CHAPTER _ _ V.

REVIEW OF LITERATURE.
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A large number of studies have been conducted on animals using various types of drugs to study their effects on behavior but only a few have been reported on human subjects in this area of research. The present review aims to emphasize those studies conducted on human subjects, especially on patients (mentally ill) population. Of course, the importance of experimental findings on animal subjects is well recognized, though animal studies are not mentioned here. Only those studies relevant either from the point of view of drugs used or from the point of view of different measures of behavior used in the present investigation are mentioned. While presenting each study, its theoretical background, aims and objectives, experimental designs and procedures have been mentioned and finally attempts have been made to look into the suggestions put forward by different authors so as to enhance further research in those respective areas.
### Review of Literature:

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1. **STUDIES WITH REFERENCE TO THE USE OF CHLORPROMAZINE (LARGACTIL) IN SCHIZOPHRENIA**

The use of chlorpromazine (Cowden et al. - 1955-56), as an adjunct to group psychotherapy has been reported in the treatment of psychiatric patients.

Eight schizophrenic patients received chlorpromazine and group psychotherapy, eight received only chlorpromazine, and 7 patients acted as control. Medication was for about a period of 5 months. Dosages started at 25 mg., t.i.d., and was adjusted thereafter according to behavior. Maximum dosage was 150 mg., q.i.d., the average 100 mg., t.i.d. No unwanted effects have been noted in the experimental groups. One hour group psychotherapy sessions, held 3 times per week. The two groups receiving the drug improved significantly more than the control in practically all measures (behavior rating scale measures were taken). The 8 patients receiving group therapy in addition to the drug showed greater improvement than the drug-only group. Chlorpromazine is an effective adjunct to other therapies when used properly, is the conclusion drawn on the basis of this study. Chlorpromazine is not effective with all types of patients.
In a study, conducted by Rinaldi, F., Rudy, L.H., Himwich, H.E. (1955-56) clinical evaluations of azacyclonol, reserpine and chlorpromazine were used on a group of 40 moderately disturbed, psychotic patients (between 40 and 70 years of age), most of whom revealed schizophrenic reactions maintained through long hospitalization. Double-blind method was followed, namely, 4 weeks of placebo, 4 weeks in which half of the patients were on the test medication and half on placebo, 4 additional weeks where the medications of the two groups were reversed and subsequent 4 weeks of placebo. The dosages of the drugs were as follows: azacyclonol, 10 mg. b.i.d., reserpine, 2 mg. b.i.d. - with chlorpromazine however, the dose was gradually increased during the initial 2 weeks so that by the end of that period each patient was receiving 200 mg., b.i.d. In the subsequent 2 weeks the dose was lowered if it seemed excessive. For some patients, on the other hand, dose was further increased (maximum 700 mg. b.i.d.) until the desired therapeutic effect was obtained.

Beneficial results were obtained with each of the three groups, but not necessarily in the same patients; nor were all patients helped by any one drug.

Consideration of the total number of patients improvements showed reserpine to be best, closely followed
by chlorpromazine, and then by azacyclonol. From the analysis of the results in relation to the different diagnostic categories, the hebephrenic and hebephrenocatatonic patients were helped most by reserpine, next came azacyclonol, while chlorpromazine was least effective. In the treatment of paranoid patients chlorpromazine was most beneficial, followed by reserpine, and then by azacyclonol. The schizo-affective patients exhibited best improvement with chlorpromazine. However, on the basis of this study, it was possible to differentiate between the use of each of these drugs in different psychiatric categories and to indicate the choice of drug that may prove most useful in the treatment of a given case.

Experimental investigations have been carried out with Largactil on chronic and acute mental patients by Szatmari (1955 - 56).

Eighty-seven chronic patients previously treated with E.C.T. and/or insulin-coma received Largactil medication. The average duration of breakdown was 6 years and 4 months and the average age 38 years and 3 months. Thirty-five acute patients received the same drug as initial treatment. The average duration of breakdown was 1 year 4 months, average age 22 years 3 months. Dosages
used were fairly systematised. Two tablets (25 mg. each) q.i.d. and every 3 days increased with 4 tablets up to 6 tablets q.i.d. Each patient stayed for 2 weeks on this dosage and then it was reduced again in 3-day intervals to the minimum dose required to maintain the clinical improvement. The maintenance dose varied from 1 to 16 tablets a day. In case of restless patients, the drug was started intramuscularly, 50 - 75 mgm q.i.d. for 3 days and then the oral administration took place beginning with 2 tablets q.i.d. All patients showed very pronounced gross psychiatric symptoms. To establish clinical improvement, 4 criteria were used: general behavior, sleep, delusional activity and hallucinations. E.E.G. recordings were made before Largactil medication and again at the peak of its effect. Fifty mg. were given intravenously and the immediate effect was observed.

The over-all improvement in chronic cases was 69% and in acute cases 60%. The transitory effects in acute cases indicate that while Largactil is extremely valuable in chronic psychosis, in acute psychotic breakdown, it has value only as a sedative. E.E.G. investigations showed that Largactil markedly decreases the muscle artefacts, decreases the frequency, and increases the voltage, causing a mild progressive synchronization.
Comparison of Prochlorperazine and Chlorpromazine in hospitalized chronic patients was made by King, D. and Weinberger (1958 - 59).

Twenty-seven male and 45 female schizophrenics who had been hospitalized an average of 13.9 and 9.6 years, respectively were assigned randomly to prochlorperazine, 100 mg. daily, chlorpromazine, 400 mg. daily, and lactose placebo (capsules were given b.i.d.) for 10 weeks. Hemograms, differentials, serum bilirubins, blood pressure determinations and urine tests for chlorpromazine were made on all patients before and 1, 3, 6, and 10 weeks after starting capsules.

All three groups showed a significant improvement after the 10 weeks ($p < .01$). The placebo group improved by 5.0 the prochlorperazine group by 7.0; and the chlorpromazine group by 8.9 points in the measures taken using a rating scale. These changes were not significantly different from each other; however men on chlorpromazine and prochlorperazine showed a significant change of 6.9 points greater than their matched controls ($0.01 < p < 0.05$). The women did not show this difference.

There was no significant change in red cell counts, hemoglobin or blood pressure during the 10 weeks of medication. Chlorpromazine tests on urines were positive
for all patients assigned chlorpromazine, varying on them from one - plus to three - plus.

A comparison of the psychological effects of acute and chronic administration of chlorpromazine and secobarbital in schizophrenic patients was made by Kornetsky and others (1959).

Twelve male schizophrenic patients (no single subtype) were selected. Their mean age was 30.1 years (range 21 - 40); mean years of hospitalization was 3.75 years (range 1 - 11.5); mean years of schooling was 12.4 years (range 10 - 16); and mean of I.Q. was 99.1 (range 84 - 127).

Acute study - one hundred and 200 mg doses of secobarbital sodium, and 100 and 200 mg. of chlorpromazine were administered on separate occasions to each subject. Each drug at each dose was given twice so that the subjects received drugs on eight separate days. In addition to the drugs, placebos were given on two separate days. A minimum of 48 hours elapsed between drug treatments. Control measurements were taken one day prior to the start of the experiment and again as its completion. Ninety minutes after the drug was given, Digit Symbol Test, Pursuit Rotal, Tapping Speed, Tachistoscope recognition of numbers and reaction
time tests were administered as behavioral measures.

Chronic study - A minimum of one week after the completion of the acute study, subjects were placed on a two week regime of chlorpromazine, secobarbital, or a placebo. All subjects received two weeks of each treatment. The first week on either drug subjects received 100 mg. at 8.00 a.m. and at 8.00 p.m. for a total daily dose of 200 mg. The second week on either drug subjects received 200 mg. at 8.00 a.m. for a total daily dose of 400 mg. Subjects were tested 90 minutes after the morning medication on the fifth day of each drug week, without giving any break-fast. The same tests employed in the acute study were used in the chronic study.

The following conclusions were drawn:
Single dose of 200 mg. of both drugs caused a significant deficit in test performance.

After 11 days of chronic administration (7 days of 100 mg. twice daily and 4 days of 200 mg. twice daily) a 200 mg. test dose of chlorpromazine no longer impaired functioning; a 200 mg. test dose of secobarbital, given after a similar schedule of secobarbital administration, still significantly reduced level of performance.
Single dose of 100 and 200 mg. chlorpromazine caused less impairment in schizophrenic patients than in normal subjects.

Secobarbital impairs performance of schizophrenic patients and normal subjects to the same extent.

A double-blind trial was conducted by Wilson et al. (1961) to investigate the effects of Thorazine (Largactil, Chlorpromazine), compazine (Stemetil, Prochlorperazine), and Stelazine (Trifluoperazine) in paranoid schizophrenia.

Eight female patients diagnosed as schizophrenia (paranoid type) were selected. Their age ranged from 26 - 39 years with a mean age of 32 years (S.D. = 3.7). The mean duration of illness was 33 months with a minimum of 11 months and a maximum of 7 years. The mean duration of present stay in hospital was 8.1 months with a range from 2 months to 24 months.

The experiment was conducted according to the double-blind method of study. Three drugs and placebo were used. These drugs were each administered in two phases as regards dose; one dosage was within the moderate range, the other dosage was considered to be sufficiently large to cause maximum movement in psychiatric symptomatology and perhaps also produce toxic side-effects.
The patient received their medicines thrice daily (7.00 a.m.; noon, 6.00 p.m.). The drugs and placebos were dispensed in identical capsules.

The project was carried out over a period of nine weeks. The first week was a period of observation so as to establish a base line of "average" and adjustment to the ward environment. Thereafter drug administration started. Drug and dosage was changed weekly on saturday morning. During the 8 weeks period of drug administration each patient had one week's administration of each drug in each of the dosage phases and two weeks placebo. Both objective and subjective methods were employed in psychiatric assessment.

Results showed that, none of these drugs had an appreciably different effect on psychotic ideation, but compazine and stelazine were definitely superior in the management of overall psychopathology.
An attempt was made to evaluate the comparative effects of three Phenothiazines drugs, Chlorpromazine (Thorazine, Largactil), Fluphenazine (Permitil, Prolxin Moditen) and Thioridazine (Melleril), and an inert placebo, upon the symptoms and behavior of newly - admitted acutely psychotic schizophrenia patients by Goldberg, S.G., Klerman, G.L., and Cole, J.O. (1965).

Three hundred and forty newly - admitted patients, randomly assigned to one of the four treatments, completed six weeks of treatment. Double-blind conditions were maintained throughout. Clinical conditions of the patients were evaluated before treatment and after six weeks of treatment, by a number of methods, including, the in-patients. The In-patient Multidimensional Psychiatric Rating Scale (I.M.P.R.S.) (Love et al. - 1962) and Ward Behavior Rating Scale (W.B.R.S.) (Burdock, et al. - 1959) completed by the Psychiatrist and Psychologist.

Results showed that, Phenothiazines, or at least the three used in this study, have a wide variety of clinical effects beyond tranquilization. Moreover, although drug effects were demonstrated on a group of symptoms usually considered target symptoms for phenothiazine treatment (Hostility, Agitation, and Ideas of Persecution), the greater drug effects were not on this group. Significant
improvement occurred on placebo, and varied in amount among the symptoms measured.

A Double-blind placebo controlled trial of chlorpromazine, using a cross-over design, has been reported by Letemendia, J.J., and Harris, D. (1967).

There were 65 male patients of whom 28 finally took part in the trial. Selection of the patients was based on certain criteria, e.g., age less than 65, at least 5 years' continuous hospitalization, no specific treatment for at least 5 years and diagnosed as Chronic Schizophrenia. The drug was given in a dose of 100 mg. thrice time a day, throughout the trial (9 medication; 9 months and total time 125 weeks for assessment) period. Medication was not started until the end of a six-month observation period, in which all the procedures of a therapeutic trial, including administration of placebo, were carried out.

Assessments were made at regular intervals throughout the trial, using a rating scale (Harris et al. - 1967). The assessments were made during the placebo period. Two further assessments were made after each group in turn had been for nine months on chlorpromazine and a final one when the both groups were again on placebo, four months after the
withdrawal of medication. In addition, patients were seen every one to two weeks to detect any obvious change at the earliest opportunity.

Only one patient out of 28 showed a definite therapeutic response. Analysis of ratings for the main psychopathological symptoms did not disclose any significant change in the group as a whole.

It is argued that the value of chlorpromazine in chronic schizophrenia has been accepted without sufficient evidence of the effect of the drug in different clinical states and the specific indications for its use. Further study of the clinical features of cases which do or do not respond to phenothiazines is required.

In a comparative trial of insulin and chlorpromazine, conducted by Markowe, Steinert and Davis (1967), one hundred previously untreated schizophrenic patients were subjects. Equal numbers of male and female patients were allotted to two equal treatment groups. They have been followed up after 10 years and of the original number, 17 were untraced and 9 had died in the follow-up period.

For the remaining 74 patients, the time spent in hospital in the ten years following the day of admission
was obtained, and these patients spent between them 27.1 per cent of the ten years in hospital. There was no statistically significant difference in hospital stay between the treatment groups, nor between the sexes. Male patients spent 32.2 percent and the female patients 20.8 per cent of the 10 years in hospital.

Fifty-four patients were interviewed by the investigators, reports from hospital psychiatrists were obtained in 12 cases and reports from relatives etc. in 6 other cases; and clinical, occupational and social ratings were made.

It was found that there was no difference in outcome of any of these rating scales between the treatment groups. However, a difference significant at the 5 per cent level, and in favour of the female patients was found in each scale.

In a collaborative study, conducted by the National Institute of Mental Health, Psychopharmacology Research Branch, (1968):

One of the principal aims was to evaluate the comparative efficacy of three phenothiazines drugs - chlorpromazine (Thorazine), fluphenazine (Permitil, Prolinx)
and thioridazine (Mellaril) - and an inert placebo, with respect to the symptoms and behavior of newly admitted ill schizophrenic patients. Attempt was also made to determine whether pattern of social and psychiatric history indicators was associated with outcome (symptom reduction) regardless of which of three phenothiazines a patient received, or whether he was on placebo.

Over 335 newly admitted patients (approximately equal number of male and female), randomly assigned to one of the four treatments, completed six weeks of treatment. Double blind conditions were maintained throughout. The patients' mean age at the time of admission was 28.2 years (Males - 27.0 and females - 29.5). Most of the female patients (74 %) were or had been married, while this was true of only 32 % of the males. The details of this research design has been reported elsewhere. At the end of the treatment period the amount of clinical change shown by the patient was rated by the research psychiatrists, psychologists, and nurses using the following scale: "Compared to his condition at admission to the project, how much has he changed? (1) very much improved; (2) much improved; (3) minimally improved; (4) no change; (5) minimally worse; (6) much worse; and (7) very much worse." The
criteria of improvement used in this study was the sum of the global change ratings made at the end of 6 weeks of study treatment rated by the specialists. On a judgmental basis, items in the history forms representing demographic characteristics, family background and environment, patient's social history, social performance and course of psychiatric illness were grouped into 34 predictor variables.

Analysis of the findings showed that, the greater differences were between fluphenazine (FPZ) and thioridazine (TDZ), with chlorpromazine (CPZ) holding an intermediate position. However, chlorpromazine resembles fluphenazine more than it does thioridazine. Moreover, all the predictors on which there are active drug differences are irrelevant to improvement on placebo.

Three categories of predictors were found:

1. general predictors, applying equally to all treatments;
2. variables which predicted outcome under placebo but not under drug treatment, or vice versa; and
3. variables which predicted outcome under one phenothiazine but not other.

The present findings on predictor pattern of social and psychiatric history may be added to two other classes of variables in which differential activity of the
phenothiazines has been demonstrated, i.e., side effects and patterns of psychotherapy. It has been pointed out that variables may predict social and occupational functioning but not the more circumscribed criterion of short-term symptom reduction used in this study. However, it has been suggested that, for more data under a greater variety of treatments will be necessary before a theoretical integration of these three domains present itself.

Clark, M.L. et al. (1972) conducted an experiment to investigate the effect of age and hospitalization on behavioral dose-response relationships using chlorpromazine in chronic schizophrenic patients.

It involved a double-blind study in which 71 chronic schizophrenic female patients, ages 18 to 60, following a 12-week drug "dry-out" period, were randomly divided into four treatment groups to receive a fixed daily dose of either placebo, 150 mg., 300 mg., or 600 mg. chlorpromazine for 6 months. Behavioral responses were monitored at regular intervals through psychiatric interviews and ward observations by nursing personnel. The psychiatric variables included the psychiatrist's clinical global impression of severity of illness and his ratings on the Inpatient Multi-dimensional Psychiatric Scale and
Behavioral data were stratified by age (≤40 or ≥40 years) and duration of hospitalization (≤10 or ≥10 years) and examined for dose-response relationships at the 12th week of treatment with either placebo or 150, 300 or 600 mg. chlorpromazine per day.

It was found that the shorter hospitalized patients (≤10 years) and to a lesser extent, the younger patients (≤40 years) as well, responded better to the higher dose (600 mg./day) whereas the longer hospitalized patients (≥10 years) and older patients (≥40 years) achieved no improvement in response beyond 300 mg./day.

Goldberg et al. (1972) made an attempt to replicate certain findings which earlier studies implied that schizophrenics could be assigned, according to their pattern of presenting symptomatology, to that phenothiazine on which they are likely to improve most.

Newly hospitalized, acutely ill schizophrenic patients between the ages of 18 and 50 were included in the study within 24 hours of hospitalization. Oral capsule medication (No. 2 opaque maroon) was supplied. A flexible
dose schedule was followed: for acetophenazine the minimum daily dose was 40 mg. and the maximum 320 mg. for chlorpromazine a minimum of 200 mg. and a maximum of 1,600 mg. per day. The average daily dose was 146 mg. for acetophenazine and 680 mg. for chlorpromazine. Patients were assessed by psychiatrist using the Inpatient Multi-dimensional Psychiatric Scale (IMPS) (Lorr, M., Klett, C.J., McNair, D., et al. - 1963) and a nurse using a short version of the Ward Behavior Rating Scale (WBRS) (Burdock, E.I., Hakeren, G., Hardesty, A.S., et al. - 1969) both prior to the start of treatment and after five weeks of study medication. Data regarding selected aspects of patients' social and psychiatric history were collected on the basis of an interview with the patient and a relative, if one was available.

Patients were randomly assigned to one of the two drugs or to placebo, producing six groups:

(1) Those patients predicted to improve more acetophenazine and who, by chance, received acetophenazine;

(2) those patients predicted to improve more on acetophenazine but who by chance were actually assigned to chlorpromazine;

(3) those patients predicted to improve more on acetophenazine but who received placebo;
(4) those patients who were predicted to improve more on chlorpromazine and who, by chance, were assigned to chlorpromazine;

(5) those patients predicted to improve more on chlorpromazine but by chance were assigned to acetophenazine;

(6) those predicted to improve more on chlorpromazine but who received placebo.

Results were found to be negative. It was possible to predict improvement generally across the two drugs but not differentially between them.
2. STUDIES WITH REFERENCE TO THE USE OF DIAZEPAM (CALMPOSE) IN ANXIETY PATIENTS:

Metcalf and Whitley (1964) made an observation using Diazepam on 401 patients undergoing E.E.G.

Most of the patients were referred for treatment by court and prison authorities. Their age range was from 17 months to 85 years. The patients were divided into four groups. The first included 298 patients who received Diazepam in oral dosages of 5 or 10 mg, (5 mg. per 5 c.c. suspension) prior to E.E.G. Of these, 185 had adequate relaxation with sleep, five had relaxation, but no sleep and 108 had little or no relaxation and no sleep. The second group consisted of 31 patients who received intramuscular Diazepam in dosages of 10 mg. (2 c.c.) prior to E.E.G. Of these, 19 had adequate relaxation and sleep, 3 had relaxation alone, and 9 had neither. The final two groups made up of 36 patients each were subjects in a double-blind study. Both groups received identically appearing tablets orally prior to the E.E.G. The dose of the active drug was 10 mg. and 26 patients had excellent relaxation or sleep, 7 good and 3 poor; one patient developed transient dizziness. Of these receiving placebo, 17 had an excellent, 8 a good and
11 a poor response. Thus, diazepam appeared to have some superiority over the placebo but not to the degree that might have been expected.

With respect to E.E.G. tracings, 53 patients (16%) in the group receiving the suspension had anterior cerebral fast activity (16 to 24 c.p.s.) but 43 of these had been receiving chronic doses of other psychotherapeutic drugs which may have been the influencing factors. On the other hand, of the 15 patients (48.4%) receiving parenteral doses who had fast activity, only two received concomitant drug therapy, suggesting that in these instances diazepam was the causative agent.

Fast activity with diazepam as noted by other investigator was usually after several days of active medication. But in this experiment, however, single doses were sufficient to precipitate fast activity especially when diazepam was administered parenterally.

While diazepam is not as effective as other medications for the induction of sleep in E.E.G. laboratory, it appears to have other activity worthy to note. Because its fast activity is relatively specific, the E.E.G. can be used as an additional and partial diagnostic tool for evaluating whether a patient has recently received this type
of medication. Moreover, in the absence of other, more classical E.E.G. abnormalities, disturbances in the production of deliberately induced fast activity (asymmetry of voltage, pattern of frequency) may be of value in detecting the presence of significant brain pathology.

Results in this study indicate that diazepam is not a suitable sleep-inducing medication for E.E.G. It may be useful, however, as a diagnostic tool.


Twenty three consecutive out-patients suffering from anxiety states were treated in a double-blind cross-over trial with the two drugs mentioned above. Each drug was prescribed for a period of fortnight, the order of presentation being randomized. Amylobarbitone was used in doses of 60 mg. t.i.d. and Diazepam in dosages of 5 mg. t.i.d. The patients were interviewed and rated on an anxiety scale (Robin et al., 1961) before commencing treatment, after the first period of treatment at two weeks, and after the second period of treatment at one month.

All 23 patients showed significant improvement \( (p < .01) \) in their total anxiety score after two weeks
of treatment. The average anxiety score dropped from 19.7 to 14.1. At the end of the month these patients remained significantly better than at the start of the trial, but the second fortnight of treatment was not contributory and indeed there was a slight overall deterioration — average scores ranging from 14.1 to 15.4 (on Wilcoxon Matched Pairs Signed Ranks Test, Siegel, 1956).

Eleven patients were treated with diazepam in the first fortnight of the trial and twelve with amylobarbitone, the order being reversed in the second fortnight. Diazepam resulted in significantly greater improvement in anxiety scores than amylobarbitone ($p = <.01$) without regard to the period during which the drugs were administered.

A double-blind drug trial with patients suffering from neurotic anxiety has been described by Kellner, R., Kelly, A.V., and Sheffield, B.F. (1968).

The purpose of this trial was to compare various methods of assessing changes in anxiety and to determine which could discriminate most effectively between the effects of treatment.

Thirty-two out-patients suffering from neurotic anxiety and attending an out-patient clinic of a day hospital
were asked to participate. Only those were selected about whom the psychiatrists agreed that they were suffering from neurotic anxiety, that there was no suspicion of another psychiatric illness, and that they were in need of treatment. There were 15 women and 9 men; their age ranged from 16 to 44 years, Mean - 28.2 years.

The methods of rating used were the sum of the scores of rating of categories of symptoms (Hamilton Anxiety Rating Scale); Global Rating and Self-rating of change (Five-point Standard Scale); the sum of scores of rating (and self rating) of the patient's individual symptoms (Target Symptoms); the rating and self-rating of the three main complaints, the check list form of the Taylor Manifest Anxiety Scale (MAS); the Symptom Rating Test (SRT); and the Maudsley Personality Inventory (MPI).

The drug compared were diazepam (5 mg. t.i.d.) and that of hydroxyzine pamoate (50 mg. t.i.d.).

A Latin Square design was used, each block lasting one week.

All rating and self-rating methods employed discriminated significantly between the effects of treatment and no definite conclusion can be drawn about the comparative value of the methods. The Hamilton Anxiety Rating,
Scale accentuated observed differences between the effects of treatment. There was hardly any difference between the effectiveness of psychiatrist’s rating and self-rating of target symptoms. The SRT check-list discriminated more effectively between treatments than the check-list form of MAS. The Neuroticism Scale of MPI remained fairly stable and did not discriminate significantly between the effects of treatment.

Diazepam 5 mg. t.i.d., was significantly more effective than hydroxyzine pamoate 50 mg. t.i.d., and significantly more effective than placebo.

Baldev Kishore et al. (1971) reported the findings of a Comparative Study of Diazepam and Chlordiazepoxide in anxiety patients.

In view of the excellent comparative results reported with Diazepam (Feldman et al., 1962; Pignataro, 1962; Erakowski – 1963; Erakowski – 1965), from the foreign medical literature, the authors of this study decided to try diazepam (available as Calmpose in India) in comparison with commonly used Chlordiazepoxide so as to find the relative value of this compound in the treatment of various psychoneurotic patients attending the Mental Hospital, Amritsar. The pilot study was undertaken to –

(i) assess the efficacy of Diazepam in anxiety neurosis;
(ii) assess its side-effects and (iii) compare its results with Chlordiazepoxide, both in the varied symptoms of Anxiety and the often associated symptoms of depression.

Twenty patients with anxiety neurosis in whom anxiety and/or depression was present as an associated symptom, were studied in a cross-over trial with those two drugs mentioned above.

All previous medication was stopped for one week before putting the patient on the drug trial. In order to have an objective assessment of the severity of patient's illness and the degree of change brought about with the treatment, each patient was rated on a specially designed anxiety symptoms rating scale and a rating scale for depression, both of them modifications of Hamilton's rating scale.

Each patient was randomly allocated to either of the two drugs, so that 10 patients received Calmpose first and were crossed over to chlordiazepoxide after four weeks, while another ten received chlordiazepoxide for first four weeks. The cross-over was done without a break inbetween the two drugs.

Patients receiving Calmpose were started on 5 mg., t.d.s., and depending on side effects its dose was reduced to 2.5 mg. t.d.s. No patient received more than 15 mg. per day.
Patients receiving chlordiazepoxide were put on 10 mg. t.d.s., and dose raised to 20 mg. t.d.s., depending on response and tolerability of the drug.

The duration of drug treatment was kept at four weeks, but where the anxiety symptoms worsened or side effects were troublesome the duration was cut short to two to three weeks.

The findings were as follows:

In the improvement of Global Symptoms of Anxiety (both somatic and psychological), calmpose was there times more effective than chlordiazepoxide and in associated symptoms of depression, calmpose was $2\frac{1}{2}$ times more effective than chlordiazepoxide.

Appreciable improvement under calmose in the total twenty cases, was recorded in 45 per cent where as under chlordiazepoxide it was recorded in only 15 to 19 per cent of the cases.

Factor analysis shows that in the somatic symptoms of Anxiety, appreciable improvement was seen in 45 per cent patients under calmose but only in 15 per cent under chlordiazepoxide. These figures for psychological symptoms' improvement was 50 per cent with calmose, and 10 per cent with chlordiazepoxide.
Calmopose gave relatively better results in the psychological symptoms Clusters than the Somatic Symptom Clusters.

The anxiety tension symptoms which were improved to the range of Good Improvement under Calmopose were - Insomnia, disturbed sleep, fears and phobias, lack of concentration, forgetfulness, palpitation, sinking of heart, breathing difficulty, irritability and intolerability of noise, adverse news or sights.

Calmopose caused a moderate improvement in the associated depressive symptoms, that is, feelings of inferiority and insecurity, worrying, pessimistic and depressed mood, whereas under chlordiazepoxide there was no improvement of these symptoms.

Under the two drugs, the only side-effect was drowsiness which was little more with calmopose. But it was less, when the daily dose was reduced.

A double-blind between-patient study (Wadzisz - 1972) was carried out in forty patients with anxiety neurosis. They were either new patients or ones poorly controlled on other therapy. Any with primary depression or known to be in early pregnancy was excluded.
The trial duration was four weeks. Patients were followed up at two and four weeks and assessed at each interview on the Anxiety Rating Scale described by Hamilton (1959).

Dosages was Oxypertine 10 mg. or Diazepam 5 mg. both t.d.s. No other psychotropic drugs were given during the trial unless a hypnotic was needed, when Nitrazepam (Mogadan) was used. Six patients in the Oxypertine group and eight in the Diazepam group received this hypnotic.

Forty patients completed the trial, and the overall sex ratio was 1.7 female to 1.0 male. Age distributions were similar in groups and the median age was 36.5 years.

The median initial score on the Hamilton Scale for the oxypertine group patients was 22 and for the diazepam group of patients was 23.

The dose of one capsule t.d.s. was considered to have been maintained by each patient.

From the patient's remarks it was apparent that drowsiness was the only side effect with either drug.

The clinician noted whether the patient had improved by the end of the trial. These results were
summarized as None, Slight, Moderate or Marked. Differences between the treatments were not significant, 60 per cent of all patients obtaining moderate or marked improvement of their anxiety state.

The changes in the Hamilton Anxiety Scores were correlated with the clinician's assessment of improvement in the patient's condition. There was a positive significant correlation between these measures of response.

(Spearman's Rank, Correlation Co-efficient, \( r_s = + 0.80 \) \( p < 0.001 \)).

Responses of the two groups to the two treatments were compared. A statistically significant improvement after two and four weeks was observed in both treatment groups, \( p < 0.01 \), improvement after four weeks being greater than after two weeks. The median improvement in the score for the Oxypertine group was 7.5 at two weeks and 14.5 at four weeks, compared with eight and thirteen respectively for the Diazepam group. Differences were not statistically significant \( (p > 0.05) \).
PART 3.1.

3. STUDIES WITH REFERENCE TO THE USE OF IMIPRAMINE (TOPRANIL) IN DEPRESSION:

In a preliminary study conducted by Azima et al. (1958-59), imipramine was administered to 63 patients: 43 females and 20 males, with an average age of 47 years, consisting of 55 depressive (35 psychotic and 20 neurotic) and 8 non-depressed neurotic patients.

The dose range was between 50 and 200 mg. daily, by mouth, with an average effective dose of 100 mg. administered for an average period of three weeks. The drug was discontinued, if no favourable response appeared after this period. The follow-up ranges from 3-6 months. The criteria of improvement consisted of four items. Symptoms' disappearance (subjective comfort), ward management, ability to go home; and ability to go to work (social effectiveness).

Side effects were minimal, appearing at the onset of therapy. Among 55 depressed patients, 24 (43.6%) showed marked and 20 (40 percent) moderate improvement, 3 slight and six no improvement. The percentage of significantly
improved cases was 83.6 per cent.

Thus, imipramine was found to be potent anti-depressant drug, with more or less specific influence on the symptom of depression, indicating of possibility of a specific effect on certain parts of the psychic structure. If its long term application proved to be as effective as the relatively short span of its usage, it might limit the use of E.C.T. considerably. The use of imipramine after 4 - 8 weeks had resulted within a week in a return of depression, indicating the necessity of long term application.

In a study (Roland - 1958-59) over a three-year period, more than 500 psychiatric patients of various diagnostic categories were treated with imipramine hydrochloride. While giving injection the dose did not exceed 150 mg. a day, and by oral administration not above 300 mg. a day, side effects were slight. As a rule, the initial response was evident within 2-3 days, while in some cases 1-4 weeks of therapy were required. The observations suggested the importance of a proper selection of the patients as to type and etiology of depression. While in a number of instances, neurotic, schizophrenic or other depressions were also benefited by the drug, particularly when used in combination with chlorpromazine, electro-shock or psychotherapy, it was concluded
that imipramine hydrochloride is primarily indicated and effective in the treatment of endogenous depression.

The action of Tofranil alone in a series of hospitalized, unselected depressed patients with different diagnoses has been reported by Kump and others (1959).

Twenty-eight male and thirty-eight female, whose ages varied between 25 and 72 years, were included, as subjects. The majority of the depressions were endogenous (28 involutional, 11 Manic-depressive), while 17 schizophrenic patients with depressive features and 10 patients with arteriosclerotic, senile or psychoneurotic depressions were also included. About one-third of these cases were chronically depressed patients, some of whom had received E.C.T., insulin treatment and different tranquilizing drugs without effect.

The drug was given by oral administration only, starting with a dosage of 75 mg. per day which was increased slowly to a mean dose of about 200 mg. per day, adjusted individually. In some cases higher dosages up to 400 mg. per day were used.

According to the authors, improvement can be observed as soon as the first or second day in some patients,
but sometimes it takes two or three weeks, and the patient who does not respond during the first three weeks, will not respond at all.

Best results were seen in endogenous depression. In this group ten patients (26%) recovered, 22 (56%) showed good improvement and seven were unchanged, schizophrenic patients did not respond as well. The mixed group was also less responsive.

From the standpoint of symptoms affected, best improvement was seen in affective depression, flow of psychological activity and alteration of thought process. In 9 patients impending agitation was observed with higher dosages. Other side effects were minor and consisted of dizziness. A slight drop in blood pressure was observed in a few patients at the onset of treatment and disappeared as the therapy continued. For some elderly patients it was desirable.

From the above it was concluded that Tofranil is the most potent antidepressive drug available at the present time, comparable in effectiveness with E.C.T. While E.C.T. may still be preferred in acute suicidal patients, it is the impression of the authors of this paper that Tofranil reduces the need for E.C.T. drastically.
Lemere (1959) reported negative results in the treatment of depression with Tofranil.

One hundred and thirty-seven patients in which depression (endogenous type) was the most prominent symptom were included.

The dose used was from one to two 25 mg. capsules q.i.d., for three or four weeks. None of the side effects was serious but dizziness, dryness of mouth, blurred vision, increased tension often caused the patients to discontinue this drug.

Only twenty-two of the one hundred and thirty-seven thought that imipramine was of help. No other patient was interested in continuing this drug beyond the first trial month. The evaluation of the pharmacological treatment of depression is especially difficult because most of these cases are self-limited anyway and whatever is being given at the time of recovery is credited with the cure. This is especially true where it is recommended that the drug be given for at least a month before judging its effect.

According to this author, in view of reports of success with this drug by others, it would seem advisable to continue clinical trials, especially control trials.
Fleminger and Groden (1961) conducted an experiment on depressive patients using Tofranil.

Fifty-five patients (35 women and 20 men) all diagnosed as suffering primarily from depressive illness were selected. The age range was 23 - 72 years. In thirty patients symptoms had been present for more than six months. The presence or absence of 12 clinical features (e.g., anxiety, apathy, agitation, early waking, etc.) before treatment were noted for each patient.

Imipramine was given orally in divided doses, but the intramuscular route was used to initiate treatment in some inpatients. The daily dose varied between 150 and 375 mg. according to individual tolerance. The majority received between 150 and 225 mg. per day, but nine patients were given higher doses. Medication was maintained for at least four weeks in all except nine patients in whom it was stopped sooner on account of side-effects.

Response to treatment was assessed at one month after imipramine was started. This was rated as either "Good" or "Bad". "Good" indicates full remission or sufficient improvement to obviate the need for other treatment. "Bad" indicates either lesser degree or no improvement, or the need to terminate treatment.
Results showed that, twelve features of depressive state and several other clinical factors were found to have no relation to the response to drug. It has been suggested that, search for factors which relate reliably to the response to this drug needs to be pursued beyond merely clinical observation.

A controlled trial of Tofranil in the treatment of fifty cases of depression was conducted by Friedman and others (1961).

Over a five month period 50 in-patients diagnosed as depression were randomly assigned to imipramine and placebo groups. Patients in whom depressive symptoms were thought to be secondary were excluded from the study. Diagnosis was based on patient's history, interview, and also degree of behavioral and subjective depression found on some questionnaires, rating scale, administered to the patient.

The tablets were administered for a standardized dosage 25 mg. t.d.s. for two days, then 50 mg. t.d.s. for two days, then 75 mg. t.d.s. for four weeks. In the majority of cases the dosage was later reduced to 50 or 25 mg. t.d.s. When the patient has either improved or was showing side-effects he could not tolerate.
Rating scales and questionnaires were re-administered at the end of the course of tablets. This was normally after 6 weeks, but in a number of cases the period of trial was shorter either because the patient was better or was discharged or his/her symptoms became so serious than it was considered unethical to keep the patient for trial. A number of patients who had been on placebo were given a trial on the genuine drug, following which ratings and questionnaire were again repeated.

It was felt that traditional double-blind method may not be applicable to an investigation of the pharmacotherapy of depression.

Taking all cases of depression together, it was found that patients on Tofranil had a significantly greater chance of improving than patients on placebo.

Endogenous and involutional depressions benefited more from the drug than reactive ones, but the most severe cases, whatever their classification, failed to respond to the drug.

It was concluded that Tofranil is of value in the treatment of less severe depressions, but in severe cases it would appear to be inferior to E.C.T.
Kateryniuk et al. (1961) conducted a clinical trial study of imipramine hydrochloride on thirty-four subjects; 18 women and 16 men, treated with the drug for 20 to 130 days (average 58 days). Diagnostic classifications were many, e.g., psychotic depression, neurotic depression, paranoid reaction, involutional depression, mental deficiency with psychosis.

Age varied from 20 - 75 years, 31 of these patients had previous hospitalization.

The average initial dose of imipramine hydrochloride, given orally, ranged from 50 - 75 mgs. per day, not exceeding 20 - 130 days, with three-fourths of the patients receiving the drug for a period of two months.

All patients were examined immediately before, during and at the end of the observation period. No allergic reactions or side effect other than dizziness, reported by two elderly patients.

According to the results, improvement with this drug observed in schizophrenics was less well sustained and fluctuating. "Pure" depression (neurotic or psychotic) abated more readily than depressive symptoms in schizophrenia and brain syndrome.
All the patients who failed to improve had earlier failed to improve on conventional treatment methods. Rees et al. (1961) reported the results of a controlled trial of Imipramine (Tofranil) in the treatment of severe depressive states.

A group of twenty patients participated in this triple-blind trial. The group consisted of 14 women and 6 men with ages distributed as follows: 20 - 29 years, 10%; 30 - 39 years, 25%; 40 - 49 years, 15%; 50 - 59 years, 20%; 60 - 69 years, 25%; 70 years and above, 5%. Seventeen out of 20 patients had previous attacks of depression.

Imipramine and inert tablets were given according to the following schedule: For the first two days four 25 mg. tablets and then the tablets were increased by two 5 mg. tablets daily to reach 10 tablets on the fifth day. This was continued for five days and then gradually reduced by one tablet daily to six tablets a day, which was continued until the 21st day. No toxic reactions were observed.

A number of clinical features relating to depressive illness were rated by physicians on a 5-point scale according to severity. Separate records were made of
nurses' observations after 24 hours. An overall grading of the patient's clinical state was made by physicians at weekly intervals.

The ratings and grading made at the end of the third week and at the end of the sixth week were the ones chosen for statistical comparison of the effects of active and inert tablets. This procedure was adopted as experience, in a pilot trial showed that the beneficial effects of imipramine often take two or three weeks to develop and that ratings and gradings made at the end of the three week period would give the best measure of the effectiveness of the drug given for the period.

Results showed that imipramine has significant beneficial effects on some severe depressive illness, though the results achieved in this study were not as good as those reported in the literature generally which give improvement rates ranging from 57% to 92%. Excluding slight improvement which is of minor significance in practice, the range was from 22% to 65%. The total percentage of moderate, marked and total improvement in this study was 50 per cent. Taking total recovery and marked improvement only the figure was 35 per cent.

In the patients who were not improved with imipramine and were given E.C.T., the improvement was so
marked and clear-cut in that there was no doubt of the superiority of E.C.T. in these patients. And only a proportion of depressive illness respond to imipramine treatment and those include both endogenous and reactive varieties there is an urgent need for further research into the attributes of the individual, whether these prove to be clinical, psychological, physiological or biochemical which are highly correlated with susceptibility to imipramine, in order to achieve more efficient selection and correspondingly better therapeutic results.

A clinical evaluation of four anti-depressant drugs (Nardil, Tofranil, Marplan, and Deprol) has been reported (Agnew, Baran, Howard, Klapman, Theodre reid (Jr.). and Stern, 1961-62).

The study was conducted for a relatively short period of three weeks time. Subjects were selected on the basis of depressive symptomatology rather than diagnostic category. A total of 26 patients were studied. The study was based on frequent closed observation of changes in clinical picture. All subjects were receiving regular treatment, e.g., individual and group psychotherapy, occupational therapy, recreational therapy. Patients were placed on a drug for three weeks. At the end of three weeks' treatment period there were thirteen evaluation forms for each.
patient describing his clinical picture over a period of five weeks. Patients were selected by the authors after study of history, psychiatric examination and physical examination. The name of each patient selected for this study, was sent to a pharmacist who assigned one of the four drugs or placebo in rotation (Marplan, 10 mg. t.i.d., for 7 days; 10 mg. b.i.d. for 14 days. Tofranil - 25 mg. t.i.d. for 21 days. Deprol - 400 mg. meprobamate + 1 mg. benadryl hydrochloride; Nardil - 15 mg. t.i.d. for 21 days).

When analysed, data were found to be inconclusive, which might have been insignificant because of small number of subjects studied in this experiment. Only conclusion drawn from the data was that all four anti-depressant drugs showed better results than the placebo.

In their study "Clinical trial with tofranil", Dube and Narendra (1962) reports the efficacy of Tofranil in case of different diagnostic groups of psychiatric patients.

Due to nonavailability of placebo, straight clinical trial without controls was undertaken in this study, Eleven cases were selected (ten male and one female), through the outdoor as they came and were admitted for this therapy. Their ages varied from 20 years to 75 years, average age being
The dose was varied according to clinical results in each case. However, the initial dose was three tablets daily and gradually increasing to nine tablets per day. The average maintenance dose was three tablets daily. The number of cases selected according to the classification of depression was as follows: Agitated Depression - 2; Involutional Depression - 1; Retarded Depression - 2; Simple Depression - 2; Reactive Depression - 2; Schizophrenia - 2. Elaborate charts were maintained for each patient marking the presence of various symptoms and noting the changes in each symptom, after two weeks of treatment.

Of the endogenous variety five cases showed complete recovery and two cases showed marked improvement.

The two psychoneurotic cases showed variable improvement in the beginning. Both cases relapsed, one having relapsed completely and one partially.

Two cases of catatonic schizophrenia showed no change. On two cases of involutional depression, and one case of retarded depression, E.C.T. had either no effect or only partial effect. These cases responded remarkably to Tofranil. In one case Tofranil was supplemented by E.C.T.

The average period of Tofranil therapy when
recovery was noticeable was two weeks. Side effects seen were rise in pulse rate, dryness of mouth, hypotension, dilatation of pupils, constipation, excitement and sinking sensation.

However, endogenous depression showed marked improvement or complete recovery in comparison with the psychoneurotic variety which showed little and schizophrenia which showed no improvement.

A controlled clinical trial (double-blind) of Imipramine (Tofranil) was conducted by Abraham, H.C., Kamter, V.B., and Rosen, I., (1963) to test the efficacy of imipramine in low dose in an out-patient setting over a relatively long period.

Eighty patients suffering from depression were selected on the basis of their suitability for out-patient treatment and the likelihood of their continuing to attend at weekly intervals for eight weeks; thus it was desirable that they should be neither too ill nor only slightly depressed. A self assessment inventory was devised to check the clinical findings. There were 26 men, with an age range of 23 to 69 years, median age 50; and 54 women with age ranging from 18 to 74, median age 42. Cases were diagnosed as reactive, neurotic, endogenous (MDE), unclassified and
and mixed.

By means of a randomisation procedure, the 80 patients were allocated in advance to four sub-groups of 20 - namely EO, EE, 00 and OE, getting placebo during 1st fortnight, 2nd fortnight, 3rd fortnight and 4th fortnight respectively. Every patient was able to receive the drug for 6 to 8 weeks of the trial period. Tablets were prescribed as follows: one tablet morning and noon for two days, then two tablets twice daily for the remainder of the fortnight. The purpose of beginning with lower dose was to facilitate drug tolerance and this initially lower dose was repeated at the start to each successive fortnight because one subgroup was then changing from placebo to drug.

Patients were rated at the beginning of the trial and weekly thereafter for severity of depression on a 3-point and a 5-point scale for clinical improvement.

The results reported are for 65 patients at the second week and 46 at the eighth.

At the end of the first fortnight all four sub-groups showed an improvement, which was significantly greater in the three on the drug than on the placebo group (EO). The mean differences between the four sub-groups
exceed the limits of chance fluctuation; analysis of variance yields an F-ratio significant at the 2½ per cent level. At the end of 8 weeks, all the sub-groups had improved further, and the differences between their mean improvements were no longer statistically significant. However, the main finding of this study was that imipramine in low dosage produced improvement in out-patients suffering from depression, but that the degree of improvement was not related to the diagnostic categories used.

Seven treatments for depression have been evaluated by a blind technique in a series of 200 female in-patients by Hutchinson, J.T., and Smedberg, D. (1963).

In this trial the patients were divided into two series of 100 patients each. Each series of 100 was divided into groups of 25 randomly, and each group was given a specific treatment. The treatments given were E.C.T., phenelzine ('Nardil'), imipramine ('Tofranil'), pheniprazine ('Carodil'), amitriptyline ('Tryptizol'), Parstelin and Chlorprothixene ('Taractan').

Treatment was given for a period of three weeks only. One investigator allocated the treatments by the method of random numbers and supervised each patient. The other investigator assessed the degree of depression on
admission, then again at weekly intervals for three weeks, so that four assessments were made. This was done on a four point scale. This investigator was quite unaware of the treatment which each patient had.

At the end of the trial the total score before treatment obtained was compared with the total score obtained after treatment.

Results showed that, E.O.T. was significantly superior to all the other treatments, while imipramine and parstelin have been significantly more effective than amitriptyline, carodil, phenelzine and Taractan, which could all be regarded as comparable in action.

A comparative, blind trial of imipramine and phenelzine in 96 cases of depression has been described by Martin, M.E., (1963).

Ninety-six patients (Seventy-nine were in-patients and seventeen out-patients) were included in the trial. There were 69 women and 27 men; their age ranged from 16 to 89 years with an average of 54.6 years. There were 95 cases of endogenous depression and one of reactive depression.

Each patient had a four week's trial of one
or other drug. Patients were randomly allotted to treatment. In order that this four weeks' period should be blind to the assessor, each patient, in addition to this active drug was given a placebo of the other. That is, a single dose consisted of one large "phenelzine" and two small "imipramine" tablets. Either the two small or the one large were placebo tablets. The daily dose of imipramine was 150 mg. or 200 mg., and of phenelzine was 45 mg. or 60 mg. The patients started with 50 mg. imipramine or 15 mg. phenelzine and increased over three days to the full dose. Two cases had maximum daily dosage of 400 mg. A few cases, in whom side-effects were troublesome, were reduced from four to three doses a day. During the four weeks' trial period no other drugs, apart from barbiturates for sedation, were given.

Each patient was seen prior to commencement of the trial, and then at weekly intervals. Rating scales recording depth of depression and accompanying symptoms as well as records of blood pressure, weight and side-effects were kept at each interview.

All patients were followed up three months after this four weeks' trial. Patients who had made satisfactory progress during the four weeks' trial continued on the same
drug; patients who had not made good progress were changed to another drug or had electroplexy.

After four weeks therapy 76 per cent of depressed patients on imipramine had improved, 57 per cent on phenelzine. After four months' therapy, 67 per cent of depressed patients on imipramine showed a satisfactory result, 49 per cent on phenelzine. These figures indicated that imipramine was a better antidepressive agent than phenelzine.

Edwards, G. (1965) conducted an experiment with a view to compare the speed of action of desipramine and imipramine in the treatment of depressive illness, with separate assessment of a number of symptoms, particularly depression and anxiety.

Ten patients were randomly allocated to either group, and a double-blind procedure was employed. Both drugs were given in a fixed dosage schedule working upto 50 mg. t.d.s. by the 5th day. No day time sedation, only amylobarbitone sodium was prescribed as night sedation.

On admission to the trial and thereafter at weekly intervals for the 4 weeks of the study patients were separately rated for depression, anxiety, insomnia, anorexia, by using an appropriate rating scale and at the
same time, blood pressure, patient's body weight and side effect, if any, were also assessed.

Results show that, desipramine appeared to produce a slightly more rapid effect than imipramine but this difference did not reach the 0.05 level of significance. The improvement over the 4-week period was significant in the imipramine group but not in the desipramine group.

The superiority of imipramine in reducing anxiety symptoms was demonstrated at the 0.05 level.

Anorexia appeared to respond more rapidly to imipramine than to desipramine, but the difference was not significant. Improvement at the end of 4 weeks was significant ($p < 0.01$) for the imipramine but not for the desipramine group.

So far as insomnia was concerned, imipramine was superior to desipramine at the 0.05 level and the desipramine group required significantly ($p < 0.05$) more night sedation. At the end of 4 weeks, improvement over initial insomnia rating did not however reach the 0.05 level in either group.

The hypotensive effect of imipramine was significantly more marked than that of desipramine, but in
neither group were there any side-effects of sufficient severity to require reduction of dose.

In neither groups did mean weight show significant change.

The conclusion drawn from these results was that desipramine, far from being the "active" metabolic of imipramine in the treatment of depressive illness, it is different and less active drug. Imipramine is to be preferred to desipramine in the treatment of depressive illness. The inference is made that, reserpine induced inactivity in the rat is not a valid model of the depressive syndrome in men.

Lafaye et al. (1965) reported the results of a comparative trial of desipramine and imipramine in an out-patient setting on 28 patients, each having a depressive syndrome as a principal clinical feature.

The 14 patients who received desipramine had a mean age of 33 years, ranging from 17 - 38 years; the 14 patients who received imipramine had a mean age of 38 years, ranging from 20 - 60 years. The severity of depression was measured by a rating scale and different diagnostic categories of depressive patients, e.g. neurotic depression,
psychotic depression, schizophrenia with depression, involutional melancholia, manic depressive-depressed were included in this study.

All patients were begun on a dose of 25 mgs. three times a day and the dose was increased as high as 50 mgs. three times a day, if the desired response was not obtained. No psychotherapy was given to these patients.

The evaluation of the patients (using rating scale) was done twice in the first week and weekly thereafter. The total score obtained on the first visit, prior to starting therapy, served as a baseline.

The efficacy of both drugs was found to be in the same range. Desipramine had a more rapid onset of action than imipramine and produced slightly fewer side-effects. The difference between the number of days for onset of action and the number of side-effects with both drugs was not statistically significant. The majority of patients on each drug responded well to treatment.

Neki, J.S. (1965) reported the results of a comparative clinical evaluation of three drugs: Tofranil (Imipramine), Niamid (Nialmid), and Nardelzine (Phenelzine) with a placebo in depressive states.
In all 200 depressive patients admitted to the psychiatric clinic, V.J. Hospital, Amritsar, India, completed the evaluation comprised of four groups of 50 patients each - three having received antidepressive therapy one on each of the three drugs mentioned above, and the fourth which acted as control received placebo tablets.

Following physical and certain biochemical investigations along with interview, patients were assigned to one of the drugs or placebo in rotation so that equal number of patients from each of the broad diagnostic categories had been placed on each of the drugs. Some other adjustments in assigning the patients to the various groups were also made in order to have a comparative view of these groups with regard to age, sex, social status, duration of illness and broad diagnostic categories.

Initial doses were given for 1 - 2 weeks, and if no significant improvement was reported, were gradually raised by unit dose increments at weekly intervals until the maximum dose (Neki - 1965) was reached - at which level the patient was kept for 2 - 3 weeks. If good clinical response was obtained with a submaximal dose, the patient was kept at that sub-maximal dose for 2 - 4 weeks. After this the dose was gradually decreased to the level of maintenance dose, and kept at that level for 2.5 weeks depending...
upon the patients' response. After that it was reduced to maximum level for another 2 - 3 weeks to prevent a relapse. After 12 weeks of treatment each patient was reviewed for the assessment of improvement. A check-list completed at this stage was compared with the one prepared at the outset.

The results showed that Tofranil has yielded statistically better results than either of the other two drugs in the treatment of unclassified depressive patients.

So far as the results in the groups of psychotic depressive alone were concerned, the differences between the means for Tofranil and placebo was significant at 1% level for 66 degrees of freedom \( (t = 4.152) \); that for Niamid and placebo was not significant at 5% level for 65 degrees of freedom \( (t = 1.448) \) and that for Nardelzine and placebo was also not significant at 5% level for 66 degrees of freedom \( (t = 1.482) \).

The difference between means for Tofranil and Niamid was significant at 1% level for 75 degrees of freedom \( (t = 2.817) \); so also for Tofranil and Nardelzine for 76 degrees of freedom \( (t = 2.998) \) but was not significant at this level for degrees of freedom for Nardelzine and Niamid.
These results indicated that Tofranil is only therapeutically effective agent against psychotic depression.

So far as neurotic depressions are concerned, Niamid is the most effective drug but the difference between means for these drugs taken in pairs, however, are not significant at 5 per cent level for the respective degrees of freedom. There is, therefore, no definitely significant superiority in the efficacy of Niamid over that of other two groups in the treatment of neurotic depression.

A study was conducted by Sandifer, M.G., and Gambill, J.M. (1965) to evaluate the efficacy of amitriptyline and imipramine in treating depressed female patients.

Patients (approximately 2,700) were consecutive female admissions, aged 40 - 59 years, presenting with depressive symptoms of sufficient severity to attain an initial score of 23 or more on the Hamilton Rating Scale (Hamilton - 1960). Finally thirty-three patients were receiving imipramine and twenty-three amitriptyline. Medication was administered in the dose of capsule - 1, four times daily (imipramine 200 mg. daily or amitriptyline 160 mg. daily) initially, and was increased to capsule - 2
thrice daily at one to two weeks (imipramine 300 mg. or amitriptyline 240 mg. daily) in the event of lack of improvement as measured by the Hamilton Rating Scale Scores. Assessments were done before medication and after 1, 2, and 4 weeks of treatment.

Results showed that, the mean changes at each interval favour amitriptyline, but none of the differences were statistically significant. As a group, the patients treated with amitriptyline achieved an 82 per cent reduction of symptoms, and the patients treated with imipramine achieved an 76 per cent reduction in symptoms. By individual patients, half in each group had 90 per cent, or more symptom removal, with a tendency favouring imipramine for complete symptom removal. However, the specific finding was that both drugs were effective and equally effective.

Imipramine was compared with desipramine in a double-blind controlled trial of sixty patients suffering from primary depressive disorders and classified aetiologically into reactive and endogenous depression (Rose and Westhead, 1967).

Imipramine was given 75 mg. daily for one week, thereafter 150 mg. daily. Desipramine was given 112.5 mg. for one week, thereafter 225 mg. daily. All the patients received thioridazine in addition to specific antidepressive
therapy and were assessed initially, and after one, two, three and six weeks of treatment, using Hamilton's Rating Scale for Depression.

The rating scale scores before and after treatment showed the patients had a mean initial score of 43.9 points; the mean 3 and 6 week scores were 10.1 and 6.6 respectively, which indicated considerable improvement in the group as a whole. Regarding the two treatments, none of the scores at any assessment differed at a significant level, the desipramine group had some advantage at the final week. Comparison of the percentage reduction in the scores, taking the initial score as 100, also showed no significant difference between the two groups.

The response after one week of treatment was shown to be a good indication of the three week outcome. Reactive and endogenous depressions responded equally well to either drug.

Dimascic and Meyer (1968) reported the effects of Imipramine on individuals varying in level of depression.

The subjects were 40 healthy non-hospitalized men between 21 to 30 years of age who scored two standard deviations either above or below the mean on the 'D' scale of
the MMPI. Twenty subjects from each depression level were chosen.

Imipramine (150 mg. daily) or a placebo was orally administered on a three-times daily schedule for a one week period. Ten "low" and ten "high" depressed subjects received imipramine and the others received placebo. Within a given depression level, assignment of subjects to placebo or imipramine was on a random basis.

Each subject was tested prior to administration of any drug and again one week later, two hours after injection of the final dose. The test battery included measure of level of depression (the 'D' scale of the MMPI) and of level of anxiety (Scheier and Cattell's 8 parallel form anxiety test).

The data on the effects of imipramine on depression and anxiety levels were analyzed in terms of the differences in scores between the predrug baseline and the final testing session. Analyses of variance were carried out.

There were considerable variation within each level of depression in the anxiety scores. That is, there were "low" depressed subjects who score high on the anxiety test and "high" depressed subjects who showed little anxiety. The analysis revealed that those individuals who were initially
"high" anxious subjects showed a significant reduction (p < .05) in anxiety level under imipramine in comparison to those who were initially "low" anxious subjects. The reduction of anxiety under imipramine just failed to reach a statistically significant level from the placebo-induced change in anxiety level in "high" anxious subjects.

Rose and Maxwell (1969) in a study attempted to throw light on the problem of prognostic factors in drug treatment of depression.

The subjects consisted of 66 males and females, aged 18 - 65 years who were all suffering from primary depressive disorders. The group was treated with imipramine (Tofranil Geigy) tablets of 25 mg. or desipramine (Pertofran Geigy) tablets of 37.5 mg. in the course of a comparative double-blind trial, one tablet t.d.s., for one week and two tablets, t.d.s., thereafter. In addition, all the patients received thioridazine (Melleril, Sandoz) 150 mg. per day.

The severity of depression was rated on the Hamilton rating scale (Hamilton, 1960), by two observers, before treatment, and after one, two or three and six weeks. In addition the following data were recorded: age, family history, neurotic traits, obsessional traits, psychopathic traits, the number of previous attacks and the duration of
the present illness, to see how these items correlated with each other and with the initial severity of depression, the final severity after six weeks of drug treatment, and the degree of improvement as measured by the Hamilton rating scale.

Efforts to predict which patients were more likely to respond to drug treatment suggest that older, more obsessional patients with previous depressive episodes are more likely to present with more severe symptoms and are more likely to have some residual symptoms; patients with a history of previous attacks of depression present with a shorter duration of illness. Lack of correlation between outcome and age, family history, and number of previous attacks were found.

Kumar, S., and Davis, R.B., (1972) designed an experiment to study the effectiveness of Noveril as an antidepressant as compared with Imipramine.

Fifty patients suffering from "endogenous" depression were selected alternately for treatment with Noveril and Imipramine. On admission the patients happened to be well-matched for age and depression scale (Davis Institute Modification of the Hamilton Rating Scale, DIMHS). The drugs were designated Noveril "A" and "B" for the purpose of the study. Dosages were adjusted in terms of tablets
to be given and for nursing purposes one 25 mg. tablet of Imipramine was taken to be equal to one 80 mg. tablet of Noveril. Patients who were suicidal or very severely depressed were also given E.C.T. They were regularly assessed to keep the number of E.C.T.'s to an absolute minimum. At the time of admission patients were assessed on the basis of DIMHS score and rating was reported after three weeks and then approximately at two weeks intervals and finally at the time of discharge from the hospital (when they were completely free from symptoms). On admission mean DIMHS Score was 27.4 for the Noveril group and 27.6 for Imipramine group. After three weeks of treatment, patients on Noveril improved by about 63.1 per cent and those on Imipramine improved by 37.7 per cent (means). This shows a difference of 25.4 per cent in the percentage of improvement between Noveril and Imipramine. One person made global clinical assessment and another rated the patient's progress independently by DIMHS; the results of which were found to correspond closely when the code was broken.

Global results were better with Noveril (not significant). Cross-over patients (changed because of lack of response or side effects) showed a clear-out superiority for Noveril, but the numbers were too small to be significant, 7 being transferred to Noveril, and 2 to Imipramine. Mean
percentage improvement in rating scale was significantly more with Noveril ($p < .05$). Mean time taken to become symptom-free was significantly less for Noveril, 2.22 and 4.83 weeks respectively ($p < .05$). Less patients on Noveril needed E.C.T. (not significant) side effects of Noveril were unimportant.

Teja, J.S., and Bhatia, S.C. (1972) conducted a 'Double-blind trial of Iprindole' and Imipramine in depressives, at Chandigarh, India, over a period of 13 months. The diagnostic breakdown of the cases and the type of drug administered was as follows:

<table>
<thead>
<tr>
<th></th>
<th>Iprindole</th>
<th>Imipramine</th>
</tr>
</thead>
<tbody>
<tr>
<td>M.D.P. depressed and Endogenous depression -</td>
<td>24</td>
<td>24</td>
</tr>
<tr>
<td>Involutional melancholia -</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Reactive depressive psychosis -</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Depressive Neurosis -</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>29</strong></td>
<td><strong>30</strong></td>
</tr>
</tbody>
</table>

The trial was conducted in a double-blind manner. A randomization order for patients was drawn before start of the trial in such a manner that by the end of the
trial each of the two compounds would have been received by 
equal number of patients.

Identical tablets with 30 mgm. of Iprindole and 
25 mgm. of Imipramine were administered in the following 
dosage schedule: One tablet thrice daily for the first week. 
Two tablets thrice daily in second, third, and fourth weeks. 
The only other drug which the patients received during the 
period of trial was a night hypnotic in the form of butobar-
bitone or pentobarbitone.

If a patient showed no improvement at the end of 
four weeks, the drugs were stopped and E.C.T. was started. 
In patients showing improvement on drug at the end of four 
weeks, the same drug in same dose was continued for another 
two weeks.

An assessment of the patient’s symptomatology was 
done by the "blind" investigator, both on clinical cariteria 
(Teja and Narang, - 1970) and Hamilton's rating scale for 
depression (1960) on days 0, 7, 14, 21, 35, and 42.

Both the drugs were found to be potent and effect-
ive agents for treatment of depressåd patients. At the end 
of four weeks of treatment imipramine appeared to be sli-
ghtly better than iprindole on clinical criteria of global 
improvement (75 % of the patients improved on imipramine and 
47.5 % on iprindole) and percentage reduction of score on
the Hamilton's Scale (66.6 % of the patients on imipramine and 48.8 % on iprindole showed a reduction of 26 per cent or more of the score). In both instances, however, differences were not statistically significant. Between the effectiveness of the two drugs, however, there was no significant difference in relation to any of the symptoms of the Hamilton's scale both at the end of four and six weeks.

The response to treatment with E.C.T. in the 19 patients who had not shown any improvement at the end of 4 weeks of treatment with iprindole (12) or imipramine (7) was very good and gratifying. It would thus seem that E.C.T. may be a good form of treatment in the psychotic depressed patients not responding to the tricyclic anti-depressants.
Martin (1960) conducted an experiment to consider the effect of depressant drugs on palmar skin resistance and adaptation.

In palmar skin resistance reflects behavioral arousal, as Duffy (1951, 1957) argued, then it should be affected by central depressant or stimulant drugs. As there was lack of clear evidence on this point (Latties - 1957; Marquis et al. - 1957), this experiment (Martin - 1960) was carried out to consider the effect of Meprobamate and Doriden on palmar skin resistance and adaptation.

The subjects were a group of twenty-four adults (undergraduate students) consisting of 13 women and 11 men whose mean age was 30 years with a S.D. ± 8 years.

Two 250 mgm. tablets of Doriden were given -- one in the morning and the other after four hours. The same time intervals were followed with Meprobamate using 400 mgm. tablets.

Apparent skin resistance was measured continuously over a period of 15 minutes, approximately 1 - 1½
hours after oral administration of the drug. The psychogalvanometer provided an overall coverage up to 1 megohm, and delivered a very small constant current of 10 \( \mu \)A. Electrodes were brassed, 1" in diameter, strapped dry to the palm by means of rubber band.

Since the nature and intensity of the disturbing stimulus is known to exert a significant effect upon adaptation, two types of stimuli were used; the first series a twenty tones (100 db. 980 c.p.s.) spaced at intervals of 30 seconds, and the second a series of questions (presented at a similar time interval), dealing with the presence of neurotic symptoms within the subject. Subjects received the stimulus through head-phones.

After three minutes recording during rest the series of tones was presented to the subject, and followed by a three minute relaxation period. Following this, experiment using a series of questions started. This procedure was repeated on three consecutive days, one day with Doriden, one day with Meprobamate, and one day with no drug.

Results showed that, the drugs raised level of skin resistance, and reduced the number of GSRs given to tone stimuli.
Venables (1960) conducted an experiment to see the effect of auditory and visual stimulation on the skin potential response of schizophrenics.

Many works on the reaction time of schizophrenics, e.g., Venables and Tizard (1958) had shown the dependence of response on the parameters of the stimulus. The value of repeating this work on voluntary responses, in the field of involuntary response, was in removing explanations of the behavior from situations where attitudinal and "set" factors may be the preferred form of interpretation to one where more physiological constructs may be evoked. With this in mind the skin potential response had been adapted for study.

The aim of this experiment was two-fold. Firstly, to provide evidence for the influence of non-specific background stimulation on the responses of active and withdrawn schizophrenics. Secondly, to provide data on rates of adaptation of electrodermal response in different subjects so that a later experiment on the intensity of stimulation might be more economically planned.

The psychiatric subjects were 32 male chronic schizophrenics of mean age = 36.6; S.D. = 9.0 years, who had been in hospital for a mean length of present admission
of 8.6 years. They were divided into the following groups -- active -- paranoid; active--nonparanoid; withdrawn -- paranoid; and withdrawn -- nonparanoid. Subjects in these four groups were allocated at random to the experimental treatments. In addition to this, there were 16 normal subjects with mean age of 46.9; S.D. = 9.0 years, a figure which did not differ significantly from that of schizophrenics.

Skin potential was measured by means of two channel D.C. amplifier. The auditory stimulus was a 90 db, 1,000 c.p.s. pure tone presented for one second through a loud speaker situated 5 feet in front of the subject. The visual stimulus was the illumination for one second of a milk white screen 1'6" x 1' and situated 5 feet from the subject at an intensity of 900 ft. Lamberts or 99 d.λ. re 10^-10 Lambert. The extraneous visual stimulus was the continuous illumination of the same screen at an intensity of 700 ft. Lamberts or 95 d.λ. Auditory or visual stimuli were used either in the absence or presence of additional stimuli of the "opposite" modality.

Confirmation of previous reaction time results was achieved by the finding of greater responsiveness of active schizophrenics in minimally stimulating conditions while greater speed of response was shown by withdrawn schizophrenics in the presence of additional stimulation.
Also in confirmation of previous results was the greater speed of active paranoid schizophrenics - in contrast to the other diagnostic groups.

Venables and Wing (1962) reported a study in which the arousal level of a group of schizophrenic patients was measured using central and peripheral indices.

Previous experiments had suggested that a relationship exists between level of arousal and behavioral withdrawal in chronic schizophrenic patients (Tizard and Venables - 1957; Venables - 1960). It had also been shown that clinically defined sub-groups of chronic schizophrenics differ significantly in degree of social withdrawal (Wing - 1960, 1961). This study (Venables and Wing - 1962) was designed to investigate further the relationship between arousal, withdrawal, and clinical condition.

In all, 55 male schizophrenics who had been in hospital for longer than two years, and whose age ranged from 20 - 60 years, took part in the study. None of the patients was put on drug. There was definite evidence, for all the patients in the series, that they had had delusions, schizophrenic thought disorder, or catatonic motor disturbances at sometime during their illness.
Each patient was rated by his charge nurse on withdrawal using items 1, 5, 16, 17, 19, and 20 of the scale described by Venables and O'Connor (1959). Withdrawal was measured by a low total score on the rating scale and lack of withdrawal by a high score.

Each patient's arousal level was measured by the method described by Venables (1961). The two-flash threshold was measured by asking the patient to indicate by pressing a button once or twice, whether he saw one or two flashes when presented with two flashes, which varied in interflash interval from 30 to 120 msec. The flash intensity was 50 ft.-L., the visual angle of the source was 1.8 degrees, and the flash length 5 msec. Skin potential was measured by a chopper-type D.C. amplifier with an input impedance of 5 megahms. Silver-silver chloride electrodes were used. High arousal was indicated by either a low threshold or a high negative potential.

Results showed a close consistent relationship in chronic schizophrenic patients between degree of social withdrawal and level of physiological arousal, whether measured centrally or peripherally. The more withdrawn the patient, the higher his arousal. The only exception of this findings was with those patients who exhibited marked coherent delusions.
Different sub-groups of patients, categorised during a standard clinical interview, did show a gradation in level of arousal which was consistent with their gradation in mean social withdrawal score.

It was also found that increased arousal affected perceptual activity in chronic schizophrenic in such a way that normal selectivity was impaired. Withdrawal from the environment - both social and material was explained in terms of protective mechanism.

Finally, there was evidence that arousal level in schizophrenics can be influenced by various drugs, particularly the newer phenothiazine derivatives, and by the social organization of the patient's environment.

Sugerman (1964) conducted an experiment on Chronic Schizophrenics.

The electroencephalogram, interpreted by the traditional method of visual inspection had proved of little use in the diagnosis of schizophrenia and the assessment of change during its course. The recent findings by a quantitative method of EEG analysis that the EEG of the chronic schizophrenics showed characteristic abnormalities of mean energy content and variability suggested that changes in schizophrenic behavior under the influence of psychotropic drug;
might be correlated with specific EEG changes.

In this study (Sugerman - 1964) quantitative EEG measures and standard behavioral measures obtained in a double-blind study were correlated over a period of one year, the subjects being 16 male chronic schizophrenic patients (mean age - 38.2 years; range 25 to 45).

Deanor, Chlorpromazine, Perphenazine and placebo were administered singly and in combination without the psychiatrists, nurses and EEG personnel being aware of their nature. Every patient was maintained without medication for at least 2 months before the study. The compounds given were deanol.

Significant correlations were obtained indicating that worsening of schizophrenic behavior inside the ward (as rated by a rating scale) was associated with decrease of coefficient of variation and increase of mean electrical energy content, while the reverse was true with improvement in schizophrenic behavior. On the basis of the results, further research in this area has been suggested.

Thimmappa (1969) conducted a study in chronic schizophrenics and neurotics to find the relationship between arousal, conditioning and learning. The sample consisted of 95 subjects - 30 male schizophrenics with 2 to 14 years of duration of illness, 30 male normals and 20
female normals, and 15 anxiety neurotics. Spiral after-effect test was used as a cortical measure and the skin resistance was used as an autonomic measure of the level of arousal. Classical finger withdrawal conditioning and verbal learning consisting of three paired-associate learning, and concept learning were also used. The Basal skin resistance was measured while the subject was relaxed. Silver/Silver electrodes with potassium chloride jelly were used in palm to palm placement. The basal level was recorded after 17 minutes of relaxation. After this subject was asked specific questions to which he or she was expected to answer by Yes or No. There was an interval of two minutes during which the resistance change was noted. There were altogether 10 questions. After this four electric shocks were given to the leg of the subject with two seconds duration. Before giving the shock the subject was explained about the nature of the shock that it would not be very painful. The mean change in resistance was noted. Four trials of Spiral-after-effect test in clockwise and anti-clockwise directions were given with an inter-trial interval of one minute. In the conditioning experiment the U.C.S. was electric shock to the finger and C.S. was a bell. The pair of U.C.S. and C.S. were given till the subject showed unconditioned response in five successive trials to the C.S. alone. Towards the end, paired associate learning and
concept learning tests were given. Analysis of variance was conducted on the data. The results showed the responsiveness on G.S.R. to the stimulation (both verbal and shock) in schizophrenics and neurotics. The schizophrenics showed lesser responsiveness than the neurotics. This lowered responsiveness in them was statistically significant. In conditioning and verbal learning the neurotics performed better than the normal group, while the performance level of the schizophrenic group was significantly less than that of the normal group. A significant negative relationship between the skin resistance measure and the duration of spira1 after-effect was observed, in the normal group. But this was not significant in the patient group. Again, a significant positive relationship between the measures of arousal and the trials taken in verbal learning were found in the normal group, and no such significant relationship was found in the patient group.

Fenz and Velner (1970) reported a study on physiological concomitants of behavioral indexes in Schizophrenia.

Reviewing the literature on arousal in schizophrenia, it was found that depending on the physiological measures used, selection of subjects and the experimental situation, schizophrenics fall anywhere along the continuum of arousal, although in most cases toward a high or
low ends of this continuum. In addition, some schizophrenics show marked and sudden shifts in autonomic activity, now being "overaroused" and now "underaroused."

A common and basic deficit in all schizophrenics lies in their inability to modulate effectively or change their level of autonomic responsiveness to correspond to variations in internal and external stimulation (Epstein - 1967). As for autonomic responsivity, so far behavioral indicants; a basic underlying deficit seems to be an inability of the schizophrenic patient to evaluate correctly the emotional demands of a given situation and to respond to it appropriately.

On this background, this study was conducted to find out autonomic concomitants to behavioral indexes in schizophrenia.

The sample consisted of 42 male subjects, 28 psychiatric patients, and 14 normal controls. The 28 patients were selected from a larger sample of patients on the basis of extreme ratings on the Phillips Premorbid Rating Scale (PRS - 1962), given independently by two experienced interviewers. The 14 controls were non-professional hospital employees who volunteered to take part in the test and were remunerated for their participation. Most patients were receiving Stelazine (Phenothiazine
group), the approximate dosage ranging 10 - 40 mg./day. No one in the control group admitted to taking any tranquilizer drugs. The patients were classified either chronic or acute on the basis of the Phillips Premorbid Rating Scale.

Recordings were obtained from a multichannel Beckman Type - R dynograph, using standard Beckman couplers. Electrodes used for electromyogram (EMG), Skin resistance (SR), direct Heart rate (HR), and Cardiotach (CT) recordings were zinc cups, 6mm. in diameter, placed in specially built plastic holders 15 mm. in diameter. The cups were filled with Beckman electrode paste and fastened to location with adhesive collars EMG electrodes were placed on both sides of a median line of the forehead; direct HR and CT electrodes were placed one slightly above the other sternally, the two electrodes in each set about 6in. apart; the SR electrodes were attached on the Volar Surface of the distal phalanges of the third and fourth fingers of the non-dominant hand.

The stressers consisted of intense audio and visual stimuli. Extraneous audio stimuli were presented through loud speakers on two tape recorders placed outside the shielded area behind and outside subject's visual field,
approximately 30 in. away, shoulder high. Three tapes were used: (a) a relaxation technique tape; (b) a continuous white noise tape, with an intensity of 110 db; and (c) an intermittent white noise tape, consisting of 20 stimuli, lasting 1 sec. each, randomly distributed between 18 and 20 sec. apart, with an intensity of 80 db. The extraneous visual stimulus consisted of four 300-w. bulbs, mounted one next to the other outside the shielded area, 6 ft. above ground and approximately 4 ft. from the subjects.

The background illumination before and during the experiment consisted of two fluorescent tubes (with a total of 80 w.); the background noise was limited to apparatus noise, such as the motor of dynograph and the switching on and off of tape recorders and lights, the room being adequately sealed from external noise.

The experimental procedure included first the relaxation tape, to help subjects to relax and to adjust to the environment. The experiment proper was then initiated and consisted of three phases: First, subjects were presented for 5 min. with the continuous white noise; this was followed by 5 min. of the same noise, plus the continuous flash of light; and this was followed by the
20 discrete white noise stimuli.

The results on physiological measures during both rest and stress periods were in agreement with the findings of a member of earlier studies, especially if the two schizophrenic groups are treated as one. Both HR and respiration rate are usually found to be much higher in psychotic patients than in normal controls (Goldstein - 1964; Venables and Wing - 1962), as are measures of muscle potential (Goldstein - 1964; Reynolds - 1962). SC on the other hand, is usually found to be lower in psychotic patients, as are the various measures of GSR (Berger - 1964). Similar findings were reported in this study. Thus, while on some measures patients may be considered over-aroused, on others they are clearly under-aroused.

Mukundan and Murthy (1970) in a study measured the skin potential response to an auditory stimulus and an electric shock of various intensities in chronic schizophrenics and normals. Further responses to anticipated stimuli in auditory modality and to electric shock were also recorded.

Taylor and Epstein (1967) mentioned a model of arousal which
is more in accord with physiological facts recognizes that as stress mounts, it triggers reactions at different points in time in different systems. Thus a greater knowledge of the different systems and their variations to different stimuli may throw more light on the problem. Hence this study (Mukundan and Murthy - 1970) was undertaken.

The main objectives considered in this study were --

(1) To investigate the theory of high level of arousal in chronic schizophrenics.

(2) To find the relationship between level of arousal and clinical (psychiatric) classification of schizophrenia.

The sample consisted of 18 male chronic schizophrenics and 8 normals. The schizophrenics were within the age range of 20 to 50 years with a mean of 35 years. The normals were within the age range of 23 to 45 years with a mean of 32 years. Silver/Silver chloride electrodes with potassium chloride electrode jelly were used. The active electrode was placed in the left hand palm and the inactive electrode also was placed in the forearm of the same hand. Skin potential recordings were taken in the initial rest period. The subject was then told that he
would hear 5 sound stimuli at increasing intensities through a pair of earphones. The change in the skin potential during one minute anticipatory period and the responses to the auditory stimulation were recorded. After a period of relaxation, the subject was told that he would receive 5 electric shocks of increasing intensities. The responses to anticipated stress and stress were recorded.

The results showed that the schizophrenics did not differ from the normals in their basal level or skin potential level during the initial rest period. However, the schizophrenic group was significantly less responsive than the normal group to the electric shocks whereas this difference was not evident during the auditory stimulation.

Chattopadhyay and Murthy (1971) in a study made an attempt to assess the level of arousal in a group of anxiety patients and thus to find out the difference, if any, in the Basal cortical conductivity of the anxiety group in comparison with that of normals.

Theoretical considerations led to the formulation of the hypothesis in this experiment that, the basal cortical conductivity of the anxiety group would be different than that of the normal group. This study was undertaken so as to validate this hypothesis further.
Fifteen males, literate, student/service holders, age ranging from 18 - 43, diagnosed as cases of anxiety by psychiatrists at the out-patient department of the Government Mental Hospital, Bangalore, were taken as subjects to constitute the experimental group in this study.

A group of fifteen literate, male nurses, (employed at the Government Mental Hospital, Bangalore), age ranging from 20 - 42, without having any psychiatric or any other physical illness were selected to constitute the control group.

Keeler's polygraph was used to measure G.S.R. Reading for each subject was taken continuously for about three minutes time, using polygraph.

Statistical treatment of the data showed that the Basal cortical conductivity of the anxiety group is significantly different ($p = < .01$) than that of the normal group.

As the population studied in this experiment was very miniscule in form, this study suggested further investigation in this area.
The relationship between vascular indices of arousal and psychometric indices of anxiety was used to assess the validity of the emotional reactivity hypothesis (Forrest and Korth - 1971).

The "emotional reactivity" hypothesis (Desiderato - 1964; Omimsky and Kimble - 1966) assumed that high anxiety subjects react with high drive than do low anxiety subjects only in situations containing some degree of stress.

Spielberger (1966) in accord with the emotional reactivity hypothesis, conceptualizes anxiety as consisting of two parts, one being a transitory state or condition of the organism and the other as a personality trait, and developed a psychometric test using the State-Trait Anxiety Index (STAI) to measure these aspects of anxiety. State anxiety consists of feelings of apprehension and heightened autonomic nervous system activity that vary in intensity and fluctuate over time. Trait anxiety refers to individual differences in anxiety proneness, i.e., to differential tendencies among individuals to respond with different levels of state anxiety in situations that are perceived as threatening.

This study investigated the relationships between psychometric indices of anxiety (Manifest anxiety...
Scale - MAS /Taylor - 1953; and STAI and vascular indices of arousal to test two hypotheses:

i) That psychometric indices of anxiety (MAS, STAI) are associated with vascular arousal of the autonomic nervous system; and

ii) to ascertain whether different base line blood pressures are associated with different anxiety level ("Chronic hypothesis" which assumes that high anxiety subjects manifest higher drive than low anxiety subjects in all situations, stressful or not; Farber - 1956 and Taylor - 1956), or if differences in blood pressure readings are evident only after subjects are placed in a stressful task (reactive hypothesis).

Three groups, each containing 10 males, were selected on the basis of high, medium and low scores on the psychometric indices of anxiety. Blood pressures were recorded using a Sphygmomanometer and taken every 30 seconds while the subjects were in stressful task. The stressful condition required a continuous matching task upon which was superimposed a shock avoidance contingency. Subjects received a shock at the pain threshold, irrespective of matching task performance, twice per minute. The task lasted 20 minutes and the number of shocks and matching
responses were taken by an event recorder. There were no significant differences in group performance.

Subjects' performances on the psychometric indices of anxiety (STAI, MAS) were compared with vascular indices of arousal (systolic and diastolic blood pressure) measured during the 20 minute shock avoidance procedure. The differential scores obtained by the subjects on the psychometric indices were ranked and separated into three groups; High, Medium, and Low. Vascular measures were taken on low, medium and high anxious groups before and during a stressful task. Support of the emotional reactivity hypothesis was obtained in that differential vascular responding occurred only during the stressful task, not during the baseline period.

18. STUDIES WITH REFERENCES TO GSR CONDITIONING:

Welch and Kubis (1947) endeavoured to investigate the effect of pathological anxiety on the rate of conditioning, in order to determine whether the rate of conditioning might be eventually a valuable objective indicator of the degree of anxiety.

The most accurate and carefully controlled studies pertaining to the rate of conditioning in patients suffering from mental disorders were made by Mays (1934),
Shipley (1934) and Pfaffmann and Schlosberg (1936). Mays endeavoured to compare "perseverational tendencies" in catatonic schizophrenics with those of normal subjects. Shipley's study was a continuation of May's investigation. He used similar sound patterns for the conditioned stimulus and the response he studied was likewise the P.G.R. In case of a loud automobile horn as the unconditioned stimulus, he used an electric shock. Pfaffman and Schlosberg used a bell as a conditioned stimulus. Schizophrenics were found to be the less responsive and at the same time had more negative reactions than either the normal subjects or the manic depressive group. Hilgard and Marquis (1940) in commenting on the work of these men stated inconsistancies in the findings made it difficult to draw any conclusion of their results. On this background this study (Welch and Kibis - 1947) was undertaken.

Two groups were used in this experiment. One group of 82 college students and the other group of 51 patients, (some of whom had anxiety and some of whom did not, according to psychiatric observation). The corresponding age range for the two groups were 17 to 53 and 16 to 54 years of age.

Instead of using a bell or buzzer as a conditioned stimulus, certain non-sense syllables of low association
value were used as conditioned stimulus. Unconditioned stimulus was a door buzzer at a distance of two feet from the subject's head and the response under investigation was the PGR detected by the Fordham two-stage D.C. amplifier. The criterion of conditioning for the test was three subessential marked responses to the conditioned stimulus when unaccompanied by the sound of the buzzer. The score was determined by counting the number of times the buzzer was sounded before this criterion was fulfilled.

All but four of the normal group had a score of from 14 to 58, while with but one exception all of the patients who were diagnosed by the psychiatric staff as having anxiety had a score of 14 or less.

The repeat correlation on 36 of the normal subjects was .88. On repeat tests given to the patients the scores in most instances increased or decreased as their anxiety increased or decreased, according to psychiatric diagnosis. Differences in age, sex, and general intelligence did not appear to affect the rate of conditioning.

Bitterman and Holtzman (1952) reported a study in which the relation between a clinical index of anxiety and behavior in a conditioning situation was studied in a homogeneous group of normal males.
Welch and Coworkers (1947; 1947; 1949) have reported a number of experiments with the galvanic skin response in which children and adult diagnosed as pathologically anxious were found to condition more readily than normal controls. Taylor (1951) studied the conditioning and extinction of eyelid reflex in high and low anxiety groups. The high group conditioned more readily than the low and tended to extinguish less readily, although the latter difference was not statistically significant. As Hilgard and Coworkers (mentioned by Bitterman and Holtzman - 1952) had noted, their approach to the problem did not suggest a relation between anxiety and simple conditioning, but the theoretical position of Taylor did lead to the expectation of such a relationship. Although extreme groups (such as psychiatric samples Vs. normal or the upper and lower ends of the distribution of Taylor Scores) had been clearly differentiated in terms of simple conditioning measures, the Hilgard experiment with a more homogeneous sample produced negative results. This study, (Bitterman and Holtzman - 1952), was designed to permit a comparison of simple conditioning scores with the results of a more extensive clinical analysis of a homogenous group of normal subjects.

The subjects of this experiment were 37 unmarried male students, between 18 - 25 years of age.
The conditioned stimulus (CS) employed in the experiment was a 5 sec., 1,000 cycle tone of two intensity produced by a Hewlett-Packward audio-oscillator and led directly, without amplification, to a small speaker attached to subject's chair. The unconditioned stimulus (US) was a 3.5 ma. shock (from a 700-v, supply through a high series resistance) to the right wrist of subject. The duration of shock was 1 sec., and its onset coincided with the termination of conditioned stimulus (CS); inter-trial inter-vals ranged from 30 to 70,secs. The presentation of stimuli on each trial was recorded on one channel of a two-channel Brush ink-writing Oscillograph (Model BL 202). Skin resistance was measured between the palmar and dorsal surfaces of subject's left hand.

All the subjects were rated for susceptibility to anxiety on the basis of psychometric indices and performance in a laboratory test situation, and in terms of their ratings they were divided into two groups. The galvanic skin response to shock conditioned more readily and extinguished less readily in the high anxiety group than in the low. In view of the homogeneity of the sample, this experiment represented a most stringent test of the hypothesis that anxiety is related to the rate of conditioning and extinction. The results suggested that conditioning scores may be sensitive enough to be of practical value in psychiatric screening especially of specialized military personnel.
franks and Laverty (1955) in a study reported the effect of Sodium Amytal on conditioning.

Sodium Amytal had long been regarded as a physiologically inhibiting drug. Both introversion - extra-
version and conditionability have been related to the cortical processes of excitation and inhibition, as conceived by Pavlov (1927, 1928, 1941). If this is so, then a drug which increases cortical inhibition should decrease condition-
ability and increase extraversion. One of the effects of sodium amytal was thought to be that of cortical depression. Hence, it was predicted that this drug would reduce condition-
ability and increase extraversion. As far as the present writers (Franks and Laverty - 1955) were aware this hypothesis had not been previously tested, although it was shown (Hil-
gard and Marquis - 1940) that other depressants such as bromide, retard the rate of conditioning and accelerate the rate of ex-
tinction.

This study was carried out upon 16 neurotic hos-
pitalized subjects, of either sex, diagnosed as dysthymics (anxiety states, obsessive compulsives, reactive depressives) and therefore expected to condition readily. All subjects were between the ages of 17 and 46 years.

Four different treatments were used, two of these consisted of different doses of amytal, one of a
placebo and one of no drug or placebo. The four different
treatments were as follows:

1. A large dose of intravenous sodium amytal. 0.5 grains
   per stone body weight, made up in a solution of sterile
   water immediately prior to injection, 1 grain of amytal be-
   ing dissolved in 2 c.c.m. of water, and injected into the right
   arm at the rate of 2 c.c.m. per unit (i.e., at a rate of 1
   grain per minute).

2. A smaller dose of intravenous sodium amytal. This dose
   was always two grains less than the larger dose would be for
   that subject, made up and injected as above.

   In practice the dosage range for the 16 subjects
   varied 4 to 6 grains for "A" and for 2 to 4 grains for "a".

3. A placebo injection of distilled water. This was in-
   jected in precisely the same manner and under the same con-
   ditions as the sodium amytal.

4. No injection at all.

More than one treatment and testing session was allocated to
each subject so that treatment comparisons could be made with
each person.

The unconditioned stimulus was a puff of air,
delivered to one eye at a pressure of approximately 65 mm. of
mercury from a distance of 2 cm. from the eye and lasting 500 milliseconds. The conditioned stimulus was a pure tone of frequency 1,100 cycles per second at an intensity of 65 dB above the subject's auditory threshold. The duration of this tone, heard through a pair of padded earphones, was 800 milliseconds. The air puff was so arranged that it began 350 milliseconds after the tone had commenced. Partial conditioning was used, the sequence being such that the reinforcement ratio was approximately 60 per cent., throughout the reinforcement trials. Thirty reinforcement trials were given, interspersed with 18 test trials, consisting of the conditioned stimulus alone. The inter-trial interval varied from 20 to 30 seconds with a mean of approximately 25 sec. After 30 reinforcement trials and 18 test trials (called acquisition test trials) had been given the subjects were given a further series of 10 consecutive test trials (called extinction test trials) so that the resistance to extinction could be measured.

The following conclusions were drawn: The two main hypothesis of this study were confirmed at least tentatively. These were — 1 that intravenous sodium amytal reduces the number of conditioned eyeblink responses during acquisition and increased the rate of extinction; 2 that intravenous sodium amytal increased the extraversion score as measure by Guilford's 'R' Scale.
The scores obtained under treatment P. were not significantly different from the scores obtained under treatment N. - nor even any trend in the data was evident. It was suggested that these conclusions should be used with caution and further experimental investigations were recommended to validate these findings.

Franks (1956) reported a study on conditioning and personality using normal and neurotic subjects.

Pavlov's (1927, 1928 and 1941) theory of cortical functioning emphasized two basic cortical processes, excitation and inhibition. In this study (Franks - 1959), Pavlov's concepts of excitation and inhibition were related to the dimension of introversion - extraversion in normal and neurotic subjects.

Twenty dysthyemic patients, 20 hysteric patients and 20 normals were tested. All subjects were aged between 17 and 47 years. Although the normal group was significantly younger than the two neurotic groups, the neurotic groups did not differ significantly in age.

The unconditioned stimulus was a puff of air, the conditioned stimulus was a tone administered through a pair of head-phones, and the unconditioned and conditioned
responses were both eyeblinks and P.G.R. changes. Partial conditioning was used, each subject being given 30 reinforcements, interspersed with 18 test trials, and 10 extinction trials. All conditioning was carried out in one session, taking approximately half an hour per subject. The 20 normal subjects were retested after an interval of 14 - 21 days.

Results showed that :-

(a) anxiety states conditioned much better than hysterics, and

(b) conditionability is related to intraversion - extraversion and not to neuroticism.

Howe (1958) in a study examined conditioned GSR behavior in hospitalized anxiety states, normals and hospitalized chronic functional schizophrenics, on the hypothesis that these three groups would involve, respectively, a descending order of total drive strength (Hull's D) with respect to such a stimulus as electric shock.

Several studies have confirmed that the neurotic subject conditions more readily in a threat situation than does the normal (Spence and Taylor - 1953; Taylor and Spence - 1954), a difference which might have been
explained by an increase in motivation derived from anxiety. The data on the conditionability of psychotics, are, on the other hand, rather scanty and unsystematic (Bender and Schilder - 1930; Mays - 1934; Shipley - 1934; and Pfaffman and Schlosberg - 1936). Some other studies (Spence and Taylor - 1953; Taylor and Spence - 1954) have reported data and deductions for psychotics with the conclusion that these subjects condition more readily than both neurotic and normal subjects. This conclusion did not support the findings of Pavlov (1951), who examined G.S.R to electric shock and to threat of shock in 450 normals and 450 psychotic subjects. Although there was little difference to the subjects' response to the shock, there was a significantly smaller response in psychotic subjects to the threat of shock. However, as data in this regard were scanty, the present study was undertaken.

A total of 60 normal control subjects was used (half of them were university students, age ranging from 19 to 24 years; half of them were males; another half was a group of 30 nurses, equal number of males and females, age ranged from 18 to 25 years).

A total of 60 anxiety patients (29 males and 31 females the ages of these patients were not recorded)
and 60 chronic functional psychotics (26 males, 34 females, mean age 32 years) was used.

The Feve method, involving impressed current, was used for G.S.R. conditioning in the circuit described by Lacey and Siegel (1948). The following conclusions were drawn:

With magnitude of response (in long conductance units) during experimental extinction as an indirect measure of strength of conditioning, the anxiety subjects showed significantly stronger conditioning than both the normal and schizophrenic subjects, the difference in response magnitude being some increasing function of the number of extinction trials, as shown by a significant interaction term. While schizophrenic subjects showed the lowest magnitude of response, it was not possible to offer proof with either a parametric or non-parametric method of analysis that this magnitude was statistically less than that for the normal subjects.

It was argued that predictions concerning the autonomic conditionability of the schizophrenic must vary with the degree of chronicity of and perhaps the amount of deterioration in the disorder with less reactivity (for
example, Hull's drive strength, \( D \), being more typical of the chronic and deteriorated case. A comparison of schizophrenic subjects who were conditionable with some who were not gave support to such an hypothesis.

Stewart et al. (1959) reported a review of the literature on classical conditioning in psychiatric patients.

The subjects were 70 in number, comprising 27 patients with manic depressive disease, depressive phase; 18 with schizophrenia; 15 with personality disorders; and 10 with anxiety neurosis. Thirty-six patients were male, 34 females; the mean age of the subjects was 39, the range from 15 to 72. None of the subjects had received any specific treatment other than night time sedation or psychotherapy, within a period of a month before the time of the test.

The conditioned stimulus was a 500 c.p.s. tone, whose intensity was about 65 decibels above the normal hearing threshold for this frequency; it was presented for 4 seconds. The unconditioned stimulus was a shock of about 46 volts lasting for one second, and immediately followed the end of the conditioned stimulus in the paired trials. Continuous readings of the skin resistance were
taken by means of Galvanometer.

The following conclusions were drawn on the basis of the findings:

(a) The subjects with anxiety neurosis took significantly more trials to become habituated to the conditioned stimulus before the conditioning trials began, than the subjects of either of the psychotic groups.

(b) The subjects with personality disorders conditioned significantly more quickly than subjects in either of the psychotic groups. The subjects with anxiety neurosis conditioned more quickly than those with schizophrenia, only between the .1 and .05 level of confidence.

(c) The subjects with anxiety neurosis and with personality disorder tend to make more conditioned responses during extinction trials than subjects in either of the psychotic groups.

(d) A high degree of correlation was found in each group of subjects between the rate of habituation to the conditioned stimulus and the rate of extinction of the conditioned response.
willett, R.A. (1960) reported the effects of depressant drugs on learning and conditioning.

Conditioning was described and analyzed by Pavlov and his associates (1927) in terms of inhibitory and excitatory neural potentials. The various phenomena associated with rote learning of nonsense syllables have been accounted for, in analogous terms, by Hull and his associates (1940). The measures of conditioning and rote learning were taken, after the administration of depressants such as Doriden and Meprobamate, with the assumption that the primary hypothesis that the extravert is likely to be characterized by an exaggeration inhibitory potential would be supported. On this background, the purpose of this study (Willett - 1960) was to repeat those of Franks et al. (1955, 1958) on eye-blink conditioning and Willett on rote learning, using the two new depressants and employing each subject as his own control.

The subjects were a group of twenty-four adults consisting of 13 women and eleven men whose mean age was thirty years, with S.D. ± 8.

The conditioned stimulus was a tone of 1,000 c.p.s. delivered at 60 d.b. above each subject bi-aural threshold, through a pair of high-quality earphones.
The unconditioned stimulus was a puff of air delivered through a plastic tube at a pressure of 65 mm. of mercury. The two stimuli overlapped in time — the tone lasting 850 msec., the puff being delivered 450 msec., after the commencement of the tone. Both stimuli terminated together. The eyeblink response was recorded by means of a photo-electric cell held in the right-hand lens carrier of a pair of spectacles frames which the subject wore. The carrier also held the open end of the plastic tube through which the puff was administered.

For nonsense syllable learning the apparatus used was similar to the standard, electrically driven memory drum used by Hull (1949) and by Hovland (1938). The subjects began the nonsense syllable task when their conditioning session was completed. The subjects were required to learn one list of 12 syllables to a criterion of one perfect repetition.

Each of the 24 subjects was seen on 3 occasions — once under Doriden, once under Meprobamate, and once without any drug. The treatment orders were so arranged that over all the group, at the end of the experiment, treatments were equally distributed amongst occasions, so that 8 people had Doriden on the first occasion, 8 on the
second, and 8 on the third. Likewise 8 subjects had Meprobamate and the "No drug" condition on the first, second and third occasion.

Two 250 mg. tablets of Doriden were given — one in the morning and the other 4 hours later. The same time intervals were followed with Meprobamate — using 400 mg. tablets.

Findings were summarized as follows:

On the basis of the hypothesis linking extraversion with cortical inhibitory tendencies it was expected that the depressant drugs would reveal extravert behavior pattern. More specifically it was expected that the drug group would have fewer conditioned eyeblink responses and would also show evidence of a decreased rate of learning.

Doriden significantly decreased the number of conditioned responses but Meprobamate, although acting in the same way, did not produce a statistically significant effect.

Neither Dorden nor Meprobamate significantly increased the number of trials taken to reach a criterion of one perfect repetition on a rote learning task,
although the mean scores were separated as expected. When
the slopes of the individual learning curves were examined,
both doriden and meprobamate were associated with shallow
learning curves, and this difference was statistically sig-
nificant one.

Certain secondary effects were examined. The
drugs did not effect any change in rate of random blinking.
Both drugs significantly increased the number of incorrect
responses given during the nonsense syllable learning when
allowance was made for the total number of errors recorded.

No reminiscence was found for any of the groups.

No regular or significant regression co-efficients
between any of the measures and the questionnaire measures
of extraversion and neuroticism were found.

Becker and Matteson (1961) conducted an experiment so as to
examine the hypotheses formulated by Eysenck (1955) and
Spence (1958) relating GSR conditioning to extraversion and
anxiety, respectively.

Using basic notions derived at least in part
from different aspects of Hullian theory, Eysenck and
Spence have developed two different but not necessarily
mutually exclusive hypotheses concerning the relationship
of personality characteristics to conditioning. Eysenck
proposed that individual in whom reactive inhibition de-
velops rapidly and dissipates slowly tend to develop extra-
verted behavior patterns. Since reactive inhibition in-
terferes with the repetition of a conditioned response,
Eysenck predicted that extraverts will condition less read-
ily than introverts. On the otherhand, Spence had hypo-
thesised that the higher emotional reactivity of the an-
xious person acts like other drives in increasing reaction 
potential during conditioning, therefore, a positive re-
ationship can be predicted between the degree of manifest 
anxiety and level of conditioning.

The impetus for this study (Becker and Matteson - 1961) came from a recent failure by Becker (1959) to find support for either Eysenck's or Spence's hypothesis when G.S.R. conditioning was used on unselected male and female college students.

Four groups of 10 subjects scoring on the extremes of anxiety and extraversion measures were selected from a group of 273 male students for conditioning. A Hunter Model GSR amplifier (using finger electrodes) with visual reading was used to measure basal resistance and resistance changes as a result of stimulation. List of words and electric shock were used.
Using a conditioned response amplitude measure for testing Spence's hypothesis, a significant positive relationship was found between anxiety and conditioning. No significant relationship was found between extraversion and conditioning when either the conditioned response amplitude measure was used or (more appropriately) when a criterion — type conditioning measure was used. The results gave clear support to Spence's theory while failed to support that of Eysenck.

1(C). STUDIES WITH REFERENCE TO EXTINCTION:

Murthy and Brains (1965) in a study reported the nature of excitation - inhibition balance in the schizophrenic and also suggested certain indications for therapeutic regimes.

The concept of excitation - inhibition in spite of the fact that it has aroused great interest in the scientific field, still remains unclear in the way it has been used by the various investigators. Hence attempt was made to probe deeper into the matter.

The purpose of this study (Murthy and Brains - 1965) was to introduce three types of stimuli and note the excitation as indicated by the PGR deflection to the stimuli with the assumption that a high PGR deflection would indicate
a high level of excitation and with the introduction of rest period, the phenomena of recovery may be looked into. Recovery from excitation (as indicated by the recovery from the original deflection) would point to a very generalized understanding of the concept of inhibition as was used by Pavlov or the concept of inertia used by Freud. Three types of stimulatory situations were grouped under the heading — (1) Impersonal (2) Personal and (3) Interpersonal. This was similar to the procedure followed by M. Williams (1963) in his investigation on the psychophysiological responsiveness to psychological stress in early schizophrenic reactions.

The experimental group consisted of 15 male schizophrenics with age range of 20 to 35 years and with duration of illness of 1 to 3 years with little response to treatment. The control group consisted of 15 normals matched with the experimental group in age, sex and education.

The following conclusions were drawn:

(1) The schizophrenics showed reaction to non-personal situations just the same way and to the same degree as normals. The rate of recovery in them was non-different from normals.

(2) The ultraparadoxical reaction of the schizophrenics
at the significant level, indicated the meaningfulness of such a reaction towards personal stress and pointed to the institution of new regimes to the behavior therapeutic approach towards schizophrenia. It appeared to be in conformity with much the psychiatric understanding of schizophrenia.

(3) The schizophrenics responded strongly as did the normals toward interpersonal stress situations, but the rate of recovery was significantly slow and different from the normals. It was suggested to take this factor into consideration along with conclusion 2 in setting up experimental regimes for the therapy and rehabilitation of the schizophrenics.

Davidson et al. (1966) reported a study in which the performance of neurotic patients on finger withdrawal and GSR conditioning to shock was correlated with several personality and objective measures of drive level and cortical inhibition.

In a previous study using normal students (Davidson, Payne, and Sloane - 1964), conditioning indices for finger withdrawal and GSR were nonsignificantly correlated with measures of introversion, neuroticism and manifest anxiety. While these results did not refute
Eysenck's (1957) theory for a relationship between cortical inhibition and conditioning, they did fail to confirm the notion implicit to his theory of a general factor of conditionability (Eysenck - 1958, 1960b). These results also failed to Spence's (1958) theory of the relationship of drive (manifest anxiety) and conditioning. Since the previous study had used a large sample of student volunteers there would have been some restriction in the ranges of their test scores. Hence, in this study, a sample was chosen from a neurotic rather than a normal population in order to obtain subjects with extreme scores on tests of anxiety, extraversion, and neuroticism.

The subjects were 40 female neurotic patients, with a mean age of 35 ± 13 years and mean I.Q. was 93 ± 12. The subjects were free from any drug at the time of the experiment. The conditioned stimulus was a 750 c.p.s. tone of 200 milliseconds duration followed 400 milliseconds later by a UCS of 200 milliseconds duration: The UCS, an unavoidable d.c. electric shock to the right middle finger, was maintained at the subjects' threshold of reaction to pain. The apparatus and procedure were the same as those reported earlier by Davidson et al. (1964).

Results supported Spence's theory of the relationship of drive level to conditioning, but were not compatible
with Eysenck's theory relating cortical inhibition to conditioning because the only significant correlations in this respect were opposite in direction to his prediction. They did give, however, partial support to Eysenck's hypothesis of a generality of conditionability, but with the limitation, as pointed out by the authors that, this finding may only appear in neurotic subjects.

Spain (1966) in a study compared a group of schizophrenic patients with normal subjects on an eyelid-conditioning task.

Experiments on classical conditioning of schizophrenic patients did not lead to clear conclusions regarding these patients' ability to acquire conditioned responses. While most experiments in the West could find no difference between patients and normal subjects (Franks - 1954; Howe - 1958; King and Landis, 1943; O'Connor and Rawnsley - 1959; Pfaffman and Schlosberg - 1939), Russian studies suggested that most schizophrenics tend to condition poorly (Lynn - 1963; Pavlov - 1941). In contrast, Spence and Taylor (1954) reported acquisition levels higher than normals, and Mednick's (1958) theory of schizophrenia also predicted that at least acute patients should condition more rapidly than normal subjects.
Work by Venables (1960, 1963a, 1963b) and Venables and Tizard (1958) suggested that schizophrenic reactions differ in many important ways according to the modality of the stimulus employed. Many different responses have been used in studies of conditioning in schizophrenia. However, while there may be some evidence that the same parameters may affect conditioning of different responses (Razran - 1957; Spence - 1958; Haggard - 1958; and Ross - 1958), there may not be experimental evidence for a factor of conditioning (Franks - 1958). Therefore, generalization from any one experiment on conditioning in schizophrenia must be limited and it might be possible that schizophrenics will condition poorly if one response is used, and rapidly if another response is chosen. On this background, this study (Spain - 1966) was undertaken.

The subjects were 32 male schizophrenic patients between the ages of 28 and 53 years, with a mean of 40.3 years, all of whom were chronic.

Eyeblinks were recorded by a pair of electrodes placed above and below the left eye. The CS was either a tone of 1,000 cycles per second and 60 decibels in loudness, or an increase in brightness of a milk glass disc, from 7 to 700 millilamberts, subtending a visual angle of about 10 degree. The C.S. was 1,000 milliseconds in duration and
the onset of the U.C.S. occurred 500 milliseconds after the beginning of the CS. The UCS was a puff of air to the zonaea lasting 160 milliseconds.

Skin potential was measured from a pair of electrodes, one on the hypothenar eminence and one on the forearm, by the method described by Venables and Sayer, (1963).

The principal findings were as follows:

a) The number of conditioned responses was shown to be related to level of skin potential in both normal and schizophrenic subjects.

b) The schizophrenic group gave more conditioned responses than the normal group and this was associated with higher skin potentials in the patient group.

c) The level of skin potential was found to be related to withdrawal and the more withdrawn subjects gave more conditioned responses.

d) A differential effect was found between normal and schizophrenic subjects and the modality of the C.S. While normal subjects gave a shorter reaction time to auditory than to visual stimuli, schizophrenics gave a shorter reaction time to visual stimuli. It was concluded that, there
was indication of a difference between schizophrenics and normals in the arousing properties of visual as opposed to auditory stimuli.

Schramm and Kimmel (1970) reported a study in relation to resistance to extinction in G.S.R. conditioning.

Silver and Kimmel (1969) reported that the administration of paired conditioning trials after the subject has made his largest C.R., has the effect of reducing resistance to extinction. The results of this study were in accord with the notion that learned inhibition acquired during the acquisition of classical conditioning - 

(a) by attenuation of the C.R. following its initial rise (Kimmel - 1966); 
(b) by inhibition of delay (Kimmel and Greene - 1964); and 
(c) by diminution of the U.C.R. (Kimmel and Pennypacker - 1962), summates with extinctive inhibition in such a fashion as to produce more rapid extinction. As was observed by Silver and Kimmel, results of this type will provide justification for the assumption that a single type of learned inhibitory process can account for all of the varieties of Pavlovian "internal" inhibition. Beyond its potential theoretical significance, the Silver and Kimmel (1969) study pointed out the practical implications for GSR conditioners interested in generating substantial resistance
to extinction in a response notorious for rapid extinguish-
ability.

Because of its possible theoretical and prac-
tical significance, it was desirable to replicate the 
basic Silver and Kimmel (1969) procedure, and at the same 
time add unpaired control groups for each experimental 
condition.

Four group of 12 subjects each received paired 
tone - shock conditioning trials. The CS was a 40 db., 
1,000 - cps. pure tone delivered via earphone, and the UCS 
was a 4.0 ma. dc. shock delivered via zinc electrodes to 
the volar surface of the left forearm. CS duration was 
5.0 sec., UCS duration was .1 sec., and both stimuli 
terminated together. The inter-trial interval was varied 
unsystematically between 30 - 70 sec., with a mean of 
50 sec. The GSR was picked up from the palm and back of 
the right hand. One group of subjects received two paired 
trials past the peak CR., 1 received 4 paired post-peak 
trials, 1 received 8 post-peak trials, and 1 received 
16 post-peak trials. Four control groups received unpaired 
tones and shocks matched in number to subjects in the paired 
groups. All subjects were then run in extinction until 
two non-responses or 50 trials occurred.

The results showed that the paired groups'
GSRs to the tone increased during acquisition, while these of the unpaired groups did not, i.e., conditioning occurred. In addition, the paired groups required a greater number of extinction trials to reach nonresponding. The number of extinction trials required in the paired groups was inversely related to the number of post-peak paired acquisition trials. The unpaired groups did not display a similar relationship.

It was concluded that post peak paired acquisition trials produce learned inhibition which transfers to extinction and summates with extinceptive inhibition to accelerate the rate of response diminution.

Lanning and Yaremko (1971) reported a study in relation to resistance to extinction in GSR conditioning.

Recent studies of classical GSR conditioning have examined the relationship between training post peak CR amplitude and resistance to extinction. Silver and Kimmel (1969) delivered 1, 2, 4, 8, or 16, conditioning trials following subject's peak CR. Except for the group that received one post peak trial, resistance to extinction varied inversely with the number of additional training trials. Schramm and Kimmel, (1970) replicated these findings omitting the 1-post peak trial group and adding unpaired control groups for
each of the remaining conditioning groups. The behavior of the control groups indicated that simple variation of the number of unpaired C.S. and UCSs was not the source of the relationship observed among the conditioning groups. Kimmel (1970) and his associated mentioned that G.S.R. conditioning involves an initial excitatory phase followed by an inhibitory phase. In this study (Lanning and Yaremko - 1971) however, it was hypothesized that the inverse relationship between post peak conditioning trials and resistance to extinction could be modified if the inhibitory tendencies accumulated during training were dissipated prior to extinction by interpolating a rest interval between the end of acquisition and the beginning of extinction.

Data collected from 26 female and 54 male college students. The C.S. was a 40 - db, 1,000 - Hz tone of 5.0 sec. duration, produced by an audiogenerator, and delivered to subject through ear-phones. The U.C.S. was a .1 sec., 2.0 mA. Shock delivered via 14 mm. zinc electrodes to the volar surface of the right forearm. The GSR was picked up as a dc resistance change from the palm and back of the left hand using electrodes. Four groups of 10 subjects each received paired tone - shock classical G.S.R. conditioning trials, differing in the number of training trials beyond peak G.R. amplitude (2 to 16), and
the presence or absence of a 5 min. pre-extinction rest interval. Four additional groups of ten subjects each received unpaired tones and shocks matched in number to subjects in the experimental groups.

The results indicated that conditioning groups without rest displayed an inverse relationship between the number of post-peak training trials and resistance to extinction, while the introduction of rest reversed this relationship. It was concluded that recent studies of post peak GSR conditioning produced results which are modifiable when appropriate inhibition-reducing operations are employed and that these operations will produce strong resistance to extinction.
Rechtschaffen (1958) in a study attempted to test various hypotheses propounded in relation to neural satiation, reactive inhibition and introversion - extraversion.

Expanding upon earlier theorizing by Pavlov, Eysenck has hypothesized that extraverts would show greater figural after-effects (or neural satiation) and more reactive inhibition (IR) on a motor task than introverts. Several investigators (Kohler and Wallach - 1944; Eysenck - 1955) had noted similarities between neural satiation and $I_R$ and had hypothesized that the neural mechanisms underlying both phenomena might be the same.

These various hypotheses were investigated in this study (Rechtschaffen - 1958) by testing 96 subjects on introversion-extraversion, visual after-effects, and $I_R$. Introversion-extraversion was defined in terms of scores on Guildford's Rhathyunda scale. Visual after-effects were measured with a specially constructed apparatus, and two measures of $I_R$ were obtained from an inverted alphabet - printing task.

The results showed that, the introversion-extraversion scores were not significantly correlated with either
amount of visual after-effect or $I_R$ measures. Amount of visual after-effect was not significantly correlated with the $I_R$ measures. An additional analysis was made comparing the 35 subjects having highest scores on extraversion with the 35 subjects with lowest scores on extraversion. The two groups did not differ significantly on the after-effect and $I_R$ measures. Thus, the results obtained in this experiment failed to support the hypotheses concerning the relatedness of the three variables mentioned above.

Becker (1960) set out a study to examine Eysenck's (1955) hypothesis that cortical inhibition is one of the bases for individual differences in extraversion-introversion.

Eysenck subsumed both satiation effects and reactive inhibition effects under the cortical inhibition concept. Secondly, Franks used the concept of cortical inhibition to refer a posal trait-like difference among individuals which was dependent of the number of stimulation of a given neural structure. Thus Franks' use of cortical inhibition was different from Eysenck's. Thus, it was found that three different hypothetical variables, all going under the heading of cortical inhibition, were assumed to be related to individual differences in extraversion-introversion.
Sixty-two college students of both sexes, (mean age of subjects 20.2 with SD of 2.0), randomly selected, were used as subjects. Measures of extraversion-introversion were derived from the Guilford and Cattell personality inventories. A variety of experimental tests were designed. While it was not always possible experimentally to separate basal and reactive effects, two of the eight experimental tests used clearly measured reactive inhibition effects (pursuit rotor reminiscence and response alternation), three fitted the definition of satiation effect (Kinesthetic after-effect, Archimedes spiral, and Necker cube difference score), while three approximated basal type measures (GSR conditioning, aniseikonic lenses, and CFF).

The findings indicated that the concept of basal cortical inhibition as used by Franks appeared to be a unitary factor, but was not found to be related to extraversion-introversion. No empirical evidence was there to support Eysenck's assumption that satiation and reactive inhibition form a unitary trait. Satiation and reactive inhibition measures were found to have some common variance with the basal inhibition measures, but they did not covary with each other. There was no evidence to support Eysenck's hypothesis that satiation measures covary with extraversion measures. There was very minimal evidence that some reactive inhibition measures covary with extraversion. However, there was equally compelling evidence to the contrary. The remark made by the author
was that, if a relationship between reactive inhibition and extraversion exists, it is probably of such a small magnitude as to be practically and theoretically trivial.

Honigfeld (1962) conducted a study in relation to cortical inhibition, perceptual satiation and introversion-extraversive.

Eysenck (1957) postulated that cortical inhibition is a major determinant of perceptual, personality and learning phenomena. Rechtschaffen (1958) failed to support Eysenck’s hypothesis that a relationship exists between figural after-effects, reactive inhibition and introversion-extraversive. In similar fashion, Becker (1960) reasoned that perceptual "satiation" measures and measures of reactive inhibition should share common factor loadings. He measured 62 male and female college students on several tests of satiation (including spiral after-effect, kinesthetic after-effect, and Necker Cube) and reactive inhibition (pursuit rotar reminiscence, and response alternate test). He reported that no empirical evidence was found to support Eysenck’s assumption that satiation and reactive inhibition form a unitary trait. Becker was also unable to support that introversion-extraversive dimensions of personality was related to either satiation or reactive inhibition.
Verification of these earlier findings was obtained as a part of a larger investigation of "neurological efficiency" - (Honigfeld - 1961). A sample of 105 subjects was composed of 81 female and 24 male college students. Variables importance for this report were the introversion-extraversion measure and the measures of perceptual satiation. Perceptual satiation was assessed by the average length of after-effect of monocular viewing of a rotating Archimedes Spiral and by several indices of apparent movement, recorded under monocular, binocular, and interocular conditions. For the assessment of introversion-extraversion aspect of personality, the R Scale of Builford and Zimmerman (1949) was used.

Results failed to support Eysenck's hypothesis. It has been commented that, Eysenck's (1955) views regarding the generality of cortical inhibition are over simplified, while Becker's (1960) suggestion of several different kinds of inhibitory cortical processes is a more valid representation of the complex nature of the phenomena investigated.

Whitmyre and Kurtzke (1962) conducted an experiment to define the role of the spiral after-effect (SAE) in patients with cerebral lesions.
Freedman and Josey (1949), Standlee (1953), Spirack and Levine (1957) reported that the Archimedes Spiral After-Effect (SAE) cannot be used as an index of memory impairment. Berger et al. related performance on spiral test to such indicators as EEG, Pneumoencephalogram, Skull X-ray, Spinal fluid characteristics etc. Blau and Schaffer (1960) reported results in contrast to Berger's findings.

On this background Whitmyre and Kurtzke (1962) in their study attempted to define the role of the spiral after-effect (SAE) in patients with cerebral lesions, by testing groups with and without clinically evident mentation deficit. In addition, the length of time which the patients viewed the rotating spiral was varied to determine if an optimum exposure time could be found to maximize the differentiation among the groups.

Three groups of 20 subjects each were selected from the Neurology and Psychiatry services of a Veteran Administration Hospital. The psychiatry (P) group consisted of patients with a clear primary diagnosis of schizophrenic reaction, and free from any neurological abnormality. The patients from the Neurology service all carried clearly established primary diagnosis involving pathology of the cerebrum. Those with mentation defects
M group) were tested separately from those without mentation defect (N group). Mentation defect was defined as the presence of impaired memory, orientation, judgment, intelligence or emotional control caused by or associated with brain tissue damage, such impaired functions having been evaluated by ordinary clinical neurological examination.

The usual eight inch 2½ convolution spiral was used at 78 rpm and viewed from a distance of 8 ft. The rotating spiral created a contracting and the expanding or reversing spiral was sought when the SAE after rotation ceased. Each subject was administered four trials at each of five exposure times: 10", 20", 30", 40", and 50". Within the P, M and N groups the order of presentation of exposure times was randomized whenever ⅔ trials at any exposure time produced a reported SAE, the subject was considered able to see the after-effect at that exposure time.

Results showed that, in no group was there a significant difference in the frequency of occurrence of the SAE, as a function of the length of exposure to the rotating stimulus. Patients with mentation changes reported the SAE with much less frequency than did the patients in the other two groups. The $X^2$ test indicated that the three groups differ significantly at every exposure
time \((p < .001)\). Two by two \(x^2\) tests revealed that at all exposure times \(P\) and \(M\) groups differ \((p < .001)\) with more \(P\) patients reporting the phenomenon. Similarly, at all exposure times more \(N\) than \(M\) patients report the SAE \((p < .02)\). \(P\) and \(N\) groups however fail to differ at any exposure time. From the above mentioned findings, it has been suggested that, patients with acquired deficits in the psychological functions of memory, orientation, judgement, intelligence and emotional control report the SAE with less frequency than either schizophrenic patients or patients with cerebral damage but without such changes in functioning.

To explain the nature and duration of figural after-effects in schizophrenic subjects, a number of questions have been raised as to whether nature and duration of treatment patients receive, experimenter's bias, etc. can influence their after-effect or it can be attributed to the incapability of schizophrenic patients to concentrate on a particular object for a certain considerable period of time. This can be answered if in a study those above mentioned variables are controlled and at the same time, duration of figural after-effect obtained in schizophrenic patients is compared with that of non-schizophrenic patients.
With this idea in mind, Kelm Harold (1968) conducted an experiment to investigate visual figural after-effect in schizophrenic and non-psychophrenic patients.

Out of 32 patients finally, 13 schizophrenics and 8 non-schizophrenics (rest others were not able to maintain constant fixation on the figures, hence their figural after-effect (FAE) was not measured) were taken as subjects. All patients did not receive any medication for at least 48 hours prior to the experiment. The mean age of the schizophrenic and non-schizophrenic groups were 33.0 and 30.4, respectively. All subjects were male, except four schizophrenic patients.

The apparatus was the same as one used in an earlier study (Prysiasmivk and Klem - 1965). The spatial relationship of the I figure, T figure, and fixation points, chosen to give optimal results, was the same as used in previous studies (Klem - 1962; Prysiasmivk and Klem - 1963, 1965). The procedure employed in this study was similar to that used earlier (Klem-1962; Prysiasmivk and Klem - 1963, 1965).

Results showed that, when tested on admission to hospital and without any medication, schizophrenic
patients have a smaller FAE than non-schizophrenic patients, and that both groups show a similar pattern of change in phenomenal displacement as a function of test time. It has been mentioned that, clinical treatment, medication, experimenter's bias etc. do not affect the direction of phenomenal displacement in schizophrenic patients. It was suggested that smaller FAE of schizophrenics may be partially due to poorer fixation of these patients on the test object.

Thimmappa (1969) made an attempt to investigate the level of arousal, conditioning and verbal learning and the relationship among them in a group of chronic schizophrenics as compared with a group of normal and neurotic subjects.

Level of arousal has been considered as a dimension in the intensity of behavior ranging from low activity found in sleep and relaxed states to the higher activities of waking and excited states and also as having driving (motivating) properties influencing the behavior and performance. Chronic schizophrenics are found to be in heightened arousal as measured on various physiological variables. The work of Venables (1967) and Claridge (1967) on psychotics, especially chronic schizophrenics, has
shown the importance, relationship and disturbances that exist between subcortical and cortical arousal.

On the basis of this background, Thimmappa (1969) in his study, along with a subcortical (GSR) measure of arousal also selected a cortical indices of arousal, obtained by the duration of the Archimedes Spiral After-effect which Claridge (1967) used as an indicator of cortical arousal.

A group of 30 chronic schizophrenics, 15 anxiety neurotics and 50 normal subjects of similar age (age ranging from 20 - 50 years) and educational level were taken as subjects. Along with other indices necessary for this study, the Archimedes Spiral was used. Four trials were given, the spiral being rotated for 30 seconds each time; trials were alternately clockwise and counterclockwise, with the rest of one minute between trials. The mean of the four scores thus obtained were taken as a measure of the subject's performance in this task.

The findings revealed that the mean duration of the after-effect in the schizophrenic group was 22.12 seconds (SD - 8.39), normals - 16.33 seconds (SD - 3.17) and in neurotics - 19.48 (SD - 4.57). Schizophrenics experienced the longest duration of after-effect than the
other groups. Schizophrenic group as a whole appeared to be more variable in their experience of after-effect than normals who are least variable and neurotic who are more variable. Differences in the groups were statistically significant \( (F = 9.23; \ p < 0.001) \). Schizophrenics and normals differed significantly on Spiral After-effect \( (t = 4.97; \ p < 0.01) \), where schizophrenics' duration of after-effect was longer than normals. Normals and anxiety neurotics also differed significantly in their duration of after-effect \( (t = 2.61, \ p < 0.03) \), where anxiety neurotics had longer duration of after-effect than normals. But schizophrenics and neurotics did not differ at statistically significant level as in case of G.S.R. However, it has been concluded that, Claridge, Harington Claridge - 1965, did find a significant difference between psychotic and neurotic groups as with normals in duration of spiral after-effect. His psychotic group largely consisted of acute schizophrenics. As acuteness - chronicity is the important variable differentiating on arousal (Venables - 1966), acute patients being less aroused than chronic, as Thimmappa's study dealt with chronic patients, the results might have failed to support the findings of Claridge. His findings of significant difference between psychotics and normals found to be in agreement with the findings of this study.
Chattopadhyay and Murthy (1971) conducted an experiment to see the nature of perceptual satiation and its effect on the cortical conductivity of anxiety patients.

Theoretical considerations led to the formulation of the hypothesis that the individual differences in satiation effect are correlated.

Fifteen males, literate, students service holders, aged ranging from 18 - 43 years, diagnosed as cases of anxiety by the psychiatrist at the out-patient department of Government Mental Hospital, Bangalore, were taken as subjects to constitute the experimental group of the present study.

A group of fifteen literature male nurses, (employed at the Government Mental Hospital, Bangalore), age ranging from 20 - 41 years, free from any psychiatric complaints or physical illness were selected to constitute the control group of this study.

As Archimedes Spiral, devised by the All India Institute of Mental Health (Psychology Department) with 20.5 cm. in diameter served as the stimulus disc. The rotation speed was 120 r.p.m. and fixation time was 30 sec. The rotation of the spiral was always in clockwise direction,
the interval between successive trials varying with the
duration of the reported after-effect by the subject. Ten
trials were given. Immediately after this, to assess the
change in basal cortical conductivity, a measure of G.S.R.
was taken, using the Keeler's polygraph.

Statistical treatment of the data revealed no
significant difference in the nature of satiation in between anxiety and normal groups. Individual differences in
satiation also did not show any definite order of change in
the basal cortical conductivity of the anxiety group as well as the normals, when comparison was made between the two
groups and between individuals within a given group.
However, population studied in this experiment was very
miniature in form and hence, further studies in this area has been recommended.

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Osgood and Suci (1955) in their article "Factor analysis of meaning," reported two factor analytic studies of meaningful judgement.

Although there were objective methods for studying many aspects of language behavior, any standard ways of measuring meaning which meet the usual criteria of measurement was lacking. This led the present authors to undertake a series of studies describing research on the development of an objective method of measuring meaning, and this article is one of those series of works.

Both the studies were based upon the sample of 50 bipolar descriptive scales. The first analysis applied Thurstone's centroid method to correlations derived from 7-step graphic scale data obtained by having 100 subjects judged 20 specific concepts against the 50 scales. The second analysis applied a new method developed by the second author to a matrix of percentages of agreement obtained by having 40 different subjects make forced-choice pairing of the polar terms themselves, i.e., without any specific concepts being judged. The evidence as a whole pointed to the existence in meaningful judgements of three major connotative factors: evaluation, potency, and activity. The evaluative factor accounted for by far the
largest portion of the extracted variance. These three factors were taken as independent dimensions of the semantic space within which, it has been suggested, the meanings of concepts may be specified.

Donald, Smith and Raygor (1956) designed experiments to determine verbal and personality correlates of satiation.

Satiation was described as the reduction in effectiveness of a stimulus with continued exposure. Walker (as mentioned by Donald et al. - 1956) has suggested a neurological basis for the satiation process involving a progressive reduction in response probability resulting from continued or repeated firing of a "reaction system," with continued exposure to the stimulus. According to Hebb (1949), it would result from continued elicitation of the relevant "phase sequence."

The personality correlates of satiation was not specified and hence, Donald et al. (1956) designed studies to determine verbal and personality correlates of satiation. Specifically, two questions were posed:

(a) is associative activity in thinking a function of satiation? and, (b) does the process of satiation operate differentially in accord with personality structure?
In study I, a word-association technique was used to determine the effect of visual satiation on thinking. The hypothesis tested was: prolonged visual exposure of a stimulus word results in a word-association response by subject which is less common than that elicited under brief exposure.

Twenty-four college students in two groups of 13 and 11, were seated before a projection screen on which words were exposed. Stimulus words were selected from the Kent-Rosanoff Word Association test. Each group was subjected to two experimental conditions, satiation and control. The satiation condition consisted of three exposure periods of 7 seconds at 3-second intervals. The subjects were instructed to fixate the word during the exposure interval and to write it as they pronounced it subvocally during each 3-second rest interval. A final 3-second delay was followed by an exposure of the same stimulus word for 40 ms. The control condition consisted of a 40 ms. exposure of each word with directions to respond in writing with the first word aroused other than the one shown. The directions for responding were identical for both conditions.

In the second experiment, to determine whether
the satiation process operates differentially in accord with personality structure, the previous procedure was repeated with a group of 36 post graduate students who had respond to a personality inventory.

The students were divided into two groups A and B. The list of 10 words were drawn from the Kent-Rossanoff list. Group A was exposed to list X under the satiation condition (prolonged exposure) and to list Y under brief exposure. Group B was exposed to list Y under the satiation condition and to list X under brief exposure.

The satiation procedure consisted of 20-second exposure period during which the subject fixated the stimulus word and repeated it subvocally, one second pause, and a ½-second exposure after which subject wrote his response. Control procedure consisted of a ½-second exposure after which subject responded to writing.

Findings confirmed the following hypotheses: Prolonged visual exposure of a stimulus word results in a word-association response less common than elicit under brief exposure.

Individuals categorized as "permeable" (sensitive, flexible, imaginative, extravert) and "impermeable" (less
sensitive to stimuli, rigid, withdrawn, introvert) differ with respect to satiation effects.

Grigg (1959) in a study tested whether the semantic differential scores of a group of normal subjects reflect greater distance between "ideal self" and "neurotic" than between "self" and "neurotic," and whether semantic differential scores obtained when judging an actual case would shift in a predicted direction as a result of experimental manipulation of the base of judgement.

Osgood's (1957) semantic differential technique is a relatively brief and computationally simple method for the assessment of the meaning that a client assigns to the "self" of "ideal self," and provides for measurement of discrepancy between these concepts. Hence, this technique was used by Grigg (1959) in a validity study of the semantic differential technique.

Using this technique, a group of normal subjects indicated greater distance between "ideal self" and "neurotic" than between "self" and "neurotic," a result which was in favour regarding the validity of the semantic differential. Later, the group was divided into an experimental and a control group and both groups read the
same favourable selection about Miss X. and then rated her
on the semantic differential. Then the experimental group
read a statement which stressed that Miss X. was not as
well adjusted as appeared on the surface, and the label
"neurotic" was emphasized in the statement. The control
group received no additional data on Miss X. Both groups
were asked again to indicate their impressions of Miss X. by
on the semantic differential. (Scale used was having
'evaluative' factor, like, good - bad, etc., 'potency'
factor like, Strong - weak, etc., and 'activity' factor
like, fast - slow, etc.). Although the experimental group
shifted in the expected direction (prediction was made before
starting the experiment that the experimental subjects'
second rating of Miss X. would be closer to their meaning
for neurotic than their first rating of Miss X.), an ana-
lysis of co-variance indicated that differences between the
changes in the two groups were not statistically significant.

Mitsos (1961) reported a study in which attempt was made to
find out the applicability of a personal construct approach
within the conventional frame work of the semantic differen-
tial.

In accord with Kelly's (1955) emphasis on the
importance of personal meaningfulness to the subject in
psychological measurement, Mitsos (1961) made an attempt to find out the possibility of employing personal constructs within the semantic differential technique.

Subjects for this experiment included 16 students of undergraduate class. Each subject was given a list of seven bipolar adjective scales (Osgood et al. - 1957) with demonstrated high factor loading on the semantic differential "evaluative" factor. The subjects were asked to think about those seven dimensions and select the three that they considered most personally meaningful in thinking about people. Each subject was then presented with seven additional scales loaded heavily on the "potency" factor. Subjects were again asked to select the three most personally meaningful. The same procedure was followed with seven scales with loadings on the "activity" factor. The ratings were completed in the conventional manner as described by Osgood.

A direct relationship was predicted between the personal meaningfulness of scales and the degree to which the concepts rated by the scale are saturated with meaning. The prediction was supported. It was also mentioned that, increased saturation did not appear to occur at the expense of "distortion" in the semantic field.
Brod et al. (1964) conducted an experiment in relation to anxiety and semantic differential responses.

An investigation by Kervick (1956) on the relationship between intelligence, anxiety as measured by the Taylor (1953) Manifest Anxiety (MA) Scale, and discrimination among concepts of the semantic differentials (Osgood, Suci and Tannenbaum - 1957) reported the following relationships: a positive relationship between I.Q. and discrimination, a zero relationship between anxiety and discrimination, and an interaction between I.Q., anxiety, and discrimination. In view of more recent results (Ware, as reported by Osgood - 1962) which suggests that there is no relationship between intelligence and responses on the semantic differential and in view of several inadequacies in the Kerrick study, it appeared that the problem required further investigation and hence, Bord et al. (1964) conducted this study to test the following hypothesis:

Following the conclusions of Ware, but in contradiction to those of Kerrick there would be no correlation between intelligence and either discrimination on response bias on the semantic differential.

Following the results of Spence and Beeveroft
(as reported by Brod et al. - 1964), it was hypothesized that there will be a positive correlation between manifest anxiety and discrimination in semantic differential responses.

It was also predicted that a positive correlation will be found between response - bias tendencies on a standard personality inventory and response biases on the semantic differential. Specifically it was assumed that a high Lie (L) score on the MMPI would indicate a tendency toward response biases. There would be, therefore, a negative correlation between L scores and differentiation on the semantic differential.

Fifty volunteer female undergraduates were administered a form of semantic differential. They were to rate 50 words on each of nine scales, three scales representing each of the three dimensions of meaning (evaluation, activity and potency) reported by Osgood et al. (1957). For each subject the following scores were obtained:

(a) a response bias on the differential defined as the use of "very" and "neutral" categories,

(b) discrimination on the differential defined as the tendency to use all categories equally often,
(c) Scholastic aptitude test scores, and 
(d) Manifest Anxiety and Lie scores.

The hypothesis that there would be a positive correlation between anxiety and discrimination and 0 correlation between aptitude and discrimination were supported by the findings. In addition, a positive correlation between Lie score and response bias was found. It was argued that the nature of a high Lie score would tend to produce this type of correlation.

Das (1964) in his study "Hypnosis, verbal satiation, vigilance and personality factors," made an attempt to find out correlation, if any, exists in between or amongst these factors mentioned above.

It was supposed that in hypnosis some kind of inhibitory processes are at work. Since hypnosis is ordinarily induced through verbal suggestions, inhibition produced in the verbal system may stand a good chance of being related to hypnotizability. Verbal satiation, therefore, may be relevant in this context to hypnotism (Das - 1964). Verbal satiation has been linked to a cognitive reactive inhibition ($I_R$) (Lambert and Jakobovits - 1960). They further suggested that satiation is a cortical phenomenon
and Lambert and his associates have repeatedly demonstrated the existence of semantic satiation.

Das (1964) in his study used 62 male postgraduate students, their ages were between 19 and 25 years.

The words (Child, We, Rich, Family, Truth) selected for satiation purpose had been previously used by Lambert and Jakobovits (1960). Verbal satiation was produced by a continuous 40-second repetition of the stimulus word at the rate of 2-4 repetitions per second. The subject was required to rate each word on nine 7-point semantic differential scales taken from Osgood, Suci and Tannenbaum (1957). Three scales for each of the three semantic factors of Evaluation, Potency and Activity were provided for rating. The scales were presented in a fixed random order to all subjects before and after satiation.

Results showed that positive correlations were obtained between hypnosis and low verbal satiation.

Weksel and Hennes (1965) reported the results of two studies which were designed to test the validity of semantic differential as an attitude measuring instrument.

According to Osgood et al. (1957), the semantic
differential yields information about the direction of an attitude (on a favourable-unfavourable continuum). This score has been referred to as the polarization score of attitude polarity. Then the degree of favourableness or extremeness or polarity would be equated with attitude intensity. (Attitude intensity was defined as the strength of feeling with which an attitude is held).

The authors of this study made an attempt to find out the direction of relationship between polarity and intensity scores.

In the first study 73 college students were administered a series of semantic differential scales using certain stereotypes and abstract social categories as concepts. In addition to the usual instructions each subject was asked to place a number from 1 to 7 in a space provided along side each scale to "demonstrate how strongly you hold this particular view." This score represented the intensity score for each item.

In the second study semantic differential scales were administered to samples of 69 sixth-grade and 58 tenth-grade students, and 566 college freshmen and sophomores. In addition to the usual instructions for the semantic differential, each subject was asked to indicate "how sure
are you about the rating you just made." This score represented cognitive certainty or intensity.

Results showed that in the first study the mean correlation for college students between polarity and intensity was .31. In the second study the mean correlation for college freshmen was .43, for tenth-grade students it was .47 and for sixth-grade students it was .62.

The findings supported that, the argument is not that polarity scores are unrelated to intensity scores, but that there might be logical reasons as well as empirical support for not accepting a model which equates attitude intensity and polarity. It was mentioned that among younger respondents the magnitude of the correlation tends to increase. The magnitude correlation for the sixth-grade subjects did not nullify the logical argument which rendered unacceptable the assumptions underlying the measurement model, although the decrease in correlation with age might have revealed something about attitude formation among young subjects.

Gibbins (1968) study was designed to investigate the nature of response styles operates in the semantic differential (SD).

It has been suggested that two response styles
operate in SD and that at least three response sets are involved in their operation. The first of the response styles was considered to be a tendency to use neutral response category, when making judgements, with a consistent frequency, i.e., a person tends to use the neutral category either frequently or rarely. The second response style was thought to be a tendency to make judgements consistently often in one evaluative direction, i.e. to judge things regularly as either relatively good or relatively bad.

A response set, it was suggested may be directly responsible for this "evaluative response style," and may be referred to as the 'evaluative response set.' It was thought that the consistent use of the neutral category may be the result of the interacting effects of two separate response sets: 'generalization' and 'extreme response set.'

Gibbins's study was designed to test the following hypotheses:

That in the use of SD it will be found that - (1) people will tend to use the neutral category in a consistent manner, using it with a consistent frequency independent of the scales or concepts being used; (2) people will tend to evaluate fairly neutral concepts in a consistent direction, either as good or bad.
The hypotheses were tested on a population of women students at a college of education. The scales used were narrower than usual, consisting only of two terms plus an intermediate neutral category. Twenty-eight concepts were judged.

Results showed that, there were a tendency to use the neutral category in a consistent manner and a tendency to evaluate concepts in the same direction. It was suggested that the tendency to use the neutral response is related to the extreme response of Rundquist (1966). The hypothesis that it is also a function of a set of 'generalization' could not be established. This evidence was in favour of the hypothesis that the evaluative response style may be partly determined by a general optimistic outlook.

Chattopadhyay and Murthy (1971) in a study made an attempt to assess the nature of satiation, using semantic differentials, in case of anxiety patients.

From the review of literature it was assumed that the individual differences in satiation effects would be correlated.

Fifteen males, literature, students/service holders, age ranging from 18 - 43, diagnosed by psychiatrist
as cases of anxiety were taken from the out-patient department of Government Mental Hospital, Bangalore to constitute the experimental group of this study.

A group of fifteen literate male nurses, employed at the Governmental Hospital, Bangalore, age ranging from 20 - 42, free from any psychiatric or physical illness were selected to form the control group of this study.

The words used for verbal satiation were - Child, Me, Rich, Family and Truth. The procedure adapted for this was essentially the same as used by Das (1964). Detailed description has been given elsewhere in this thesis and hence, need not be repeated.

A measure of cortical conductivity following satiation was also taken through GSR readings using Keeler's polygraph.

The statistical treatment of the data did not reveal any significant difference in satiation aspect, in between normals and anxiety patients. Attempt was also made to find out the correlation, if any, in between verbal satiation and perceptual satiation. No significant correlation was found. This negative correlation was also supported by previous findings. The cortical conductivity
after verbal satiation also did not show any significant change when comparison was made between two groups and between individuals in one group. However, population studied in this experiment was very miniature in form, hence, further study in this area has been recommended.
4. STUDIES WITH REFERENCE TO HABITUATION:

Harper et al. (1965) reported the results of forearm blood flow in normal subjects and patients with phobic anxiety states.

In 1938, Grant and Pearson, who developed forearm plethysmography to determine blood flow mainly in the skeletal muscle rather than the skin, noted transient increases in forearm flow with mental arithmetic. This response was studied in a more detail by Abramson and Fennis (1940). Their conclusion that mental arithmetic produced an increase in forearm flow due to vasodilation in the forearm muscles was confirmed by the work of Brod, Fencel, Hejl and Jirka (1959) who attributed the change to emotional stress.

The mechanism underlying this effect has been investigated by Barcroft, Brod, Hejl, Hirjarvi and Kitchin (1960) who reviewed the evidence of other workers and concluded that both a humoral mechanism and a cholinergic nervous mechanism involving sympathetic vasodilator fibers to skeletal muscle were operative. They pointed out the similarity of this circulatory response to the stress reaction observed when the cat hypothalamus was stimulated.
During a faint, whether induced by haemorrhage or by strong emotion, the forearm blood flow had been shown to increase inspite of the dramatic fall in systematic arterial pressure which occurs (Barcroft, Edholm, McMichael, Sharpey-Schafer - 1944; Brigden, Howarth, Sharpey-Schafer - 1950; Greenfield - 1951). This effect is also due to an active vasodilatation of muscle blood vessels and physiological studies have confirmed Lewis's (1932) conclusion that the fall in blood pressure during a faint was due to peripheral vasodilatation rather than to cardiac inhibition. Emotion is one of the commonest precipitants of fainting although the mechanism remains incompletely understood.

Thus, the physiological enquiries reviewed above suggested that it would be profitable to study forearm blood flow in neurotic subjects prone to attacks of severe anxiety.

Twenty females, ten normals and ten patients suffering from phobic anxiety states were drawn as subjects. The patients were all undergoing active treatment which was not interrupted for the study, but they were all still subject to anxiety symptoms and the investigations were performed during the early phase of treatment before any
radical amelioration had occurred. In addition to night sedatives three subjects were receiving amylobarbitone by day, and three were receiving chlordiazepoxide combined with an amine-oxidase inhibitor. One patient was receiving "Pars-telin" tablets. Three were receiving injections of intravenous thiopentone. The mean age of the patient group was 40.4 years and of the normal group 26.4 years. All the patients were found to have a neuroticism score on the Maudsley Personality Inventory, which was significantly higher than the normal group. All the measures of blood flow were carried out on the right arm, with the subject in sitting position, using a mercury-in-rubber resistance strain gauge plethysmograph as described by Whitney (1953), except that the gauge was not compensated for thermal changes.

Results showed that mental arithmetic stress was associated with a significant elevation of forearm blood flow in both groups. There were no statistically significant differences between the normal and neurotic groups in respect of resting flow, peak flow during stress, and after stress scores. Results also suggested that an elevation of forearm blood flow may be found to be associated with the subjective experience of acute anxiety, but not with depression. Finally, the usefulness of this method was recommended.
Koopke and Pribram (1966) undertook an experiment to study the course of habituation and to determine the relevance of certain variables during habituation.

Sokolov (1960) conceptualised a stimulus in two parts - onset and prolongation. He hypothesised that the prolongation of a stimulus will produce unconditioned inhibition, which will become conditioned to the onset of the stimulus, thereby producing response decrement and habituation. The habituation had been explained as conditioning in which stimulus onset will act as a CS and stimulus prolongation as a US for inhibition. "During habituation, conditioned inhibition accrues to stimulus onset, thus causing the response decrement characteristic of habituation." This formulation suggested stimulus prolongation or duration as a relevant variable in habituation. It was expected that greater prolongation would facilitate the development of conditioned inhibition, thereby producing faster habituation. In order to investigate this hypothesis, habituation of the GSR as a function of stimulus duration was studied.

Sokolov reported that, once habituated, subjects will orient to changes in the temporal characteristics of the stimulus experienced during habituation. In an
attempt to replicate this finding the durations of the stimuli were varied subsequent to habituation.

A number of investigators have shown that, within a given response mode, "spontaneous activity" is likely to be strongly related to reactivity of stimulation (Johnson - 1963; Lacey and Lacey - 1958). In this study, the relation between spontaneous activity and habituation was investigated.

Habituation of GSR to repeated stimulation with tones of either 2- or 20 sec duration was investigated with 40 college students. Subsequent to habituation, stimulus durations were reversed immediately for half the subjects and after a number of additional trials for the remaining subjects. Speed of habituation did not vary with stimulus duration but was significantly related to "spontaneous activity." Orienting to the reversal in stimulus duration was indicated by an overall increase in latency and an increase in response duration for subjects changed from a 2- to a 20 sec. stimulus.

Gaviria (1967) in an experiment studied habituation to and magnitude of electrodermal, plethysmographic, and heart rate changes in response to 4 auditory stimuli.
This study was prompted by the observation of Holzman et al. (1966) that when people listen to their own voices they show a stronger electrodermal, electromyographic, and plethysmographic responses than when they hear the voices of other persons.

Twenty members along with their wives participated as paid volunteers. Their ages ranged from 20 to 53 years. Four auditory stimuli - noise, the subject's own voice, the subject's spouse's voice, and unknown person's voice were used. The stimuli were recorded on tape loop cartridges. The rates of electrodermal response habituation as well as the magnitude of electrodermal (skin potential and skin resistance), plethysmographic and heart rate responses were recorded.

The results showed slower habituation of electrodermal responses and greater plethysmographic responses to noise than to any one of the voices. Plethysmographic responses were also greater and more frequent to the known voices than to the unfamiliar ones. No pattern of responses were found in the magnitude of electrodermal or heart rate initial responses. However, no analysis of a possible amplitude decrement pattern during the habituation series was carried out.
Kimmel and Goldstein (1967) conducted an experiment so as to determine whether any difference in retention to habituation might occur when stimuli of different sense modalities were used.

In spite of the accepted fact (Rosvold - 1959) that removal of the eliciting stimulus results in recovery of the habituated response, it seemed reasonable to ask whether some retention of habituation might be revealed in number of trials needed to reach a criterion of habituation when subjects were rested sometimes after initial habituation. Since habituation may be due to a process analogous to Hull's reactive inhibition ($I_R$), an analogy supported by the fact that it accrues to an extent is inversely related to the temporal interval between stimulations, it might be expected that conditioned inhibition ($S_{IR}$) would develop as a consequence of the dissipation of $I_R$ during non-responding. Accordingly, it was hypothesized that subjects would require fewer trials to achieve the same criterion of habituation of the GSR when tested 1 and 2 weeks after an initial session. It was also assumed stimuli of different sense modalities may show some difference in retention of habituation.

Twenty-six subjects (student volunteers) were assigned randomly to two groups, to receive either auditory or visual stimulation (14 auditory, 11 visual).
Subjects came to the laboratory on 3 successive weekly sessions and received repeated presentations of a white light or a 1,000 - cps tone until a criterion of habituation of the GSR was reached. Stimuli were presented at varying temporal intervals between 30 and 90 sec. to overcome any tendencies toward temporal conditioning. No stimulus was intentionally presented during spontaneous GSR activity.

There was a significant reduction in the number of trials to criterion from session to session for both stimuli, while neither sense modality nor the Modality X Sessions interaction effects were significant. On the first session, habituation was characterised by a drop in response magnitude, followed by some increase, and, finally, an additional drop. The average magnitude of response on the first trial of each session did not reduce significantly from session to session, but the average magnitude of response on the second trial of each session did. The results were interpreted to mean that some retention of habituation from session to session occurred (i.e., there may be something "learned" in habituation) and it was conjectured that conditioned inhibition associated with response-produced stimuli might have been responsible for some of the retention effect.
Gelder and Mathews (1968) in a preliminary study attempted to relate forearm blood flow to a subjective assessment of anxiety during the imagination of phobic scenes.

Forearm blood flow was thought to be a potential value in the assessment and treatment of phobic states, especially in systematic desensitization therapy. Previous attempts to use physiological measures (e.g. skin conductance measures -- Hoenig and Reed - 1966; Seager and Brown - 1967) have not been systematic enough to provide any reliable evidence concerning the posited mechanisms of desensitization. It was thought that psychophysiological measure sensitive enough to record changes related to small increment of anxiety would be of practical usefulness. On this background, this study was taken into consideration.

A total of 19 phobic out-patients were examined. The mean age of all subjects (17 women, 2 men) was 30 years (range 19 - 48). A waterbath plethysmograph, similar to that described by Barcroft and Swan (1953) was used and the method resembled that described by Kelly (1966) with the exception that volume changes in the plethysmograph were registered via a transducer on a Grass 5 polygraph.

Four tasks (Mental arithmetic, Neutral image, Low stress, High stress) were performed by each subject
with rest periods between each one. Following each task or rest period the patient was briefly questioned about his emotional state and asked to rate any anxiety experienced on a scale from 0 (no anxiety) to 5 (panic).

Results showed that blood flow readings associated with mental arithmetic were significantly higher than for any other condition, while blood flow during the high stress phobic scene was significantly higher than that during all conditions except mental arithmetic. Mean blood flow during the low stress phobic scene was significantly higher than that in four of the five rest periods, while blood flow during the neutral scene was not significantly higher than any other condition. The association between forearm blood flow and subjective anxiety rating was estimated. High correlations between blood flow and subjective anxiety were found. It was suggested that this method may be used to assess response to brief imagined stressful situations similar to those used in desensitisation treatment. Further work using simultaneous recording of several physiological measures of arousal was suggested.

Kelly and Walter (1968) in their study reported the relationship between clinical diagnosis and anxiety, assessed by forearm blood flow and other measurements.
Anxiety may be present to a greater or lesser degree in almost every psychiatric syndrome. The ability to quantify of the degree of anxiety present in an individual patient has important implications for diagnosis, treatment and prognosis. "Basal" forearm blood flow has been found to be a valid and reliable index of anxiety and had been used in this study to measure the amount of anxiety in different diagnostic groups.

Two hundred and three patients and sixty normal controls were examined. Measurements of forearm blood flow, heart rate, blood pressure and anxiety self ratings (The Taylor Manifest Anxiety Scale, Neuroticism and Extraversion were also measured) were made under basal (resting) condition for 15 minutes, and during experimentally - induced anxiety produced by 2½ minutes of harassing mental arithmetic. The method employed in this study was adopted previously in a study by Kelly (1967).

Highly significant differences were found between 41 patients with chronic anxiety states and 60 normal controls. The mean "basal" forearm blood flow of the anxious patients was more than twice as great as that of the controls.

Basal forearm blood flow placed nine diagnostic
categories and normal controls in the following rank order of decreasing anxiety: Chronic anxiety state (4.45), agitated depression (3.54), chronic schizophrenia (3.31), obsessional neurosis (2.65), phobic state (2.26), normal control (2.21), hysteria (2.20), non-agitated depression (2.13), personality disorder (1.90) and depersonalization (1.84). The rank order was consistent with other physiological work and with clinical experience. The difference between the group means of the different diagnostic categories was significant in over 50%. This was the highest degree of differentiation of all the parameters used.

There was a highly significant positive correlation between "basal" forearm blood flow and other measures of anxiety, i.e., The Taylor Scale of Manifest Anxiety, "basal" anxiety self rating and "basal" heart rate. This suggested further evidence of the validity of forearm blood flow as a good objective index of anxiety.

The Taylor Scale, "basal" heart rate and anxiety self-rating differentiated well between patients and controls, but showed fewer significant differences between the patient groups than "basal" forearm blood flow.

Chronic anxiety states had been characterised by high levels of "free floating" anxiety and had high
"basal" forearm blood flows, heart rate and anxiety self-rating. Patients who suffered from phobic states did not have high levels of free floating anxiety and their "basal" values were within normal limits.

Patients with chronic schizophrenia had high basal forearm blood flow, heart rates and anxiety self-rating, but showed a poor response to the stressful stimulus.

Patients with non-agitated depression had a mean "basal" forearm value which was very similar to that of normal controls. This parameter may not be a measure of depression, as the remark was given by Kelly and Walter. If anxiety was conspicuous in a clinical setting of depression leading to agitation, a high "basal" forearm blood flow and anxiety self-rating was found.

The patients with primary depersonalisation had the lowest mean "basal" forearm blood flow and almost the highest anxiety self ratings.

There was a trend which did not reach a significant level for patients with obsessional neurosis to have a higher mean "basal" forearm blood flow than other psychoneurotic patients, excluding chronic anxiety group of patients.

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Patients with hysteria had a low mean forearm blood flow and anxiety self rating during both resting and stress measurements, which supported the view that hysteria is often associated with low level of anxiety.

The diagnostic and prognostic implications of forearm blood flow was recommended.

Ritter et al. (1968) conducted an experiment to study short term habituation in human subjects by a method which provided a stimulus by stimulus analysis of averaged evoked responses.

Several human studies employing average evoked responses (AERs) have reported habituation to auditory and photic stimuli (Bogacz et al. - 1960; Garcia - Austt et al. - 1961, 1964; Garcia - Austt - 1963; Walter - 1964; Perry and Copenhaver - 1965). With the exception of Walter (1964), who claimed that responses recorded from the frontal region suddenly diminished sometime during the presentation of the first 20 - 100 stimuli, decrements in the amplitude of AERs had been found to be gradual, occurring over many hundreds of stimuli. But the inference that these decrements reflect loss of attention seemed questionable since behavioral and physiological indices of arousal and attention had been shown to decrease rapidly during the first
few repetitions of a neutral stimulus (Sharpless and Jasper - 1956; Sokolov - 1963; Thompson and Shaw - 1965).

Studies of habituation using the AER technique have averaged responses to 20 or more stimuli, thus changes in evoked responses occurring within the first block will be obscured by the averaging procedure. If short term decrements in AERs can be demonstrated, and reversed by appropriate disinhibition procedures, it was assumed in this study that, such changes might reflect neurophysiological processes associated with the rapid development in attentiveness and orienting behavior which occurs during habituation.

Nine normal adults, the three authors of this paper and six "naive" volunteers, served as subjects. Trapezoidal tone bursts, 30 msec. in duration (rise and decay time 5 msec.) and approximately 60 db above the subjects' absolute threshold, were delivered binaurally through earphones. The usual frequency employed was 1000 c/sec. In the experiments involving change in pitch a 2000 c/sec. tone was also used. Evoked responses were picked up from chloride silver disc electrodes used (placed at F2, C2, O2, and T2, each referred to the linked ears).

Tones delivered every 2 sec. resulted in a rapid drop, during the first few stimuli, in the amplitude of
the positive component of vertex responses which peaks between 150 and 200 msec., but no similar change was found for tones delivered every 10 sec. The rapid drop for the faster rate of stimulation was considered to have only the appearance of habituation, and was viewed as reflecting refractoriness within the auditory system. On the other hand, when the first stimulus was presented in an unpredictable manner it elicited a large positive component with a peak latency of about 300 msec. Similar responses were obtained when an unpredictable pitch change was presented in an effort to elicit dishabituation. Predictable pitch changes did not produce these results. The 300 msec. component was seen as reflecting a shift of attention associated with the orienting response.

Bishop and Kimmel (1969) reported a study to ascertain the retention function of habituation.

Habituation has been differentiated typically from "changes in the physiological state of receptor (sensory adaptation) and effector (fatigue) organs (Kimmel and Goldstein - 1967) and from learning, which refers to changes that occur with reinforced practice and are relatively permanent" (Kimble - 1961). Habituation being a "temporary" state (Rosvold - 1959), has been usually excluded from
the category of learning. Recent research has led some investigators to question this position and to suggest that habituation may profitably be viewed as a variety of learning (Kimmel and Goldstein - 1967).

Assuming habituation to be a variety of learning, it seemed reasonable to investigate the extent to which habituation would be retained over time without practice. This study employed a variety of time intervals to ascertain the retention function of habituation. Since classical conditioning is a widely accepted, simple kind of learning, it was thought appropriate to compare the retention of habituation with the retention of simple classically, conditioned responses.

One hundred and ninety-four female students were assigned randomly to either a conditioning group (N = 97) or an habituation group (N = 97) and were tested at one of six time intervals (immediately, 20 minutes, 1 day, 1 week, 4 weeks, or 6 months) following an initial "learning" session. All groups contained 16 subjects with the exception of two 6 months groups, both of which had 17 subjects. The subjects were assigned to treatment conditions randomly.

For habituation subjects, the initial and test sessions consisted of habituation to a criterion of
two consecutive non-responses. The initial session for conditioning subjects consisted of as many pairing of CS (tone) and UCS (shock) as were necessary to reach a conditioning criterion, while the test session involved extinction to a criterion of two consecutive non-responses. A comparison in the habituation groups of the magnitude of response of the first trial in test and in the initial session revealed a substantial decrement for group tested one day or less after the initial session, while minimal decrements were observed for the longer interval groups. Three trials measures revealed differences for the most part in the same direction as the magnitude measure. Data obtained from conditioning subjects revealed no significant differences between groups: CRs were observed to be retained almost totally over the periods of time studied. This has been suggested on the basis of these findings that, there is something learned and retained in habituation and that the forgetting is similar to that observed in other learned (e.g., verbal) material. The study showed, in addition, that habituation is not retained to the extent to which conditioning is.

Gabriel and Ball (1970) using G.S.R. and Finger Plethysmograph (F.P.R.) measures made an attempt to investigate some of the factors which affect orientation response (O.R.) magnitude for tactile stimuli.
Theories which attempt to account for the OR following habituation of autonomic responses (e.g., Sokolov - 1960, 1963) assumed the OR to be related directly to stimulus novelty. Question raised regarding the role of stimulus simultaneity. That is, following habituation to Locus A, will single stimulation (S.S.) of Locus B alone produce a greater O.R. than double - simultaneous stimulation (D.S.S.) of A plus B, or will the OR to A plus B exceed than to B alone? Sokolov's theory would seem to favour superiority of DSS over SS since DSS may have two novel components (locus and number of stimuli), while S.S. may have only one (Locus). Alternatively it may also be argued (Gabriel and Ball - 1970) that D.S.S. will produce a smaller OR than S.S. (or greater generation of habituation) due to a subtractive effect on O.R. magnitude of a stimulus to the habituated locus. To provide informations on these questions this study was conducted by Gabriel and Ball (1970).

The subjects were 48 normal adults ranging in age from 18 to 35 years. The G.S.R. electrode and plethysmograph transducer was fastened to subject's left hand and the five fingers of the right hand were each gently held in an extended position by rubber bands. The subject was blind - folded and seated on an adjustable metal chair.
After instructing subject to remain relaxed but alert, head phones conveying 80 db. of white noise were positioned, and the experiment began. Following nine tactile stimulations of one of four fingers, GSR and FPR orientation responses were observed at three novel finger-tips. OR stimuli were either single stimulation (SSs) of the novel finger-tip, or simultaneous of novel and original finger-tips (DBSs). Trials of habituation to the original finger-tip were interspersed among the test trials. The FPR data suggested that DSS is more effective OR producing stimulus than SS, and that OR magnitude is inversely related to proximity of habituation and test finger-tips. The GSR showed reduction of the OR for some pairs of adjacent (highly proximate) habituation and test finger-tips. The reduction depended upon an interaction of the stimulus factor with relative position of habituation and test loci. Even under adjacent conditions, ample GSR - ORS occurred when either the habituation or test finger-tip had high licalizability.

Rosenberg (1970) reported a study the aim of which was primarily at the examination of the forearm blood-flow responses of normal subjects to a number of stimuli.

Forearm blood-flow plethysmography has been proposed by Kelly (1966) as an objective measure of anxiety.
But the relationship between the level of blood-flow at rest and the level attained during stress, as well as the significance of this difference has been the subject of controversy. Hence, Rosenberg (1970) made an attempt to study the relationship between stress, anxiety and forearm blood-flow.

Twenty-six male subjects were tested and a group of 23 chronic alcoholic subjects were also examined for purposes of comparison. The apparatus used to record volume changes was a modified version of that described by Kelly (1967).

The readings of the resting ("basal") forearm blood flow were obtained, and the lowest three were noted. Following this, the subject was told that the experimenter wanted to measure his (S'S) responses to a series of electric shocks applied to an anterior aspect of the left fore-arm. Readings were taken changing the interval time in between two shocks. After this step of the experiment, the subjects received 10 regularly spaced shocks (lasting for a brief period), but the subject was not told how many or how often the shocks would be given. After this, the subject was given further 10 irregularly spaced shocks (given within a 100-sec. period) but he was informed that shocks would be given at irregular intervals. Following
this, the subject was allowed to rest until the level of blood flow returned to the previously recorded resting level. He was then given mental arithmetic problems to solve quickly while continually being harassed and criticized. In the alcoholic group, the electric shocks were omitted.

With repeated regular shocks, habituation of the vasomotor response occurred and anxiety became less intense. These changes appeared to be related to the subject's ability to predict accurately the intensity and frequency of the stimulus. Mental arithmetic under harassment produced a more gradual but greater rise in blood flow without an equal rise in anxiety. Alcoholic subjects who were judged to have limited motivation and ego strength showed a significantly lower vasomotor response during mental arithmetic. It was concluded that changes in forearm blood flow observed during stress were not related to an increase in anxiety only. The response seemed to depend also on the significance of the stimulus to the subjects, his psychiatric status, and his level of motivation.

Jeffrey et al. (1971) in their study investigated the effects of differential instructions on response habituation and responses to novelty.
Previous research dealing with habituation has demonstrated that instructions affect responding (Maltzman and Raskin - 1965). These studies gradually examined responding to a single stimulus. The object of this investigation was to focus subject's attention separately on either the first or second stimulus of a two element sequential compound and to compare rate of habituation as a function of these instructions.

A second question dealt with the orienting response. Badia and Defran (1970), found that omission of the first or second element of the two element sequential compound produced orienting responses (ORs) which were presumably due to the novelty of the situation. In this study subjects were instructed to judge the intensity of the second stimulus element across all trials to determine if differences occurred. When the second stimulus element was omitted, subject was confronted with both novelty and a situation where the instructions made it possible to carry out the task.

This study was carried out by presenting subjects with repeated trials of a two element sequential compound and then omitting either the first or second stimulus element. The subjects were instructed to concentrate on either the first or second stimulus.
In each of the four groups, 15 female volunteers were randomly assigned. Four groups of 15 female subjects differed with respect to order of presentation of sequential stimuli (light-tone or tone-light) and instructions (concentrate on first or second element of the sequence). All groups received 21 trials of the sequence except on trials 11, 14, 16, and 20, when light was omitted.

The compound stimulus was composed of 750 Hz, 60 db. (re 0.0002 dyne/cm²) tone and a 1 - in. , 6-w, jewel lamp positioned 4 ft. in front of subject. An audio-oscillator produced the tone via Koss earphones (Model SP - 3XC). Intensity was measured at the earphones using a General Radio Sound level meter. A Grass (Model 7) polygraph and preamplifier (Model 7P-1) were used to record GSR.

Response habituation showed both an order effect (p < .01) and an order X instructions interaction (p < .05). The subjects with instructions to concentrate on the first element of the sequence showed less habituation. Some ORs to omission of one element of the compound did occur.

In a study conducted by Nobel and Lader (1971) forearm blood flow and pulse rate of depressed patients were recorded.

Previous investigation (Pollitt - 1965)
suggested that hypothalamic dysfunction may play a role
in the etiology of those depressed patients in which phy-
sical symptoms predominate. Physiological studies on
depressed patients also suggested hypothalamic disturbance.
Depression is associated with an increase in plasma corti-
sol secretion (Board, Wadson and Persky - 1957; Doig,
Mummev, Wills and Elkes - 1966). Dexamethasone, which
acts on the hypothalamic - pituitary axis, does not sup-
press high cortisol secretion in severely depressed patients,
although it does suppress cortisol secretion in less se-
verely ill patients and on recovery (Rarroll, Martin and
Davies - 1968). The plasma cortisol response to hypo-
glycaemia may be reduced in depression, again suggesting
a hypothalamic - pituitary intensity in these subjects
(Carroll - 1969).

Retarded depressives show a reduction in the
amount and variability of palmar sweat gland activity as
assessed electrically (Lader and Wing - 1969). The se-
cretion of sweat and saliva is mediated autonomically and
hence is secondary to control by hypothalamic centers.

Specific vasodilator nerves are responsible
for the increase in muscle blood flow which occurs during
anxiety and the stress of mental arithmetic (Blair, Glover,
Greenfield and Roddie - 1959; Barcroft, Brod Heal, Hirsiarvi and Kirchen - 1960). There is also evidence that vasodilation is secondary to hypothalamic control (Ganong - 1969). There are few studies of the cardiovascular accompaniments of depressive illness, but raised pulse rate and muscle blood flow has been reported in agitated depression (Lader and Wing - 1969; Kelly and Walter - 1969). Hence, this study was undertaken.

The subjects were Maudsley Hospital in-patients whose primary diagnosis was depression and who were treated with E.C.T. They were free from any physical ailment. All drugs (apart from night sedation) were stopped for ten days before assessment. Although 34 patients were tested prior to a course of E.C.T., and of these 31 were retested two weeks after their last E.C.T. The patients' age ranged from 19 to 64 years. There were 12 men (mean age 44.3 years; ± 13.6) and 22 women (mean age, 35.7 years, ± 11.4).

Blood flow was measured using a water-filled plethysmograph and the standard technique of intermittent various occlusion (Barcroft and Swan - 1953; Kelly - 1967). During recordings a wrist cuff inflated to 200 mm. Hg. occluded the blood supply to the hand, and a cuff on the
5. STUDIES WITH REFERENCE TO REACTION TIME:

Tizard, J., and Venables, P.H. (1955), in a study, carried out in a London Mental Hospital replicated the experiment conducted by Rodnick and Shakow (1940) on "Set in the schizophrenic as measured by a composite reaction time."

Rodnick and Shakow (1940) believed that by complicating the reaction time situation somewhat it is possible to obtain a composite measure of several aspects of his function which will be of more clinical value than simple reaction time itself; at the Worcester State Hospital they and their colleagues have labored to devise "set indices" to differentiate patients from control groups, and to assess the effects of drugs on patients. Hunt and Cofer (1944) say of Rodnick and Shakow's set index that it is "the only score known to us that has differentiated any diagnostic group from a normal group without any overlapping." According to Hunt and Cofer, it demonstrates that schizophrenics do not sustain a high level of readiness to respond to environmental stimulation.

In this study by Tizard and Venables an attempt was made to repeat Rodnick and Shakow's study with minor alterations in techniques.
Subjects were 25 chronic schizophrenic men aged 25 - 35, none was receiving any physical treatment at the time of the study. A control group of 10 mental defectives and another 10 colleagues of the authors were also tested.

The timing apparatus consisted of an electrically operated stop-watch graduated in one-hundredths of a second. As a warning signal a bell was rung for about one fifth of a second. The reaction time stimulus was a light which came from a torch bulb over which a paper cap was fitted.

Results were similar to those obtained by Rodnick and Shakow, in that the schizophrenics were slower and more variable than the controls. Also unlike the controls, the schizophrenics tended to be quicker in response when the signals were presented at irregular intervals than when they were presented at regular ones, if the interval between a warning signal and the stimulus was greater than 4 seconds. Results confirmed Rodnick and Shakow's hypothesis that schizophrenics suffer from defects of mental set.

Venables and Tizard (1958) conducted an experiment to investigate the effect of auditory stimulus intensity on the reaction time of schizophrenics.

Two earlier studies (Venables and Tizard - 1956
a, b) on the reaction time (RT) of schizophrenics have shown that as the intensity of visual stimulus is increased beyond an optimum point, RT to the stimulus increases. This "paradoxical" increase in RT is not shown by normal subjects, whose RT decreases as the intensity of visual stimulus increases.

Studies by Pieron (1919) and Okochie (1954) have shown that with normal subjects the RTs to auditory stimuli also decrease as the intensity of the stimulus increases. The present experiment was carried out to determine whether with schizophrenics the effect on R.T. of a strong auditory stimulus would be similar to the paradoxical effect of a strong visual stimulus.

A preliminary experiment with five female schizophrenics and an auditory stimulus of 1,000 c.p.s. at intensities of 30, 45, 60, 70, and 90 db presented through earphones indicated that no paradoxical effect was present and the relationship was one of decreasing RT to increasing auditory stimulus intensity. This finding, which was contrary to that which had been obtained with visual stimuli with schizophrenics, made further experimentation necessary.

To establish that the experimental conditions
and type of subjects were similar to those with which paradoxical effects had been observed in the previous studies using visual stimulation, subjects were tested with visual as well as auditory stimuli. Subjects were allocated at random to one of two groups, one of which made 20 consecutive responses to each of 5 intensities of visual stimuli, and then to each of 5 intensities of auditory stimuli, while the other group responded first to five auditory intensities and then to the five visual intensities.

The subject reacted to the appearance of the stimulus by switching it off with a small toggle switch, after which he returned the switch to its previous position to await the next stimulus. Auditory stimuli of frequency 1,000 c.p.s. were presented by means of ear phones fed from a pure tone audio-generator. Twenty responses were given to each intensity of stimulus and a three-minute rest period was allowed between each series of twenty responses. Measurement of the time was made to the nearest milli-second. Sixteen male and sixteen female schizophrenics were tested. The mean age of male patients was 38.3, S.D. 7.28 years and of females 43.6, S.D. 9.8 years. All were non-paranoid chronic schizophrenics who had been in hospital longer than two years.
Findings have shown no evidence for the appearance in schizophrenics of paradoxical increase in reaction time with increase in auditory stimulus intensity. This phenomenon has previously been established for schizophrenics with visual stimulation, and the present findings gave, with visual stimuli further evidence of its existence.

One deduction which can be made on the basis of above mentioned findings concerns the site of function of the paradoxical effect. As the final effector pathway is common to RT experiments testing both the visual and auditory modality it is evident that the paradoxical effect may be considered as having its origin at a point in either the receptor organ or in the cortex before the effector pathway. Much further work however, must be carried out as suggested by the present authors to establish whether this schizophrenic anomaly of function can be considered central or peripheral.

The effects of Chlorpromazine and Secobarbital on the reaction time of chronic schizophrenics have been reported by Wynne and others (1958).

Twelve male schizophrenics were given a simple visual reaction time test (RT) after oral administration of
chlorpromazine and secobarbital. RT was tested under two conditions: irregular, where preparatory intervals were presented randomly, and regular, where the same preparatory intervals were given in consecutive order. Results indicated that secobarbital tended to improve performance, while chlorpromazine tended to worsen RT performance. Results are different from those obtained by other investigators who have observed facilitation in schizophrenic psychomotor performance after chlorpromazine and deficit in performance after barbiturates.

Lang, P.J. (1959) investigated the effect of aversive stimuli on reaction time in schizophrenia.

A number of theories (Cameron - 1944; Hunt and Cofer - 1944; Wittman - 1937) have suggested that impairment of schizophrenics on psychomotor, verbal and concepts tests is attributable to lowered "motivation", i.e., attitudinal variables such as indifference to the task or uncooperativeness. Cohen (1956), Cavanagh (1958), and others (Pascal and Swensen - 1952; Rosenbaum, Grisell and Mackavey - 1957a, 1957b) reported that schizophrenics responding under escape conditions show a reduction in psychological deficit on tasks ranging from concept formation to simple reaction time (RT). Their findings imply that
the task becomes more "need relevant" in this context.
The subject (S) overcomes his uncooperativeness or indifference to the task stimulus in an effort to escape the aversive stimulus (i.e., negative incentive). However, it is possible to explain the improvement of the schizophrenic subjects particularly on the reaction time tasks, in terms of stimulus dynamism. The simultaneous presentation of the aversive stimulus and the discriminative stimulus may result in a greater "arousal" effect, in Hebb's (1956) terms, than is obtained by the latter stimulus alone. Differences in the improvement of normal and schizophrenic subjects when aversive stimuli are introduced may reflect a difference in response of normals and schizophrenics along the intensity dimension of the stimulus. The findings cited by Sands and Rodnick (1950) that schizophrenics show a "normal" G.S.R. to an intense sound stimulus and a greatly diminished G.S.R. to the word "ready" seems relevant to this point.

On the basis of the above background, attempts have been made by Land, P.J. (1959) to test the hypothesis propounded by Cameron - 1944; Hunt, Cofer- 1944; Wittman - 1937, by introducing aversive stimuli (Shock, unpleasant "noise") into the experimental situation in ways designed to raise the motivational level of psychotics to
perform. This study (Lang - 1959) was designed to examine this proposition for a disjunctive reaction time task and to clarify the role played by the aversive stimulus in modifying the schizophrenic response.

The subjects for this experiment were 70 male chronic schizophrenic patients and 30 normal males. All subjects performed a visual reaction time and received sound which was presented twice at both .40 sec. and 1.30 sec. and three times at .80 sec. The sequence of duration was random.

Avoidance (AV): The "noise" was presented after a time interval subsequent to the light and was maintained for 1.20 sec. Depression of the correct key before the end of the time interval presented the "noise" from coming on.

Information (INF): The "noise" was presented at low intensity subsequent to the visual stimulus. The pattern of presentation was the same as that described for the AV condition.

Following the stimulation trials, 21 post stimulation trials were given, 63 test trials into three series of 21 trials each — prestimulation, stimulation and post-stimulation. The prestimulation trials were conducted under the usual conditions of administration for an RT task.
All subjects were simply instructed to respond as quickly as possible. Subjects were divided into five groups—control, escape, avoidance, extinction and information—and during stimulation trials they performed under one of the following conditions:

Control (Co): The "noise" was not presented.

Escape (ES): The "noise" was turned on simultaneously with the light and terminated by a correct response.

Extinction (EX): The noise was turned on simultaneously with the light and maintained for fixed duration, for each block of seven trials, in which no sound was presented to any group. Instructions were the same for all groups indicating that subject should respond to the appropriate key as quickly as possible.

Analysis of the data showed that, none of the experimental conditions appreciably altered the performance of normal subjects. However, schizophrenic subjects performing under Escape, Extinction and Information conditions displayed greater improvement than controls.

The results confirmed findings of others (Cohen -1956; Pascal and Swensen -1952; Rosenbaum et al. -1957a) that under conditions of aversive stimulation (escape),
schizophrenic subjects showed a greater decrement in RT than schizophrenics performing under the usual conditions of administration. However, the suggestion that improvement in performance under escape conditions may not be a function of the reinforcing effect of termination of the aversive stimulus was borne out. The fact that schizophrenics were able to improve their performance would suggest that response latency is not circumscribed by some organic defect of the peripheral nervous system (Lang - 1959). This failure of chronic schizophrenics to perform at the level of normal subjects seems related to a fundamental inability to make adequate use of stimuli in the usual experimental setting. Shákov's concept (1950) of an inability to maintain set appears to fit the data, both in terms of readiness to respond to a specific stimulus and "readiness to respond to a generation from a group of stimuli."

Martin (1960) conducted an experiment to consider the effects of depressant drugs on reaction times (RT) and 'set.'

A great deal of work had been carried out in the past on the human reaction time, but in spite of this there were a great many aspects of it which had received little attention and about which no clear evidence was available. The effect of drugs on RT was one of them. Hence,
this experiment (Martin - 1960) was undertaken.

The subjects were a group of 24 adults (undergraduate students) consisting of 13 women and 11 men whose mean age was 30 years with SD ± 8 years.

Two 250 mg. tablets of Doriden were given — one in the morning, and the other after 4 hours. The same time interval were followed with Meprobamate using 400 mg. tablets. In the case of both drugs a period of 45 minutes was allowed to elapse between administration and the commencement of testing. On the "No drug" day the subject rested during these delay periods.

The measure of RT obtained was that of pressing a telegraph key with the preferred hand upon hearing the signal to respond (a 70 db 1,000 c.p.c. tone) which was presented through headphones. A preparatory signal was always given before the signal to respond. This preparatory period was regular in the first series of stimuli and irregular in the second series as follows:

Series (i): RT's were obtained to 20 tones which were regularly preceded by a warning tone at an interval of 3 sec.

Series (ii): The 20 signal-to-respond tones were preceded by a warning tone at a time interval which varied from 3 sec.
to 18 sec. About 15 sec. time elapsed between the subjects' response and the presentation of the next preparatory tone.

There were three clear findings from this experiment:

1. RTS were longer in a series with irregular preparatory periods;

2. Meprobamate had no deteriorous effect on RT. Its means were almost identical with no-drug means, and in fact it was very slightly superior to them;

3. Doriden did lengthen RTS, although only in the irregular series.

It was mentioned that the attitude of vigilance was apparently impaired to a greater extent by the drug than the straight forward response as such.

The effects of Meprobamate on the performance of a five-choice serial reaction time task has been reported by Claridge (1961).

The experiment described here arose out of two earlier tests of Eysenck's drug postulate that central depressant drugs increase cortical inhibition while both studies report similar effects of depressant drugs on pursuit
rotar performance and reminiscence, it was unclear from the data whether the impaired performance found was due to an increase in inhibition or to a decrease in excitation, or both. In order to throw some light on this issue, the effect of meprobamate on a more suitable serial reaction time was investigated.

The subjects used were 20 male soldiers, all volunteers, who were employed as either male nursing orderlies or clerks or on general duties in a military psychiatric hospital. They were allocated at random to two experimental groups: Group D receiving meprobamate and Group P receiving a placebo. The mean age of Group D was 21.5, S.D. - 1.29 years and of the P group 26.1, S.D. - 7.02 years. Assessments of intelligence and personality were made using Progressive Matrices and Maudsley Personality Inventory respectively.

The task was a five-choice serial reaction time test, the apparatus being constructed by P.H. Venables from a design based partly on that described by Leonard (1953). It consisted of a display panel set at 15 degrees from the vertical and containing five lights placed 2 in. apart in a horizontal row. In front of each light and in the horizontal plane was a key 5 in. long and 1⅔ in. wide. The
subject was asked to press the key corresponding to the light. The order in which lights were illuminated was a random one over a series of 50, except that no light appeared twice in succession. Subject's response, both correct and incorrect, were registered on a moving drum event recorder and a simple counter allowed the experimenter to note down scores for each minute of performance.

All subjects were administered three tablets a day for a period of three days. This was a common clinical dosage which was hoped it would stimulate clinical conditions of usage more closely and have a more clear-cut effect on performance than the single tablet often used in this kind of experimental study.

In case of Group D each tablet contained 400 mg. of meprobamate so that prior to the testing session, subjects in this group had consumed 3.6 g. of the drug. The tablets administered to Group P were inert, but identical in appearance with those given to Group D.

Each subject was given a written schedule of the hours at which he was to take each tablet. These were 6 a.m., 10 a.m., and 2 p.m.; the subject coming for testing as far as possible about one hour after taking the last tablet.
tablet on the third day. Following the test, the subject worked for a further period of one minute so that a reminiscence score could be obtained.

Results provided considerable support to Eysenck's drug postulate when applied to serial reaction time performance. As expected from Eysenck's postulate, the effects of meprobamate were revealed mainly towards the end of the work period, far-off in performance during the second half of the test being significantly greater in the drug than in the placebo group. This was thought to be due to the combined cumulative effects of reactive and conditioned inhibition. Measures of these variables in terms of reminiscence and errors respectively showed that differences between drug and placebo were in neither case significant. No difference was found in starting level in the drug and placebo groups, but a comparison with a third group who had previously performed on the task with no treatment indicated a marked "placebo reaction" in those receiving dummy tablets. There was sufficient evidence from the data for the three groups to conclude that an effect of central depressants is probably to decrease excitation as well as increase inhibition. It was suggested that the appropriate excitatory variable involved was drive rather than habit strength. The
hypothesis was proposed that the habit variables $S^H_R$ and $S^I_R$ were secondarily affected following a primary effect on the drive variables, $D$ and $I_r$.

In an experiment the effect of the preparatory interval (PI) on simple reaction time (RT) in schizophrenic and normal subjects was investigated by Zahu, T.P., Rosenthal, D. and Shakos, D. (1961).

The effects of the PI depend not only upon its absolute length but also upon the context in which it occurs. A previous paper (Rosenthal, Lawlor, Zahu and Shakow - 1960) advanced the suggestion that each of the two contexts (regular - irregular) was governed by its own set of variables and that they could be studied separately. The main content of this paper was with the effect of varying the context of the $P^I_S$ in a regular procedure. More specifically it is with the effects of varying the order of presentation of successive series of RT trials with $P^I_S$ of varying lengths.

Two experiments were conducted using a regular procedure.

In experiment I, the $P^I_S$ were presented in order of increasing length (ascending) and of decreasing
Seven chronic schizophrenic and 11 normal subjects were used.

The subject was required to operate a telegraph key. Two methods of testing RT were used. In both, the subject's task was to lift his finger from the telegraph key at the onset of the tone. A 0.2 second light flash was the warning stimulus, and the length of the time between the light and the tone, was, the PI.

In method NR (No ready) the subject was instructed to depress the key shortly after his preceding response. If the key was depressed within 5 seconds of the preceding response, the light - tone sequence automatically began 8 seconds after the previous response, regardless of when, during the 5 second period the key was depressed.

In method VR (verbal ready), the subject was instructed that after the experimenter had recorded the previous RT and reset the timer, the experimenter would say "Ready" and then when the subject was ready he was to depress the key. When the subject depressed the key, there was a 0.3 sec. delay before 0.2 second light flash which initiated the PI.
Each subject was tested in eight sessions, four with NR, four with VR. Each session consisted of five series of 14 trials each. The $P_i$ were presented in an ascending order (2, 4, 6, 8, 10 sec.) and descending order (10, 8, 6, 4, 2 sec.). The sequence of condition was constant for all subjects.

In experiment II, 12 schizophrenics and 9 normal subjects were taken.

Method VR was used, modified from that of experiment I. The PI was initiated solely by the subject's depressing the key. Each subject was given 10 successive trials on each of 5 different $P_i$: 1, 2, 4, 7, and 15 sec. In the first session, the $P_i$ were presented in descending order (descending 1) and in second session in ascending order, and in the third session the descending order (descending 2) again.

Results showed that, when successive series of $P_i$ were presented in order of increasing length (ascending), $RT$ was in increasing function of PI length for both groups, but the slope of the curve (in graphic representation) was significantly greater for the schizophrenic subjects. When reverse (descending) order of presentation was used, the RTS of the patients tended to the same
for all \( P^I S \) and relatively slow, whereas the curve for the normal subjects was virtually identical to that for the ascending order.

The data indicated, in general, a greater susceptibility of the effects of context of \( P^I S \) on the part of schizophrenic subjects. More specifically, these subjects showed an inability to recover from an inadequate set or response pattern which had been produced by unfavourable external conditions. The data, as the authors said, cannot be accounted for by the concepts of fatigue or reactive inhibition. However, series of long \( P^I S \) could conceivably lead to a "withdrawal" reaction, characterised by the perservation of minor sets, or to a general change in the level of arousal in schizophrenic subjects.


(a) confirm previous observations (Huston, Shakow, and Riggs - 1937) that the slope of the negative relationship between reaction time (RT) and the length of the preparatory interval (PI) was steeper in schizophrenic than in normal subjects, and

(b) investigate the effects of the PI on one trial on RT to the subsequent trials (PPI).
Two experiments were reported, the second being essentially a replication of the first under slight changed conditions.

In the experiment I, 12 schizophrenic patients were used, none of the patients had had drug therapy for at least several months. A group of normal subjects was also taken.

The subject was told that his task was to lift his index finger from the telegraph key as quickly as possible after onset of a tone. He was instructed that the experimenter would say "ready" before each trial.

After the subject depressed the key hearing "ready" signal, there was a 3-sec. delay, a 2-sec. light flash (warning signal) and a further delay (PI) before the onset of the tone. This procedure was repeated on each trial with only the length of the time being varied. The subjects were given two identical blocks of 36 trials with a 3-minute rest interval between blocks. PIs of 1, 2, 4, 7, 5, 15, and 25 seconds were presented in an irregular order, the same for all subjects in which every PI followed every other PI at least once in each trial block.

In the experiment II, the schizophrenic group
consisted of 13 men and 18 women. The normal subjects were from the same population as in experiment I.

There were three modifications of the procedure from that used in experiment I.

(i) The omission of the warning light, as some of the more disturbed patients used to be confused by this.
(ii) Only 5 PIs were used here 1, 2, 4, 7, and 15 seconds.
(iii) Two non-identical series of 26 trials each were given separated by a 3-minute rest period.

The results of the two experiments were dealt with together. In each experiment the slope of the PI curve (solid lines) for the patients was stiffer. That is, the curves relating the PI with RT were significantly steeper for the patients even when differences in "baseline" RT level were controlled for. Another analysis that was made of the effect of the PPI was to compare RT on the trials in which the PPI was shorter or equal to the PI with the trials on which the PPI was longer than the PI. The means for the differences between the two conditions were found to be significantly different from zero at below the 0.1 level in all cases. In experiment I, this difference was greater for the schizophrenic than for the normal subjects, but
not significantly so. In experiment II, however, the difference was significantly greater for the schizophrenic patients \( p < .01 \). The significance of the combined experiments was tested by Stouffer's method (cited in Mosteller and Bush - 1954). This test showed the combined result to be significant at below .01 level. It was concluded that the length of the PPI relative to that of the PI is a more important variable in the RT performance of schizophrenic subjects than it is for normal subjects, even when differences in baseline RT level are taken into account.

In their study, "Reaction time and prognosis in acute schizophrenia," Cancro, r., Sutton, S., Kerr, J., and Sugerman A.A., (1971) reported the predictive value of reaction time (RT) and its relationship to other predictors.

In 1937, Huston, Shakow, and Riggs published their classic study on RT in schizophrenia. Their tranquilizer-free schizophrenic sample showed a greater mean RT as well as significantly greater within group and within individual variations than normals. They concluded that their patients did not "attain as high a level of preparation as normal subjects, that the patients vary more within themselves in the height of preparation attained from reaction to reaction, and that the patients do not maintain
their level of preparation as consistently as the normal subjects."

Rodnick and Shakow (1940) conducted an experiment utilizing preparatory interval (PI) of varying duration as an estimate of a person's ability to reach and maintain the high level of preparation or set necessary for meeting recurrent environmental stimulation. Their study revealed that even normal subjects under certain conditions were unable to take advantage of a regular PI. However, the failure to take advantage of regular PI did not occur in the normals until some point between 20 and 25 seconds. In the schizophrenics the failure occurred after about 5 or 6 seconds. These investigators computed a "set index" which was devised so as to separate the schizophrenic and the normal subjects without overlap.

Mowrer (1941) reported a series of experiments in which he studied RT as a function of the sequence of the modality of sensory input. He found that RT was lengthened when a stimulus was presented in a sensory modality differing from the stimulus which preceded it. Kriegel and Sutton (1969) and Sutton et al. (1961) independently investigated the phenomenon which Mowrer had reported. Their results indicated that under certain conditions the
effect of a previous sensory experience persisted longer in a schizophrenic than it did in a normal.

The role of prior events has also appeared as an important variable in the PI studies (Kriegal, J. and Sutton, S. - 1971; Sutton, S. and Zubim, J. - 1964; Zahn, T.P., Shakow, D., And Rosenthal, D. - 1961). Zahn, T.P., Rosenthal, D. and Shakow, D. (1963); Zahn, T.P., Shakow, D. and Rosenthal, D. (1961) have shown that the RT of schizophrenic patients is affected not only by the PI, but also by the duration of the PI relative to the PI of the immediately preceding trial. In both the Sutton and Shakow studies, immediately prior events have a disproportionate effect on the RT of the schizophrenic patient. Zubin (1970) has recently considered both the modality shift and PI findings as reflecting a common effect and proposed a model involving the concept of facilitatory and inhibitory residues or traces left by prior stimulating events. In terms of this model, the finding for the schizophrenic patients are seen as evidence for a longer persistence of such traces in schizophrenic.

Unfortunately much of this work was done years ago when data were not collected on variables which are now recognized as important, including the more precise
discrimination of subgroups of patients, such as the process-reactive distinction. The therapeutic requirements of patients today, especially with the emphasis of community psychiatry, are such that most patients are receiving pharmacological treatment before RT studies can be done.

As early as 1960, Freedman, Deutch and Deutch showed that a single dose of hydroxyzine would bring the RT of schizophrenic children closer to normal. The restriction of a population of schizophrenics to only those patients who are drug-free or who could be taken off drugs, would result in the selection of a sub-population that would be highly unrepresentative. A somewhat different approach was taken in this study (Ganero - 1971). The primary goal was to explore the relationship between RT and outcome, i.e., to ascertain the value of RT as a prognostic indicator. The rationale was that RT measured something basic to the psychopathology of schizophrenia, and, therefore, should be related to outcome. The secondary goal was to study the relationships between RT and known prognostic indicators.

Thirty acute, male admissions with a senior staff's diagnosis of schizophrenia were admitted to the study. The patients were drug-free and were not given any long acting sedatives or tranquilizers throughout the
period of testing. They were hospitalized between 2 and 3 weeks when the RT's were obtained so that the confounding effect of variations in duration of pre-testing hospitalization did not pertain. The RT measure was a simpler finger lift response to a quasi-random series of four stimuli; red and green lights and low and high tones. The RT data were classified according to the stimulus presented on the preceding trial. RT's to stimuli preceded by the same stimulus – (category I); RT's to stimuli preceded by a different stimulus in the same sensory modality (ipsimodal RT; Category II). And, RT's to stimuli preceded by a stimulus in the other sensory modality (cross-modal RT; Category III). Patients were classified as a process or reactive on the basis of the Phillips Rating Scale (PRS - 1953) – a measure of premorbid withdrawal. The other predictors included were marital status, social class, duration of previous hospitalization, acuteness of onset, depressed mood, abstract attitude, conceptual plasticity and field independence. The outcome measure was the total number of nights spent in any mental institution during the 3 years of follow-up.

The results indicated that simple RT scores to light and sound were significantly correlated to length of hospitalization for both process and reactive patients.
The correlations ranged from .40 to .53 and averaged .50 for the combined group. The ipsimodal and cross-modal data did not significantly improve prediction of hospitalization for process schizophrenics but did for the reactive cases. RT is not correlated with premorbid adjustment, thought disorder, field independence and several other predictors of outcome. This suggests that, it measures a relatively independent variable. While the clinical measure of the thought disorder was the best single predictor, the simple RT to light added 17 per cent of additional variance. This result indicates the value of using RT measures in a variety of clinical situations.

However, as cited by Cancro et al. (1971) a major defect of this study is the absence of repeated RT measures during follow-up period. This deficiency highlights the need for longitudinal studies in schizophrenia as a function of the clinical state of the patient. We need to know what variables change and in which direction over the course of the disorder. Until this basic need is met we shall be continuing to ignore, so to say, a critical source of variance.
Time perception and distortion have been long considered as important behavioral facts of psychopathological conditions. Though there has been much theorizing concerning the relationship of temporal experience to the emotional or neurophysiological etiologies of psychopathological states, relatively few experimental studies in this area have been reported.

In their review of experimental studies of time perception, Wallace and Rabin (1960) stressed that the few studies of time distortion by psychopathological subjects have cast little light on the nature of the underlying processes.

The past few years have seen a proliferation of studies and theorizing about the relationship of personality and emotional characteristics of subjects to their perceptual and cognitive processes (Pearl, D. - 1963). While there has been controversy concerning the specific processes involved, the majority of such investigations have been consistent in finding that affective and perceptual processes interact.
studies with schizophrenic subjects (Daston - 1956; McGinnies and Adornetto - 1952; Zahn - 1959), have indicated that perceptual thresholds and estimation of size are dependent upon the emotional concomitants of the visual stimuli.

The prominence of emotional factors and conflicts in schizophrenia suggests that affective factors may be integrally involved in the distortion of time perception frequently found in schizophrenic subjects (David - 1963). In line with other findings concerning perceptual accuracy, time perception distortion should be a function of the emotional state or conflict a schizophrenic subject is in at the time his perception of time passage is obtained. The perception of the exposure time duration of stimuli with symbolic threat which tap known conflict areas of subjects should be more distorted than perceptions of temporal duration of relatively non-conflict-laden stimuli (Pearl, D. - 1963). Falk and Bindra (1954), have reported that subjects under stress tend to overestimate time intervals.

Lhamon, W.T., and Goldstone, S., (1956) conducted an experiment on schizophrenic patients in relation to time perception. Schizophrenic patients often make statements to the effect that "time is standing still" - (Lhamon et al., - 1956). It was because of such observation and also
because of a general interest in the time sense, that this experiment was undertaken.

Thirty-seven schizophrenic patients were compared with 41 control subjects with respect to their estimation of one clock second's duration. The mean age of the patients was 33 years; there were 34 men and 3 women. In most instances, patients consisted of a chronically ill population. The mean age of control group (college students, 31 men and 10 women) was 27 years.

A modified Hunter Timer (1949) activated an audio oscillator that delivered through head phones a tone of approximately 725 c.p.s. for selected duration of between 0.1 and 2.0 seconds. The apparatus allowed duration to be presented in step intervals of 0.1 second. Amplitude of the seconds was comfortable and constant. The apparatus had a repeat reliability of 1% and delivered selected durations within a reliability of 5%.

The sounds were presented to all subjects through earphones. The subject was required to report whether the duration he heard was more or less than one second. It was found that random presentation of durations gave results similar to a modified ascending—descending method; the latter method was used because of greater ease of testing.
Twenty alternating runs of ascending and descending durations were provided, starting at 1.0 second. If the subject reported "more" to the initial 1.0 second stimulus, the first run descended by 0.1 second step intervals and terminated when the subject reported "less" - on three consecutive occasions. The subsequent run started 0.1 second below the last of three consecutive reports of "less" and ascended by 0.1 second step intervals the patient or subject reported "more" on three consecutive occasions, whereupon the ascending run terminated. In the event that the patient or subject reported "less" to the original 1.0 second stimulus, the first run was of an ascending nature until three consecutive reports of "more" were given, when the run terminated, the subsequent run being of descending nature. Subjects were unaware of the length of the duration to which they responded. After 20 runs a one minute rest was allowed. After the rest period, the subjects were provided with five consecutive one second durations, with instructions that these durations were exactly one second long and that they were to use this information in the following test, subjects were then retested immediately in a manner identical with the procedure prior to information with 10 ascending - descending runs starting at 1.0 second.

A log-normal distribution of second estimation
points (S.E.P's) was found (the log mean approximates the median). Before information the "median" SEP for the control group was 0.538 seconds; for the schizophrenic group, 0.308 seconds. The smaller mean log of schizophrenic group differed significantly (p less than 0.005) from the mean log S.E.P. of the control group. It was suggested that both groups tended to overestimate the duration of one clock second and that, this tendency was more marked in schizophrenic group. It was of interest that 42% of the control group had an S.E.P. of 0.63 second or more, while only one patient, or 3% of the schizophrenic group showed an SEP this large. In the test period following the five 1.0 sec. informational durations both patients and control subjects had an increase in the "median" SEP in the direction of, but not reaching 1.0 clock sound. Healthy controls changed from 0.558 to 0.762 seconds with information, while the schizophrenic patients changed from 0.308 to 0.668 seconds. The patient group, however, was more variable after information than the control group. This variability of the patient group after information reflected the tendency of this group to "undershoot" or "overshoot" the mark (one sec. clock time) on being tested immediately after having been given information as to the real length of a clock second. It seemed apparent that the control subjects became more homogeneous as a group with respect to their estimate of
one second following information about the exact length of such duration, while the schizophrenic patients were relatively less homogeneous as a group in this respect immediately after such information. The change in mean log SEP of both groups before and after information was statistically significant (p less than 0.005).

The finding that the schizophrenic patient was likely to overestimate the duration of a clock second to a greater degree than the controls, was apparently in line with clinical observations of the inner-directed, autistic person's tendency to overestimate temporal events based upon external occurrences (Lhamon, W.T.; Goldstone, S. - 1956).

It may be that schizophrenic patient's autistic separation from external events association with his passivity prevents full utilization of sensory and motor cues in making consensually valid temporal judgements (Lhamon, W.T.; Goldstone, S. - 1956).

The derived SEP, or a subject's private notion of the duration of a clock sound, was found to be surprisingly stable over the approximately 10 minutes required for the test procedure. However, the nature of variation of the SEP over hours or throughout days or weeks in
a normal or a patient population is not known (Lhamon, W.T.; Goldstone, S. - 1956). It is not known whether remission in the patient group would be accompanied by a lengthened SEP (Lhamon, W.T.; Goldstone, S. - 1956). In addition to the described findings, there was preliminary evidence (Lhamon, W. - 1953) of a variation in the personal estimate of a second with fatigue, with alteration of metabolism, with the degree of boredom, and with administration of certain pharmacologic agents.

RABIN, A.I. (1957) reported an experiment on time examination of schizophrenics and non-psychotics. Previous investigators, for example, Dobson (1954) reported study which dealt with estimation of brief periods of time. But perception of longer intervals may be similar/different from estimating short intervals (Gilliland, A.R., Hofeld, J.R. and Eckstrand, C. - 1946) of time. The estimation of longer periods of time, according to Woodrow (1951), is in need of more study and investigation. Accordingly, Rabin's (1957) study aimed to investigate the estimation or "judgement" of "long" periods of time (minutes and hours) by schizophrenics and non-psychotics and to see to what extent the reported "impaired judgement" in schizophrenia would extend to the estimation of time as well.
There were two groups of subjects. The experimental group consisted of 20 schizophrenics ranging in age between 18 - 40 and equally divided between the sexes. In control group were 20 non-psychotic individuals of individuals of the same ages and the same properties of males and females. This group was made up of hospital personnel, a vocational guidance case, and a few psychopathic personalities.

Each subject was interviewed individually and was examined with the Wechsler Bellevue (entire scale or part of it) and with the Rorschach test. At a convenient point during the examination period (usually at the approximate mid-point of the session) each subject was asked, "How much time has passed since you entered the room? Guess as closely as you can." At the close of the testing session the subject was asked a similar question. Thus, two time estimates, for one-half (approximately) of the length of the interview and for the entire interview, were obtained.

The shorter periods estimated ranged from 25 to 59 minutes with a median 34 and the longer periods from 60 to 160 minutes with a median of 88. The length of the periods to be estimated varied from case to case; they were not standard periods. However, the variation in
the length of periods had no effect upon the estimates. The correlation between length of the actual periods and the accuracy of estimation was .08, which was statistically insignificant.

Results of this study justified the following conclusions: Mere inspection of the range of the percentages of both groups readily revealed striking differences between them. The range for the schizophrenic group was 17 - 300 and 17 - 164 per cent for the first and second periods respectively. The non-psychotic group showed consistently narrower ranges of 28 - 139 per cent for the two respective periods. The judgement of "long" time intervals was significantly poorer in schizophrenics than in non-psychotics. Another interesting findings was the relative stability of the time estimation ability or judgement. Co-efficient of correlation (rho) between the first and second period estimations were .76 and .75 for the schizophrenics and non-psychotic groups respectively.

Costello, C.G. (1961) reported a study which was mainly concerned with the predictions from the drug postulate of Eysenck's (1955) theory of cortical excitation-inhibition as to the effect of depressant drug - meprobamate - on time estimation.
Frankenhaeuser (1959) has presented evidence showing that increasing the amount of mental content by increasing the amount of external stimulation made the objective second seem subjectively longer whereas a decrease in the amount of mental content had the reverse effect. In so far as an increase in inhibitory potential can be assumed to reduce the amount of mental content one would predict that depressants would make the objective second seem subjectively longer. Frankenhaeuser (1959) reported that 200 mg. phenobarbital and 10 mg. metamphetamine produced significant changes in present time estimates in line with the above prediction. Goldstone, S., Boardman, W.K., and Lhamon, W.T. (1958) have also reported evidence on the effect of 0.2 g. secobarbital (quinalbarbitone) and 15 mg. dextro-amphetamine which were in line with the above prediction. The longer production of 10 and 20 seconds intervals after intravenous injections of isomyl (amylobarbitone) reported by Hormia (1956) and also in line with the prediction since a decrease in the subjective length of the objective second would be expected to lead to longer predictions.

Frankenhaeuser (1959) also presented evidence indicating that more was retained of the time units within
a given intervals under conditions which favoured retention of the events which occupy the time period than under conditions which impede retention. Since an increase in inhibitory potential would be expected to impede retention it can be predicted that stimulant drugs would increase the time retained and depressant drugs would decrease the time retained. Frankenhaeuser's (1959) results with secobarbital and dextro-amphetamine were in line with prediction.

With this background in view, the prediction tested in Costello's (1961) study was that meprobamate as a depressant drug would produce a decrease in the reproduction of time intervals.

Llewellyn - Thoams (1959) described a technique which amplifies a subject's error in the reproduction of time intervals by using positive feed-back. The technique used in this study (Costello - 1961) was based on that of Llewellyn - Thomas.

A buzzer was used as the standard. The subject was instructed to press the key as soon as the buzzer stopped (buzzer was sounded by the E), and thus sounding the buzzer again, and to keep the buzzer sounding by holding the key down for a period which he estimated to be the same as the standard. Five seconds after his judgements, the
subject was presented with a further stimulus period which was his own reproduction of the last stimulus. The cycle was repeated ten times. The buzzer was sounded initially for 5 sec. or 10 sec., these periods were the initial standards and the order of presentation of the two periods was counter balanced for the subject's use.

Each subject was given two treatment - (1) Placebo, (2) 800 mg. meprobamate on two different days, the order of treatment being counter balanced. On each day, the subject was tested 1½ hours after administration of the treatment.

There were 12 male and 12 female subjects. The ages of the sample ranged between 17 and 47 years with a mean of 29.95 years. All were volunteers.

Results showed that — the drug tended to produce a decrease in the reproduction of the time periods as predicted, but the effects were not significant. Negative correlations were found between extraversion and the reproduction of the time periods under placebo conditions, but none of the correlations were significant. Negative correlations were also found between extraversion and the effects of drug on the reproduction of time, but none of the correlations were significant.

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Lynn, R. (1961) reported the results of an investigation, designed to examine introversion - extraversion differences in judgements of time.

Previous to this experiment, an attempt was made by Claridge (1960) to apply Eysenck's (1957) theory of introversion - extraversion to the problem of time errors. The hypothesis advanced by Claridge is as follows: the first stimulus produces both excitatory and inhibitory effects, the inhibitory effects reducing its perceived intensity or duration. This hypothesis accounts for the preponderance of negative time errors (overestimation of time is called as negative time error and underestimation as positive time error - Lynn, 1961) that most investigators have reported. It also follows from this hypothesis, taken in conjunction with Eysenck's postulate that extraverts generate reactive inhibition more quickly and dissipate it more slowly than introverts, that extraverts should show larger negative time errors than introverts. Claridge - (1961) verified this hypothesis using judgements of intensity of sound and duration of time. A tendency for hysterics to show greater negative time errors than dysthymics in judgement of time intervals had also been reported by Eysenck (1959b).
Llewellyn - Thomas (1959) had published a new procedure for obtaining time judgements designed to maximize individual differences. This procedure involved the use of a positive feedback technique in which the subject was required to make a judgement of a standard and was then presented with his judgement as his new standard and so on over a number of trials. Any tendency to error became cumulative with this method. With this view as background, Lynn's (1961) study aimed to investigate introversion—extraversion differences in judgements of time.

The subjects were two groups of 20 introverted and 20 extraverted male university students. Introversion—extraversion was assessed by the Maudsley Personality Inventory (Eysenck - 1959a). The introverts scores 6 - 18 on this scale and the extraverts between 29 - 44.

The procedure followed that of Llewellyn - Thomas (1959). The apparatus consisted of a light that could be switched on with two keys, one of which was held by the experimenter and the other by the subject. The subject was told by the experimenter that he (E) would switch on the light for a brief interval and following this the subject should switch on the light and attempt to keep it on for the same intervals and the duration of each trial might differ in length, this was also the subject was told.
first standard was 15 seconds, and there were 9 further trials in which the subject was successively given his last judgement as his new standard. The interval between trials was approximately 5 seconds.

The results showed that there were no differences between introverts and extraverts on the first five trials, but that differences in the direction predicted by Eysenck's theory emerged from trial 6 and became statistically significant at the .05 level on the last three trials. The results did not replicate the findings of Claridge and Eysenck exactly, since they found significant introversion - extraversion differences on a single trial. It was not easy, as Lynn mentioned, to account for this discrepancy, since the procedures used appear to have been same. Nevertheless, the hypothesis that introversion - extraversion differences in time judgements do exist received some support from this experiment. Further, Eysenck's theory that these introversion - extraversion differences reflect differences in the generation of reactive inhibition entailed the prediction that the differences would become greater as the trials proceed, since reactive inhibition would not dissipate fully in the inter-trial interval.
Sieman, A.W. (1962) conducted an experiment to study the effects of anxiety and impulse control on the estimation of time.

Previous investigators, e.g., Eskin, M.E., and Kofka, J.S. (1952), found that stress tends to increase subject's estimation of the duration of "chronological" time. Rosenzweig and Koht (1933), suggest that this is due to some kind of wishful-thinking mechanism, as if subject wished that more time had elapsed and the stressful situation was over. An alternate explanation, based on a learning theory approach to stress and anxiety (Child, I.L. - 1954; Taylor, J.A. - 1955) is that, time estimation under stress presents a much more complex stimulus situation, producing in subject a greater number of response tendencies. Spivack, G., Levine, M., and Sprigle, H. (1959) have reported significant positive correlation between intelligence and time estimations which were obtained by the production method. But since this kind of task apparently measures subject's estimation of duration as well as his impulse control capacity (Singer, J.L., Wilensky, H. et al. - 1956; Spirack, G., Levine, M., and Sprigle, H. - 1959), it is not clear whether intelligence is merely related to impulse control or also to the estimation of duration.
The aim of Siegman's (1962) study was to investigate the relationship between intelligence and the verbal estimation of elapsed time.

The subjects in this study were 36 undergraduate students and each subject was presented with the following time intervals, 20, 5, 20, and 5 sec., the beginning and end of each of which was marked by the click of a stop watch. The intervals between stimuli were 5 seconds. In order to control for the serial position effect which was found by previous investigators (Eson, M.E., Kofka, J.S. - 1952; Falk, J.L., Bindra, D., - 1954). One half the group was presented with the stimuli in order which they are listed, and the other half in the reversed order. The repeated estimations of the same two time intervals were obtained in order to ascertain the reliability to subject's estimations. All subjects were told not to count off the sounds and not to use mnemonic devices, that the purpose of this study was to determine how they felt various periods of time were like. Subject's impulse control level was determined by means of motor - inhibition task (Io). In this task, subjects were asked to trace a 2½ inch circle on onion-skin paper as slowly as possible. All subjects had previously taken the Taylor Manifest Anxiety Scale (MAS) and a general intelligence test
tasks (e.g., a vocabulary test, a digit symbol test, an arithmetic test, a similarities test, etc.)

A significant positive correlation was obtained between subject's MAS scores and their estimation of a 20 sec. and a 5 sec. time interval. While intelligence was clearly not a significant source of variance in subject's time estimations, the negative correlations between impulsivity control and time estimations were nearly significant. Anxiety, but not intelligence, was found to be a significant source of variance in subject's performance on a motor impulse inhibition task.

Pearl David (1963) conducted an experiment to test the hypothesis that, schizophrenics would exhibit greater distortion in estimation of duration time for stimuli relevant to their major conflicts than for other stimuli. Three groups, each consisting of 16 subjects who were homogeneous with respect to essential factors for the experiment, necessary, were formed. A factorial Latin square design was used for the data obtained following the techistoscopic presentation at 4 exposure times of 4 pictorial stimuli. Results demonstrated that greatest distortions occurred for conflict pictures at the .001 level. Distortion elicitation of the aggression stimulus was greater
than other stimuli at .001 for the combined schizophrenics, an effect not found with normal control subjects.

In an experiment conducted by Carlson, V.R., and Feinberg, I., - (1968), on individual variations in time judgement and the concept of an internal clock, time judgements of 1 - 10 sec. by the methods of estimation, production and reproduction were obtained from 20 normal subjects and 20 schizophrenic patients.

Many account of time perception involve some form of analogy to a clock (Carlson, V.R.; Feinberg, I. - 1968). However, different methods of obtaining time judgments have not yielded the straight forward mutual consistencies one might expect if such analogy were useful (Clausen - 1950; Du Preex - 1963; Kruup - 1961; Ochberg, Pollack and Meyer - 1965; Siegman - 1962; Wallace and Rabin - 1960; Warm, Morris and Kew - 1963). Such an apparent inconsistency may be due to a lack of explicitness as to just what the analogy implies, an attempt to set forth its essential requirements, at least for relatively short time intervals, was made in this experiment (Carlson, V.R., Feinberg, I. - 1968).

The analogy consists basically of a comparison
of one clock, a hypothetical one, with another, E's real clock. There was therefore only one fundamental variable to assess, namely the rate at which the internal clock runs relative to the rate of the real clock. For convenience the "running" of the internal clock was referred to as counting on the part of the subject(S), but the clock itself should be understood theoretically to mean whatever process may exist that renders S capable of counting at a regular rate whether he counts overtly or not.

In the method of estimation, E presents an actual time interval and S names the number of seconds he judges to have elapsed. If the given interval is 4 sec., and S counts at the rate of 2/sec., he will count to 8 during the interval and E will plot 8 against 4. If E presents 2 sec., S will count to 4 and E will plot 4 against 2.

In the method of production, E names the given time interval and S is required to hold down a key (or otherwise cause a real clock to operate) for the amount of time he judges to be equivalent to the stated interval. If the given time interval is 4 sec. and the S counts at the rate of 2/sec., he will release the key at the end of 2 sec. and E will plot 2 against 4.
In the method of reproduction E presents an actual time interval, operationally as in the method of estimation, and S holds the key down for a judged equivalent interval, operationally as in the method of production, neither E nor S overtly naming the interval. If E presents 4 Sec. and 5 counts at the rate of 2/sec., then in order to be consistent with the result of estimation, 8 becomes the effective given time interval to be produced. At the rate of 2/sec. S will count to 8 in an actual interval of 4 sec., and E will plot 4 against 4.

The present investigation (Carlson, V.R., Feinberg, I. - 1968) was directed toward determining whether the functions are linear for the range of time intervals from 1 to 10 sec., and whether individual mean responses to the time values 1 - 10 sec. are related to slope or to intercept values.

Ten male and ten female junior college students constituted the normal group, (median age for each sex was 19.5 years), and 26 male and 28 female schizophrenics (unselected with respect to subtypes; median age for male--$7.66 years, and for female 35.5 years) constituted the experimental group.

A response key was connected to a circuit
permitting the key to operate an interval timer or an elapsed timer, depending upon the method of time judgement. For estimation, the response key started the interval timer, which turned on a light visible to subject for the duration of the selected time interval. For production the response key operated the elapsed timer and light for as long as the key was held down. For reproduction the first depression of the key operated the interval timer and the second depression operated the elapsed timer, the light coming on at the first depression, going off at the end of the time interval, coming on again at the second depression, and going off at the second release of the key. As this procedure was difficult, a simpler, more conventional procedure was used with the schizophrenic subjects. On estimation or reproduction trials E started the interval timer and turned the light on for the presented durations, the procedure otherwise being the same as for the normal subjects.

Each session was made up of 30 trials plus repetition of any trials on which mis-trials occurred. The integer time values 1 - 10 sec., were presented randomly each once for each method within the restriction that neither the same method nor the same time value was allowed to
occur more than twice on successive trials. The criteria for mistrial was failure to respond or improper operation of the response key, inspite of repeated presentation. All subjects were tested on two sessions with at least one day and usually several days intervening.

It was originally intended to classify subjects according to the significance or non-significance of curvilinearity in the functions. It became apparent that, significant curvilinearity occurred at about the chance expected frequency (5% of the instances at the .05 level). Only one normal S and schizophrenic subjects showed significant curvilinearity (p ≤ .05) in the same direction for both sessions for any method, and the linear regressions were highly significant in three instances (p < .001). The intent to form a group of subjects with curvilinear functions was therefore abandoned.

Overall regression analyses were performed on the time scores separately for each method and separately for the normal subjects and the schizophrenics. The linear regressions were all highly significant but none of the deviations from linear regression reached significance. There was therefore no contradiction to use of the linear intercept and slope coefficients as adequate representations
of the Response X Time Functions. Individual mean responses for subjects failing to meet the criterion for significance of regression were highly reliable and highly correlated with the intercepts of the functions, indicating that level of response is not necessarily a valid of measure of time judgement.

Johnson, J.E. and Petzel, T.P. (1971), in an attempt to find out temporal orientation and time estimation in chronic schizophrenia mentioned that, research on time estimation in schizophrenics has yielded inconsistent results. There is agreement that schizophrenics are poorer than normals in estimating "long periods" of time (Rabin, A.I. - 1957; Wallace, M. and Rabin, A.I. - 1960; Dilling, C.A. and Rabin, A.I. - 1967). However, some studies demonstrated disruption of temporal estimations only in long time intervals (Rabin, A.I. - 1957; Dilling, C.A. and Rabin, A.I. - 1967), while others have also found evidence of temporal disturbance in brief intervals (Johnson, H.M. - 1939; Adler, N. - 1954; Lhamon, W.T. and Goldstone, S. - 1956).

In addition, the errors in time estimations by schizophrenics have not manifested a trend in direction of errors; rather, there have been reports (Johnson, H.M. - 1939; Dobson, W.R. - 1954; Rabin, S.I. - 1957; Wallace, M.

On this background, the purposes of the study by Johnson, J.E. and Petzel, T.P. (1971) were to:

(a) correct the methodological deficiencies of the temporal orientation studies cited above and compare the ages reported by chronic schizophrenics with their actual ages;

(b) determine whether the time estimations of brief intervals given by chronic schizophrenics differ from those of normals; and

(c) determine if there is a consistent direction of error in time estimations by those patients.

The schizophrenic group consisted of 40 hospitalised patients (20 male and 20 female) who had not received drug treatment at least 4 weeks of ECT at least 2 months prior to testing. The control group consisted of 40 subjects (20 male and 20 female) selected from the patient files of a general practitioner. The criteria for control subjects included no history of psychiatric illness or use of psychiatric medication. Both groups were matched for age, education and I.Q.
Each subject was then asked to estimate passage of time in two conditions. In condition A, subjects estimated how many seconds passed in an unspecified period of time. They were asked how much time passed from when the experimenter said "start" until he said "stop". The actual period was 30 seconds in all cases. In condition B, the subjects were to estimate a specified period of time; that is, they were asked to indicate when 30 seconds had passed after the experimenter gave them the signal to start.

Results showed that — in condition A, there was a greater tendency for the schizophrenics to over-estimate the passage of an unspecified period of time (M = 55.8 seconds) than normals (M = 40.4), (F = 4.45, df = 1, 76, p < .05). Of the 40 schizophrenics, 35 overestimated the actual time, whereas only 25 of the normals overestimated the length of the period (X^2 = 3.33, df = 1, .05 < p < .10).

On the other hand, the results of condition B indicated that schizophrenics underestimated the passage of a 30 sec. period (M = 20.1 sec.), whereas normal subjects were more accurate (M = 29.88), (F = 14.28, df = 1, 76, p = <.01). In this case, 36 schizophrenics compared to 24 normal underestimated the length of the 30 second period (X^2 = 4.80, df = 1, p < .05).
The above mentioned findings disagree with the conclusion that temporal disturbance occurs only over long periods of time (Dobson, W.R. - 1954; Rabin, S.I. - 1957; Dilling, C.A., and Rabin, R.I. - 1967) and agree with others who have found evidence of temporal disturbance in brief intervals (Johnson, H.M. - 1939; Adler, N. - 1954; Lhamon, W.T. and Goldstone, S. - 1956). Moreover, the present results indicated that there is a trend in direction of error (Johnson, J.E. and Petzel, T.P. - 1971). The data suggested that schizophrenics may experience time as passing more slowly than normals, since they reported that an unspecified period of 30 seconds was nearly twice that long. The findings that they also consistently estimated a specified period of 30 seconds in two-thirds of the actual time supported this view.
PART—II

7. STUDIES WITH REFERENCE TO TWO—FLASH—THRESHOLD.

Goldstone (1955) conducted an experiment to find out the relationship between flicker fusion measurements and anxiety level.

Krugman (1947) reported the results of an exploratory study which suggested that sensitivity to a flickering light (flicker fusion threshold) was inversely related to anxiety level. Results of several other investigations summarised by Landis (1951) and Simonsen and Brozek (1952) demonstrated a relationship between flicker sensitivity and fatigue, impaired oxygen circulation, ingestion of central and autonomic nervous system stimulants and depressants, ophthalmologic pathology in any part of the visual pathway, central nervous system pathology, cardiovascular function, and possibly anxiety. On this background this study was undertaken and the flicker fusion measures included were the following:

(a) Flicker fusion threshold (FFT); the measure of sensitivity to flicker, and

(b) slope, the measure of intrasubject variability or precision of judgement.

Seventy-four subjects were selected—serially
from the patients and their relatives attending out-patient psychiatric clinic and were separated into the following groups according to the anxiety criteria as described below:

33 high - anxiety patients, 18 low - anxiety patients, 2 high - anxiety normals, 21 low - anxiety normals, 33 total high - anxiety, 39 total low - anxiety.

This study employed an electronically activated "glow modulation" tube which illuminated a 5. mm., circular test patch mounted in a black box at 1° visual angle. The patch appeared as white light at a brightness of .35 ml., and the light - dark ratio used was 60 : 40 over the entire frequency range.

All subjects received a 3- min. adaptation period followed by a method of limits flicker fusion test. Alternating runs of ascending and descending flicker rates were presented. The duration of stimulus presentation was 1.5 sec. and the step interval was .5 cycle per second. Three blocks of five ascending runs alternating with 5 descending runs were used, separated by a 30- sec. rest. The percentages of reports of flicker for each frequency in the last 20 trials were plotted on normal probability paper. The following reliable differences were found:
(a) Those groups designated high anxiety had a lower FFT than those groups designated low anxiety, suggesting reduced sensitivity to flicker associated with high anxiety.

(b) Those groups designated high anxiety had a greater individual variability of judgements than those groups designated low anxiety.

(c) Those groups designated high anxiety had a greater decline in sensitivity to flicker (FFT) associated with continued exposure to the flicker test than those groups designated low anxiety.

Morfarland, R.A. et al. (1958) made an attempt to find out alterations in critical flicker frequency, if any, as a function of age and light - dark ratio.

One of the important organismic variables known to influence critical flicker frequency (OFF) variation among individuals is chronological age. Simson, Enser, and Blankstein (1941) and Brozek and Keys (1945) reported a definite decrease in OFF for subjects over 40, but little change in OFF was found before this age. Misjak (1947) studied subjects ranging in age from 7 to 89 years, and found that average OFF declined rather regularly from age...
20 to 89, but not without considerable individual variation. Another study by Copping (1951) has established that the OFF - age function is linear and negative from the age of 20 to 90.

While it has been generally accepted that OFF would be negatively correlated with age, there had been little uniformity in previous studies in the characteristics of the test field, especially in the light : dark ratio (LDR) of the flicker cycle. Further more, since only a few studies used more than one LDR, little systematic informations were available on the comparative sensitivity of the fusion threshold when the light - time proportion (LP) of the LDR would vary. On this background, this experiment made an attempt to establish more precisely the nature of the relationship between foveal OFF and chronological age by - (a) using a number of different light : dark ratios, and (b) employing a large sample of subjects covering an age span of 76 years.

Binocular critical flicker frequencies (OFF's) were determined for 160 subjects ranging in age from 15 to 89 years. The light pulses were in the form of square wave activating a glow modulator tube. The ratio of light-time/dark-time in the flicker cycle was varied systematically
from 2/98 to 98/2. The test field consisted of a circular test area of .6° subtense shown at the centre of a circular 17° surround. Tests were made at surround luminances at 25.6 and .04 ml.

The results were:

(a) The relationship between OFF and age was found to be linear and negative for all LDR level.

(b) The decrement of OFF with age might have been a function of light - time percentage of the flicker cycle. The differentiation between age groups was more pronounced at the lower light - time percentages.

(c) The light - time percentage at which the maximum OFF occurred was a function of chronological age of subject.

(d) The change in the surround luminance resulted in a shift of the position of the OFF - LDR curves, but the shape and slope of the curves were not altered.

On the basis of the results it was suggested that the use of lower levels of light - time in the flicker cycle, rather than the conventional 50 : 50 LDR, would enhance the sensitivity of OFF as an indicator measure.

Holland (1960) designed an experiment in order to exami
the effects of depressant drugs on some perceptual processes.

The design of this experiment was mainly to examine the compounds Meprobamate and Doriden from two viewpoints: The empirical and the rational. The former examination had been based upon the proposition that the two agents differ in their chemical structure but that their behavioral differences would remain obscure. The rational examination had been based upon the established relationship between personality and drug action which had been formerly stated as the extraversion/drug hypothesis. Although in the main, the drug hypothesis advanced by Eysenck had been formulated on differences existing in the performance of chemically "depressed" and "stimulated" subjects, it had relevance in this study (Holland - 1960) because of the basically "depressive" characteristics of both the tranquilizer and the hypnotic, which by hypothesis, would be expected to increase cortical inhibition and decrease excitation, thereby changing task performance of those functions dependent upon them.

On the empirical level both the drugs selected were supposed to have some effects on all the tests (static ataxia, OFF etc.) given. Here the influence of those two drugs mentioned above had been discussed in relation to critical flicker fusion (OFF) frequency.
The subjects were a group of 24 adults consisting of 13 women and 11 men whose mean age was 30 years with SD ± 8 years.

The instrument used was a modified moving arm type 315/466. Flicker was provided by a pulse generator, and the neon activated through a finger key.

Two 250 mg. tablets of Doriden were given - one in the morning and the other 4 hours later. The same intervals were followed with Meprobamate (400 mg. tablets).

Results indicated that the CFF threshold was low because of both the drugs used.

Hieatt and Tong (1969) in a study reported the differences between normals and schizophrenics on activation - induced change in two-flash fusion threshold.

Research relating brain stem stimulation and cortical selectivity by Lindsley (1957) led Venables (1963) to utilise a score from a perceptual discrimination task (two-flash fusion threshold T.F.T.) to examine hypotheses relating arousal level to perceptual dysfunction and schizophrenic symptoms. Other work failed to confirm the results (Hume and Oldridge - 1965), possibly due to the
unsuitable method of determining T.F.T., a method of constant stimuli. This study was based on the proposition that perceptual functioning would be related to arousal level, and also attempted to resolve confusions arising from earlier studies by control of possible sources of error in the experimental situation. Two hypotheses were posed in this study:

(a) Normals, paranoid schizophrenics, and non-paranoid schizophrenics would differ in T.F.T.;

(b) induced arousal would differentially affect T.F.T. for the three groups.

The subjects, all male, were 16 non-paranoid and 16 paranoid schizophrenics, mean age 33.8 and 39.3 years, all hospitalised longer than 6 months, and 16 normals, mean age 36.4 years.

The apparatus was a timing control device for producing flashes from a cathode ray tube behind the display screen at discrete 1 ms. intervals between 10 and 209 ms. Each flash was of 50 ft. L, illumination, fade time 5 microseconds and 5 ms. duration. The two T.F.T. measures were - (i) the modified method of constant stimuli used by Venables; and (ii) the modified method of limits used
by Pearson and Tong (1968). While seated at a table in the dark-room the subject was required to regard a screen and report whether he perceived one or two flashes of light. In all cases there were two flashes but of varying inter-flash interval (I.F.I.). The T.F.T. score was the longest I.F.I. in milliseconds at which the subject perceived the two flashes as one.

The heart was used as an indicator of physiological arousal and was continually monitored during all sessions. During the two high arousal sessions the subject performed a non-distracting pedalling activation task whilst seating at the viewing table, T.F.T. being measured by one of the two methods before and during activation. For the two low arousal sessions - the appropriate T.F.T. measure was also obtained twice but with a four minute rest interval and no activation during the session.

Results showed that, under non-activated conditions heart rate differed significantly (p = .05) between the three groups. It was mentioned that, if the heart rate is regarded as an indicator of arousal level then the groups differed in respect to resting arousal level. The activation task significantly increased heart rate for all groups but there were no significant differences between the groups.
Under non-activation conditions the mean Pearson T.F.T. differed significantly between the groups. The activation task did not significantly affect the Pearson-Tong T.F.T. for the combined groups, but did have a significant differential effect bringing about a decrease for normals and an increase for schizophrenics, the paranoid showing the greater increase.

In general, the results indicated that, the paranoid and non-paranoids showed perceptual discrimination differences under low arousal conditions and that induced high arousal had a differential effect on patients and normals. The normals decreased their T.F.T.s and the schizophrenics increased, the paranoid more so. A lower T.F.T. score implies greater efficiency in perceptual discrimination. In terms of Yerkes-Dodson explanation, as mentioned by Hieatt and Tong (1969), the subjects with low T.F.T.'s under low arousal conditions (e.g., normals) may not be sufficiently aroused to perform with their maximum perceptual efficiency. On further arousal they would further decrease their T.F.T.'s, i.e., improve discrimination. However, subjects whose resting level of arousal was beyond that required for optimal discrimination, would following an increase in arousal, show an increase in T.F.T. This finding fits the present results and suggested
that both groups of schizophrenics function under chronically high arousal, the paranoids being the more highly aroused. Scrutiny of medication records gave no indication of a drug artefact.

Miller (1969) in a study measured the effect of a controlled auditory stimulus over a wide range of amplitude on a visual response measure, critical flicker fusion frequency (OFF).

Gorrell (1953) studied the effects of high (2,400 - Hz) and low (270 - Hz) tones on OFF and concluded that both auditory stimuli lowered the fusion threshold, the higher tone more than the lower. He did not however, report the amplitude of the auditory stimuli. Levine (1958) tested several intensities of pure tone (1,550 - Hz) on two subjects and concluded that there was an enhancement of flicker discrimination up to a certain intensity level of sound and then a fall in OFF at intensities above this level. Davis (1966) accepted the phenomenon of inter-sensory effects in both positive (facilitatory) and negative (inhibitory) direction. On this background, this investigation (Miller - 1969) was undertaken, which varied the amplitude of a sound stimulus through a wide range and measured the effect of this on a visual response.
Five male university students between the ages of 19 and 52 years were chosen. All subjects had normal distance vision.

A sine wave generator delivered the auditory stimulus to padded earphones. Flicker was produced by rotating an opaque circular disc 8 in. in diameter. When the disc was rotated a light/dark ratio of approximately 1/6 was produced. Starting below threshold, flicker was increased by the experimenter until fusion was indicated by the subject. The ascending and descending trial rates were averaged to yield the datum of one trial.

Result showed that, auditory stimulation exerted a significantly curvilinear facilitatory effect on OFF, dependent on the amplitude of the sound. Peak facilitation occurred at approximately 90 db. It has been suggested that the reticular ascending activating system as a brain structure is likely to be involved in mediating intersensory effects.

Gruzelier et al. (1972) reported the results of three experiments in which the relation between two-flash thresholds (TFFs) and electrodermal activity - Skin conductance level (SCL) and skin potential level (SPL), of paranoid and nonparanoid schizophrenics was examined in activated and nonactivated conditions.
While it has been widely suggested that schizophrenia involves disturbance of arousal processes experimental investigation in this field has produced few uniform results. Experimental findings revealed significant but opposite correlations between the same variables, namely skin potential level (SPL), regarded as an index of autonomic arousal, and two flash thresholds (TFT), known to vary with changes in central arousal. Venables (1963) in two experiments, obtained negative correlations with chronic non-paranoid schizophrenics and positive correlations with paranoid schizophrenics and normal controls. Lykken and Maley (1968) found negative correlations between TFT and both SPL and SCL with patient controls, while with non-paranoid schizophrenics correlations between TFT and SPL were positive and between TFT and SCL varied around zero.

The discrepancy between these studies may arise through differences in the methods of measuring TFT and SPL, in the nature of the groups and in the experimental conditions. Furthermore, arousal has not been taken as a unitary dimension and the relation between the measured indices may be non-monotonic. The experiments which will be reported here were designed to examine these possibilities using TFT, SPL, SCL and heart rate (HR), and measuring their variation over a number of sessions, in
activated and non-activated conditions, with particular interest in their co-variation within rather than between individuals.

Levels of activation were varied within a session by having the subject pedal a bicycle ergometer under differing loads. The two-flash light source was a cathode ray tube. Flashes were 1 msec in duration with an intensity of 360 foot Lambert and were viewed binocularly from a distance of 8 feet. Two methods were used for obtaining TET. The first one consisted of traditional method of limits (TET ML) with alternating ascending and descending series, each beginning at a different interflash interval (IFI) and then varied in intervals of 2 msec. The second method consisted of two-alternative temporal forced choice procedure (TFT FC) whereby a double flash of variable IFI was presented one second before or after a single flash. The double flash was varied over five IFIs with a duration of 40, 50, 55, 60, 65, or 70 msec. and selected so that two fell below and two above that IFI closest to ML threshold.

In the experiment I, the aim was to evaluate the bicycle ergometer as a means of varying simultaneously SC, HR and TET. Subjects were 12 male students, ages 20 through 28, mean 23 years. In the experiment II, the aim was to measure arousal using different indices, e.g.,
HR, TPT, SCL, SCH, etc. The subjects were 18 male schizophrenics, 12 non-paranoid (ages 24 to 43 years, mean - 33 years) and six paranoid (ages 31 to 42 years, mean - 37 years) respectively. Twelve male nurses (age range 26 to 57 years, mean - 33 years) served as controls.

In the third experiment, the aim was to examine whether the non-paranoid schizophrenics would manifest an increase in TPT and decrease in SCL with increased activation. The subjects were 36 male schizophrenics, 24 non-paranoid (ages 19 to 46 years, mean - 36.0 years) and 12 paranoid (ages 24 to 47 years, mean - 38 years) plus 12 male nurses (ages 23 to 44 years, mean - 34 years).

Results showed that, at low levels of skin potential and skin conductance the two-flash thresholds of the controls were positively related to skin potential and skin conductance whereas at higher levels of skin potential and skin conductance, and in activated conditions, a negative relation was found. In general, the two-flash thresholds of both schizophrenic groups were negatively related of skin potential and skin conductance in non-activated conditions; when activated the paranoids showed the same changes as normals while the non-paranoids showed raised two-flash thresholds and lowered skin conductance level. Activation increased HR and SPL for all groups.
These findings were interpreted as showing the operation of inhibitory processes, consonant with the concept of protective inhibition, elicited as somatic arousal increases in non-paranoid but not paranoid schizophrenics.
PART II

8. STUDIES WITH REFERENCE TO

KINESTHETIC FIGURAL AFTER EFFECTS

Assumptions proposed for a brain model (Klein and Krech - 1953) suggested the hypothesis that if prolonged exposure to stimulation results in decreased conductivity (satiation) of cortical tissue, this effect will be particularly marked where there exists severe brain lesions. The purpose of the experiment conducted by Klein and Krech (1953) was mainly to compare brain-injured and controls on degree and rate of satiation after exposure to a kinesthetic stimulus, and on the extent and rate of recovery (dissipation of satiation).

Hospitalized 12 male patients with cortical lesions of varying severity and locus were compared with equated hospitalized controls (N = 16). Subjects were blindfolded and were instructed to rub the sides of a 2½-inch wide standard for 30-second, 60-second, 90-second, and 120-second periods. After each period they judged the width of a 1½-inch test object by adjusting a tapering scale. Persistence of the effects was measured 5 minutes and 10 minutes after the last satiation period. To form individual's baseline in judgements, control
measurements were taken prior to satiation.

Consistent trends observed were - (a) frequency and intensity of satiation effects were significantly greater in the brain-injured; (b) the brain-injured reached maximal satiation more quickly; (c) the satiated state persisted longer in the brain-injured, recovery being less pronounced; (d) correlations of satiation indices with neurological ratings ranged from +.65 to +.92. The results supported the "cortical conductivity" concept and the suggestion that a generalised effect of severe brain injury is lowered conductivity. Tumour cases showed alterations which approximated those of diffuse non-tumor lesions, especially in rate of recovery, which was excessively slowed. It was suggested that a broader organismic imbalance rather than merely the local changes in specifically affected regions may be an important source of variations in conductivity.

If the concept of "reactive inhibition" of Pavlov and Hull is indeed essentially identical with the factors involved in Kohler's "satiation," then it would follow that satiation is related to personality, on this ground, —

Eysenck, H.J. (1955) made an attempt to work out a dynamic theory to account for a number of experimental findings in
the field of personality related to the concept of extraversion - introversion. It was predicted that hysteries would be differentiated from dysthyms in the speed of arousal, strength, and length of persistence of figural after-effects.

The subjects used in this experiment were 14 males in each group. The average age of the two groups were 29.14 (hysteries) and 34.23 (dysthyms). The differences in between two groups regarding age, intelligence etc. were insignificant.

The apparatus used in this experiment and procedure adapted were taken from Klein and Krech (1953) who used it in their work on cortical conductivity in the brain injured.

Results showed that -

(a) hysteries developed satiation and figural after effects more quickly than did dysthyms;

(b) hysteries developed stronger satiation and figural after effects than did dysthyms;

(c) hysteries developed more persistent satiation and figural after-effects than did dysthyms.

The differences were statistically significant.
Prolonged inspection of an object in the Kohler-Wallach (1944) paradigm produces figural after-effects (FAE) which may persist for long periods of time. The longevity of these phenomena was first noted by Kohler and Wallach (1944) and additional information has been provided by further studies of both visual and kinesthetic FAE (Kohler and Wallach - 1944; Hammer - 1949; Kohler and Fishback - 1950). Any FAE is maximum immediately after its induction, and then dissipates slowly, with a negatively accelerated decay function which may never return to the original pre-inspection level, thus leaving a residual FAE which Kohler has called the "permanent" FAE or "permanent satiation."

Although Kohler and Dinnerstein (1947) provided some incidental observations on the persistence of the kinesthetic FAE, systematic studies of such persistence was lacking. This had led the present authors to undertake the present study.

The apparatus and technique used in the measurement of kinesthetic FAE were similar to those used by Kohler and Dinnerstein (1947).
Subjects were divided into 3 groups: Group I (N = 11), the control group, was given no inspection at any time, but spent 1 min. between the pretest and the post-test at rest between the inspection bars without touching them. Group II (N = 14), the 1-min. group, was given 1 min. of inspection between the pre-test and the post-test. Group III (N = 14), the 5-min. group, was given 1-min. of inspection between the pre-test and the post-test, and 4 min. off further inspection following post-test.

Kinesthetic FAE measures were obtained on three groups for five successive days. Evidence for significant residual FAE was obtained, by plotting daily pre-inspection matches. The greater the daily inspection, the greater the residual FAE 24 hour later; the rate of growth of residual FAE also varied monotonically with the amount of daily inspection. It was mentioned that, satiation effects may persist lawfully over relatively long periods of time.

Bourne and Beier (1961) conducted an experiment to assess the effect, of duration of inspection upon kinesthetic figural after-effect.

In a study of the temporal factors influencing visual figural after-effects (FAE), Hammer (1949) found that magnitude of FAE increased as duration of stimulation with
an inspection figure increased. But there has been no
rigorous study of the temporal factors in kinesthetic FAE
comparable to Hammer's study for vision.

This led Bourne and Beir (1961) to design an
experiment to assess the effects of duration of inspection
on kinesthetic FAE.

Measures were obtained on 50 subjects at five
different durations of stimulation with an inspection block.
The inspection durations were 0, 30, 60, 90 and 120 seconds;
the inspection block had a width of 2 inches; the test
block had a width of 1.5 inches. Order of presentations
for the inspections durations was varied within a 5 x 5
Latin square which was replicated 10 times. The subject
made width estimates for the test block by gripping this
block in the right hand while surveying a scale graduated
in width with the left. Measurements of FAE were computed
after taking ± into account constant error.

The results were:

Kinesthetic FAE in the form of significant underestimation
of test block width were found. Constant error in judg-
ment, practice and certain individual differences were
ruled out as explanations for the effect.
Magnitude of FAE increased significantly with successive measurements and stimulations with the inspection object.

Duration of stimulation with the inspection object was a significant variable affecting FAE. The effect appeared to increase to a maximum of 30 and 60 seconds inspection, at a rate somewhat greater than found for the visual FAE.

Qualitatively, FAE in kinesthesis parallels those found in vision, but the results of this experiment suggested that the two modalities differ widely either in amount of effect developed in the same inspection time, or in rate of decay of effect over rest.

Meier (1961) designed an experiment to demonstrate the interrelationships among kinesthetic figural after-effects (KFA), reminiscence and personality variables.

Investigations of the interactions among personality, learning and perceptual variables (Eysenck - 1955; Gibson - 1933; Klein and Krech - 1952; Kohler and Dinnerstein - 1947; Kohler and Wallach - 1944; Livson and Krech - 1955; Worthheimer and Jackson - 1957; Worthheimer, Levine, and Worthheimer - 1955) have pointed out the possibility of generating
and testing hypotheses relating behavioral variables hitherto considered independent and theoretically disparate. Eysenck (1955) extended Hullian concept of reactive inhibition ($I_R$) to individual differences. Assuming that kinesthetic figural after effects (KAE) is a function of generation of $I_R$ and personality differences, Eysenck (1955) predicted and found more rapid development of KAE in hysterics than in dysthyrmics.

Since neither of these studies had simultaneously considered learning, perceptual, and personality variables, the necessary empirical foundation for extending $I_R$ to explain individual differences and for postulating corresponding cortical processes appeared to be incomplete.

On this background Meier (1961) designed an experiment to demonstrate some inter-relationships among kinesthetic figural after effects (KAE), reminiscence (Rem) in motor learning, and personality variables. Five hypotheses were tested: individual variation in the magnitude of KAE varies negatively with the amount of Rem in inverted alphabet printing; individual variations in the persistence of KAE varies negatively with the amount of Rem; personality variables, as measured by MMPI and psychiatric classification, are related to Rem and KAE; the size and persistence
of KAE vary positively with age and negatively with size vocabulary. Rem varies negatively with age and positively with size vocabulary.

The sample consisted of 120 mixed psychiatric and non-psychiatric hospitalized males, age being 45 years or less and those who did not receive any drug for 2 weeks prior to the investigation. The tests used were Inverted alphabet printing (Krautzke - 1946) and kinesthetic after effect test, adapted by Klein and Krech (1952). The procedure outlined by Krech for kinesthetic after effect test was used. In addition to these two tests, MMPI and Shipley-Hartford Scale were used.

Results showed that, the amount of Rem varied negatively with the magnitude and persistence of KAE. Two empirically derived MMPI Scales differentiated High from Low Rem scores upon cross-validation, but failed to account for variation in KAE. Similarly, two sets of MMPI code rules separated along the Rem criterion when cross-validated. Rem varied with psychiatric classifications as psychotics exhibited lower scores than non-psychotics and hysterics showed higher scores than dysthymics. KAE failed to relate with psychiatric classification at conventional significance levels. Size of vocabulary and age varied
with Rem and KAE in accord with prediction, but the correlations did not reach significance for the age and KAE relationship.

Although some of the variation in Rem could be accounted for by MMPI variables and psychiatric classification, these measures of personality did not relate to KAE. It has been assumed that the relationships between Rem, KAE, age and vocabulary may derive from some neural processes involving the generation and dissipation of $I_r$.

Singer and Day (1965) reported the results of two experiments using kinesthetic after effect, with two different purposes.

The temporal determinants of the spatial after-effect from kinesthetic stimulation have been investigated by Bakan, Myers, and Schoonard (1962), Bourne and Beier (1961), and Carlson (1963) all of whom used the traditional task involving judgements of the width of a bar before and after stimulation by one of different width. In an earlier study (Day and Singer - 1964) consistently large ($4 - 5^\circ$) and reliable kinesthetic after effects were obtained in a task requiring manual judgements of the horizontal after motion of the extended arm and hand across a slanted
bar. But no quantitative data were available on the determinants of this particular form of the kinesthetic after-effect.

This being the background, Singer and Day (1965) in their investigation made an attempt to establish the relationship between the magnitude of kinesthetic after effect and time of stimulation on the one hand, and its dissipation over time on the other, in two experiments.

The first experiment was concerned with the relationship between the size of the kinesthetic after effect and duration of stimulation (15, 30, 45, 60, 75, 90, 105 and 120 seconds). The second experiment was to establish the dissipation functions for the kinesthetic after effect for two stimulation times, 30 sec. and 90 sec.

The apparatus was adapted from similar experiment used in an earlier investigation (Day and Singer - 1964). In the first experiment, 10 high school students (2 boys, 8 girls) whose age ranged from 13 to 17 years acted as subjects. In the second experiment, there were 2 groups of 12 adult male and female subjects all of whom were either graduate or senior students of psychology. The task required kinesthetic judgement of the horizontal following controlled rhythmic stimulation of the extended hand across
a slanted bar. In experiment I, the after effect was shown to increase with stimulation time. In experiment II, the size of the after effect was similar immediately following 30 and 90 sec., stimulation but the rate of dissipation was greater for the shorter than the longer stimulation. Since with the method of adjustment dissipation is rapid during the adjustment period, the development function of experiment I has been interpreted as representing a joint function of stimulation time and differential dissipation rates.
shagass (1954) used the Sedation Threshold (S.T.) test as a method for estimating tension in psychiatric patients.

A pathological degree of tension occurs in many psychiatric conditions. A method of estimating degree of tension objectively and quantitatively would have many clinical and research applications, and the main purpose of this investigation was to develop such a method.

Data were derived from the 80 technically satisfactory tests which were carried out on Psychoneurotic and Schizophrenic patients. The patients were classified in the following groups: (a) 54 patients (18 males and 36 females) with psychoneuroses of various types; (b) 15 patients (9 males and 6 females) who were considered to be pseudoneurotic schizophrenics; (c) 11 schizophrenics (6 males and 5 females), psychotic at the time of testing, 5 of whom were chronic and 6 acute cases. Age ranges were 19 to 55 (median 31.7 years) for the psychoneurotic group, 19 to 39 (median 28.0 years) for the pseudoneurotic schizophrenics, and 16 to 22 (median 21.7 years) for the schizophrenic group.

Development of the procedure was based on the common clinical observation that sedation tolerance and degree of tension are closely related. Sodium amytal was
administered intravenously at a constant rate while the E.E.G. was recorded. The discovery of a definite point of inflection in curves of E.E.G. amplitude plotted against amount of sedative provided an objective threshold value. The E.E.G. threshold point usually coincided with onset of slurred speech.

The E.E.G. S.T. was found to be highly correlated with clinical ratings of degree of tension of 69 psychiatric patients (including 54 psychoneurotics), who were not psychotic at time of testing; the correlation was low in a group of 11 psychotic schizophrenics.

Frequency analyzer studies in 10 tests confirmed the quantitative E.E.G. aspects of the S.T. method. They also showed that with progressive sedation, the amplitudes of the frequencies in the frontal E.E.G. were increased in an orderly progression from the faster to the slower frequencies.

It was concluded that the S.T. method seems to hold exceptional promise as an objective psychiatric test, provided that it is properly developed.

Shagass and Naiman (1955) carried out an experiment using the Sedation Threshold (S.T.) technique to find out the relations if any, in between manifest anxiety and Ego function.
There have been no previous attempts to correlate clinical findings in a control group with the sedation threshold. This study was carried out for two purposes: (a) to determine whether the threshold measures manifest anxiety in non-patient, and (b) to test two predictions, based on the hypothesis that impairment of ego functions, such as reality contact, lowers the sedation threshold.

In 45 non-patient (control) subjects there was a high positive correlation between the S.T. and the number of symptoms of manifest anxiety elicited in a psychiatric interview. There was also a significant relationship between the threshold and the score on a self-administered symptom inventory (Saslow Screening Test; as mentioned by the authors).

Psychiatric patients included 11 with organic psychoses, 11 with acute schizophrenia, 22 with agitated depression, and 34 with chronic schizophrenia. In the psychotic group as a whole there was no statistically significant correlation between the S.T. and clinical appraisals of degree of tension or manifest anxiety. Among the chronic schizophrenics there was a significant positive correlation, which was smaller than that found in psychoneurotics or in controls.

From the ego impairment hypothesis, it was
predicted that the chronic schizophrenic group would have higher thresholds than apparently equally tense patients with acute schizophrenia or agitated depression. It was also predicted that the organic psychoses group would have lower thresholds than any other subjects.

The procedure followed was that described by Shagass (1954) earlier.

The results confirmed both predictions which were formulated in relation to ego impairment hypothesis.

It was concluded that the S.T. is positively correlated with degree of manifest anxiety and negatively correlated with degree of impairment of ego functioning. Since the ego impairment factor is important mainly in psychotics, it was concluded that the S.T., as a measure of manifest anxiety, is most applicable to non-psychotic subjects.

The role of reticular system has been emphasized while discussing the findings. It was concluded that the phenomena related to the sedation threshold may be most readily understood in terms of the functions of reticular formation.

Shagass and Mihalik (1956) conducted an experiment using
the Sedation Threshold (S.T.) test as an objective measure to differentiate between neurotic and psychotic depression.

Several psychiatric nomenclatures differentiate several categories of depressive syndromes, such as manic-depressive, involutional and reactive depression. One of the main concepts underlying this classification is that neurotic and psychotic depressions are different. This concept is not universally accepted (Shagass and Mihalik - 1956), and it has been criticized by several workers.

As the disagreement concerning the differentiation between neurotic and psychotic depression is based upon conflicting interpretations of clinical observations, it was felt that the problem might be clarified by the addition of new objective data. The main purpose, therefore, of this study was to apply the sedation threshold (S.T.) test to study of depressive states, with particular emphasis upon the problem of distinguishing between neurotic and psychotic depression.

For this study, 182 patients of the following diagnostic categories were taken: Psychotic depression, Schizoaffective psychosis with depression, "hysterical" depression, Neurotic depression and Anxiety State.
The procedure for determining the S.T. was that described by Shagass (1954, 1955), where the slurred speech served as a rough guide to the S.T., while E.E.G. change was the precise guide.

Results were as follows:

(a) Sedation thresholds of patients with neurotic and psychotic depressions were markedly different; The test differentiated between these groups with about 95% accuracy. Age difference was not an influential factor. Thresholds were low in psychotic depression, regardless of the degree of agitation or history of previous depressive episodes.

(b) The threshold of patients with anxiety states were similar to those of patients with neurotic depressions and almost always higher than those of patients with psychotic depression.

(c) Patients with high S.T. (neurotic depression and anxiety states) were treated with E.C.T. much less frequently than patients with low S.T. (Psychotic and "hysterical" depressions). When E.C.T. was given, the short-term therapeutic response of the high threshold patients was significantly poorer than that of the low-threshold group.
(1) The S.T. of psychotic depressive patients who had received E.C.T. prior to testing were higher than those of patients not recently receiving such treatment.

The following conclusions were drawn:

(1) The S.T. appears to be a valid objective method for the differential diagnosis of depressive states.
(2) The results supported the validity of the concept which distinguished between neurotic and psychotic depressions.
(3) The relationship between the S.T. and depression was probably secondary to the effect of another factor, degree of impairment of ego functioning, on the threshold.
(4) The S.T. appears to have some validity for predicting the outcome of E.C.T.

Bradley and Jeavons (1957) conducted an experiment to assess the effect of chlorpromazine and reserpine on sedation and convulsive thresholds in schizophrenic patients.

From previous literature it was found that these two above mentioned drugs, not only potentiate the action of central depressant drugs, but may also increase convulsions. This study was an attempt to throw further light on their action in men.
The group of patients chosen for this investigation consisted of chronic catatonic schizophrenics (either in stupor, semi-stupor, or had definite stuporous episodes).

The method used was to establish the control sedation threshold (S.T.) and control convulsive threshold in each patient and then to repeat these, first after pre-medication with chlorpromazine, and then following reserpine. The method of administration of chlorpromazine (CPZ) was to give 50 mg. intramuscularly at 8.00 a.m. and again at 8.00 p.m. on the day before the experiment and further 50 mg. one hour before the recording was started. The same procedure was used with reserpine but in this case the dose was 2.5 mg. for each intramuscular injection. None of the patients had received any treatment with drugs for several months before the investigation was carried out.

For the sedation threshold test though it was thought that Shagass's technique would serve the purpose, because patients selected for this study were mute, modification of Shagass's technique was necessary. The only clinical threshold which could be assessed was failure to respond to a verbal command to open the eyes. The convulsive threshold was established with hexasol, the method used being based on that of Ulett et al. (1955).
Results showed that after chlorpromazine there were significant changes in the sedation thresholds in a number of patients. These changes were consistent, being a lowering of the S.T.

Following reserpine, in normal clinical doses, neither the S.T., nor the convulsive threshold showed any significant change. The same was true of the convulsive threshold after pre-treatment with chlorpromazine.

It was concluded that both the methods had to be modified before they could be used. The convulsive threshold was found to be fairly easy to establish accurately; with regard to the method for establishing S.T., it was felt that this has to be used with care in patients incapable of full co-operation.

Shagass (1957) carried out an experiment to test the utility of the Sedation Threshold to reflect some factor which is of importance to the neurophysiology of psychiatric disorder.

The sedation Threshold (S.T.) is a clinical neurophysiological test, which determines the amount of intravenous amobarbital sodium required to produce certain EEG changes, accompanied by slurred speech. Previous investigations have shown that threshold to be related to several
significant psychiatric variables, such as degree of manifest anxiety. The purpose of this study was to further the aim of defining the neurophysiological factor, measured by the S.T., by testing the hypothesis that the S.T. is a function of the rate of depressant action of amobarbital on brain activity.

Subjects for this study were 399 psychiatric patients and 45 non-patients. The procedure followed was that described by Shagass (1954). Continuous EEG's were recorded from transverse frontal and sagittal frontal-central placements. The amplitude of frontal fast activity was measured and plotted against the amount of drug, which contained a clear inflexion point, occurring about the time when speech became slurred.

Analysis of the data showed that the amplitude of frontal fast frequency activity produced by amobarbital, could provide an acceptable index of rate of depressant action which was required to test the hypothesis mentioned above. The mean amplitude at the threshold, which represents a particular level of depressant action, was approximately constant for groups of subjects with different thresholds.

The rate of increase of mean amplitude, which
could be taken as the index of depressant action, was amenable to quantitative expression as the slope of a rectilinear function, when the logarithm of amplitude was used in calculation. In confirmation of the hypothesis, there was a highly significant inverse correlation between the sedation threshold and the index of rate of depression action.

In contrast to the S.T., fast frequency amplitude as an absolute value, either before the injection or at threshold, was not significantly related to psychiatric diagnosis. Amplitude at threshold was correlated with amplitude before injection, but neither value was significantly correlated with the S.T.

From the conclusion that the S.T. is a function of rate of depressant action of amobarbital, it was suggested that it measures a time characteristic of neuronal activity, which is probably an important factor influencing cerebral excitability.

Thorpe et al. (1957) conducted an experiment to assess the objectivity of Sedation Threshold test.

During the course of a preliminary investigation into the general usefulness of a patient's Sedation Threshold as measured by the onset of slurred speech, the authors were
impressed by the apparent lack of objectivity of the onset of slurred speech, and by the disturbing possibility of its being affected by the clinical picture presented by the patient during the course of the amobarbital sodium. As a result, this study was an attempt to assess the amount of agreement among observers with regard to the onset of slurred speech following the injection of amobarbital sodium.

Seven consecutively admitted male patients were given intravenous amobarbital in accordance with instructions given by Shagass (1954); i.e., amobarbital sodium was injected intravenously at the rate of 1 c.c. every 40 sec., each cubic centimeter containing 0.5 mg. of amobarbital sodium per Kg. of the body weight. Twenty five seconds after each injection the patient was asked to repeat the following words: Siesta, Saucer, Sociology, Solicitor, Somerset, House, British constitution and Massachusetts. Injections were continued until the patient was no longer able to repeat the words, or until the amobarbital sodium was all given.

The whole procedure was recorded by a tape recorder. The seven recordings were subsequently played during a medical staff meeting, when 16 members were present.
Results showed that the 16 listeners were unable to agree regarding the onset of speech slurring. In conclusion, speech slurring was regarded as too subjective to be of general use and its objectivity was questioned.

Refinement of the then concept of Sedation Threshold, so as to make its measurement more objective, was suggested.

Boudreau (1958) in a study reported the reliability of the Sedation Threshold test.

During the last few years a number of articles have been published on the Sedation Threshold test. By means of this method, there were obtained a number of interesting findings which seemed to warrant further investigation and hence this study was taken into consideration. The purpose of this study was -

(1) to test the reliability of the technique and to determine how accurately it could be reproduced;

(2) to examine the correlation of the Sedation Threshold (S.T.) with certain diagnostic categories and with manifest anxiety, and

(3) to evaluate the stability of the threshold in non-patient controls or in-patients whose psychopathology remained constant.
Patients were selected on the basis of the degree of manifest anxiety they demonstrated and the diagnostic category into which they fell. A total of 60 tests were performed on 36 patients and 3 controls. Of the patient group, 25 were female and 11 male, the ages ranging from 18 to 72 years. The three non-patient controls were nurses who exhibited no psychopathology either clinically or as detected by MMPI testing prior to S.T. determination.

The procedure adapted was almost similar to that described by Shagass (1954) with minor variations, following the technique used by Thorpe and Barker (1957).

The following conclusions were drawn:--

Because of various technical difficulties, the Sedation Threshold (S.T.) is difficult to determine and often equivocal. In this study, there was, however, a definite correlation between S.T. and various diagnostic categories, particularly as applied to Shagass' concept of psychotic and neurotic depression. Yet no correlation existed between manifest anxiety and the threshold. In addition, the S.T. was not found to be a stable value in control subjects or in a patient whose psychopathology did not change clinically.
Kawi (1958) reported a study using the Sedation Threshold test on psychiatric patients.

This study was undertaken to investigate the relationship between various manifestations that have been designated "anxiety" and the amount of central nervous system depressants — namely, amobarbital sodium and ethyl alcohol — required to produce the levels of the Sedation Threshold (S.T.). The assumption was that the psychological state of the organism determines, to a large extent, his reaction to the drug. The study was also to investigate the psychological changes as a result of the administration of these two drugs.

A group of 24 male patients presenting varying degrees of "anxiety" were taken with the conditions that it was their first admission to psychiatric hospital and with an age range of 16 - 36.

On each subject the following data were obtained:

- An evaluation of the degree of the anxiety using three measures: Clinical judgement, the figure-drawing test and Taylor's Anxiety Scale.

The Sedation Thresholds for amobarbital sodium and ethyl alcohol. The performance on four psychological and psychomotor tests under the effects of amobarbital sodium and
ethyl alcohol, and a no-drug condition.

E.E.G. readings of the brain waves under the effects of amobarbital sodium, ethyl alcohol and a "no-drug" condition.

The amount of amobarbital sodium in grammes or of ethyl alcohol in cubic centimeters, per 10 lb. of body weight that was required to produce slurred speech was taken into consideration. This modification of Shagass's technique of the Sedation Threshold (S.T.) was adapted so as to meet the objectives of this investigation.

The injection of amobarbital sodium was made up so that 1 c.c. of sterile water contained 1.5 grams (0.10 gm.) of amobarbital sodium. The drug was injected intravenously at the rate of 1 c.c. per 40-sec. interval. This was followed by a 20-sec. period during which the subject was tested for slurred speech. This injection, followed by testing, was repeated in the same way until the subject had manifested slurred speech on two consecutive testing periods.

The apparatus that was employed to administer ethyl alcohol intravenously consisted of a container for each of the following solutions: first, isotonic saline solution and, second, a solution of pure ethyl alcohol.
and isotonic saline solution in the proportions of 15 c.c. of 95% ethyl alcohol to 85 c.c. of isotonic saline solution. The tubes from these containers ran to a Y-connector, which was equipped with a two-way stopcock, so that the solution in either bottle may be infused. With this type of apparatus, the infusion could be administered by gravity. The whole apparatus was sterilized previous to injection. The rate of flow was adjusted, using clamps, to 20 c.c. per minute. The point of the S.T. again, was that at which the subject manifested slurred speech on two consecutive testing periods.

Results showed that there was a significant positive correlation between the sedation thresholds for amobarbital sodium and ethyl alcohol. These thresholds were also significantly correlated with the clinical judgement of anxiety. The S.T. for ethyl alcohol was significantly correlated with Taylor's Manifest Anxiety Scale. Since slurred speech was the only criterion for reaching the level of the S.T., it was tested for reliability by studying the relationship between the sedation threshold and the performance on the psychological and psychomotor tests. The per cent deterioration or improvement on the projective and psychomotor tests was found to have no significant correlation with the doses of the drug that produced the effect, thus asserting the reliability of the
s.T. as a specific level of psychological functioning with slurred speech as one of its clinical manifestations.

Martin and Davis (1962) conducted an experiment in order to assess the sleep thresholds in depression.

Although Shagass' view seems to imply that "excitation" and conversely "inhibition" are gross unitary factors, there are of course many ways of assessing C.N.S. excitability in the sense of measuring different aspects of C.N.S. activity. It seems equally likely that such measure as autonomic and skeletal muscle activity also relate to C.N.S. "excitability", and, incidentally to clinical assessment of anxiety and tension. As there have been relatively few studies which specifically investigate autonomic activity in depressed patients, the present study was undertaken.

In this study attempt was made first to reproduce Shagass' findings as a whole by using the technique of administering sodium amytal to depressed patients to obtain their sleep thresholds. At the same time this study obtained several autonomic and skeletal muscle recordings as well as a number of ratings and questionnaire scores which could be correlated with the sleep threshold measures.
The patients studied were 30 consecutive admissions to one female ward, in whom a diagnosis of a primary depressive illness was made. The patients' ages ranged from 11 - 59 years (Mean 41.2). Duration of illness - 3 months. No drug was given for 24 hours before testing.

The clinical features of retardation, agitation and anxiety were rated on a 5-point scale. In addition a number of variables relating to depression were scored from the Item Sheet of the Institute of Psychiatry.

The normal subjects were all volunteer women (N = 12). They were not taking drugs, and their age ranged from 24 - 40 years (Mean = 28.0).

The procedure was carried out in a standard ward bed room. Subjects were given details of the test they were to have. Electrodes were fitted for recording (when the subject was lying on a bed) skin resistance, heart rate, and forehead muscle tension, and continuous records were obtained throughout the whole procedure.

After an initial period of rest to accommodate the subject to the situation, the sodium amytal solution was injected intravenously at the rate of 0.5 mg./Kg. body-weight every 40 seconds, and the tape recorder started on
which digits were played black at the rate of one every two
seconds. (Digit doubling technique was followed). The
criterion of sleep was verbal unresponsiveness to stimuli.

Data revealed that there were no significant
differences between the groups on the amount of sodium amytal
required to reach the sleep threshold (Endogenous, reactive
and indeterminate groups of depression). Similarly
there was no significant correlation between the sleep
threshold and clinical ratings of agitation, retardation,
anxiety, severity of depression or with factor scores from
a factor of "psychotic depression."

Scores on the MPI and MAS showed that in general
the patient groups were higher on neuroticism and anxiety
and lower on extraversion than the normals. The personality
scores did not, however, correlate significantly with
the sleep threshold data.

Claridge et al. (1963) in an experiment... attempted to find
out the relationship between the sedation threshold and
autonomic lability.

In a previous paper (Claridge and Harrington — 1960), it was demonstrated that by using a modified ver-
sion of the Sedation Threshold technique, originally des-
cribed by Shagass (1954), it was possible to differentiate
neurotics diagnosed as hysterics and those diagnosed as anxiety states (dysthymics). In keeping with Eysenck's theory of neurosis (1955) and drug action (1957), it was found that dysthymics had significantly higher threshold for sodium amylobarbitone than hysterics. In addition, supporting the earlier findings of Claridge (1960) and again Eysenck's theory of personality, dysthymics were found to have significantly longer visual after effect to a rotating spiral than did hysterics. It is true that some workers have, without success, attempted to demonstrate a relationship between Sedation Threshold (S.T.) and autonomic responses. Ackner and Pampiglione (1958), for example, reported negative findings in this respect, while Shagass (1958) himself found no correlation between the S.T. and the blood-pressure response to mecholyl (Funken-Stein test). However, in recent years, some doubt has been cast (Seager - 1960); (Thorpe and Barker - 1957) on the reliability of Shagass' Sedation Threshold technique, which with a variety of modifications has been used by most workers. By using what has proved over several years to be a more reliable index of the S.T., it was hoped that less equivocal evidence would emerge of a relationship between autonomic response and barbiturate tolerance.

In the series of studies described here, the
relationship was examined between the blood pressure response to three physical stressors and the basic measures used by Claridge and Herrington (1960), viz., S.T., Archimedes Spiral after-effect, and the two scales of Maudsley Personality Inventory.

The investigation was carried out on 32 neurotic (mixed neurotics) and 13 normal subjects, with mean age of 24.3, S.D. 4.40 years, and 23.4, ± S.D. 5.03 years respectively.

The S.T. was determined in each patient according to the method described by Claridge and Herrington (1960).

A four - throw spiral was used. Two trial of one minute each were given, the visual after-effect being recorded in seconds.

All blood pressure readings were taken by auscultation with the subject in a standing position. The systolic and diastolic blood pressures were taken once a minute for three times in order to obtain a basal reading. The subject was then asked to plunge the whole of the opposite hand into a vessel containing water kept, as far as possible at a constant temperature of 4° centigrade. The systolic and diastolic blood pressures were then taken once every half-minute for a further three minutes. The blood
pressure taken prior to the cold pressure test was referred to as pre-stress blood pressure and that taken after cold pressure was referred to as post-stress blood pressure measures.

Results showed that, by partialling out the relationship between pre-stress level and post-stress change, consistently positive correlations were found between S.T. and blood pressure rise, although only in case of one measure of the diastolic response was this significant. The spiral after-effect correlated significantly and positively with the pre-stress blood pressure level, which in turn, showed a near zero correlation with S.T.

These results were considered sufficiently encouraging for further investigations to be carried out, using more adequate measures of autonomic function. They were also held to support the view that it is necessary to hypothesize two sources of arousal to account for some of the postulates of Eysenck's theory of personality.

Martin and Davis (1965) in an experiment made attempt to find out the effect of Sodium Amytal in patients with depressive illness.

The studies were described. The first aimed
to repeat certain aspects of the work of Shagass et al. (1956) on sleep thresholds in which reactions to sodium amytal was correlated with clinical groupings. Clinical findings of this experiment have already been reported (Martin and Davis - 1962). The major purpose of the second experiment was to investigate further the question of whether there is differential responsiveness between depressive groups to sodium amytal, and whether differences exist between groups in levels of autonomic and muscle activity. The results of the previous experiment were in the main negative in these respects, but it seemed that several improvements could be made in the method of administering the drug.

Subjects were depressive patients and volunteer normal controls, all females, age range 18 - 59 years. Patients were classified into three groups, as follows:

(a) mainly endogenous (N = 12);
(b) mainly reactive (N = 9); and
(c) indeterminate (N = 9).

Measures of heart rate, skin resistance and muscle activity were taken into consideration.

In the first study, Shagass' technique of
intravenous administration of Sodium Amytal was used. This was modified in the second experiment, in which the
constant/fusion technique was used; control groups re-
ceived saline or no treatment. In addition to the three
measures above, digital Systolic blood pressure was re-
corded continuously. This was the only physiological mea-
sure which showed a significant drug effect, all the other
measures showing reduced activity over time irrespective of
treatment. No differential effect was observed on the di-
fferent categories of depression.

Vahia and Bagadia (1965) carried out a study with a view to
test the reliability and validity of Sedation Threshold Test
as defined by Shagass.

In Psychiatry, as objective criteria of diagno-
sis, prognosis and treatment are lacking, it was therefore
thought that if Shagass' test is found useful as an objective
measure, clinical work in psychiatry will be on a much more
sound and scientific basis. On this background, the pre-
sent study was undertaken.

During 1958 - 1959, 27 patients were taken up
for the test, and in all 35 tests were administered. Dur-
ing 1960 - 1961 - 1964, patients were given the test and
in all 90 tests were administered.
After taking detail case history, physical examination was done, body weight and blood pressure were noted. A four point rating scale was employed. No. 1 was meant for normal levels of tension and No. 4 for maximum degree of tension.

A routine EEG of the patient was taken beforehand preferably on the previous day. When the patient was lying on bed he was interviewed for about ten minutes by non-psychiatrists for the assessment of clinical tension. This was followed by venepuncture, and a minute later a brief control EEG was taken. Following this 1 c.c. of Sodium Pentothal was injected at intervals of 40 seconds. The solution of the sodium pentothal was prepared in such a way that the patient got 0.5 mgm. of the drug per Kg. of body weight every 40 seconds. The patient was asked to pronounce some difficult words like "Chakravarti", 'British constitution,' "Rashtrapathi," etc., 25 seconds after injection of 1 c.c. of solution. The amount of drug in c.c. at which the patient's speech was slurred was noted. The amount of drug with which the patient slept, was also noted; and the last 1 c.c. of the drug being given after the patient slept. E.E.G. recording continued all the time for 10 more minutes after the last injection.
Sedation Threshold (S.T.) was worked out in the following way -

Wave amplitudes of bi-frontal tracings were measured. The amplitude of all waves of 15 to 80 cycles per second occurring in sequence of two or more were measured. The samples for measurement were taken from the period of 25 to 40 seconds and 0 to 10 seconds of the next period. Amplitude of wave during a period of two seconds showing the maximum fast activity was taken and the average was found out. This was then converted into micro-volts.

The following findings were noted:

The correlation between clinical tension and S.T. as well as that between diagnostic categories and S.T. was noted to some degree. The results were not statistically significant. Valuable information was obtained from follow-up tests. Out of the twelve patients, correlation between clinical improvement and clinical slurring was seen in 5 cases, whereas, in case of E.E.G. - S.T., 9 out of 12 showed good correlation — the consistency and reliability seemed to be promising. This shows the value of S.T. in the objective assessment of improvement and the efficiency of treatment.
Perez - Reyes and Chapel Hill (1968) conducted an experiment to find the differences in sedative susceptibility between types of depression.

Shagass et al. (1956) reported that psychotic depressed patients differed significantly from neurotic depressed patients in the amount of sodium amobarbital necessary to produce a specific end point of sedation. This end point was characterized by onset of slurred speech as well as by certain specific changes appearing in the EEG-frontal fast activity. Unfortunately, although this finding was later confirmed by Bouéreau (1958) and Nymgaard (1959), other authors tried to utilize Shagass' technique reported considerable difficulty in determining the Sedation Threshold (S.T.) point by the speech and/or the EEG criteria. The theoretical as well as the clinical importance of a difference in Sedative Susceptibility between types of depression motivated the present authors to investigate further this problem.

More than 1,000 in-patients, were clinically screened and evaluated by means of a psychiatric interview, from within this group large population 190 patients with depression as the primary symptom who fulfilled specific diagnostic criteria for either "neurotic" or "psychotic"
types of depression were utilized as experimental subjects. All patients were treated within the first four days of hospitalization and before any somatic treatment was initiated.

The technique for the determination of the GSR inhibition and sleep was as follows: With the subject lying comfortably in bed and after an initial rest period of five minutes duration, a slow continuous intravenous drip of normal saline solution was started and maintained for a second five minutes period to allow the subject to accommodate to the needle in his arm. Following this, the subject listens to and repeats a series of three grouped digits, such as, 676, 778 etc., played from a tape recorder at intervals of 20 sec. After three digit repetitions and without informing the subject, administration of sodium thiopentonal solution was begun. This solution was prepared individually in such a manner that injection at the rate of 1 cu. cm. every 20 seconds results in the administration of 0.5 mg./Kg. of sodium thiopental per minute. The injection of the drug was continued through the interval at which the GSR disappears and until the subject no longer responds to the digits and was pharmacologically "asleep." The amount of sodium thiopental in mg/Kg. of body weight necessary to completely abolish the GSR activity measured the GSR inhibition threshold and that necessary to reach a point at which
the subject no longer responded and was "asleep" measured the sleep threshold.

The following conclusions were drawn:

The group of neurotic depressed patients had the highest, the normal group intermediate and the psychotic depressed patients, the lowest GSR inhibition and sleep threshold mean values. The differences between any two of these groups were statistically significant (p<0.001).

In order to determine whether the increased susceptibility to sodium thiopental sedation occurring in the psychotic depressed patients was characteristic of the psychotically depressed process and not just an attribute to psychoses in general, the GSR inhibition and the sleep thresholds of 12 acute schizophrenic patients were determined. The mean GSR inhibition was 4.62 ± 1.475 mg./Kg. and the mean sleep threshold 5.05 ± 1.567 mg./Kg. Comparison of these values with those obtained in the psychotic depressed group indicated the presence of significant differences (p<0.001).

This result suggested that the low susceptibility to sodium thiopental sedation of psychotic depressed patients is characteristic of the psychotically depressed process and not of psychoses in general.

On the other hand, the decreased susceptibility to sodium thiopental sedation detected to occur in the
Neurotic depressed patients was not exclusive of them, and it appeared to be related to the presence and level of anxiety. Thus, 12 acutely anxious patients, which presumably had higher levels of anxiety than neurotic depressed patients had higher threshold values. Mean G.S.R. inhibition threshold was $5.99 \pm 2.907$ mg./kg. and the mean sleep threshold, $6.24 \pm 2.730$ mg./kg.

Parekh (1970) carried out an experiment using the Sedation Threshold test so as to evaluate the difference in sedation threshold (S.T.) if any, among normals, neurotics and schizophrenics.

A re-awakening of interest in the relationship between drug tolerance and personality differences has been witnessed during past two decades while Shagass' sedation threshold method provided a promising tool for investigating this relationship. Eysenck's analysis of differential drug susceptibility in terms of differences in central inhibition offers a broad continuum of frame work for further experimental study of the problem. It is felt that Claridge's technique can become a useful diagnostic tool. The modification employed of this technique needs confirmation of its reliability. On this background the present study was undertaken.
This study aimed to evaluate the differences in S.T. if any, among normals, neurotics and schizophrenics in both the cases of inter and intra group comparisons. Attempt was also made to find out the effect of variables like age, I.Q. and weight on S.T. in different diagnostic groups.

Thirty male schizophrenics (Simple = 3; Catatonic = 10; Hebephrenic = 4; Paranoid = 5; Unclassified = 8) were taken. Mean age 28.38 (years) ± 5.88; Mean I.Q. = 109.3 ± 4.1; Mean body weight = 109.6 ± 8.9. The duration of ailment ranged from 15 days to 6 years (13 with a duration of 6 months or less).

The neurotic group comprised of 27 patients (Anxiety State = 13; Neurotic Depression = 7; Obsessive-compulsive state = 2; Hysteria = 5). Mean age = 26.65 ± 5.00; Mean I.Q. = 105.6 ± 2.3; Mean body weight = 118.6 (lbs) ± 14.0. The duration of illness ranged from 15 days to 3 years.

The normal group consisted of 10 subjects. Mean age = 29.2 ± 5.2; Mean I.Q. = 113.7 ± 5.3; Mean body weight = 115.6 ± 13.5.

The educational level for all the three groups
The procedure followed for the S.T. experiment was that described by Claridge and Herrington (1960) with slight variations.

Analysis of the data revealed the following:

No significant difference in the mean S.T. among normal, neurotic and schizophrenic groups have been found.

Significant differences in the mean S.T. of normals and dysthyminic and normals and anxiety (states) patients were found.

Intra-group analysis of neurotics showed that there was significant difference between mean S.T. of Hysterics and dysthyminics, Anxiety state and Hysterics, Hysterics and Neurotic depressives.

There was a highly significant difference between the mean S.T. of Acute and Chronic schizophrenics.

Intra-group analysis of schizophrenics showed that there was a significant difference in mean threshold of simple and paranoids.
It was noticed that variables like age, I.Q., and body weight did affect S.T. in schizophrenic group as they were significantly correlated.

Further investigation in this line was recommended.