PROBLEMS IN METHODOLOGY.
CHAPTER - III.

Problems in Methodology :

I. Problems in determining the value of the findings obtained on the basis of the experiments on animals and also in their application to and extrapolations from the animal laboratory to the clinic. 83 - 89

II. Terminological distinctions and semantic differentiations, e.g., arousal; (i) Source; (ii) Uses. 89 - 97

III. Units of Measurement. 98 - 100

IV. Standard instrumentation and controlling the affecting factors. 100 - 102

V. Problems in relation to the selection of areas to be investigated in drug research 102 - 105

VI. Difficulties in relation to choice of measures. 105 - 111
All mental activities are the resultants of the integration of a person's psychologic and somatic functioning, as influenced by the world in which he lives. Thus, in many contemporary studies of behavior, we find one basic assumption common to all, i.e., behavior patterns of living organisms are related directly or indirectly, to events taking place in biological sub-systems within the organism. Evidence of the validity of this assumption now covers a wide territory from the demonstration of relations between gene-controlled enzymes and behavior dysfunctions, e.g., phenylketonuria (Garrod - 1923, as discussed by Uhr and Miller - 1960) to present studies of psychopharmacology (Miller - 1960), to their promise of major contributions to the treatment of mental illness.

Traditionally drugs have been used in the field of psychiatry mainly because of their possible use in therapy, and because they have been called upon, occasionally, to deal with complications arising out of their use, such as intoxication and addictions. Consequently, the bulk of research on such agents has consisted of therapy - oriented studies, the results of which are expressed in terms of
per cent "cured" or "improved", and interest in one drug or another has waxed and waned in parallel with initial optimism and subsequent pessimism regarding therapeutic results (Wikler - 1955 - 56). This is still true to day and such emphasis on therapeutic results has served to obscure the potential use of chemical agents in the development of a science of human behavior, upon which rational therapy, pharmacological and other might be based. And this interest in turn, has to be helped to bring forward the concept of 'experimental psychiatry' in literature (Wilker - 1955-56).

It can be sometimes contended (Rothlin - 1954) that since drugs alter behavior in an "un-natural" or "abnormal" manner, they can yield no information on how the brain functions "naturally" or "normally." The fallacy inherent in this objection can perhaps be revealed best by asking for a definition of "natural" or "normal" (Wilker - 1955-56). In what sense, as Wikler put it, are any of our experimental procedures "natural?" When and where, in nature, do nerve fibers become isolated in a saline bath, or does brain tissue become homogenized in a test tube?

In a very important sense, all of our experimental procedures are "un-natural" (Wikler), for experimentation involves controlling variables, and controlling variables involves alteration of "natural" phenomena in an "unnatural"
way. In other words, our conceptions of "normal" brain processes are constructions from observations of the effects of isolating variables in an "abnormal" manner, and such conceptions are continually subject to revision as new variables are discovered (Wikler), the alteration of which modifies behavior. In the accomplishment of this task, drugs which alter behavior can be used as devices for detection and manipulation of significant variables, for this is precisely the sort of investigation that is involved in explaining drug actions.

Although it is quite logical and readily accepted that the behavioral effects manifested by a drug are mediated by various physiological and biochemical subsystems, at our present stage of knowledge a considerable gap remains between the theoretical concepts used in physiology and biochemistry and those used in the behavioral sciences, and therefore, explanations available from the former two disciplines may not enhance understanding in the latter (Peterson - 1966). Thus, what Uhr and Miller mentioned in their book "Drugs and Behavior" in the year 1960, seems to hold good even to-day,. To paraphrase — the methodology of behavioral research has not yet reached the stage of sophistication and clarity of the physical sciences. As in the physical sciences we distinguish between the methods used in
applied and those used in pure or theoretical research, however, in the field of psychiatry, for instance, specialists frequently employ tests and experiments to assist them in the empirical manipulation of clinical problems, while at other times their principal interest seems to be the theoretical explanations or dynamic understanding of relationships. These two orientations should be distinguished, namely the empirical — manipulative one, in which the investigators are primarily interested in establishing the effects of certain agents on psychological processes and in the resulting qualitative data, and the theoretical — understanding orientation, in which they are mainly concerned with the clarification of action mechanisms of a physical or psychodynamic nature and with the elucidation of psychopathological phenomena as such. But in doing so, we encounter certain problems which may briefly be discussed as follows:

In the first half of the twentieth century although many techniques were developed to describe, analyze, control and predict behavior, most of the experiments were conducted on animal subjects and hence, there has been a great lacuna in determining the value of such findings in the field of psychopharmacology and also in its application
to and extrapolations from the animal laboratory to the clinic (Peterson - 1966; Thompson et al. - 1970). Studies of drug induced changes of behavior are usually based on visual observation and seldom are quantified, systematic or prolonged (Paton - 1962). In animal experiments mostly emphasis has been placed on changes in electrical phenomena, conditioning and instrumental responses (Abramson - 1957; Braceland - 1959; Featherstone and Simon - 1959; Otis and Bosley - 1960; Pennes - 1958; Whilelock - 1956, 1957). In neurophysiology and psychology also, as brought out in a symposium on First International Pharmacological Meetings, 1961 (discussed by Paton - 1962), that few attempts have been made to study the relation between the brain and spontaneous behavior (Brazier - 1959; Delafresnaye - 1954; Harlow and Woolsey - 1958; Jasper et al. - 1958; Jasper and Smirnov - 1960; Jeffress - 1951; Ramey and O'Doherty - 1960; and Wotslenholme and O'Connor - 1958).

One of the difficulties in interpreting the results of animal experiments lies in the fact that it is impossible to know how an animal feels. For example, after administration of a drug, an animal may cease to show signs of the fear which had been induced in it during a conditioning experiment. The explanation may be that the drug is a
true tranquilizer and has allayed fear selectively, leaving the animal virtually normal, or the animal might no longer show fear because it feels too ill or else has forgotten the recently learned routine, so that the whole situation is different (Laurence - 1966). Almost a similar view has been given by Pollard and others (1962). To paraphrase — when it is appropriate and essential that the initial bio-assay of psychoactive drugs is undertaken by animal experimentation, it is quite apparent that where the effects of the drug is going to be primarily on psychological functioning, animal studies have obvious limitations. Micro-electrodes placed in selective brain areas have indicated the locus of drug action, biochemical measurement has shown changes in neuro-humour metabolism, and behavioral changes — from gross observation of the animal to alteration of conditioning response patterns have been measured. But the final test of psychotrophic drugs has to be with human subjects, whose psychological functions can not only be tested objectively but also can give valid subjective descriptions of the drug effects. This is also important mainly because, as Laurence (1961), pointed out, that the problems involved in psychiatry are more difficult than in any other branches of medicines where animal experiments can often be devised to approximate human disease. Animal
experiments which throw light on the function of simpler nervous system should not be despised, although care must obviously be taken to avoid over-enthusiastic extrapolation from them to man.

Apart from this, we consistently seem to suffer from terminological problems and semantic distinctions and thus a consensus as to what behavior is, what type of behavior would be appropriate for drug research on human subjects (especially psychiatric patients) in laboratory conditions is not yet clear.

Similar problems arise regarding the selection of areas to be investigated in such experiments. Thus, let us take the concept of 'arousal' as an example. There are three sources with different methodologies and slightly varying notions that have contributed to the concepts of arousal.

First, the concept of arousal developed as an intensity with which behavior occurs. This is largely from the work of Duffy (1951, 1957), Freeman (1948) and others. The second, the "activation" referring to the level of alertness of the organism as derived from the work in neurophysiology and electroencephalography (Jasper - 1941; 1958; Moruzzi, Magous and others - 1949). And thirdly,
the concept developed through the learning theorist's search for a satisfactory measure of drive (Malmo - 1958, 1959; Grey - 1964).

Duffy, to start with called "energy mobilization" elaborating on the Cannon's (1929) use. According to Cannon it is during the intense emotions (e.g., fear, rage) the energy is mobilized in the body for the reaction "fight" or "flight"). For Duffy, energy mobilization need not be specific to emotion only. For every activity and behavior the underlying source is a level of energy. The speed and intensity with which responses occur are dependent on the level of energy inside the organism at that time. Energy mobilization is a dimension of the organism itself as all behavior can be characterized in its energy level. She was largely concerned with the general level of arousal in the organism through several activities rather than with any specific activity. Her concept is devoid of any "steering" function and is quite apart from the stimulus situation. The level of energy or arousal is varied during the several stages of the organism (from deep sleep to highly aroused state) irrespective of the stimulus situation which has got important effect on behavior. She also relied on muscle tension (1932) and Palmar conductance (Freeman - 1948) as measures of arousal. The main indices for
the measurement of this type of arousal have been chiefly through autonomic measures (Heart rate, Blood pressure, Respiration, Palmar conductance and Muscle tension).

Neurophysiological work through EEG findings first revealed that there is a pattern of wave characterizing the main psychological functioning from deep sleep to highly alerted state of activity (Jasper - 1941). It has been thought of as a good support to the theory of arousal as a continuum or dimension of behavior.

The discovery of Moruzzi and Magoun (1949), as we have already mentioned in previous chapter, of the reticular activating system as a controller of alerting mechanism, gave impetus to an increased number of work clarifying further the nature of arousal. With EEG the term is usually called "activation" (Lindsley - 1951). The continuum of activation or arousal is supposed to be largely the function of the cortical bombardment by the ascending reticular activating system such that the greater the cortical bombardment the higher the activation (Hebb - 1955; Malmo - 1959; Berlyne - 1960).

The French and the Soviet school of investigators of the Orienting reflex (Sokolov - 1963) distinguished two
kinds of reflexes: The first is called "alerting" or a surprise reaction (by Gastaut) and a "generalised" orienting reaction (by Sokolov). They are characterized by the higher frequency of EEG systems over the whole of the cortex, increase in arousal lasts for long and is quickly habituated.

The second is the "investigating" (Gastaut) or "localised" (Sokolov) reaction which results from the further repetition of the stimulus and habituation. The EEG synchronization is confined to the specific cortical areas, reaction subsides quickly and is more resistant to habituation. This appears to correspond to the specific projection system of the ARAS.

Behavior theorists (Lindsley - 1951; Hebb - 1955; Malmo - 1959; Berlyne - 1960) also found similarity between these two functions of the ARAS and the cortex and certain behavior in learning and other situations. Lindsley's "activation" pattern depending on the desynchronization in the alpha in EEG, - clearly referred to the general ("generalised" reaction) arousal pattern in the organism. Similarly Hebb's "arousal function" also referred to the general arousal level in comparison with his "cue function" referring to the localized reaction. If arousal, has a gearing function, cue function is that of steering the
arousal into a specific activity demanded in the situation.

Concept of arousal developed as a drive state by learning theorists is largely attributed to Hebb (1955), which was later greatly elaborated by Malmo (1959). Hebb first gave the idea of a general drive state of an organism distinguishable from the particular drive state and having its own effect on performance and learning. And this general drive level Hebb called "arousal function".

With this background in mind, one can distinguish several usages of the concept of arousal.

**Orienting Reaction**: (OR):

This is a part of arousal reaction arising out of any novel, conflicting or conditioned stimuli whereas arousal includes all these plus a general state of arousal of the organism along with those stimuli and several other conditions (which are known as determinants of arousal). It is to the generalized (tonic) orientation reaction that the level of arousal is more specifically related in distinct-\$t\$ with the localized OR.

**Activation**:

Though the terms activation and arousal are
synonymous, activation is usually in vogue with EEG and with theories of neurophysiological workers and behavior theorists. Most often activation is spoken as continuum, distinguishable on various activity by the EEG wave pattern.

**Anxiety:**

Anxiety as such arouses the various functions of the organism. Spence and Taylor equated this with drive level. Anxiety too has a continuum from low to high, having its effect on learning and performance. Having equated anxiety with drive, the inference has been drawn that anxiety and arousal are synonymous. More so because anxiety is generally constructed without having any particular stimulus and anxiety being an important character itself of every individual. But increase in arousal (psychological functioning) may not always give rise to anxiety, though arousal beyond its optimum level to an individual does result in anxiety. Hence, this is a question of individual difference.

**Drive:**

Increase and decrease in drive are synonymous with increase or decrease in arousal state. Drive is characterized by two functions: energizing and directing.
It is to the energysing part of the drive that the term arousal can be applied which varies independently of directive aspects. Moreover, any strong (intensive) stimulus (internal or external) induces drive (Miller and Dollard - 1941). Intensity of the stimulus is also a determinant of drive, as it is of arousal.

**Behavioral Arousal:**

The term is used by Malmo (1957), and later being supported by others (e.g., Duffy), which has more of psychological meaning emphasizing the total behavior and its states of arousal irrespective of the specific neurological and autonomic correlates. This is the meaning with which the present study deals. Behavioral arousal does not imply the outward activities (like shouting, running, etc.) which may even be the reverse of the internal arousal state or of the alerting, vigilant state of the mind referring to the general state of the psychological functioning (Duffy - 1957).

Apart from these, we also encounter problems in the selection of different parameters. Thus, e.g., increase palmar conductance and muscle tension was thought to be an increase in one's general state of arousal. Even now though this claim holds valid to a little extent, it has to
meet with several findings to the contrary. Both Lacey and his co-workers (1953) and Malmo and Shagaaås (1949) found individual differences irrespective of the situation in autonomic reactivity, or more specifically the differences in the different physiological measures. An individual may be a hyper-reactor in one measure (e.g., GSR) but in another he may be a hypo-reactor (e.g., heart rate). Hence, it may not be advisable to take any one measure to assess one's general arousal level, because, increased arousal in any one measure may not correspond to the other measures. The individual has his own measure of reactivity which has been called "individual — response specificity" or autonomic stereotypy by Lacey et al. (1953). Similar principle has been postulated by Lalloo and Shagaås (1949) which they call "Symptom specificity" or "Physiological specificity" as it is used later by Malmo (1959). While measuring autonomic and skeletal muscle functions in patients they found that cardiac patients responded to stress with acceleration of heart activity, hypertensive by rise in blood pressure, and patients with complaints of headache had a higher level of muscle activity in the fore-head than those without headache. From this they concluded that "stress" does not activate all physiological systems, but only the specific physiological mechanisms underlying the somatic complaints.
There are several experiments in this field which may be either specific to their particular study, or they need replication and confirmation with more number of studies employing the same condition, or the use of several measures together at the same time. It seems, the latter would need more sophisticated technical excellence in terms of the several amplifying units and recording devices. Duffy (1957), Malmo (1959), on the other hand, while discussing this problem mentioned that though the correlation is low among several measures of arousal the fact is that, there does exist a correlation which is positive, which shows an agreement amongst measures in direction. Moreover, specific measures taken may not be individual's specific reacting system, yet he does show a slight increase in that measure. Only the increase may not equal to his specific — reacting measure; but nevertheless, it is indicative of one's increased arousal. However, with fewer measures the inter-individual comparisons may be difficult but may not be so in case of intra-individual assessments.

Apart from the problem of how many measures of autonomic functions should be taken into consideration for an assessment of arousal there are many other problems associated with each measurement. In fact most of the studies undertaken by different workers with the same
measure become incomparable, shows divergent results and often conflicting, which may be mainly because of the lack of generally acceptable standardization in measurement. Nor would it be possible as yet to develop standard instrumentation and measures, with the fast advance in modern technology and electronics where each year with new improvements finds the previous instrumentation obsolete (Woodworth and Schlosberg - 1955). However, for each measurement there are certain factors which are known to affect and by recognizing these factors one may maximize the comparability of any measurement. For example, the G.S.R. First of all the use of different types of electrodes by different workers virtually minimizes any comparison. Now it is generally agreed that the silver-silver chloride are better ones as they minimize the polarization which may otherwise change either the voltage potentials or apparent resistance. The size of the electrodes and the area themselves affect the resistance. Hence, the need standard type and size of electrodes, similarly with the amount of current passed. (However, detailed discussion on these points may be found in Venables and Martin - 1967; Martin and Venables - 1966; and Woodworth and Schlosberg - 1954).

Another problem comes with the units of measurements used in such experiments. What are the meaningful
reliable and valid units of measurement (e.g., initial or and change resistance score in GSR? Systolic and/or diastolic pressure of blood?) The immediate concern is the Law of Initial Values. In the earlier works, generally measures of autonomic nervous system (A.N.S.) were taken after a presentation of stimulus. It was realized later that any A.N.S. response to stimulation is a function of the pre-stimulus level and it is a homeostatic function. This problem was first formulated by Wilder (1957). "This basic biologic law states that there is a specific inverse relation between the intensity and direction of a response to a stimulus, on one hand, and pre-experimental level of a function tested on the other" (Wilder - 1957). And the relation is homeostatic, the higher the pre-stimulus level of functioning, the smaller the response to a function — increasing stimulus,(e.g., G.S.R.: lower the initial value/"basal" or pre-stimulus level of conductance, higher the conductance to stimulus). Hence, the need for both the Initial and Response measures and to arrive at a score that is likely to be sound from the physiological point of view. Neither of these two measures can be considered alone. That is, one cannot compare the individuals with their initial levels, for which an initial score of 70 e.g., one may be asleep while the other wide awake. Similarly
with the response level which is directly related to one's initial level. These problems are of greatest complexity while interpreting skin resistance and GSR results.

Certain other factors which affect the results of such experiments are — temperature of the body, humidity, etc.

The temperature of the body affects the skin resistance. Kuno (as discussed by Martin - 1960) has argued that except the palms of the hands and soles of the feet in all the other areas in the body the sweating is caused by the heat. This means that sweating in all parts of the body (except palms and soles) cannot be the measure of arousal. Only in the palms of the hand and soles of the feet the sweating occurs due to sensory stimulation and mental stress. Still the effects of temperature in these regions on skin resistance have been investigated (Venables + 1955; S.B.G. Eysenck - 1956) and found to have certain effects on certain groups. That is, the relationship is found in neurotic group above an effective temperature of 66° F, but not in the comparable normal group.

Similarly the humidity (Venables - 1955), the diurnal periodicity (resistance more during night than the day) and
muscular tension (Freeman - 1948) are found to affect the skin resistance.

By controlling the above mentioned factors one can enhance the comparison and communications among the various studies with skin resistance. GSR has been taken as an example to convey the complex problems of measurement because of its high sensitivity, the widest usage and also as one of the measures of the present study. However, many problems exist in relation to other measures also which are being used for experiments conducted in laboratory conditions.

Apart from this, the greatest problem confronting one attempting to correlate the clinical action of drugs in mental illness with laboratory data is the lack of general acceptance of any single hypothesis for the pathogenesis of these disease. Indeed, even the diagnostic classification of disorders such as the schizophrenic reaction is subject to debate, (Eysenck - 1960).

Since the basic cause of most psychiatric diseases are unknown, treatment usually needs to be symptomatic (Dally - 1967). It is inevitable therefore, as Dally mentioned that, two or more drugs may sometimes have to be given concomitantly. An antidepressant drug such as
imipramine or phenelzine may improve depressive mood but fail to alleviate agitation or anxiety without the aid of a tranquilising drug. Schizophrenic symptoms will respond to a phenothiazine derivative but depression and anergia may remain and delay full recovery unless an anti-depressant drug is also given. Similarly it may be necessary to combine drugs with such physical treatment as E.C.T. or modified insulin. Psychotherapy and moral support particularly in treating neurotic conditions, will usually be needed in addition to drugs if maximum improvement is to occur (Dally - 1967).

Problems also arise regarding the methods employed or techniques used for the assessment of behavior. Several techniques have been devised for studying behavior of animals in relation to experiments with drugs. Although scientifically sound, most of these techniques may not be appropriate/valid for studying behavior of human beings in relation to experiments with psychotropic drugs (Peterson - 1970). Peterson has provided a succinct statement regarding the difficulties in using some of these techniques in case of human subjects. "Most of these methods although scientifically sound, lack a certain relevance to one of the major goals of psychopharmacology — that is, relating findings to the behavior of man — for he is an animal
notoriously malleable and subject to learning or conditioning effects. Man, for example, is not prone to audio-genic seizures nor does he spin web — Shakespeare to the country" (Peterson - 1970).

However, as the present study is mainly concerned with the behavior of human subjects (psychiatric patients) in relation to certain drugs used in this study, attempt will be made to discuss those techniques used for the assessment of human behavior while conducting experiments in laboratory situations.

Information on the behavior of individual may be obtained by three methods (Miller - 1960) mainly.

First one, of these may be called Introspection. A distinction however, should be made between naive inarticulate self-observer, the naive but sensitive and articulate person, and finally, the scientifically trained subject who is observing himself.

The second of these is known as observation by others. This is most commonly practiced clinical method. Again a distinction must be made between the data provided by the untrained and the sophisticated observer. Special devices such as rating scales and Q - Sort techniques, etc.,
are frequently employed to render the data obtained by introspection or observation of others more precise. But in doing so certain other difficulties arise.

A difficulty that arises in the observation method is the attempt to quantify certain characteristics observed in the behavior of the subject. No two raters may be equal in their assessment. Secondly, when subjects are asked to quantify their difficulties (e.g., use of Max Hamilton's Anxiety Scale, etc), how reliable is the patients' subjective measure? No two subjects may give equal judgement regarding this; how to eliminate their tendency to over-estimate their complaints or difficulties?

On the basis of symptoms when a case is diagnosed, it is quite likely that no two specialists may have the same opinion as regards the severity of the symptoms and hence, there may be differences in doses of drugs prescribed to the patients suffering from the complaints having same intensity. In this connection also mention may be made of the wide variation in "Optimum dose" which has been reported for all tranquilizing drugs and thus presenting another problem in research design (Koegler and Brill - 1967).

However, rather heroic efforts have been made,
as mentioned by Proteus (1957), by some devisers of rating scales of behavior to objectify their observerations. Ideally such scales are superior to those that make use of generalized subjective characterizations. But from the practical stand-point they require more detailed and faithful reporting by psychiatric aids. Moreover, the cataloguing and recording of overt incidents may give only the bare outlines of the behavior but none of the shanding (Proteus - 1957). We need, therefore, specific information as to what behavior traits have been changed through drug administration, and to what degree and in which direction.

The third method is known as Tests. Tests may be of different types depending upon the nature of the investigation done by the experimenter. Broadly these may be divided into the following aspects:

(a) **Psychological**:

The tests used for purely psychological investigation may be Projective methods — which reflect complex changes in a person's psychic functioning, such as Rorschach test.

The test may be of Psychometric type (Miller - 1960) for instance, the well known intelligence tests or
tests used for assessing other cognitive functions, e.g., memory, learning, etc.

Another type of psychological test procedure aims at the quantitative determination of basic psychomotor and perceptual functions, e.g., tapping speed.

Certain rating scales, questionnaires, etc., are also being used to know the personality aspect of the individual.

Still another method of testing a person's behavior involves physiological procedures which leave the patient quite passive as in studies of Polygraph recording of the autonomic responses of a person.

(b) Neuro-psychological and Electrophysiological :-

Recently neuro and electrophysiological techniques have undergone rapid advancements and have contributed importantly to the understanding of basic drug mechanisms (Peterson - 1970). When applied to the problems of psychopharmacology, neuro-physiological and electrophysiological studies attempt to elucidate drug effects on such disparate phenomena as the mass electrical activity of the cerebral cortex (EEG) in man to the action potentials of single neurons in the brains of animals (Peterson - 1970).
One technique, the neuropsychologist makes use of is ablation (Butter - 1969). An investigator can ablate a particular part of a nervous system of an animal and then study the resulting impairment or alteration in behavior. An important adjunct to this method is the study of behavioral changes in humans whose brains have been damaged or are diseased. By means of this techniques, it is possible to determine what parts of the brain are necessary for a particular kind of behavior to take place in a normal manner. For example, following ablation of a particular region of the brain, a subject does not respond to visual stimuli, one may conclude that this region of the brain is necessary for vision.

Another method which a neuro-psychologist uses is recording the electrical activity of the brain (Butter - 1969). According to current views, as discussed by Butter, the brain is a complex communication system in which the units of information are electrical pulses. The brain's electrical activity may be measured by placing probes, referred to as electrodes, on the surface of the brain or within the brain itself, and then amplifying the weak signals by means of conventional electronic amplifiers. This method has provided information concerning the physical
characteristics of neural messages and the pathways they follow through the nervous system. Moreover, by observing the behavior of the subjects while the electrical activity of their brains is recorded, it has been possible to infer what events occur in the CNS when subjects are in various states, such as sleep or waking.

Still another method used by neuropsychologists is Electrical stimulation of the brain (Butter - 1969). The brain not only generates electrical signals which may be recorded but is also responsive to electrical stimulation. An electrical current passed through an electrode implanted in the brain may cause the subject to respond in a particular manner. Depending on the site of stimulation, the behavior may be of different types. Electrical stimulation is thus an important technique for determining what areas of the brain control motivational processes.

There are still other techniques (Butter - 1969) that neuropsychologists have borrowed from the neural sciences. For instance, they use methods developed by anatomists in order to study microscopically the fine structure of the nervous system. By means of anatomical techniques one can, for example, trace the pathways over which sensory information is conducted into the CNS and,
determine the parts of the brain to which these pathways lead.

(c) **Pharmacocochemical Aspect**:

Another set of techniques involve the use of chemicals so as to assess behavioral changes following administration of certain chemical agents into the organism.

A number of chemical events take place within the nervous system, as in other body systems (Butter - 1969). Some of these are related to metabolic processes common to all body tissues. Other biochemical events which take place in the CNS reflect its own unique functions and are important factors in the regulation of behavior (Butter - 1969). In consequence, the study of normal CNS biochemistry is a valuable approach to the study of CNS. Moreover, the analysis of biochemical changes associated with different behavioral states and the effects of biochemical alterations on behavior are important research tools in the study of brain—behavior relationships.

It is apparent from the above discussion that the modern approach to the study of behavior is mainly from a neuropsychological point of view, hence, unlike any other branch of psychology, this approach is not restricted
to any one particular process. Rather it is a way of approaching a broad range of psychological processes. Thus, combination of different techniques seems to be helpful especially in an attempt to find out drug behavior interaction. Because if a drug has got single biochemical action, this action can be manifested in a number of areas in the nervous system. Despite these advances, however, the interpretation of neurophysiological data concerning drug action remains especially difficult, since even if a drug has a single biochemical action this action can be manifested at a number of areas in the nervous system.

Relating neurophysiological data to the behavioral actions of a drug is even more difficult, for it is not necessarily true that those structures which display the greatest electrical changes in response to drug administration are those which are related to the observed behavioral changes (Wikler - 1959; as mentioned by Peterson - 1970). This view has also been supported by Peterson (1970). "The drug-induced manifestations in behavior may be brought about by changes at chemical or anatomical levels which are not directly expressed as new patterns of electrical organization" (Peterson - 1970). In addition, regarding the usefulness of combining several of the characteristics of different techniques used for the drug-behavior interaction, Miller (1960) has mentioned that the classification
of exploratory methods used in psychopharmacology is rather simplified, and in practice one will frequently encounter experimental designs which combine several of the characteristics of different basic methods.

In the present investigation, not a single measure, but a multiple approach for the study of behavior has been taken into consideration. What Peterson has pointed out in the year 1970, seems to hold good even today that, "clinical research in psychopharmacology is not a homogeneous endeavor. There are many levels and each with its own purposes and goals." A detailed explanation of the different techniques used in this study will be given later, although each of the techniques used has its own limitation, each has its own purposes and goals, and hence the necessity of a multiple approach in a study of drug - behavior interaction. However, the essential factor which makes a research method scientific is the systematic approach, and the most important factors in determining the value of any particular method of investigation are its reliability, validity, its objectivity and practicability.