Psychopharmacology and Personality

JOSEPH ZUBIN and MARTIN M. KATZ

DRUGS occupy a unique place among the various factors which bring about changes in behavior. Relief from intractable pain, operative pain, psychotic and neurotic symptoms, seasickness, headaches, fatigue, boredom, the induction of moods, and the facilitation of learning and sleep are but a few of the alterations which psychopharmacological agents attempt to bring about.

The implications of these various drug effects on the physiology, biochemistry, and overt behavior of the organism have drawn research workers from many diverse disciplines to the field of psychopharmacology. The research literature, in the general area of drugs and personality, reflects interests in (1) behavior theory and personality measurement, (2) the nature of drug action, and (3) the interaction between these two, that is, the influence of personality factors on reaction to drugs and the effects of drugs on personality.

The study of psychopharmacology and personality change is very much in its infancy and suffers from a lack of sound, testable theory and adequate methodology to apply to its problems.

Personality Measurement

In a discussion of the effects of drugs on personality—or indeed a discussion of whether or not there is, or can be, any experimental evidence for such effects—the present vague status of the concept of "personality" has to be dealt with. Obviously, only a concept which is relevant to experimental investigation can be accepted for our purposes. Such a concept of personality must permit change and its detection. As everyone would agree, the concept of personality, as representing the unique pattern of behavior of the individual, is no more than a scientific model. If it has ceased being a useful model, we ought to discard it. If it is still useful in the study of behavior, it ought to be retained.

Traditionally, measurement in personality has been introduced at two different levels, depending upon the model of personality adhered to by the investigators. A review of the various scientific models proposed for personality indicates the following models: (1) differential, (2) clinical, (3) personalistic, and (4) neurophysiological. In the differential model, an analysis of behavior into traits is made first and then techniques are chosen for assessing these traits. The

---

Joseph Zubin, Ph.D: Department of Mental Health, State of New York; Department of Psychology, Columbia University, New York City. Martin Katz, Ph.D: Chief, Special Studies Unit, Psychopharmacology Service Center, NIMH, Bethesda, Md.


The preparation of this report was supported in part by NIMH Grant 1541. The authors are grateful to Miss Jean Andersen for her assistance in the preparation of this manuscript.

Psychopharmacology and Personality

JOSEPH ZUBIN and MARTIN M. KATZ

DRUGS occupy a unique place among the various factors which bring about changes in behavior. Relief from intractable pain, operative pain, psychotic and neurotic symptoms, seasickness, headaches, fatigue, boredom, the induction of moods, and the facilitation of learning and sleep are but a few of the alterations which psychopharmacological agents attempt to bring about.

The implications of these various drug effects on the physiology, biochemistry, and overt behavior of the organism have drawn research workers from many diverse disciplines to the field of psychopharmacology. The research literature, in the general area of drugs and personality, reflects interests in (1) behavior theory and personality measurement, (2) the nature of drug action, and (3) the interaction between these two, that is, the influence of personality factors on reaction to drugs and the effects of drugs on personality.

The study of psychopharmacology and personality change is very much in its infancy and suffers from a lack of sound, testable theory and adequate methodology to apply to its problems.

Personality Measurement

In a discussion of the effects of drugs on personality—or indeed a discussion of whether or not there is, or can be, any experimental evidence for such effects—the present vague status of the concept of "personality" has to be dealt with. Obviously, only a concept which is relevant to experimental investigation can be accepted for our purposes. Such a concept of personality must permit change and its detection. As everyone would agree, the concept of personality, as representing the unique pattern of behavior of the individual, is no more than a scientific model. If it has ceased being a useful model, we ought to discard it. If it is still useful in the study of behavior, it ought to be retained.

Traditionally, measurement in personality has been introduced at two different levels, depending upon the model of personality adhered to by the investigators. A review of the various scientific models proposed for personality indicates the following models: (1) differential, (2) clinical, (3) personalistic, and (4) neurophysiological.1 In the differential model, an analysis of behavior into traits is made first and then techniques are chosen for assessing these traits. The

---


trait theorists have approached measurement by assembling independent but additive factors of personality which they sought to identify and then measure. Their primary statistical tool is factor analysis. In the clinical model, normal personality is regarded as the central portion of behavior which in the extremes are psychopathological. The basic approach here is the identification of types of behavior over many dimensions and the attempt then to isolate the measures which characterize these types. These holistically oriented investigators begin with a totality and try to analyze it through measurement. The personalistic approach is geared to the single individual, considering each person as a separate universe. The neurophysiological approach is more like the differential, except that it deals with behavior reflecting brain function rather than with behavior reflecting organized traits. For the purpose of this study, measurement in the field of personality can be thought of as the attempt, first to isolate, but then to synthesize the dimensions on which the behavioral uniqueness of the individual rests.

No matter what organizational principles may be postulated (needs, traits, etc.), personality is inferred from behavior. It might be interesting to classify observable behavior into its parts in order to recognize that sector for which a concept of personality is useful. Behavior includes parts which are overdetermined by biology and hence highly predictable, for example, reflex action, imprinting, and other natively endowed behaviors. It also is composed of parts that are overdetermined culturally, for example, language, food habits, dress, etc. While these two types of overdetermined behavior are highly consistent and characteristic, they do not differentiate among individuals in the same social-cultural and biological subgroup, and hence are not useful in predicting individual systematic behavior. There is a third class of behaviors, which may be regarded as accidental or erratic and unsystematic, which are not useful in prediction. The rest of behavior may be sampled for its usefulness as measures of personality.

It seems that personality is here to stay no matter how much objectively minded psychologists may disdain it. Our problem is to find a suitable model or structure for it, which can be examined scientifically and from which testable hypotheses can be drawn. An evaluation of the present status of the concept of personality in drug research will be gained from the review of the methods now in use in attempting to measure the influence of personality on drug response and the changes in personality brought about by drugs.

Nature of Drug Action

Pharmacology is the study of the interaction of exogenous chemical agents (drugs) with the endogenous chemical substances of a living organism. Within the general body of pharmacology, the study of chemical interactions which involve the central nervous system is designated as psychopharmacology if those chemical interactions lead to changes in behavior, or, neuropharmacology if they lead to merely local neural changes.

Since the nervous system is itself composed of chemical substances, and is characterized by ongoing chemical processes, one can readily see why a knowledge of neurochemistry is so essential for the understanding of psychopharmacology. Unfortunately, the science of neurochemistry is also in its infancy, and the knowledge that is available requires
a high degree of specialization for its understanding. Consequently, many behavioral scientists are reduced to the status of watching a "blackbox" from the outside to note the effects of the exogenous factors that are added to it. Hopefully, this is only a temporary state in the preparation of research workers in this field.

In considering the variety of techniques which may be useful in gauging the effect of drugs on the behaviors which reflect personality, it is necessary to bear in mind that the drugs bring about their physiological effects through alterations in the biochemical milieu of the nervous system. Since we are not concerned with peripheral or segmental aspects of the central nervous system but with its higher centers—those which presumably are concerned with personality—we must look for techniques which measure behaviors altered by alterations in brain function.

**Review of the Literature**

The question of whether drugs are capable of producing changes of an enduring nature in the personality is still very much an open one. A definitive answer to the question will require less ambiguous evidence than is so far available. Most of what is known in this area is derived from studies in which drugs are administered on an acute basis (single dose) and the methodology which would be appropriate for assessing changes of any depth has usually been lacking. Methods of measurement developed in the field of personality have, however, made a contribution to our understanding of the mechanisms of drug action.

Studies with normals are characterized by an avoidance of the more potent tranquilizers, despite the fact that this class of drugs has had the greatest impact in the clinical area. This restriction is based partly on practical considerations. These drugs are more potent, can have more disturbing side effects, and their general effects are not as well understood as those of the older stimulants and sedatives. This is especially troublesome to the nonclinical investigator who may be using drugs to study other phenomena and prefers to confine himself to those drugs on which a good deal of information is already available. On the other hand, chronic studies, that is, drugs administered over extended periods of time, have usually been carried out by clinical investigators. Here it would seem that the opportunity for exploring the more profound effects on personality would be greater. Unfortunately, methods which would be appropriate for the investigation of such changes are usually not included in these studies because of the following: (1) the investigator's assumption that profound changes will not occur; (2) the lack of adequate methodology for dealing with the problem; and (3) the lack of training in experimental methodology of clinical investigators.

Results from clinical investigations of the tranquilizers and the work with the psychotomimetics would lead one to think that basic changes are certainly possible, and that there is a great need for the application of more appropriate methods. The problem is somewhat like that encountered in the investigations of the effects of psychotherapy. The field of personality suffers, in general, from a lack of adequate methodology for studying basic change. Inventories are influenced by factors which have nothing to do with the aims of these studies, that is, social desirability. The record of projective techniques in formal research is still not very laudable despite some of
the newer promising approaches to quantification, and the relating of performance measures to personality factors is still in a very early stage of development.

**Influence of Personality on Drug Action**

One relatively consistent finding is that atypicality of drug response and increased reactivity to drugs are related to "personality maladjustment." This stems from the work of von Felsinger, Lasagna, and Beecher in which maladjustment as measured with the Rorschach was related to atypical or unusual patterns of response to different drugs, from Kornetsky and Humphries' finding that extent of deviance as measured by several MMPI scales was positively related to the amount of subjective effect derived from a given drug, and that the factor of "neuroticism" on the Maudsley Personality Inventory is related to the likelihood of a toxic reaction to methympentynol. With regard to the problem of predicting response to drugs from personality type, van Ree was able to demonstrate a relationship between introversion-extroversion as measured by the Maudsley Medical Questionnaire, to type of reaction to LSD, though the data analysis is somewhat sketchy in this research. Introversion was more likely to lead to a "schizophreniform" (withdrawal) reaction under LSD; extroverts tended to react to LSD with a "manic" reaction. Klerman and Dimascio are using MMPI patterns along with several other indices to separate out two contrasting somatotypes, and have been successful to some extent in predicting differential reactions to drugs.

Individual "atypicality" of response to drugs is apparently almost as common as typicality. Von Felsinger, Lasagna, and Beecher found approximately 50 percent of subjects on such drugs as morphine, amphetamine, and phenobarbital produced atypical responses. The relating of personality factors to individual differences in drug response would seem to be, then, a natural direction for research in this area to take. For the most part, the techniques for classifying subjects into personality types have not been highly refined and the unresolved conflict between the holistic and the trait approaches tends to inhibit this kind of research. General traits, such as neuroticism, deviance, introversion-extroversion, look promising as predictors, but other more specific traits have not been experimented with to any great extent. The work of the Michigan group, which employed a large number of specific personality variables from the

---

4 C. Kornetsky and O. Humphries, "Relationship Between Effects of a Number of Centrally Acting Drugs and Personality," *Archives of Neurology and Psychiatry*, 77 (1957), 925-927.
MMPI, CPI, EPPS, and Cattell’s 16-PFT, was very discouraging in this respect. Despite some limited findings, careful analysis failed to relate any of the measures to drug effects.9

When one is attempting to link up a single trait with drug response he has, however, to contend with the fact that his subjects, though having one personality trait in common, are also likely to differ in other traits and thus make it impossible to relate the trait in question to the drug. This, in addition to the impreciseness of our measures of traits, makes this particular predictive approach highly tenuous. On the other hand, the holistic approach introduces another set of methodological problems. A personality type implies a pattern of characteristics. It becomes difficult to find subjects who match all of the required characteristics and difficult to set up objective criteria for determining whether they do. The holistic approach is usually forced to settle for less precision in the typing of people than it would like, which then makes it difficult adequately to test the predictive hypotheses. The more general traits, such as introversion-extroversion and neuroticism, seem to represent a compromise here and have in fact worked reasonably well as noted. The Klerman-DiMascio work and the patterning approach to the MMPI used by Heartzen and Hill and by Belleville10 with several types of psychopaths demonstrates, though, some real promise for the patterning approach.


Effects of Drugs on Personality

If work in the predictor area is still very much in an exploratory stage, results from research on the effects of drugs on personality are probably even less definitive. If we accept the assumptions that personality structure is highly stable and that drugs produce only temporary effects, one should not then expect drugs to produce any profound effects on personality. Most investigators in this area have learned to operate with these assumptions and, consequently, attention has been focused on the measurement of those aspects of personality which also have a somewhat temporary quality. These are the aspects of “mood” or “affect.” It should be noted also that the field is influenced by the pharmacological and clinical nomenclature of drugs which tend to emphasize the effect on mood as against other possible effects. The majority of psychotropic drugs are classified, for example, as sedatives, stimulants, tranquilizers, and antidepressants. Where the major interest is in the concept of mood, these drugs have become highly useful tools in its study. Nowlis and the group at Rochester (with the study of mood as a prime concern) have contributed to the methodology in this field by constructing an inventory to assess the various mood factors.11 The Clyde Mood Scale as another instrument of this type was developed specifically for the measurement of drug effects and has been used in a wide variety of studies.12 These inventories, because they offer added refinement to the measurement of subjective effects, tend to supplement older symptom questionnaires in


studying drugs and, in many cases, replace them. In the long run, their promise would seem to lie in their ability to provide data on differential mood patterns in reactions to various drugs, which should also help in refining the nomenclature. At present, there are little data of this type available.

Other promising approaches to the measurement of affect under drugs come from the field of verbal behavior. Gottschalk and Giesler have developed and partially validated measures of anxiety and hostility with the verbal sampling method and have demonstrated its sensitivity to the effects of perphenazine in reducing the hostility of patients. It has the advantage of avoiding some of the methodological difficulties of inventories and may provide some sort of bridge toward more objective methods in this area. Other work on verbal behavior is particularly relevant to problems in this area and will be gone into in greater detail later in the study.

As far as the concept of mood is concerned, we will probably always want to ask the patient how he feels after the administration of a drug, but given the difficulties with inventories, that is, halo effects, response sets, and the like, we would prefer to have other more objective indices of his affect state.

Mood, however, as Nowlis and Nowlis and Kubie point out is not al-

ways so temporary. We sometimes use the concept to denote a fairly stable characteristic of temperament. Kubie conceives of this more enduring mood concept as a basic emotional attitude, that is, pessimism or optimism. Do drugs have any effect on this aspect of personality? From what has been learned through acute (single) dosage studies, the likelihood is small. To determine whether changes of this type will occur under chronic administration, one would have to apply methodology from the personality area which is aimed at assessing durable change in the basic structure. This has not been done and the reasons may be tied to our lack of adequate methods.

Basic emotional attitudes, perceptions of and attitudes toward self and others, and mechanisms for dealing with anxiety are some of the fundamental characteristics of the concept of personality structure, and the available methods for measuring these phenomena have not turned out to be wholly reliable or satisfactory. This, of course, becomes a problem only if we think that drugs are at present capable of promoting such changes or that new drugs will appear which will force these issues. Clinical experience with chronic administration of tranquilizers has certainly raised these questions, and the psychotomimetics have produced profound effects in people, which, we must continue to admit, are not fully understood. These questions remain open.

The Testing of Theory

With regard to either of the central problems, the personality factors which

influence drug response or the effects of drugs on personality, we are presently forced to work with a great many unknowns. It may be that the technical problems of objective measurement in this field are less of an obstacle where the research is guided by an explicit and testable theory.

In this respect, Eysenck's work represents one of the few attempts to follow a program of research on drugs and personality which is aimed at systematic testing of hypotheses within an explicit theoretical framework. His theories of drug action, which are based on those of McDougall and Hull, have to do with the differential effects of stimulants and depressants on cortical excitation, and have resulted in a series of discrete hypotheses and experiments. There is broad and selective application of experimental psychological methods and the results have been very helpful in providing information on the effects of standard drugs on a wide variety of behaviors.

It is worth noting that the testing of his predictions failed as often as it succeeded in giving significant support to the predictions. It is difficult to attribute this lack of consistency in confirmation to any specific aspects of Eysenck's theory, but he seems to be operating with several questionable assumptions. For example, he oversimplifies the action of d-amphetamine and sodium amytal when he designates one a "standard stimulant" and the other a "standard depressant." As demonstrated in previous work with these drugs, they are not as consistent in their effects as he proposes. His tendency to work with very few subjects in most of these experiments only helps to exaggerate this problem. There is little sound information on the effects of these drugs on cortical excitation, and his assumptions in this area are again of a highly speculative nature and represent a somewhat oversimplified picture of neurophysiological processes. Nonetheless, the data add to our general knowledge about the effects of contrasting drugs on psychological functions and the systematic nature of the research program contributes to the needed theoretical stimulation in this field.

**Summary**

On the basis of previous findings, the question of the durability of the effects of drugs on personality still appears to be an open one. Drugs administered acutely produce only short-term changes. There is a need for more chronic dosage studies and a need for the inclusion in such studies of methods which are appropriate to measuring the long-term effects on personality. Personality measures so far have been more helpful on the predictive side than they have in the assessment of drug effects. This applies particularly to research in which general rather than specific traits have been related to drug response. More refined techniques are now available for measuring the effects on subjective mood, and objective measures of affect are becoming available. These techniques will assist in the specification of mood patterns for various classes of drugs and contribute to improvements in the precision of nomenclature in this area. The available data, then, do not provide definitive answers concerning personality change, but from this brief review of findings and methodological problems, it would seem that research which is guided by explicit theory can contribute

---

a more systematic base for the gathering of this information.

A Model for Studying Drug Effects on Personality

The Variables

The study of personality, concerned as it is with such phenomena as motivations, feeling, organizing principles of experience, and behavior, suffers greatly from a lack of adequate criteria with which to measure its characteristics. The history of personality measurement has involved a continuing search for those external behaviors which are most relevant to the understanding of the intervening internal phenomena. In seeking appropriate techniques of investigation in this field, the following elements require attention: (1) the behavior to be measured; (2) the environmental situation in which the behavior takes place; (3) the individual under observation; and (4) the chemical agent.

In a previous study a classification of the types of measurable behavior that can be observed under controlled conditions, and which presumably reflect brain function as discussed earlier, has been provided. By utilizing the classical categories of physiological, sensory, perceptual, psychomotor, and conceptual responses as the basic types of responses of which human beings are capable, it is shown that each of these types of responses can be found under each of the classes of stimulation, ranging from the idling state, in which no stimulus is applied, through energy stimuli and signal stimuli. (For the definitions of these terms see Burdock, Sutton, and Zubin, 1958).

The idling state is merely the initial state of activation present when the stimulus is applied—and can vary the entire gamut from drowsiness to extreme alertness. Energy stimuli refer to those stimuli whose physical energy is in some way related to the intensity of the response, while in signal stimuli no such relationship exists, the stimulus merely serving to trigger the response.

This, however, deals only with two aspects of experimentation—the stimulus and the response. In order to deal with the total spectrum of possibilities, not only the stimulus but all the parameters of the various facets which determine a response would have to be included. The variety of facets on which a response may depend are shown in the following equation based on Graham: \( R = f (S, R_c, I, O, H, \ldots, Xi) \), where \( R \) represents the response as a function of \( S \), the stimulus characteristics; \( R_c \), the receptor organ(s) on which the stimulus impinges; \( I \), the possible instructions for carrying out the task to be performed; \( O \), the possible states of the organism at the time the stimulus is applied; \( H \), the varieties of histories which may characterize the organism with reference to the task under consideration; and \( Xi \), possible facets which have, so far, gone unrecognized but which are needed to explain the residual but systematic variation.

Each of the facets consists of many possible parameters—for example, the stimulus facet consists of intensity, spatial extent, temporal duration, wavelength of energy, etc. Each experiment represents a selection from the Cartesian product of the multiplicities of possible parameters in each facet. If these pa-

---

20 Ibid.
22 J. Zubin, "Discussion of Introduction to Facet
rameters are sufficient to predict the response in a sample of individuals, we can end the equation with H. However, if a systematic residual variance appears which is not attributable to variations in the parameters of the facets, it may be necessary to introduce an additional facet of parameters, the X’s, to take up the slack.

It may eventually be discovered that these X parameters correspond to personality traits such as impulsiveness, anxiety proneness, and the like. If we eventually find endogenous factors such as components of body fluids, or exogenous factors such as past traumas which are the underpinnings of such personality traits, we would attribute them to the state of the organism (O) or to history (H), where they would rightfully belong.

It should be noted that only the first three facets—S, the stimulus properties; Rc, the receptor organ; and I, the instructional variables—are subject to direct manipulation by the experimenter. The state of the organism, O, is only partly under the control of the experimenter. Such factors as age, sex, and psychopathology cannot be manipulated, but subjects can be selected according to these parameters. The same holds true of H, the previous history of the organism with reference to the task at hand.

One of the valuable assets of the facet equation stems from the fact that we can titrate changes brought about through the drugs by means of alterations in values of some of the parameters in the three manipulatable facets—S, Rc, and I. Suppose a drug raises the threshold for perception of light; the increase in the intensity of light necessary to attain threshold value is in a sense a measure of the effect of the drug in terms of illumination units. Thus, the effect of the drug can be titrated by increases in intensity, or temporal duration, or area of stimulation. This titration may lead to an understanding of how and where the drug brings about its effects. By triangulating the drug effect against changes in intensity across modalities, or with temporal duration or spatial extent, deeper understanding of the biochemical nature of the drug and how and where it interacts with the neurochemistry of the organism may eventuate. When the response of the organism to various stimuli is examined while the organism is under the influence of a drug, some consideration of the new idling state produced by the drug must be undertaken. To distinguish such states from the unrestricted free idling state, the drug can be designated as a load and the new idling state under the influence of the drug can be referred to as being under a load. Thus, a load is a constraint imposed on the organism prior to measurement of the behavior being investigated.

If the drug is considered to be a stimulus and is the only stimulus used, no special problem is encountered, since a measure of a particular ongoing activity, such as blood pressure in the idling state, can be readily obtained and the change produced by the drug noted. A direct approach to the discovery of changes in behavior attributable to drug effects utilizes the idling state itself as the vehicle for detecting the change, and no new stimuli except the drug need to be introduced.

The introduction of a chemical agent may alter the idling state and also bring about changes in ongoing behavior. If
these behaviors are to be measured, in the spirit of this direct approach, they must be of a variety that does not need a controlled external stimulus for elicitation. Physiological activities fall into this category as do highly practiced behaviors such as conversation, writing, reading, walking, and swimming.

Physiological measures like blood pressure, heart rate, and similar vegetative functions have long been used as measures of drug effect, because severe changes in these functions are a threat to survival, and also because they yield good quantitative indices. In searching for conceptual changes induced by drugs, speech or verbal behavior can serve a similar purpose in tapping the conceptual level as do blood pressure and heart rate in tapping the physiological level. For this reason, studies of verbal behavior before, during, and after drug administration can yield meaningful data.

A Measure of the Conceptual Response

The utilization of verbal behavior as a measure of drug effects already has an extensive literature, although most of it deals with uncontrolled clinical observation. The parameters of verbal behavior which have been measured under drug effects are (1) fluency, (2) intelligibility, (3) grammatical structure, and (4) conditionability.

These, however, do not exhaust the possible parameters that could be employed. Frieda Goldman-Eisler has proposed additional variables concerning relative rates of speech and respiration, and the predictability of words in a given context. She has related changes in speech rate, breathing, and muscle tension to interview content. Certain relationships seem to have been found between the objective measures and stages of "catharsis or abreaction through talking." These relationships might be studied with respect to certain personality factors as well as with respect to the course of the psychotherapeutic process.

The parameters described above can be utilized in the evaluation of drug effects. An example of the application of some of these methods to the investigation of chlorpromazine is afforded by the work of Salzinger and his coworkers in the Biometrics Research Laboratory. It was possible to demonstrate a lawful reduction in rate of speech with increase in dosage in 25 mg steps in one normal subject. A comparison of the control conditions and the largest dosage condition (125 mg) in three other normal individuals corroborated this finding. On the other hand, a schizophrenic subject who had been reinforced for self-referred affect statements rather than speech in general (as had the normals mentioned above) did not show a decrease in speech rate but rather in affect statements. This suggested the hypothesis that chlorpromazine influences behavior only through its effect on the reinforcement which controls the behavior. A further effect of the drugs consisted of interference with the extent to which context controls the emission of words. Thus, the "intelligibility" of speech under the influence of chlorpromazine was lowered as measured by the Cloze Technique.

As far as the general conclusions of the study are concerned, it is reasonable to say that it demonstrates that greater stimulus control over behavior produces more lawful results in response to drugs.

The extent of control over the behavior is revealed by the fact that the normal subject who was reinforced for speech received the maximum number of reinforcements over all dosages despite changes in speech rate. There were relatively few degrees of freedom left for him to vary in and, therefore, little chance that variables, other than those applied systematically, would have any effect.

Further evidence for the point that more stimulus control allows the drug effect to reveal itself more lawfully has been found in weight judgment experiments. The time required for judging heaviness of weights varied more lawfully under conditions where a heavy weight had been introduced before each standard weight than when this anchor was not introduced.

A Measure of the Physiological Response

In the previous examples we dealt with the effect of chlorpromazine on an ongoing conceptual function—speech. Here the effect of increasing dosage is to interfere with the ongoing conceptual activity and presumably, if the dosage became large enough, greater and greater conceptual distortion would occur until finally the physiological component would overwhelm the individual and put him to sleep. Let us now examine the influence of the drug on an ongoing physiological function—pupil dilation and contraction. Ordinarily, the pupil diameter waxes and wanes to changes in light intensity (a sensory-physiological response), but it also responds to conceptual stimulation accompanying fear, anxiety, and the like. To the latter it dilates, but only light can cause it to contract. The contraction has been related to parasympathetic innervation while the dilatation has been related to sympathetic activity. When a low dosage (50 mgs) of chlorpromazine is injected in a normal individual, the diameter of the dark adapted pupil remains unchanged as compared to the predrug state.

However, repeated stimulation with brief light stimuli (1 millisecond in duration) prevents the pupil from recovering to its initial size during the interpulse periods of darkness. The undrugged pupil, on the other hand, can readily accomplish this recovery during the several seconds of the interpulse period. Otherwise, the pupillary response to the light pulse shows no differential between the drug and control states. Thus, even the small 50 mgs dosage of chlorpromazine, which requires fine biochemical tests for its detection, shows its effect on an ongoing physiological response.

A single, relatively high dosage of chlorpromazine used in the normal individual (125 mgs) causes profound sleepiness, slight ptosis, and other reportable side effects. From the point of view of pupillary measurement, the diameter of the pupil after thirty minutes in darkness is more contracted, or smaller, than in the predrug or idling state. However, the response to light stimulation seems to be the same as for the lower dosage. This would be consistent with a reduced sympathetic tonus which would tend to reduce the dilation of the pupil. Incidentally, the findings for acute schizophrenics, not under drugs, was that they are characterized by a smaller dark adapted pupil diameter than normals. In other words, schizo-

---

phrenics seem to show a reduced sympathetic tonus.

The Integration of Response Levels

Before considering the interdependence of the response levels in a total behavioral event, it is well to clarify some basic assumptions regarding the two extreme ends of the spectrum—physiological and conceptual responses. The physiological response is elicited by any stimulus which excites the central peripheral or autonomic nervous system. Physiological responsiveness underlies all levels of responses, but there is no reason to assume an identity between the physiological aspects and the total response. By conceptual responses, we mean responses based on previous experience—on the stored memories of the organism. This conceptual response must, to be sure, have neurophysiological concomitants, but its primary essence is its dependence upon prior experience. As one goes from physiological to sensory, perceptual, psychomotor, and conceptual responses, the importance of prior experience and reinforcement increases. Regardless of whether the stimulus is an external object or event, or an internal spontaneously occurring event, the conceptual response is highly dependent upon memory storage which, in turn, may depend on intricate neural or protein organization.

To understand the interdependence of response levels, we must consider the threshold response. Determination of absolute thresholds is usually regarded as belonging to the category of sensory response. The determination of the presence or absence of light or sound stimulation is a psychophysical process which has a long history and in practiced hands is said to yield results which reflect the sensitivity of the organism to such a high degree that variations in threshold determination have been attributed to fluctuations in the stimulus, rather than fluctuations in the response. More recently, however, Swets has pointed out that the absolute nature of the threshold is very much in doubt, and the very existence of thresholds has been questioned.

The redesigning of the classical threshold experiment to include “catch” trials during which the experimenter actually does not present a stimulus, provides a new perspective on threshold determination. Apparently, the number of times a subject gives an inappropriate response (that is, reports presence of stimulus when there is none, and vice versa) depends on the proportion of trials during which the stimulus really is or is not presented. For example, if the stimulus is presented in 90 percent of the trials, the expectancy created by the induced set is such that during the catch trials (when the stimulus is not presented) the subject will report it as present (false alarm) 62 percent of the time; but, when it is present, he will report it absent (misses) only 3 percent of the time. On the other hand, in a series of trials in which the stimulus is presented in only 10 percent of the trials, the comparable figures are 4 percent false alarms and 72 percent misses. The introduction of rewards for correct responses (saying yes when the stimulus is on and no when the stimulus is off) and of punishments for incorrect responses is another method for manipulating the results.

Apparently the expectancies experienced by the subject and his system of values regarding monetary or other rewards and punishments loom large in determining sensory responses. These are definitely conceptual components (based on memory storage), and hence sensory responses can no longer be regarded as independent of the other systems of response.

Now let us examine one situation where the conceptual and physiological responses have to coexist in order to bring about a given pattern of behavior, and where it seems possible to prevent this pattern from occurring if one or the other component meets interference. The reaction of a subject to a frightening object involves the entire spectrum of responses from the conceptual to the physiological. Thus, following the usual analysis the sighting (sensation and/or perception) of a fear-inducing object leads to an immediate appraisal of its dangerous character (conceptual—based upon prior experience) and is accompanied by visceral (physiological) excitation and leads to flight (psychomotor). The initiating sensory or perceptual response and the final psychomotor response seem to have been taken for granted by most theoreticians, but the relative importance and temporal sequence of the conceptual and physiological components have given rise to one of the classic controversies in psychology.

Attempts have been made to demonstrate the relative importance of these two components experimentally. Experiments by Maranon, confirmed later by Cantril and Hunt and Landis and Hunt demonstrated that the physiological response induced by an injection of adrenalin does not by itself yield a genuine experience of fear in which all the components are activated. Though the sympathetic discharge (physiological) common to strong emotional states was present (palpitation, tremor, face flushing, etc.) a full-blown emotional state did not develop (no psychomotor response), because conceptually there was no basis for it. The subjects knew the source of their physiological reactivity and did not have to "fear" it (conceptual) or run away (psychomotor).

A subject, however, can sometimes experience a genuine emotion after the injection of adrenalin if he spontaneously generates a conceptual response suitable to the occasion. Thus, one of the subjects reported "I seemed oppressed with a vague fear of something—"

33 Some disagreement regarding the psychomotor aspects of emotional behavior is raised by Bull (Nina Bull, "Towards a Clarification of The Concept of Emotion," Psychosomatic Medicine, 30 (1945), 210–214, and "The Attitude Theory of Emotion," [New York: Nervous and Mental Disease Monograph], No. 18.) in which the perception of an emotion producing stimulus gives rise immediately (through some organic linkage such as neural predisposition) to a motor attitude which then leads to the emotional state and to action (see Arnold, op. cit., vol. 1, p. 150). This has not been verified experimentally.

feeling much the same as when I’d lain awake all night, frightened that Bill might die." 88 In her case, a genuine fear seemed to have taken place.

An example of how the elimination or reduction in the physiological component will interfere with an expected response is the experiment of Schachter and Wheeler. 87 They induced the conceptual component (evoking stored memories) by a comic film which elicited laughter and euphoria in most people. They blocked the physiological response in one group by administering 25 mgs of chlorpromazine and contrasted the behavior of this group with another which had been given 1/4 cc of epinephrine solution (1:1000 solution of Suprarenin) and with a third group given a placebo.

The group which received adrenalin showed the highest degree of overt amusement or euphoria, the placebo group was second, and the chlorpromazine group showed the least amount of euphoria. Apparently, the sympathetic pattern elicited by adrenalin seems to be able to enhance the expressions of emotional states while the blocking agent (chlorpromazine) reduces it considerably. Thus, emotional expression can be brought under the control of chemical agents.

The contrast between the physiological and conceptual component has occurred in several other experiments, though the experimenters were not always aware that their work was focused on this problem. It has been known for a long time that such techniques as psychosurgery reduce the conceptual aspects of pain (anticipation, fear, anxiety), while the sensory threshold for pain remains unchanged. 89 More recently, Beecher has concluded that both placebo and active drug treatments are more effective in bringing about relief when conceptual components (stress and anxiety) are present, and are not as effective in relieving the simple sensory pain responses. 90 Similarly, Wikler and his colleagues have shown that morphine is more effective in reducing the tendency to overestimate pain induced by electric shock when considerable anticipation (through induction of anxiety or fear) of the pain is promoted by the experimenter. 91 When no anticipation of pain is introduced, morphine does not interfere with the accurate subjective estimate of pain as gauged objectively by the intensity of an electrical current. Here again, the conceptual component is the one which morphine seems to influence most, leaving the sensory aspects untouched.

The role of the conceptual or cognitive component is further stressed by Beecher and his coworkers. He found that 10 mgs of morphine increased subjective responses of friendliness in one test environment (in which the needs of the subjects were supported) and decreased it in another environment in which their needs were frustrated.

We can subsume the facts of social facilitation in drug studies under the conceptual component, since a subject’s awareness of his colleagues and their mood is probably based more on con-

88 Cantril and Hunt, op. cit., p. 303.
ceptual than on physiological factors. Whether the presence of others alters directly the biochemical balance within the organism and thus brings about a different interaction between the chemical agent and the endogenous chemicals within the organism, or whether the presence of others serves indirectly to distract the individual from paying as much attention to his inner goings-on or to orient the expression of his feelings regardless of his physiological responses remains a question for further examination.

Some animal experiments also throw light on the relative importance of the conceptual and physiological components. An example of the importance of the conceptual or stored memory component is afforded by Harlow's experiments with the mothering behavior of monkeys who are themselves raised on surrogate mothers. Though these mothers experienced the entire physiological cycle of gestation, they do not have the conceptual or stored memories of their own mother's behavior nor of play experience with their siblings. Without this conceptual component, they fail to care for their offspring. On the other hand, in Birch's rats, the mothers who possess the conceptual component fail to mother their offspring if the chain in the physiological component is broken by interfering with the self-licking sequence mechanically.

This was accomplished by placing a collar about their necks to prevent them from licking the fluids emanating from their vaginal areas during the gestation period. In their next pregnancy, when no such interference occurred with the physiological cycle, normal mothering behavior ensued.

Following the same pattern of analysis, Seymour Fisher has manipulated the conceptual component directly by varying the instructional variable or set in drug studies. He has shown that dextroamphetamine, compared with placebo, has its greatest effect in elevating mood and facilitating psychomotor performance when subjects expect to be aroused by the drug. When the same drug is given to subjects who think they are being given a depressant, there are no differences in effect between drug and placebo. Here again arousal of the conceptual component acts to make certain the appearance of the mood or the emotional state, and the arousal of a contrary conceptual component tends to reduce it.

Perhaps the waning of sexual arousal with age can be placed in this framework. While the conceptual component provided by visual, auditory, tactual, and olfactory stimulation may still operate, the absence of physiological reinforcement through depletion of endocrine supplies may eventually extinguish even the conceptual arousal. One wonders whether the rise in threshold for anxiety and other psychopathological feelings in psychosis after ECT, lobotomy, and some drugs may not reflect the same type of process—that is, reduction in the involvement of the sympathetic nervous system, with subsequent extinction of the conceptual component of anxiety.

---


depression, and the like. If we assume that the emotion of anxiety permeates the conceptual behavior of the patient, and that this conceptual anxiety produces reverberations in the physiological responses of the patient and sets up a vicious circle of mutual reinforcement between the conceptual and physiological component, it becomes possible to understand how interference with the physiological component may bring about a reduction in anxiety. If the conceptual response of anxiety continues, but the physiological component is reduced by therapy, the conceptual anxiety will eventually be extinguished for lack of physiological reinforcement. This, then, represents a direct attack on the physiological component in order to eliminate the conceptual component.

An example of a direct interference with the physiological component preventing a full-fledged emotion from arising may be inferred from the work of Steinberg et al. They... found that an amphetamine/barbiturate mixture markedly increased the exploratory behaviour in a Y-maze of rats which had not been in the maze before, but that the drug mixture had no such effect on rats which had had repeated previous experience of the Y-maze. It is possible that these differential effects could largely be accounted for in terms of fear reduction by means of the drug mixture: "inexperienced" rats were afraid of the new environment and, therefore, responsive to fear-reducing medication; "experienced" rats had presumably already overcome their fear of the environment, and so the drug mixture had no effect. Amphetamine/barbiturate mixtures are often used in psychiatry in the treatment of anxiety states. 45

From the point of view of the paradigm that we have presented for the interaction between the conceptual and physiological components, we may regard the failure of the "inexperienced" rats to show fear as the effect of an interference with the sympathetic arousal. The drug mixture prevented this arousal, and hence only the conceptual component (perception of the environment as strange and "potentially dangerous") was operative. Since the conceptual component alone is insufficient to evoke a full-fledged emotion of fear, the competing drive of curiosity took over, leading to the uninhibited exploratory behavior which is normally expected in a rat in a nonfearful new environment.

If we utilize the same paradigm it becomes possible to explain the extinction of the conditioned emotional response in rats, by postulating that chlorpromazine prevents the sympathetic arousal when the conditioned tone is heard. 46 The conceptual experience which the tone induces is insufficient to arouse a full-fledged experience of fear, and therefore the rat blithely keeps on pressing the bar as if it heard nothing. Similarly, the patient under chlorpromazine can experience episodes which ordinarily would arouse his anxiety but which fail to do so because the chlorpromazine prevents sympathetic arousal. It would, of course, be extremely enlightening if it could be demonstrated experimentally that chlorpromazine actually interferes with sympathetic arousal by direct recording of electric potentials.

By the same token, one may view psychotherapy as a direct attack on the conceptual component in emotional disorder. Once the conceptual component is reduced, it will in turn gradually bring

45 Hannah Steinberg, Ruth Rushton, and Christine Tinson, personal communication.
about the extinction of the sympathetic component because of the reduction in the interaction between the two. Behavior therapy perhaps is explicable on this basis. For example, the reduction of tics may be accomplished by separating the psychomotor response from its conceptual (anxiety) substrate. By repeatedly practicing the tic without the anxiety accompaniment, the link between the two can be eventually extinguished.47 Similarly, hysterical blindness can be eliminated by conditioning to light and thus breaking the link between the sensory-perceptual component and the conceptual fear or anxiety.48

To summarize, both the conceptual component of a given pattern of behavior or emotion as well as the physiological are necessary for the existence of the pattern. Thus, our analysis of behavior into the five components of physiological, sensory, perceptual, psychomotor, and conceptual responses seems useful, since it permits experimentation with each of these components so that the nature of the total response can be better understood.

The Individual Under Observation

The individual under observation is sometimes naively regarded as representative of all other individuals who might be selected at random. This is a tenuous assumption. First, the subject usually is a person who has volunteered for the experiment, and there is considerable evidence that volunteers may not represent the general population.49 Secondly, there is a tremendous difference among individuals in response to drugs.

One important source of variation in response to drugs is the subject’s own body chemistry. While drugs may bring about certain expected changes in most people, it should be remembered that the enzyme systems of individual subjects are quite distinct and may respond quite deviantly to certain ingested chemicals. For example, while most individuals will respond within given limits of tolerance to insulin, a diabetic may not show the same response. But even normal body chemistry shows considerable variation, as Roger Williams has shown.50 Just how these deviations affect behavior still remains to be determined.

In considering the individual under observation, one might liken the relationship between personality and drugs to the relationship that exists between personality and disease. The most tenable hypothesis today regarding mental disorder and personality is the hypothesis of independence, that is, that there is no relationship between premorbid personality and the occurrence of psychopathology.51 Once the disease occurs, however, the personality of the patient may determine the direction the disease will take. Similarly, the effect of the drug may correlate with the kind of personality the subject possesses.

Because of the difficulties presented by present-day typological approaches, it might be useful to eliminate them en-

tirely and substitute more empirically determined subgroups utilizing some new statistical developments along the lines indicated by Mahalonobis’ distance function. Since the Mahalonobis distance function is applicable only when the subgroups or types that exist in the population are already known, we cannot make use of this method. Instead, the test profiles of each possible pair of individuals in a given group can be compared and the standardized distances between these profiles computed over each of the tests in the profile. These distances may then be decomposed into discrepancies in shape and in level. On the basis of these two kinds of discrepancies, the whole population can be fractionated into homogeneous subgroups or types.

The Chemical Agent

The drug itself presents a series of problems with regard to measuring its effects on behavior. One of the stumbling blocks to research in this area is the lack of a universally accepted general system of drug classification. Tentative classifications have been based on either the chemical structure of the drug, the site of the drug action (acting on heart, thyroid, etc.), or its mode of action (anti-depressant, sedative, etc.).

Isolated knowledge of the chemical structure of a drug has been of little relevance for the psychopharmacologist until now. He has been more concerned with the site and mode of action, especially the latter. Unfortunately, research on the mode of action has revealed considerable variability among subjects, and such classifications are decidedly tentative and occasionally misleading.

One of the most serious drug problems is that of dosage. What may be a “load” for one person may be no load at all for another. The characteristic differences between individuals with regard to minimally effective dosage and maximally effective dosage may be likened to the effects of a snowfall on the landscape. If the snow is heavy enough (maximum dosage) it will cover the whole landscape uniformly and hide any individual differences in its parts. If the snow is not sufficiently heavy, though it falls on all parts alike, the forms it assumes are, to paraphrase Thoreau, “as various as those of the twigs and the leaves which receive it.” In submaximal dosages, the personality of the subject may be a more important predictor of the behavioral change than the drug itself.

Perhaps the effects observed in the middle range of dosage, between little or no drug and maximum dosage, is the resultant of the two contending forces which we have described earlier—the conceptual and physiological. In the lower dosages, the conceptual factor, induced either by the instructional variable, or by spontaneously generated expectancy, may be the prepotent factor. As the dosage increases, the physiological and sensory responses begin to play more and more important roles. Finally, when the maximum dosage takes effect, the role of physiological and sensory responses are fully in command. Perhaps, we will some day find that the point of inflection in the dosage curve indicates some sort of balance between the two factors contending for control of behavior, the conceptual and the physiological components. This conceptual

---

84 Kornetsky and Humphries, *op. cit.*
component especially when triggered systematically from within, may be the personality characteristic with which this chapter is concerned. For low dosages, personality is in command regardless of the nature of the drug. For the maximum dosage, the physiological component takes over regardless of personality.

Dosage curves have to be developed for each individual to determine the range of change in behavior characterizing a given individual. These dosage curves may differ from person to person in level of dose necessary to bring about a given change in performance and in the shape of the dosage curve. It is necessary to find a way of grouping people into homogeneous groups with regard to these dosage curves and the distance method suggested previously may prove suitable.65

At the present time, because of the lack of knowledge about drugs and because of the lack of knowledge about personality, drug investigations are limited to a specific type of behavior investigated with regard to a specific type of drug, without the scope necessary to transcend individual function and individual drugs. As our knowledge increases, greater scope can be given to these investigations. Apparently dosage curves are superior to single measurements with single dosages.

But dosage is only one of the factors to be taken into consideration in producing a given effect. Leake suggests the following formula: 56

\[ I = f \left( \frac{D_{a}}{\tau_{b}}, P, S \right) \]

Where \( I \) = intensity of the action of a chemical on biological material

\[ D = \text{dosage expressed in terms of mass of chemical per mass of living material} \]

\[ \tau_{a} = \text{rate of absorption and distribution of the chemical through the living matter} \]

\[ \tau_{b} = \text{rate of detoxification or excretion of the chemical from the living matter} \]

\[ P = \text{physical chemical properties of the chemical which really determines the activity of the chemical on living material} \]

\[ S = \text{the specific and peculiar characteristics of the living material concerned, including its organizational status (in terms of macromolecules or ecological milieu), its age, its metabolic state, its "allergic" sensitivity, its pathological status, and such integrating factors as enzyme symptoms and sex.} \]

All of these factors are capable of precise scientific study and the expression \( D(\tau_{a}/\tau_{b}) \), the product of the dosage by the ratio of the rate of absorption and distribution to the rate of detoxification and excretion, gives the concentration of the drug in the living tissues at any time after administration. It is this concentration, with its mass action effect, according to Leake, which is a predominant factor in drug action.

New Directions and Prospects in Psychopharmacology

In contrast with the rather continuous progress made in pharmacology under the impetus of the sudden appearance of the tranquilizers and energizers, the progress in psychopathology has been rather meager. The psychopathologist has apparently been caught off guard. While pharmacology and psychopharmacology have made great practical strides forward, the strides in personality measurement, for example, are notably absent.

Why has there been so little progress in the development of the relationship

---

56 Zubin, Fleiss, and Burdock, op. cit.
between pharmacology and personality? Pharmacology is undergoing a revolution. Until recently, progress in the discovery of new drugs depended on chance only. While this is still true, certain principles have been developing as guide lines for the synthesizing of new compounds that are predicted to have certain properties. One of these principles is the antimetabolite principle, which may be briefly stated as follows: There are a certain number of chemical substances which are vitally essential to metabolism. If any of these vital compounds is missing or in short supply, normal processes fail to occur. Sometimes an excess of the vital substance also interferes with normal processes. It has been found that if the chemical structure of one of these metabolites is changed in any one of several defined ways, the molecule which results is not able to substitute for the metabolite in living processes. Instead, this new substance has the capacity to evoke in the organism the specific signs of deficiency of the metabolite which it resembles. It is as if it serves as an inadequate key in the lock of the metabolic process. It gets stuck in the lock and prevents the genuine metabolite from entering and opening the door to the progress of the metabolic process. Such antagonists, or antimetabolites, can be used to control an excessive amount of the metabolite, for example, antithyroxine for the control of excess thyroxine.

Another principle is that of biochemical individuality. In brief, this principle states that an examination of the biochemistry of each individual would reveal reliable and consistent differences between individuals which could be found useful in the classification of people into relatively homogeneous subgroups. Another emerging principle is that of regional organization of the neurochemistry of the nervous system. In contrast with the earlier studies of brain function in which the brain tissues were macerated and chemical tests applied to the resulting mass, the newer approach rests on the hypothesis that the brain is compartmentalized, and that the particular site of a chemical reaction in the brain is equal in importance to substrate and enzyme activity in determining outcome.

While these new principles seem to keep the field of pharmacology stirring, the field of personality measurement has reached a static plateau cushioned by factor analysis on the one hand and by psychodynamics on the other. In contrast with the revolution in pharmacology, personality is in the doldrums. Results from research on the effects of drugs on personality are, therefore, not very definitive.

It seems that we have gone as far as we can go with the present methods of investigating personality through psychometric methods (inventories and rating scales) and perhaps also through psychophysical and other experimental methods. Perhaps our stimuli penetrate the web of personality only superficially and not with sufficient reliability. The individuality of the person is lost in a maelstrom of insufficiently reliable indicators produced by tickling his epidermis. New methods are required. It might be possible temporarily to replace psychophysics, on the basis of which much of our testing is done, and clinical methods, through which most of our classification is done, by psychochemistry. If we could begin to cluster people

---


58 Williams, op. cit.
into subgroups in accordance with the changes that occur in their ongoing behavior under various dosages of specific chemical substances, we might strike at a deeper layer of personality. These new subgroups, obtained through the clustering on the basis of similarities in shape and level of dosage curves for a variety of selected chemical agents, on a variety of ongoing naturally occurring activities like conversing, writing, walking, or engaging in other highly practiced activities, might serve as new starting points for the investigation of like-structured homogeneous subgroups.

With the similarity of response to drugs in these basic activities established, we could begin looking for other variables which a given like-minded group of individuals may possess in common and thus provide a new typology to replace the present unsatisfactory personality variables by means of which we attempt to classify people or predict change. The kinds of stimuli which we utilize now in our experimental approaches to assessing personality are evanescent. Intermittent light for flicker fusion, tachistoscopic exposures for concept elicitation, inkbLOTS for mental content, and the like, merely touch the surface of behavior. They can hardly evoke as much response as a drug which influences the total nervous system. Perhaps after we have discovered the natural lines of cleavage in human populations through psychochemical methods we can return to a study of the psychophysical and psychometric functions that now hold the field.

Conclusions

Our survey of the relation between psychopharmacology and personality change has forced us to realize that neither of these two fields is sufficiently defined to enable us to make definitive conclusions regarding their interaction at the present time. Both fields are themselves at a low level of articulation and any attempt at studying their interaction is very hazardous.

We have not yet reached an integrative state in psychopharmacology, nor in personality or in their interaction. Perhaps we never will. As the Abbé Galan said without discouragement, “Science is plutôt destiné à étudier qu’à connaître, à chercher qu’à trouver la vérité.”

On the positive side, however, we have drawn up a model based on some of the assumptions and definitions arising from the observations that the literature and our own work have provided which may have heuristic value. Let us regard the behavioral change accompanying any drug dosage as an interaction between the ongoing brain activity present when the drug enters and the effect of the drug. We can relate the former, the ongoing brain activity, to the conceptual or cognitive component, that is, memory storage, which, if it is systematically characteristic of the individual, may be designated as personality. The immediate drug effect on the brain may be equated to the physiological, sensory, and perceptual aspects of behavior. As the dosage rises from 0 to a maximum, the role of the conceptual component declines and the role of the other components rises. That is why it is so important in drug research to specify the state of the organism, its environment, and the ongoing conceptual trend, as well as the dosage. When these factors are specified, it becomes possible to in-

tegrate observed results that now seem contradictory under one model. This includes such events as the contradictory effects under various instructional and situational variables, placebo effects, and drug effects which will elicit hostility in one situation, friendliness in another, elation in still another, and apathy in still another.

The model of the interaction between the conceptual and other components permits a systematic investigation of testable hypotheses which may accomplish for our generation what psychophysics accomplished for the gay 90's. But we must not dally too long. Let us hurry up and develop psychochemistry while the drugs still work!

CRITICAL EVALUATIONS

The Status of the Personality Model

PETER B. DEWS, M.D.: Harvard University, Department of Psychiatry

The personality model has not been, and does not promise to be, useful in understanding behavioral effects of drugs.

PERSONALITY is inferred from behavior, say the authors. "Obviously only a concept which is relevant to experimental investigation can be accepted for our purpose." In these unambiguous terms we are notified from the start that we are dealing with an essay in an area of science whose major spokesmen have precluded the possibility of ever being proved wrong. The revealing exchange with Eysenck, for example, leaves the impartial reader with the impression that Eysenck is safe, by his own criteria, from refutation.

Pharmacology, Behavioral Pharmacology and Psychopharmacology

Although the title is "Psychopharmacology and Personality," the authors really deal with pharmacology and personality. The authors discuss principles of pharmacology and their relevance to personality changes due to drugs, rather than principles of psychopharmacology. More specifically, they discuss behavioral pharmacology (since this is a scientific essay) in relation to personality changes. The theoretical formula of Leake for the intensity of a drug action is putatively applicable in pharmacology in general. Even the idea that a drug may effect conceptual and physiological substrata of personality and lead to opposing effects is familiar in pharmacology, in the guise of drugs that are said to have direct and indirect effects. It is well, of course, that general principles of pharmacology be given due regard. It is also desirable that the particular principles of behavioral pharmacology be given
their due regard, especially when we are discussing matters such as personality, which can only be inferred from behavior.

One principle of behavioral pharmacology is indeed stated clearly and repeatedly: the effect of the drug depends on the ongoing activity. Why do the authors not go further and consider how particular attributes of the behavior—its temporal patterning, the intensity level of the particular activity, the exact contingency relations of the behavior with stimuli, and other factors revealed by modern behavioral pharmacological work—relate to personality determinants?

I think there are two reasons. The first is that most of our understanding of behavioral pharmacology has come from experiments on animals. When people consider personality they tend to narrow their views to studies on human subjects. Yet, most of what is said in this study on pharmacology, and all that is said in some sections, for example, that on antimitabolites, derives from work on animals. This is rightly considered relevant. By the same criteria, the effects of drugs on behavior in experimental animals is relevant.

The second reason is less obvious but more important. It derives from the implicit assumption that while personality can only be inferred from behavior, there may yet be systematic and recognizable changes in personality, due to drugs, that can be recognized and studied independently of the study of changes in behavior; indeed, that systematic relationships may be revealed in personality changes that could never be recognized from studies of mere behavior. The authors themselves use an analogy: blood pressure, heart rate, and similar vegetative functions are useful physiological measures, just as certain behavior changes are useful because they are measures of personality changes. However, a physiological pharmacologist would not think of a drug effect on blood pressure or heart rate as a “measure” of the drug effect. It is the drug effect. He would be concerned thereafter with mechanism—whether the receptors for the drug were in myocardium, carotid sinus, or medulla oblongata—not with what inferred inner physiological system the drug effects “measured.” Reversing the authors’ analogy, the behavioral effects of drugs are the effects and the interpretation of these effects in terms of personality is useful only if it deepens understanding and helps generalization. I agree with Zubin and Katz that the concept of personality is no more than a scientific model that must justify its retention by its usefulness.

The Personality Model in Behavioral Pharmacology

The burden of justification thus falls on the proponents of a personality model interpretation of behavioral effects of drugs. Even though the concept of personality may linger on, objective scientists have the right, not merely to disdain it, but to ignore it if it is not useful. Zubin and Katz do not cite a single example which illustrates the usefulness of the interpretation of a drug effect in terms of an effect on personality. They classify the drug effects in terms of level of observed behavior and class of stimulus; the implication is that classification in terms of personality variables is not useful at the present time. Moreover,

---

they suggest that we may have gone as far as we can with present methods of investigating personality, so that the forecast for the future is dismal. The inescapable conclusion is that the personality model has not shown itself to be useful. Did Zubin and Katz come to the same conclusion but hesitate to be churlish and state it baldly? It may have been difficult to do in a chapter titled “Psychopharmacology and Personality” in a book titled Personality Change.

In questioning the value of the personality model in behavioral pharmacology we are not denying that hereditary and experiential factors may influence the behavioral effect of a drug. Genetic psychology and experiential determinants of patterns of behavior are becoming active fields of study. Such work will, we hope, lead to generalizations and conceptions—a model, if one chooses to call it such—useful in understanding behavioral effects of drugs. Such a model, derived from experimental results, would deal with many of the problems for which a personality interpretation is now sought; but the model will be so different from current personality models that it would be a travesty to consider it a neopersonality model, especially since its development will owe nothing to personality theory.

Some Comments on Pharmacology

The consideration of psychological topics is excellent, as is to be expected from these authors. The treatment of peculiarly pharmacological matters is less authoritative.

First, there is a matter of definitions. Probably no neuropharmacologist would agree that his job is merely to study local neural changes that do not lead to changes in behavior. Rather, neuropharmacologists study the neural substrata of behavioral effects of drugs; the behavioral effects are the effects of the drugs, and the mechanism is neural. Of course, we may likewise regard the changes in the brain as the effects of the drug. The mechanism then becomes the physicochemical reaction between cell and drug, which in turn has an atomic mechanism, and so on. Mechanism in pharmacology is a very relative term. As for definitions, as a matter of usage the term psychopharmacology seems to have been preempted by people working in clinical situations; experimental scientists prefer to call themselves behavioral pharmacologists.

The reviewers suggest an explanation of effects of amphetamine-barbiturate mixtures on the behavior of rats in a Y-maze as interference with sympathetic arousal by the mixture. Pharmacologically, amphetamine is a sympathomimetic drug, and barbiturates do not antagonize sympathomimetics; so the suggestion of interference with sympathetic arousal is not merely gratuitous but contrary to the relevant information on the drugs. Indeed, the justification for dragging anxiety into a discussion of the experiments is too tenuous to be worthy of an attempt at interpretation.

The reviewers quote with approval the antimetabolite principle. The principle is exceedingly appealing. However, it should be indicated that not a single major pharmacological agent has resulted from application of the principle. Reserpine, the phenothiazines, imipramine, and related drugs—meprobamate, chlor Diazepoxide, and lysergic acid diethylamide—all owe nothing to the principle for their discovery. Matters may change in the future, but one begins

---

to suspect that the principle may be yet another idea that was plausible, worthy of careful evaluation, but ultimately not useful.

**Conclusion**

The authors have put all people interested in behavioral pharmacology in their debt by their careful and sympathetic review of the mutual effects of drugs and personality factors. That the review was sympathetic makes their seeming conclusion the more convincing: that the personality model has not been, and does not promise to be, useful in understanding behavioral effects of drugs.

**The Function of a Model**

WAYNE O. EVANS: U. S. Army Medical Research and Nutrition Laboratory, Fitzsimons General Hospital, Denver, Colorado

The only criteria for evaluating frameworks of analysis are pragmatic applications and the aesthetic needs of the individual.

The authors have presented, in essence, a taxonomic framework of behavior designed to serve as a map for the location of particular variables existent in psychopharmacological research. This map can be thought of as a three-dimensional set of coordinates:

1. Level of behavioral analysis
   a. Physiological
   b. Sensory
   c. Perceptual
   d. Psychomotor
   e. Conceptual
2. Class of stimulus
   a. Idling state
   b. Energy variables
   c. Signal variables
3. Element of investigation
   a. Behavior measured
   b. Environment of measurement
   c. Individual studied
   d. Chemical agent administered

By the use of these coordinates, a particular experiment may be conceptually located within a systematic framework of analysis.

A danger arises from the presentation of any such systematic framework, and particularly from the one so well articulated and convincingly presented as in the present article. This danger is the tendency to reify the model. Although the authors correctly note that the function of the model is heuristic, it is all too easy for us to forget that alternative frameworks could as justifiably be developed to encompass the various observed relationships between drugs and behavior.

The function of a systematic frame-
work is to provide an investigator with a language system for the description of variables of interest to himself. If an investigator has a framework explicitly enunciated, it aids him in describing, relating, and remembering observed relationships. Its utility, however, stems solely from its applicability to concepts of use to the particular scholar. The framework itself is never true or false in an absolute sense; it is useful only for a given purpose.

The present article proposes a framework of description which can be of great use to an experimental psychologist. On the other hand, an individual with other interests might propose a system based on concepts such as ego strength or libidinal drives with equal rigor and justification. Ultimately, a particular scholar must ask himself: "Which descriptive framework is most useful to me in order to talk about, think about, and remember the observed relationships I believe to be important?" Pragmatic applications and the esthetic needs of the individual are the only true criteria for the evaluation of such frameworks of analysis.

Drug Effects and Stimulus Control

The authors mention that situations can exist in which greater stimulus control over behavior can produce more lawful results in response to drugs. It would seem only fair to note that the converse may also be true. Situations can exist in which an overdetermination by external stimuli can completely mask the behavioral expression of drug action. In a recent experiment, Hawkes and his colleagues demonstrated that an effect of drug action on the judgment of short-time intervals could be found using the "method of production"; whereas, when the "method of reproduction" was used, no drug effects could be observed. The methods of "reproduction" present an external stimulus of a given temporal length to which the subject responds by a behavioral estimate. On the other hand, in the "method of production" the subject must respond solely on the basis of internal cues in producing an estimate of the passage of time.

Thus, in this particular case, the addition of external stimuli so overdetermined the response that the subtle effects of the drugs on inherent "biological clocks" could not be observed. Only by depriving the subject of his external supports for time judgment could the effect be demonstrated. Unfortunately, once again we note a situation-drug interaction which will not allow us to make any general statements. The role of stimulus control in drug experiments will depend on what we are trying to measure. Part of this apparent complexity may be an outgrowth of a lack of clarity in the definition of the term "stimulus control."

Summary Comment

In evaluating the present manuscript as a whole, one can not help but be impressed by the logical structure developed by the authors. Their delineation of the various complexities and the enormous number of variables, important to psychopharmacology, is an important contribution to a field that has too often assumed a simple interaction between

Toward a Systematic Psychopharmacology

DANIEL X. FREEDMAN: Professor and Chairman of Psychiatry, University of Chicago

All behavioral or physiological effects of drugs that are observed by design, prescience, or fortune must further be investigated in terms of the underlying mechanisms in order for us to attach meaning to the congeries of findings. Much more empirical data is necessary; generalization is not yet the privilege of psychopharmacology.

PSYCHOTROPIC drugs should eventually reveal significant information about the way behavior is organized, since these drugs alter the factors which normally control behavior. The normal ranges and values of signals governing behavioral sequences, their duration, intensity, and patterning, can clearly be altered by chemicals; these agents affect the operation of various interacting biochemical sequences and, thereby, the chemical milieu in which numerous component systems of neurones operate. Psychopharmacology was, barely a decade ago, more a hope than an area of inquiry; progress in empirical work has been astounding. While the basic controls normally regulating neurochemical, neuronal, or behavioral systems are barely discernible, the identification of central biochemical sequences (if not their precise controls) has advanced. The regional and fine structural characteristics of these biochemical systems (and their differentiation and partial independence from classical neuroanatomical systems) are becoming rapidly mapped. Further, drugs have revealed that there are chemical controls over certain components of such basic behaviors as eating, drinking, and mating. If it is permissible to cite clinical evidence, largely and unfortunately omitted by Zubin and Katz, psychotropic drugs have revealed that the organization of deceptively familiar behaviors—such as sedation—is far more complex and interesting than once was assumed; the associations and dissociations of which the nervous system is capable are revealed, if only in the observation of behavioral sedation in the presence of psychomotor activation, as with the tranquilizers. Our notion of the appropriate time base over which to monitor rates of change of behavior subsystems has been enhanced by observing...
sequences of changes occurring with antidepressants or with lithium in mania (in which psychomotor activity often shifts several days or weeks prior to changes of mood and the “conceptual” organization and direction of behavior). There are interesting sequences of interactions of neurobehavioral systems consequent upon chemical changes; analysis of these components of behavior is as likely as systematic changes in physiological or biochemical response to reveal the significant dimensions for which behavioral science searches under the rubric of personality. Neurochemically differentiated dimensions of behavior are revealed in the different chemical and behavioral response to certain psychotomimetics. A response of heightened awareness with diminished control over input occurs with LSD-25, mescaline, and congeners or with toxic doses of amphetamine, drugs which affect brain serotonin and norepinephrine. There is an amnestic and confusional response to, or sleep deprivation resulting from, cholinolytic compounds such as atropine or Ditran, which shift levels of acetylcholine, but not the indole or catecholamines. Basic sequences and components that organize behaviors are becoming segregated and identified. In the process questions arise, concepts are to be reexamined, and methods devised that are appropriate to the development of a systematic psychopharmacology.1

Such a development requires empirical data—a lot of it—and data gathered with some systematic intent. This gathering must be guided, not only by theory, which at every level in neuro-psychopharmacology is frequently evanescently grounded, but by the problems posed by preceding experiments. This means that intensive study of a single drug is often necessary before one can sort facts of basic importance from trivial findings. The ability to recognize the difference requires experience with the variables and contexts involved. In view of the multiple relevant disciplines and their rapidly changing status, few well-grounded and experienced workers are as yet available.

Basic to the appreciation of a systematic psychopharmacology are facts which even medically trained persons too often forget. Every drug has an action on bodily systems; no drug effect is, or could be, simply confined to behavioral effects. No differentiated behavior is controlled simply and solely by biochemical changes; whether mood or the response of isolated gut is observed, surrounding conditions influence response. Even the much misunderstood placebo response to a bioactive agent can be investigated in terms of mechanism, duration of action, and the prior and concomitant characteristic response; the role of anticipation in a condition—for example, pain—plays a role in the probability of placebo response. Moreover, what is true of one drug and condition, as morphine and pain, will not likely be true of another, as chlorpromazine and schizophrenia. Generalization is not yet the privilege of psychopharmacology.

In addition, dose, route, and rate of administration and intrinsic rates of change of the neural or behavior subsystems under study will affect response just as much as purported personality variables. These variables, incidentally, appear to have been the most difficult to specify empirically—more difficult, for example, than crude somatotypes or reaction-disposition variables. Items and clusters and typologies, which to even relatively unbiased clinicians appear to

---

lack validity, evoke the suspicion that they are mysterious by-products of test instruments and mathematical treatments because they are in fact rarely tested for their dynamic role or function in an ongoing system. In biochemistry it is possible to fracture cells into any kind of component fractions; but multiple approaches (microscopic, biochemical, biophysical, pharmacological) are required to reconstruct the appropriate fractions and elements in order to emerge with a picture of structure-integrated function. It would seem mandatory in psychopharmacology that any physiological or behavioral effects of drugs that are observed by design, pre-science, or fortune be further investigated in terms of the underlying mechanisms in order for meaning to be attached to the congeries of findings. The wishful hope that drug-induced physiological or biochemical changes would quite simply reveal systematic personality differences is yet a hope. As yet, there is no empirical evidence that individual differences at the biochemical level are behaviorally consequential.

If pharmacological data are useful to this field, it is clear that at times a different dose of the same drug should for practical purposes be considered a different drug. In the rat, for example, a dose of chlorpromazine a thousandfold less than is required for grossly observable effects can block the observable effect of LSD, while normal dosages will compound and confound the effects of LSD. Prior state is probably the most crucial variable to control; the dose of amytal required to sedate an excited catatonic could be lethal to a normal person. The cardiovascular response to chlorpromazine can be quite different in schizophrenic populations than normals, as shown by Yates and Kornetsky, and the behavioral response to phenothiazine similarly differs according to prior state or population variables. Finally, behaviors are built up of complicated sub-sequences of response and, as Zubin and Katz note, subjective perception of change is consequential to changes observed in man. Why man is so sensitive to drugs, why lower dosages are usually required in primates than in submammalian creatures, why addictive behavior is vastly easier to create in man, why long-term changes in personality can be induced in man (as with alcohol addiction), has not been systematically investigated, although these questions are important to a systematic psychopharmacology.

I remark on these matters because I am not in sympathy with either the approach or the emphasis of Zubin and Katz. At the same time, I have used their article in teaching and appreciate their effort. The article is clearly written, valuably documented, and courageous in its conception of psychopharmacology, but it is generally irrelevant to the critical problem of advancing substantive knowledge of psychotropic drugs. It is not problem-centered, nor is it mechanism-centered. It is method-centered, and restricted at that. With its stress on models and theory and an entirely premature urge to generalize—not about one, but all drugs—it is hardly the article required by psychologists skilled in experimental design but untutored in the intricate by-ways of chemical-behavioral interactions. Our lack of systematic empirical knowledge in sufficient depth, either at the level of pharmacological action or behavioral effect, about even a few common drugs—morphine, certain barbiturates, amphet-

---

2 For expositions of signal detection theory, for example, see Goldiamond in Solomon, op. cit.
amine, let alone alcohol—indicates the gap between these well-intentioned schemes and the "front lines" of the struggle between ignorance and information. It is all too tempting to treat drugs as an independent variable easily manipulated by shifting dosages. One then merely produces the "appropriate" measures of personality, cleverly inserts the "proper" condition into the experimental design, and proceeds to crank out data, the interpretation of which can rest on whatever scheme of pharmacodynamics happens to be popular at the moment. This is certainly not what the knowledgeable authors intended, but this is what I find students frequently believing.

The facts of life in psychopharmacology have not been conveyed in this article. It is not sufficiently stressed that each drug presents different issues and special substantive problems and research questions; it is from this structure of sequences of empirical data that the critical questions with which psychopharmacology will be concerned will be derived. It will not do simply to apply the well-worn methods of personality testing to drugs and build thereby a generative discipline. There is the lure of oversimplification in treating a drug as a stimulus, since its various stimulus qualities, its functions as a condition or state in sequences of behavior, become lost over time. It is tempting to forget that "personality" measures devised for one purpose may not tap the valid sequences of controls that determine results at another time or in another context. I am positive that the authors do not need to hear this, since they speak to these points at various, albeit scattered, junctures throughout the article. The formulae they cite contain the relevant parameters that cause such practical difficulties. However, I would rather see a clear-cut acknowledgment, even in their basic definitions, of the fact that neuropharmacology is basic and important to psychopharmacology, and I would revise their definitions as follows: The consequences to behavior of local neural and chemical changes that can be detected with appropriate design and technique comprise psychopharmacological studies. Those operations directed to measurement of neural or chemical parameters of drug action comprise the work and knowledge of neuropharmacology.

Such a consistently and firmly held viewpoint would encourage less causal interpretation of pharmacological parameters relevant to drug effects, and less sanguine generalizations and oversights. For example, drugs have different periods of action: the knowledge of these may indicate whether one is dealing with primary or tertiary consequences of the interaction of drug and organism. It is not true, as the authors suggest, that tissue concentration of any drug is a reliable index of the appropriate period of drug action. A common sedative barbiturate is concentrated in the testes, a fact which may or may not have behavioral relevance.

Zubin and Katz survey approaches to the objective study of personality excellently. That the authors themselves do not in fact provide a basis from which research strategy and tactics in psychopharmacology can be derived is a fact stressed only because one feels at times that they are loading themselves with such a burdensome task. We still need essays that will attempt the following: When and why a particular population should be selected for study; whether highly controlled and designed
behavioral studies should precede basic pharmacologic data; whether drug action on a specific neurochemical system is similar or different in different species, and how such differences or regularities might be related to effects; whether designs, tests, and questionnaires should be generated for the specific drug tested; whether groups of drugs or a single drug should be tested extensively and why; what dose ranges are relevant and for what substantive question; what use should be made of clinical data or the data of experiments of direct tests and observation or of "reflective inquiry"; and when during an experiment this should be done.

The fact is, the field is not quite ready for this article. However, as experts on the effects of particular drugs begin to compile systematic studies, we should make useful instruction available to investigators as well as hypotheses that characterize a mature field.

Drug Responses and Personality

KARL RICKELS, M.D.: Associate Professor of Psychiatry, University of Pennsylvania

The authors' breakdown of behavior analysis into five components is not very useful to the clinical psychopharmacologist. The fact that something is easy to measure does not mean that the results from such measurement will be meaningful to the clinician or theoretician.

To discuss the whole area of psychopharmacology and personality from all its various aspects is a most difficult task. The authors have certainly, within the space limits allotted to them, performed a most formidable and comprehensive task.

Though I realize that all the areas of personality and their relationship to psychopharmacology could hardly be covered fully, I still feel that the authors have treated many relevant areas too cursorily. I refer particularly to the attempt to analyze behavior into traits by factor analytical approaches, spearheaded by such a researcher as Raymond Cattell. The area of states vs. traits vs. neurotic symptomatology needs a much more extensive study and discussion. One of the reasons for not discussing this area more intensively is probably the paucity of published research that has used factor analytic methods in the evaluation of drug effects.

The area of personality and its effect on drug action is a very complicated one. The lack of any real definition of personality makes a discussion even more difficult. For example, it could be shown that certain personality variables, such as compliance, hostility, dependency, ego strength, and even verbal intelligence, effect drug and placebo responses differentially in controlled clinical trials.
A still unsolved problem for the clinician is to predict which personality type will respond best to a given drug. Different personality types, traits, profiles, and predictor and demographical variables will effect drug response differently and often cancel each other out in their effect on treatment outcome. One variable may further and the other may decrease drug response.

Most psychophysiological laboratory studies investigate areas easily measurable by present-day methods, such as driving behavior, general performance, motor performance, stress response, cognitive and perceptual functions. Such areas are interesting from a theoretical point of view, but may have little meaning for the clinical psychopharmacologist. The fact that something is easy to measure—for example, tapping speed—does not mean that such a measure will provide meaningful data for the clinician or even the theoretician.

One also wonders whether these measures give more information about response styles than about personality aspects. For example, studies carried out with tranquilizers in normals, particularly college students, may provide results that are meaningless for the understanding of the action of drugs in the anxious neurotic patient. The student with a high Taylor Anxiety Scale may be a quite different individual from the highly anxious neurotic patient with many neurotic symptoms. Drugs that produce a decrease of performance in the “normal” may produce improved performance in the highly anxious patient. Thus, it is most important to study drugs in the environment in which they are to be used clinically.

Turning to the discussion of drug effects on personality, one again notes the lack of a definition of personality. Are mood scales really personality measures or are they not? Is personality changeable, and can it be altered by drugs? Or is personality stable, uninfluencable? One wonders if, in the purest sense, personality should be stable and not be altered significantly by medication. If one agrees with Kubie that even certain mood patterns may be “stable,” indicative of a characteristic temperament structure, one should not expect great change through drug therapy. On the other hand, many mood measures are personality symptoms, not measures, and easily influenced by treatment. The response to treatment, as measured by different mood measures, may well depend on such a composition of scales. If a mood measure is symptomatically oriented and measures flexible mood, a result can be expected. If a mood scale measures temperament and constant behavior, not much effect of drugs can be expected. The basic questions are: What aspect of the “observed behavior” or “personality” is permanent? What is a long chronic adjustment period? What is produced, or exaggerated, by the emotional problem of the neurotic patient?

The authors’ suggested breakdown of behavior analysis into five components—physiological, sensory, perceptual, psychomotor, and conceptual responses—is not as useful to me as a clinical psychopharmacologist. For me, personality aspects such as hostility, dependency, anxiety traits and states, and ego strength have greater clinical and theoretical meaning for the understanding of drug responses in neurotic patients.

In summary, I should like to congratulate the authors for their most interesting and thorough presentation. My com-
ments are not intended as a criticism of all aspects of the authors’ presentation, which is excellent. They should rather be considered to be my reflections on the whole area of drugs and personality and its meaning for psychiatry from the viewpoint of a psychiatrist and clinical psychopharmacologist.

On Drugs and the Person

EBERHARDT H. UHLENHUTH, M.D.:
Associate Professor of Psychiatry, Henry Phipps Psychiatric Clinic, Johns Hopkins Univ., Baltimore, Md.

The authors may be too pessimistic in suggesting that the usual psychometric methods, such as inventories and rating scale, have exhausted their usefulness. It seems that our measuring instruments may be serviceable, but our concepts at once too vague and too narrow.

Many of the issues raised by Zubin and Katz are central in current psychopharmacologic research. Recent clinical studies increasingly suggest the value of considering the response to medication as an interaction between the effects of the drug and the personal characteristics of the patient.

Some of these studies imply the “differential” model by quantitatively assessing selected patient characteristics. In this approach the total response to medication is viewed as the sum of several partial responses, each related to a measured characteristic of the patient. This model finds mathematical representation in multiple regression or multiple correlation techniques. Another group of these studies implies the “clinical,” holistic, or typologic model. In this approach the drug response is viewed as a function of the patient’s membership in a group. The patient’s membership in such a group is established by comparing his descriptive profile on a number of measured characteristics with “standard profiles” established for each group under consideration.

The typologic approach to predicting an individual’s response is limited by the number of types defined. The alternative approach, weighting his scores on a number of continuous measures in accord with previous experience, offers greater flexibility in predicting the response for any individual. In this sense,


the second method approximates in principle the "personalistic" model which is so natural to the practicing clinician.

Both approaches consider drug response in relation to different patterns of personal characteristics. The more limited success of earlier investigators in relating single traits to drug response suggests that a more complex description of the person, in terms of an integrated group of characteristics, is useful in understanding the interaction between the drug and the person.

Perhaps Zubin and Katz are too pessimistic in suggesting that the usual psychometric methods, such as inventories and rating scales, may have exhausted their usefulness for the time being. In the light of more recent successes, it seems that our measuring instruments may be serviceable, but our concepts at once too narrow and too vague. The advent of the electronic computer permits the application of comprehensive quantitative formulations and compels precise specification. Hopefully, these new capacities may help to resolve the problems, especially acute in complex psychological situations, of joining together adequate concepts and methods in the same investigation.

Zubin and Katz note that the definition of "personality" remains a central and thorny issue. The studies cited above describe patients primarily in terms of the symptoms they exhibit at the start of drug treatment. The relevance of such descriptions to studies on the influence of personality upon drug response hinges largely on the usual assumption that psychopathology partly reflects the patient's personality. Zubin and others have challenged this assumption. Psychopathology, as embodied in the usual clinician's diagnosis, often fails to correlate with drug effects, with Overall's descriptive types, and, indeed, with the diagnoses of other clinicians. These considerations suggest that it is premature to dismiss the possibility of relations between psychopathology and premorbid personality before viewing the results of more sensitive studies.

The concept of personality offered by the authors, in connection with their "Model for Studying Drug Effects on Personality," deserves some comment. They leave the reader with the impression, perhaps unintended, that the formal aspects of conversing, writing, walking, or other activities constitute descriptions of personality. These, like all responses, reflect the interaction of personality and situational variables, including drugs, at the moment of observation. However, it is difficult to see how the particular responses suggested should provide a clearer index to personality than do moods or attitudes. Why not apply to such "conceptual" responses the ingenious idea of determining characteristic dosage curves?

More impressive, perhaps, is the authors' failure to discriminate between response and response tendency, a distinction nicely made by Cattell. Surely the notion of trends or qualities relatively stable over time is central to any concept of personality and crucial to studies of drug effects upon personality. From this viewpoint, the "effect of a drug upon personality" implies, at the

---

very least, some change in response
tendencies persisting over a period far
beyond the discontinuation of the drug.
In the authors' terms, this could mean
a stable shift in the "idling state" or in
the characteristic dosage curve for some
response. This requirement is no more
than we ask of any other treatment (situ-
tional variable) purported to influ-
ence personality.
Adequate studies of such effects re-
quire relatively lengthy and intensive
follow-ups of subjects, like those em-
ployed in evaluating the psychothera-
pies. Perhaps such studies might at this
stage of the game be best conducted in
conjunction with intensive psychother-
apy, as suggested by Ostow. The path
toward solutions for this and other prob-
lems presented by Zubin and Katz cer-
tainly will lead through some fascinat-
ing aspects of both psychopharmacology and
personality study.


---

**Summaries**

**Zubin, Joseph,** and **Katz, Martin M.**:
"Psychopharmacology and Personality"

The behavioral change accompanying
any drug dosage can be regarded as an
interaction between the ongoing brain
activity and the effect of the drug. The
former is related to the conceptual com-
ponent which may be designated as per-
sonality. As the dosage rises from zero to
a maximum, the role of the conceptual
component declines and the role of other
components increases. That is why it is
so important in drug research to specify
the state of the organism, its environ-
ment, and the ongoing conceptual trend,
as well as the dosage.

**Zubin, Joseph, et Katz, Martin M.:**
"Psychopharmacologie et Personnal-
ité"

La modification du comportement qui
accompagne tout dosage de drogue peut
être considérée comme une interaction
entre l'activité cérébrale en cours et
l'effet de la drogue. La première dépend
des composantes conceptuelles qui peu-
vent être désignées comme la per-
sonnalité. A mesure que le dosage aug-
mente de zéro à un maximum, le rôle des
composantes conceptuelles décroît et le
rôle d'autres composantes augmente.
C'est la raison pour laquelle il est si im-
portant dans toute recherche sur les
droges de préciser l'état de l'organisme,
son milieu ambiant et la tendance con-
ceptuelle en cours, aussi bien que le
dosage.

**Zubin, Joseph, y Katz, Martin.:** "Psico-
farmacología y Personalidad"

El cambio en el comportamiento que
acompaña a cualquier dosificación de
drogas puede ser considerado como una
interacción entre la actividad cerebral
en curso y el efecto de la droga. Aquélla
está relacionada con el elemento conceptual que puede ser designado como la personalidad. A medida que se aumenta la dosificación, desde cero al máximo, el papel del elemento conceptual disminuye y el papel de los otros elementos aumenta. Por ese motivo, es tan importante en la investigación de drogas, precisar el estado del organismo, su medio ambiente y la tendencia conceptual en curso, así como la dosificación.

Zubin, Joseph, and Katz, Martin M.: "Psychopharmakologie und Persönlichkeit"

Die Änderung im Benehmen, die eine Begleiterscheinung jeder Arzneidosierung ist, kann als eine Wechselwirkung zwischen der stattfindenden Gehirntätigkeit und der Arzneiwirkung angesehen werden. Erstere ist verbunden mit dem begrifflichen Einzelteil der als "Persönlichkeit" gekennzeichnet werden kann. Während die Dosierung von Null zur Maximalquantität ansteigt, nimmt die Rolle des Begriffsbestandteils ab, während die Rolle der anderen Bestandteile ansteigt. Daher ist es in der Drogenforschung so wichtig, den Zustand des Organismus, seine Umgebung, die derzeitige Begriffstendenz, sowie auch die Dosierung zu spezifizieren.

Zubin, Розеф и Кац, Мартин М.: "Психофармакология и индивидуальность"

Изменение в поведении сопровождающее любую дозу лекарства может рассматриваться, как взаимодействие между продолжающейся мозговой деятельностью и результатом принятия лекарства. Мозговая деятельность связана с компонентом понятия, которое можно назвать индивидуальностью. По мере увеличения дозировки от нуля до максимума, роль компонента понятия уменьшается, а роль других компонентов увеличивается. Именно поэтому так важно в исследовании лекарства точно указывать на состояние организма, на окружающую его обстановку и на продолжающуюся тенденцию понятия, а также и на дозировку.