DRUGS AND PERSONALITY
I. THEORY AND METHODOLOGY

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INTRODUCTION

FEW people would be inclined to underrate the actual, and, even more, the potential contribution which the study of the effects of drugs on personality can make to psychiatry. The large number of research papers in this field contributed both by psychiatrists and psychologists bears witness to the interest in this field, as does also the testimony of Freud, who is reported by Ernest Jones to have given it as his opinion that in due course pharmacological treatment of psychiatric disorders would oust all others.

When we compare the potential usefulness of drugs with our present knowledge of their effects, and the clinical use made of them at the moment, we cannot but note the wide gap which separates expectancy from achievement. Empirical studies there are many, but they are frequently contradictory and bedevilled by many experimental, statistical and methodological errors. Clinical applications show frequent failures to obtain expected results, and a general difficulty of predicting the reactions of individuals to the given drugs, to say nothing of the eternal problem of dosage. The present position, therefore, cannot be regarded as satisfactory either from the research or the applied point of view.

The writer has elsewhere suggested that personality tests and methods of treatment can be grouped according to whether they derive from notional, empirical, or rational considerations (10). *Notional* in this context is taken to mean a procedure which is based simply on a hunch or a vaguely felt analogy. A procedure is called *empirical* when there is some independent evidence that it does what is claimed for it, although any theoretical background there may be for such a procedure is purely *ad hoc*. A procedure is called *rational* when it derives through a more or less rigorous process of deduction from an empirically supported and theoretically integrated set of postulates, theorems and axioms. The same terms may be applied to the study of drug effects, and it may be claimed that in this field also progress has been delayed by the prevalence of notional and purely empirical studies, and the comparative absence of any rational system which would allow us to predict the effects of groups of drugs, and to test these predictions in terms of the usual hypothetico-deductive methods of science. In the present paper the writer has made an effort to provide such a theory and to discuss certain relevant aspects of methodology and experimental design; subsequent papers will deal with experiments conducted in an attempt to test deductions made from theory.

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McDougall's Chemical Theory of Temperament

The theory which will be proposed here has certain important similarities to one proposed almost 30 years ago by William McDougall (17) and, as a comparison of these two theories will be instructive, a brief outline of McDougall's hypothesis may not be out of place. He began by accepting the existence of a continuum or dimension of personality corresponding to Jung's factor of extraversion-introversion: "I suggest that all personalities can be arranged in a single linear scale according to the degree to which this factor is present in their constitution . . . such a distribution of a temperamental trait is most naturally explained by the influence of some one chemical factor generated in the body and exerting a specific influence upon the nervous system in proportion to the quantity that is produced and liberated into the blood stream." McDougall confessed himself puzzled by the problem of which was the positive and which the negative state. He finally came to a somewhat arbitrary decision: "In all probability extraversion is the positive state, introversion the negative, that is to say, extreme introversion represents a defect, a minimal quantity or minimum rate of secretion of the postulated substance—(let us call it X); and extraversion in its various degrees is a consequence of correspondingly large quantities or rapid rates of secretion of X." How is this secretion supposed to act? McDougall begins by explaining his theory of introversion: "The introvert . . . is the man in whom the lower levels of the nervous system are constantly subjected to a high degree of inhibition by the higher cortical activities, and of the lower inhibited functions the most important are the affective or emotional-conative functions of the thalamic region . . . Thus the introvert, by reason of the predominant activity of his cortex and in virtue of its restraining or inhibitory effect on the outflow of thalamic excitation in its normal or direct channels of emotional expression, is a man in whom thought seems to flourish at the expense of emotion . . . introversion seems then to be the natural consequence of the great development and free activity of the cortex."

McDougall then goes on to postulate that there is an increase in introversion as children grow up into adults corresponding to the greater functional dominance of the cortex. However, "Nature has provided an antidote against such increasing and excessive introversion. It has generated in the tissues, or in some tissue unknown, an extraverting hormone, or endocrine substance, the function of which is to prevent, to diminish in some measure this inhibiting, paralysing influence of the cortex upon the more primitive, lower level functions of the nervous system. The man who is constitutionally provided with a large amount of this antidote to cortical inhibition is the extravert."

We now come to the pharmacological aspect of McDougall's theory. "How . . . may we conceive the postulated internal secretion X to work upon the brain to maintain various degrees of extroversion, to antagonize and moderate the inhibiting influence of the cortex? I suggest that we may find the clue to a simple, intelligible and adequate hypothesis in consideration of the influence of alcohol upon the brain functions (and of ether and chloroform), and that the phenomena of alcoholic intoxication go very far to justify the hypothesis. . . . I have observed in a number of cases that the markedly extraverted personality is very susceptible to the influence of alcohol. A very small dose deprives him of self-restraint and control and brings on the symptoms of intoxication, all of which are essentially expressions of diminished cortical control over the lower brain levels. The introvert, on the other hand, is much more resistant to alcohol. He can take a considerable dose without other effect

than that he becomes extraverted . . . Alcohol, in short, seems to be an extraverting drug pure and simple so far as its influence on the nervous system is concerned."

McDougall now formally states his hypothesis. "In order to explain extraversion, I make, then, the simple assumption that in the extravert some tissue (or tissues) normally and constantly secretes the extraverting substance X, a substance whose action upon the nervous system is very similar to that of alcohol (ether and chloroform); that is to say, I assume that the extraverting internal secretion X acts directly upon all synapses, raising their resistance to the passage of the nervous current or discharge from neurone to neurone. I make also the highly probable assumption that the synapses of the various levels of the nervous system are in the main solidly and stably organized in proportion to the phylogenetic and ontogenetic age of the levels in which they occur. In other words, I assume that the synapses of the high levels are the less solidly organized, have higher resting resistances, and are less stable, more subject to variations of their resistance by a variety of influences, including the chemical ones of strychnine, alcohol, and the postulated substance X."

Having stated this formal hypothesis, McDougall goes on to explore some of the theoretical connections with abnormal mental states. He argues that extraverts are more prone to hysteria, hypnosis, trances, automatic actions, crystal visions and so on, while introverts are more prone to neurasthenia, schizophrenia and insomnia. "All these differences seem to mean the greater liability of the extravert to suffer dissociative effects in the nervous system, whether local, as in local functional paralyses and anaesthesias, or general, as in general amnesia, trance, hypnosis and sleep. And this is to be expected; for, just as alcohol is a dissociative drug, which acts first and most intensely upon those most delicately organized synapses that are involved in the latest acquired and highest-level processes of the cortex, subserving self-conscious control and self-criticism, and involving the reciprocal play of one cortical system of highest level neurones upon another, so also the extraverting substance X may be supposed to affect most markedly these higher level synapses, maintaining during waking life an incipient state of dissociation and rendering easier the onset of all more pronounced states of cerebral dissociation, from normal sleep and alcoholic intoxication to hypnosis and functional paralyses and amnesias. In short, the introvert is liable to disorders of continuing conflict, because conflict cannot readily be obviated by dissociation; while the extravert readily finds relief from internal conflict through the onset of some complete dissociation between conflicting systems and tendencies."

This, then, is a brief outline of McDougall's hypothesis, which to the writer seems plausible, ingenious and extremely fruitful. It has been almost completely neglected by psychologists and psychiatrists alike for a variety of reasons, some of which may be worth stating. In the first place, McDougall does not provide objective measures of extraversion-introversion which might be used to identify any given person's position on the continuum, and which might be used to measure the shift of that person's position on the continuum subsequent to the administration of the given drug. His argument is confined to observational methods whose unreliability was becoming more and more apparent in the 1930's as a result of psychological investigation. As we shall have occasion to point out later in connection with the methodology of drug research, objective methods are absolutely essential in the testing of a hypothesis such as that advocated by McDougall. Thus the work of Shagass (21, 22) is a striking confirmation of McDougall's observation quoted above that "the markedly extraverted personality is very susceptible to the influence of alcohol" while "the

introvert, on the other hand, is much more resistant to alcohol. He can take a considerable dose without other effect than that he becomes extraverted." But this demonstration had to await the elaboration by Shagass (21, 22) of an objective method for measuring the intoxication threshold, or "sedation threshold" as he calls it.

The second reason for the failure of McDougall's hypothesis to be widely accepted lies in the mysterious nature of his substance X. This appears purely *ad hoc*, is not integrated in any way with the existing body of psychological knowledge, and does not conform with the rules science lays down for the introduction of hypothetical constructs and intervening variables. In the third place, McDougall was rather half-hearted in his specification of the relation between temperament and drugs. His main interest obviously being in substance X, drugs are only introduced into the paper by virtue of the hypothetical similarity in action between alcohol and X. A last reason may be found in the general tendency of psychologists at the time McDougall's article was written to disown higher-order concepts implying generality in the personality field (such as extraversion-introversion), and to seek instead for specific stimulus-response connections (5). All these reasons working together may explain, but cannot justify, neglect of McDougall's contribution.

The Drug Action Postulate

Much of the present writer's work in the experimental field has been devoted to an attempt to fill in the gaps in McDougall's theory. Thus a certain amount of effort has been applied to the formal proof of the existence of a personality dimension analogous to the concept of introversion-extraversion as advocated by Jung and McDougall (3, 4, 5). This has been accomplished in terms of objective tests which can be used as an operational definition of this dimension. The success which has accompanied this demonstration suggests the possibility of using tests of this type in a verification of deductions made from any theory of drug effects on extraversion-introversion.

The writer has also attempted to integrate McDougall's mysterious substance X with the general body of modern psychological theory by postulating that, as Pavlov had already suggested, personality differences between extraverts and introverts are mainly due to disturbances in the cortical excitation/inhibition balance, in the sense that extraverted behaviour patterns are produced by excessively strong reactive inhibition and/or excessively weak excitation, while introverted behaviour patterns are produced by excessively weak reactive inhibition and/or excessively strong excitation (6, 7). The terms excitation and inhibition in this connection are molar concepts clearly defined in the systematic writings of Pavlov and, more particularly, of Hull; therefore, their use should not be understood to imply any physiological hypothesis, although the recent work of Eccles (1) has given some hope that a physiological and neurological substructure for these molar psychological concepts may yet be achieved.

In thus bringing into line the major concepts of modern learning theory and of personality theory, the writer was also able to add one of the prominent groups of data from the study of perception by demonstrating that satiation phenomena as demonstrated by Köhler, can be explained in terms of the same inhibitory mechanisms postulated above. Experimental evidence regarding this whole scheme has been supplied in a number of recent publications which should be consulted by those interested in the general theory of extraversion-introversion (8, 9, 11, 12). Here only two further points will be noticed.

In the first place it was demonstrated, as had already been postulated by Jung and McDougall, that hysterics and psychopaths show a strong tendency to be extraverted in their behaviour and their test scores, while dysthymics tend to be introverted in their behaviour and their test scores (3, 4, 5). (The term "dysthymic" was introduced specifically by the writer to cover the neurotic syndrome characterized by manifest anxiety, reactive depression and/or obsessive compulsive symptoms. It was introduced because of the uncertain meaning and obsolete nature of the terms "psychasthenia" and "neurasthenia" sometimes used by older writers in this connection.)

In the second place it was demonstrated that brain damage in general, and, particularly, damage to areas 9 and 10 in the frontal part of the cortex, had an extraverting effect on behaviour, and produced a general increase in cortical inhibition in the individuals operated on or subjected to accidental damage (6, 18, 19, 20). This finding is of course in line with McDougall's conception of the cortex as an inhibiting centre for lower level activities; the damage (inhibition) of an inhibiting organ has precisely the effect of his postulated factor X.

The link between drug action on the one hand and learning theory on the other (and therefore through learning theory with personality theory, as briefly indicated above) was adumbrated by Hull (15) in a pioneer paper on the influence of caffeine on rote learning. Basing himself on a quotation from C. L. Evans (2) to the effect that caffeine had a marked tendency to eliminate internal inhibition, Hull made certain predictions on the molar effects which should follow in human rote learning from the administration of this drug. Thus, he argued that if, as Lepley (16) had shown, the bowing of the serial learning curve is due to internal inhibition, then the administration of caffeine, by eliminating such inhibition, would reduce the degree of bowing observed. Working on only eight subjects, he failed to find the predicted effect, but found instead that "the subjects as a group showed a fairly definite tendency to give more anticipatory reactions after taking caffeine, the mean percentage of increase being 33, with a probable error of 7 and a satisfactory critical ratio of 4·7". This effect can be predicted from the hypothesis that caffeine eliminates internal inhibition; as anticipatory reactions are supposed to be held in check by these inhibitions, they would therefore be released by their elimination. However, Hull appears to have regarded this experiment as a failure, and never returned himself to this vital area.

We are now in a position to put in the form of a postulate the expanded theory adumbrated by McDougall and Hull. This postulate reads as follows: *Depressant drugs increase cortical inhibition, decrease cortical excitation and thereby produce extraverted behaviour patterns. Stimulant drugs decrease cortical inhibition, increase cortical excitation and thereby produce introverted behaviour patterns.* This postulate was informally suggested in a previous paper, but has not hitherto been stated in any formal way (6). It should be noted that the terms "depressant" and "stimulant" are here used in their pharmacological sense as listed by Goodman and Gilman (14); it would be valuable to know the chemical and biochemical properties characterizing these drugs and causing the opposing effects, but such knowledge does not appear at present to be available. It should also be noted that in many cases drugs which fall in one or the other of these two groups have side effects which may be so strong as to cancel out the predicted effects; thus many excitant drugs are also sympatheticomimetic. It is important in submitting the postulate to experimental investigation to choose drugs having as few side effects as possible. We shall refer to this problem later on in this paper.

We may now note some of the ways in which the present theory differs from, and may be said to improve upon, that of McDougall. In the first place, the drug action postulated is stated in terms of two reasonably well defined groups of drugs whose existence is clearly recognized by pharmacologists and whose contradictory properties are well known. In the second place, the effects postulated can now be deduced directly from a general theory of behaviour. This point can be illustrated by reference to Figure 1 which shows the postulated correspondence between drug effects and the various levels of our behaviour-personality theory. These relationships should be borne in mind during our discussion of the methodology of drug research which forms the next section of this paper, and which amplifies this point in considerable detail. In the third place, we do not have to rely, as did McDougall, on simple observation, but are enabled to test our deductions with reference to objective laboratory procedures in the fields of learning and conditioning, of perception, and of the work decrement. These are important advantages, as by making predictions more precise and more objective, we also make the theory more incisive, and easier to disprove if in error.

Causal level:	Excitation—Inhibition.
Clinical-behavioural level:	Dysthymia—Hysteria.
Test level:	Introversion—Extraversion.
	Stimulant—Depressant.

FIG. 1.—Drug effects and three levels of investigation proposed in the text.

METHODOLOGY OF DRUG RESEARCH

The success or failure of any theory depends essentially upon the ability of that theory to enable investigators to make clear-cut deductions and testable predictions. It is part of the duty of anyone proposing such a theory to indicate the types of prediction which he would regard as crucial to the correctness or incorrectness of his theory. It is this task to which we must now turn.

Roughly speaking, we have open to us three avenues corresponding to the three levels (causal, clinical, and test level) indicated in Figure 1. Thus at the clinical-behavioural level our theory would imply the prediction that *stimulant drugs produce dysthymic symptoms and behaviour patterns, and a reduction in hysterical symptoms and behaviour patterns. Conversely depressant drugs produce an increase in hysterical symptoms and behaviour patterns, and a decrease in dysthymic symptoms and behaviour patterns.* This is probably the least useful type of prediction because of the great observational difficulties which impede objective determination of the predicted results.

At the test level, we would predict that *any test which has been shown to differentiate reliably and validly between introverts and extraverts will, when applied to subjects who have been administered a stimulant (or depressant) drug, show shifts in scores in the direction characteristic of greater introversion (or extraversion).* In view of the large number of tests covered by this deduction and the objective nature of the scores obtained, this is a useful and valuable type of prediction. We might add to it, in parentheses, a similar prediction derived from the fact that brain injury appears to have extraverting consequences, namely, that *the effects of depressant drugs are similar to those of brain damage as far as objective psychological tests are concerned. Conversely, the effects of stimulant drugs are opposite to those of brain damage.*

At the third level, and this may be regarded as the most fundamental of all, we are dealing with the hypothetical causal factors underlying both clinical behaviour and test scores. Our predictions here would therefore be in terms of

the theory of excitation-inhibition, and can be applied directly to the field of drug studies without necessarily going through the intermediate state of being applied to the dysthymic-hysteric differentiation, or that between extraverts and introverts. (Hull's (15) prediction, mentioned above, would be of this type.)

While the last type of prediction is the most advanced theoretically, and the most fundamental psychologically, it is also probably the one presenting the greatest difficulties. The theory of excitation and inhibition is nothing like as rigorous, definite and clear-cut as one would like it to be, and the failure of an experiment to satisfy the drug postulate may be due to a mistaken application of the general behaviour theory, rather than to an error in the drug postulate itself. This of course should not deter the investigator from making predictions of this kind and testing them regardless of the outcome. The results would almost certainly be of considerable interest from the point of view of learning theory, as well as from that of the study of drug effects. Indeed, one of the most important outcomes of the study of drug effects might be a clarification of certain puzzling features in learning theory, and the growth of a methodology for verifying or disproving certain assumptions of learning theory.

Nevertheless, from the point of view of making predictions which are crucial for our postulate, it would seem advisable to choose tests whose use can be justified at all three levels, i.e. tests whose theoretical derivation at the causal level is clear cut, which are known to differentiate between dysthymics and hysterics, which are known to distinguish between normal introverts and normal extraverts, and which are known to be affected by brain damage in a certain manner. An example of such a procedure is that of conditioning. Ease of conditioning is clearly determined by the growth of excitatory potential and the relative absence of inhibitory potential, while difficulty in the forming of conditioned reflexes is clearly related to the presence of strong inhibitory potential and the relative weakness of excitatory potential. Thus, on the causal level conditioning techniques present as clear-cut a prediction as we can make.

At the other two levels, work in our laboratory (11, 12) has clearly shown that eyeblink and PGR conditioning differentiate at a very high level of reliability and validity between hysterics and dysthymics, and between extraverts and introverts. Similarly, there is in the literature a good deal of evidence to the effect that brain operations tend to have an inhibitory effect on conditioning. All in all, then, the results from these various sources indicate that if our postulate is correct, *depressant drugs should produce a decrease in the rate of conditioning, while stimulant drugs should produce an increase in the rate of conditioning.*

The evidence regarding this prediction has been reviewed by Franks and Trouton (13), who have also performed an experiment using eyeblink conditioning as the dependent variable. By random allocation of subjects they made up three groups, one of which, the control group, received a placebo, while the other two received sodium amytal and dexedrine respectively. The results were very definite and in conformity with our hypothesis as will be seen from Figure 2. The group which had been administered the sodium amytal conditioned least well, the group which had been administered the dexedrine conditioned best of all, while the group which had been administered the placebo was intermediate. This experiment may serve as an example of the type of prediction which can be made with the greatest confidence from our postulate.

The research design used by Franks and Trouton has been illustrated in

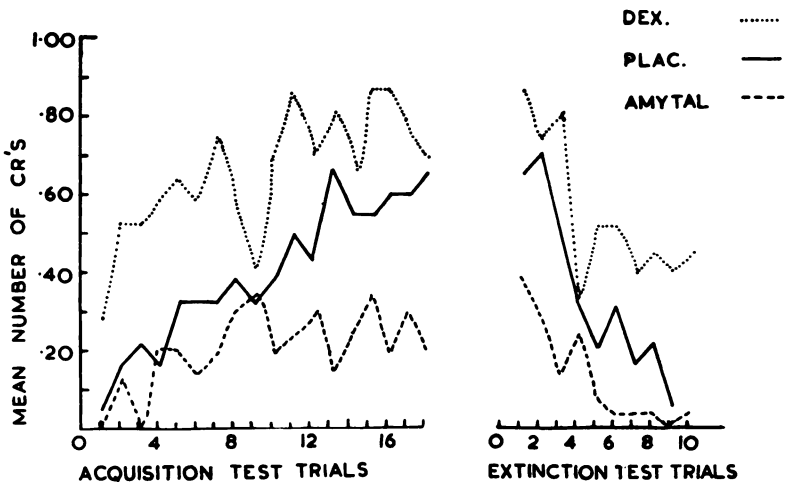

FIG. 2.—The rate of conditioning and extinction under dexedrine, placebo, and sodium amytal

Figure 3a. It will be seen that it does not depend in any way on the assessment of the personality of the subjects prior to the experiment. Subjects are randomly allocated to control and experimental groups, and what is studied is the *general* effect of the drugs under investigation on what might be called the *standard subject*. This paradigm is of course capable of certain improvements. Thus the same group of persons might be tested three times under placebo, depressant and stimulant drug conditions, so that each subject would constitute his own control. This is possible in perceptual experiments, but not in conditioning and learning experiments where nearly all the improvement in performance takes place during the first session. Other improvements in the experimental design contingent upon the one suggested above might include the assessment of the standing of the subjects on the extraversion-introversion continuum, and the calculation of possible interaction effects in an analysis of variance design. However, these refinements do not in any way affect the general principle of this design, which is probably the most widely used of all.

A rather different design is illustrated in Figure 3b. This design makes use of the known position of groups of subjects such as dysthymics and hysterics on the introversion-extraversion continuum, and thus explicitly contravenes the random sampling technique of design A. This design harks back to McDougall's observation that extraverts need less alcohol to reach a point of intoxication than introverts, who with the same amount of alcohol simply become more extraverted. Such a research design requires an objective *terminus ad quem*, i.e. the terminus of an "intoxication threshold" which would enable us to ascertain the amount of alcohol required by different groups of subjects to reach the same level of cortical inhibition as defined by this threshold.

The only example of the use of such a technique which the writer has been able to find is a study by Shagass (21, 22) using what he calls the "sedation threshold" of sodium amytal. The sedation threshold is an objective pharmacological determination, which depends on EEG and speech changes produced by intravenously given amylo-barbitone (amytal) sodium. "Amylo-barbitone sodium is given intravenously at the rate of 0·5 mg./kg. of body weight every 40 seconds. The patient is tested for slurred speech, and the injection is continued at least

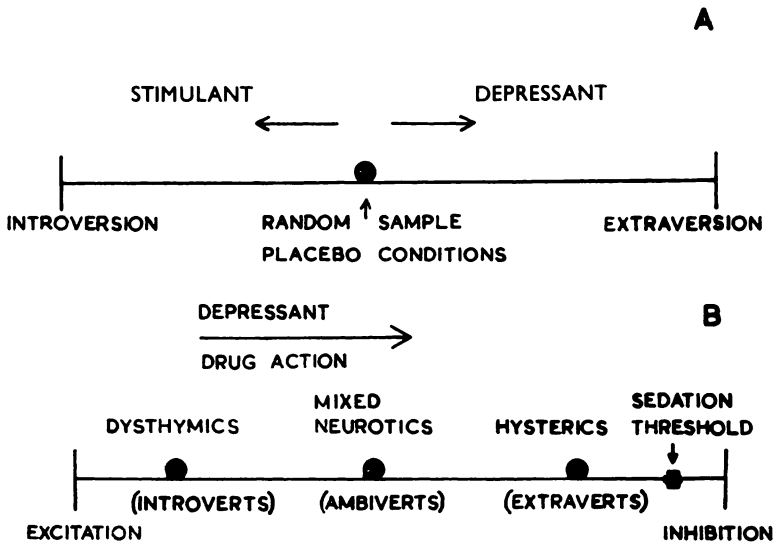

FIG. 3.—Two fundamental research designs for the study of drug effects.

80 seconds after slurred speech is noted. Continuous EEG's are recorded from transverse frontal and sagittal frontocentral placements." Figure 4 shows that sodium amytal produces a rather striking increase of fast frequency (15–30 c.p.s. activity). The amplitude of this fast frequency is taken by Shagass as a

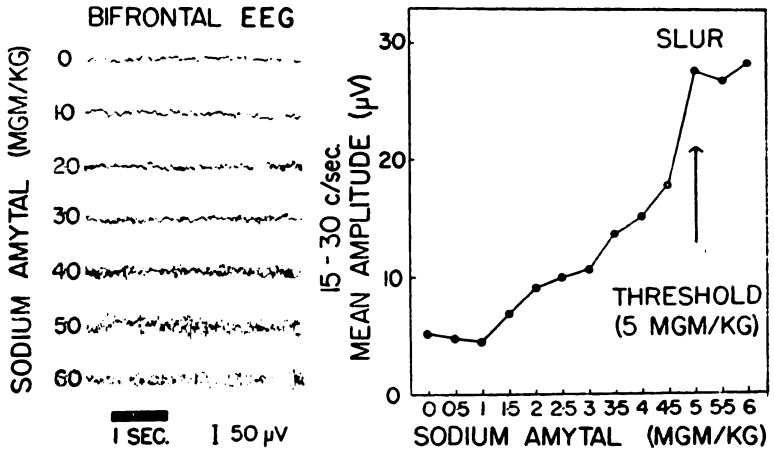

FIG. 4.—Effect of sodium amytal on bifrontal EEG. Note progressive increase in fast frequency amplitude. Arrow points to inflexion point in the amplitude curve, which indicates sedation threshold.

response to the drug and the dosage-response curve plotted. "The typical curve has a sigmoid shape and contains a point of inflexion, preceding which there is a sudden increase in the amplitude of the fast activity, and following which the curve tends to plateau. This inflexion point generally occurs within 40 seconds (0·5 mg./kg.) of the time when slurred speech is first noted, and the slur and inflexion point are used together as indicators of the threshold. The threshold

is the amount of sodium amytal, in mg./kg., required to produce an inflexion point in the 15–30 c/seconds amplitude curve, which occurs within 80 seconds (1 mg./kg.) of the time when the slur is noted. The slur localizes the threshold roughly, the EEG inflexion point does it more precisely . . . The measurement is highly reliable; its probable error is no greater than 0·5 mg./kg. of body weight. Age, sex, and previous intake of sedatives in usual psychiatric dosage have not been found to influence the threshold."

According to the theory outlined in this paper (which was developed before Shagass's work was known to the writer), we should be able to make a very definite prediction. Sodium amytal, being a depressant drug, would be postulated to increase inhibition. An extravert, whose cortex, according to our theory, is already in a relatively inhibited state, should require comparatively little sodium amytal before reaching the critical sedation point; such a person should have a low sedation threshold. The introvert, on the other hand, whose cortex is in a state of considerable excitation and low inhibition, would require a considerable amount of sodium amytal before reaching the critical sedation point; he would be predicted to have a high sedation threshold. If we express this general hypothesis in terms of neurotic groups and their standing on the extraversion-introversion continuum, then we would expect psychopaths to have the lowest threshold, followed by hysterics. Mixed neurotics would be intermediate and anxiety states, obsessionals and reactive depressives would have high sedation thresholds. An experiment along these lines was carried out by Shagass; his results are given in Figure 5. It will be seen that these results bear out our prediction in every detail.

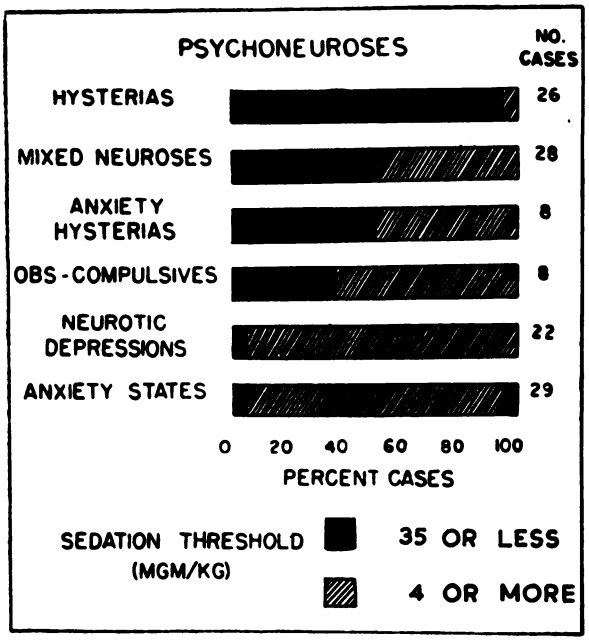

FIG. 5.—Differentiation between psychoneurotic groups by a division point between thresholds of 3·5 and 4·0 mg./kg.

This design too, of course, is capable of certain interesting modifications. If something corresponding to the sedation or intoxication threshold could be found at the introverted end of the continuum, we would predict lower thresholds

for dysthymics than for hysterics, and quite generally a reversal of the relations found on Shagass's research. Thus the same groups of patients at different times might be given different and opposing drugs as well as placebos. However, such developments depend on the discovery of such threshold effects for excitation drugs, which might possibly be looked for in EEG patterns corresponding to wakefulness as opposed to sleep.

Drug Study and Behaviour Theory

The practical usefulness of the successful elaboration of a theory of drug action on personality will be too obvious to require any further comment. The writer would like to stress, however, the point already mentioned in a previous section, namely the reciprocal interaction between a theory like that outlined here and general behaviour theory. It is customary in the work of Hull, Pavlov, Spence, and their followers to attribute certain psychological effects to hypothetical constructs and intervening variables like excitation or inhibition, without proving that the inhibition responsible for, say, reminiscence effects is the same inhibition which is responsible for, say, serial learning position effects. While it is very likely that phenomena which obey the same laws do, in fact, depend upon the same hypothetical constructs, a more formal demonstration or proof would seem to be required. Such a proof, in the writer's opinion, can be furnished most easily by reference to the field of individual differences and drug effects.

This general view can perhaps be illustrated best by reference to a hypothetical example. Let us suppose that two experimental phenomena, A and B, are supposed to be produced by the mechanism of inhibition. One method of proving that this was so would be to demonstrate on the physiological-neurological level that the underlying processes in the central nervous system were identical. Such direct proof would of course be the most satisfactory method of dealing with this problem, but unfortunately the possibility of such a demonstration is extremely remote at the present time. Consequently, we must look for some other method of proof.

To aid us, we have two postulates, which include the factor of inhibition in a manner experimentally independent of phenomena A and B. We have, first of all, the temperamental postulate stating that inhibition is stronger in extraverts than in introverts, and we have the drug postulate stating that depressant drugs increase inhibition whereas stimulant drugs decrease inhibition. Proof of these two postulates lies in tying them up with phenomena C, D, E. . . . N, which form part of the general inhibition theory. We can now apply these postulates to phenomena A and B and state that if these *are* phenomena produced by the general factor of inhibition, then (*a*) both A and B should be more pronounced in extraverts than in introverts; (*b*) both A and B should be more pronounced after the administration of a depressant drug than after the administration of a placebo; and (*c*) both A and B should be weakened after the administration of a stimulant drug as compared with the administration of a placebo. These are testable predictions which enable us to answer our original question regarding the status of phenomena A and B in learning theory, and they at the same time give us information regarding the status of phenomena A and B within personality theory, and within the theory of drug effects. Thus, this mutual interweaving of data from different and hitherto largely isolated fields within the general field of psychology constitutes the main claim of the temperamental and drug postulates to the attention of psychologists and psychiatrists interested

in fundamental theory and in the integration of the biological sciences concerned with the study of human behaviour.

These mutual interactions may also be used to solve certain problems in the pharmacological field. Thus it is often found that drugs have very diverse effects on people, so that one and the same dose of a drug given to two people may produce an apparently strong effect in the one and almost no effect in the other. Altogether it has been found impossible to rationalize the amount of drug which ought to be given in order to produce similar results. Pharmacologists of course have worked out certain rules. There is, for instance, the theory of what is called the "therapeutic ratio", which is obtained by dividing the lethal dose by the therapeutic dose. Then there are such rules as those of Clark, Young, and Cowling, relating to age, and the various rules relating dosage to body weight (14). In practice these rules appear to have very little value, particularly where stimulant and depressant drugs are concerned.

The reason for this follows directly from our postulate system. It appears obvious that in terms of that system, the most important variable in predicting the effects of the drug, and in prescribing the particular dosage required for a specific purpose, would be the excitation-inhibition ratio obtaining within the particular person concerned. This ratio would not be likely to be very highly correlated with weight or any of the obvious surface characteristics which are taken into account by pharmacologists at present. Thus, to provide a given effect, such as the reaching of the sodium amytal sedation threshold, the dosage required is clearly related to the position of the subject on the extraversion-introversion continuum. That position, as Shagass's results show, correlates far more highly with the dose needed than does any of the variables at present used by pharmacologists to assess the amount of drug required. It is likely that we can explain in a similar way the differential effects of various doses of alcohol. It is also likely that the same rule would apply in the opposite direction, such that introverts would require relatively little dexedrine or caffeine to reach a level of excitation (sleeplessness?) which could only be reached by extraverts after a considerably larger dose of these drugs had been administered.

It will be seen then that the theory here proposed makes possible the beginnings of a rational solution to a number of problems in drug administration. While the theory is not in any sense quantitative as yet, there is no reason to expect that if our hypotheses have been at all along the right lines, such quantification should prove difficult or impossible. In the writer's view, the next point of advance in the study of the relationship between drugs and personality will be that of developing truly quantitative relationships on the rational basis provided.

SUMMARY

A theory has been developed in this paper linking the action of depressant and stimulant drugs with increases in cortical inhibition and cortical excitation respectively. These terms are used in the sense given to them by Pavlov and Hull, and thus the theory proposed links up modern behaviour theory with drug action. As a further step, the personality dimension of extraversion-introversion (hysteria-dysthymia) is introduced by a postulate, formally stated in a previous paper, relating strong excitatory potential to introversion and dysthymia, and strong inhibitory potential to extraversion and hysteria.

A discussion is given of the possible range of deductions which can be made from the theory suggested, and some confirmatory experiments are quoted, dealing with conditioning and the sedation threshold. A detailed discussion is also given of methodological problems arising from attempts to verify deductions from theories such as the one proposed.

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