DRUGS IN PSYCHOLOGY

*A Commentary on Travis Thompson and Charles R. Schuster's
Behavioral Pharmacology*¹P. B. DEWS²

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Behavioral pharmacology is the offspring of a union between experimental psychology and experimental pharmacology, fostered and indeed force-fed by clinical psychiatry. Like most children, it feels that it is understood by neither of its parents and has some sense of grievance and exasperation as a result. Like most parents, however, both experimental psychology and experimental pharmacology have been influenced and changed by contact with their offspring. Some lifelong principles of psychology have been found wanting when viewed through the eyes of the unprejudiced child. The wonderfully fine fabric of the clothes of some Emperors of Theory can be seen through the eyes of the child to be not merely invisibly fine but simply nonexistent, revealing many distinguished psychological and psychiatric theorists to be wearing nonexistent jackets and even nonexistent pants.

Pharmacological ways have been extremely powerful in physiology and biochemistry. Examples are the pharmacological experiments of Langley, Loewi, and Dale. These led to understanding of the organization of the autonomic nervous system and then naturally to current development of understanding of neurohumoral processes in the central nervous system which in turn will surely increase enormously our understanding of the functional organization of the central nervous system. Other examples are the way in which studies of metabolic inhibitors and mode of action of chemotherapeutic agents have contributed to understanding of biochemical processes in cells. By pharmacological ways is meant simply study of the modification of

biological function by deliberate addition of chemical substances. Pharmacology is starting to make comparable contributions to psychology. The dissection of physiological function by pharmacological tools has been more exquisitely discriminating and at least as revealing as dissection with a surgical scalpel. The brain is much more difficult to dissect in a meaningful way by surgical means than other physiological systems, while drug effects on the brain are at least as selective as outside the brain, so the relative contribution to be made to psychology by pharmacological means would seem greater even than for physiology. Needless to say, the scalpel and the drug are not mutually exclusive but rather complementary approaches.

In view of the high and increasing frequency with which psychologists give drugs, a pharmacological approach may no longer seem to require advocacy. There is more to the pharmacological approach, however, than including a drug as a treatment element in a Graeco-Latin design. Just as physiological psychologists have found that there is more to physiological psychology than the techniques of making holes in the head—that they must know anatomy and neurophysiology and histological techniques for localization of lesions and so on—so must the pharmacological psychologists know pharmacology and subservient physiology and biochemistry, not to mention physical chemistry. The rewards will be great; the contributions of pharmacological psychology as a whole will be at least as great as the contributions of physiological psychology to psychology as a whole and the time will come when every department of psychology will want to have a pharmacological psychologist, as today it wants a physiological psychologist.

It is against this background that we must view the first textbook devoted to Behavioral Pharmacology. A first textbook in a subject is

¹Englewood Cliffs, N.J.: Prentice-Hall, Inc., 1968. Pp. xvi + 297.

²Reprints may be obtained from P. B. Dews, Laboratory of Psychobiology, Department of Psychiatry, Harvard Medical School, 25 Shattuck Street, Boston, Mass. 02115.

a recognition of "coming-of-age." To old timers, an 18- or 20-year-old human subject is never fit to cope with the world, but tradition and their own insistence determine that they must. The immaturity of behavioral pharmacology is made starkly clear by this book. Of the approximately 250 pages of text, about half is a superficial review of psychological and pharmacological topics, certainly relevant to behavioral pharmacology, but not particularly behavioral pharmacology. So behavioral pharmacology is covered in some 125 pages, liberally sprinkled with figures. What a contrast to Goodman and Gilman (1941) and to Stevens' Handbook (1951). There turns out to be sadly little behavioral pharmacology that can be presented with textbook finality. However, we must judge a young subject, human or scientific, by whether it is headed in the right direction and showing evidence that it will prosper and contribute rather than by what it has accomplished. The likely contributions of behavioral pharmacology have already been pronounced to be very great. We must judge a textbook on a young scientific subject by whether it will help people coming into the field to understand the direction in which the subject is heading, and by whether it will help them to contribute. Appraised thus, I think the book emerges as a valuable contribution.

A textbook must present what is known with reasonable certitude in a subject. It must not indulge in polemics and it must not devote much of its space to explaining why it is not covering certain topics. It would have been easy but inappropriate in this book to devote a chapter to explaining why drug effects on learning were not being discussed (neither "learning" nor "acquisition" appears in the Index). That a textbook writer cannot use his pages to defend his selection of topics makes him susceptible to charges of narrowness or arbitrariness. Thompson and Schuster play the game according to the rules; they permit themselves no more than an occasional remark as to why they judge great areas of "psychopharmacology" to lack the scientific requirements of behavioral pharmacology and so to be unworthy of coverage in a textbook. They also recognize they will be criticized (see, for example, p. 229). A reviewer is under no such constraints. Let me, then, take up some representative topics that are not in-

cluded in the book, and explain why I think the authors were correct to exclude them. Even if our reasons differ, we come to the same conclusion. Four topics will be discussed: effects of drugs on motor capabilities, sensory functions, motivation, and learning. Each of these types of effect would be immediately accepted as meaningful by most people outside the field of behavioral pharmacology, *i.e.*, the effects would fit in to the general preconceptions most people have about behavior and drug effects on behavior. Why are such "meaningful" topics given such short shrift in the book?

Effects on Motor Functions

Behavior is almost exclusively the consequence of skeletal muscle activity, so modification of motor function must change behavior.

Properly coordinated muscle activity involves integration on anterior horn cells of information from proprioceptors (themselves in some cases modulated by special efferent discharges, and from pyramidal, extrapyramidal, and cerebellar circuits. There would seem to be many opportunities for pharmacological interference here, and indeed, there are. Ataxia can readily be produced by barbiturates and alcohol, and, with chronic large doses, a Parkinsonian syndrome with phenothiazines. Yet this type of effect does not seem to be of great importance in the peculiarly behavioral effects of drugs; the effects of the motor disabilities do not seem to extend much beyond the direct consequences of the disabilities themselves. Let me illustrate.

People with severe motor disabilities may have otherwise normal behavior. Similarly, grossly impaired animals may behave as normally as possible with their remaining capabilities. A striking example was a pigeon responding under an FR 30 schedule, a schedule which, of course, engenders a high, sustained rate of responding up to the time of presentation of the reinforcing stimuli—in this experiment, food. Conventional apparatus was used. The food was presented in a movable tray which came within access of the pigeon for 4 sec through an aperture in a wall of the experimental space. The response key was above the food aperture in the same wall. Pecking on the key continued normally even when the bird was under the influence of large doses of

phenobarbital, but when the food became accessible, the ataxic pigeon put its head against the wall and outstretched its wings to maintain balance during transfer of beak from key to tray. The time involved in these maneuvers was such that the beak arrived in the food tray as the 4-sec access concluded; so the pigeon got no food. After the reverse balancing routine, the pigeon got its beak back to the disc, whereon was executed normal FR 30 performance; and so on. At all times, the behavior of the pigeon was entirely normal within the limits imposed by the ataxia. While the gross topography of the behavior was changed, the relative tendencies of different behavior to emerge at different times and in the presence of different stimuli was substantially normal.

The minor tranquilizers such as meprobamate are also called skeletal muscle relaxants. The implication is a Jamesian "I feel tranquil when my skeletal muscles are relaxed." Yet the reason these compounds are thought about this way is more historic than inductive. Mephenesin, the parent compound, was discovered through its ability to antagonize strychnine, preventing muscle spasms. Meprobamate came from a search for a longer-acting, orally active drug with the properties of mephenesin. Meprobamate does have so-called interneuronal blocking actions in the spinal cord, yet it is less active in this regard than mephenesin, while meprobamate is a much better "tranquilizer". Chlordiazepoxide, which is similar to but more active than meprobamate as a drug affecting behavior in a similar way, is much less active in interneuronal blockade. The quantitative dissociation of the characteristic behavioral effects from the muscle relaxant effects means that the latter cannot be a major cause of the former.

Finally, profound behavioral effects of such drugs as phenothiazines and morphine may be produced with no detectable motor disability.

The most characteristic and interesting effects of behavior affecting drugs is in changing the likelihood of occurrence of different responses from time to time, rather than in affecting the competence to execute the responses. It follows that we should assess behavioral effects of drugs primarily by studying dependent variables informative of probabilities of different responses. Thompson and

Schuster are therefore right in their emphasis. Rate of responding is generally the best estimator of probability.

Effects on Sensory Functions

Effects of drugs on sensory functions have been considered as separable into effects of drugs on sensory processes proper and then effects on the control of behavior by the perceived sensory stimuli in discriminative behavior.

The most dramatic effect of drugs on sensation is the induction of hallucinations. There is a high degree of selectivity here, both in that only some drugs will produce hallucinations, and hallucinations are characteristically modality specific, usually visual. The occurrence of hallucinations is affected, like all behavioral effects of drugs, by circumstances, being most likely to occur in the absence of preemptive actual visual stimuli.

Study of hallucinations has been greatly hampered by lack of methods of study in experimental animals. A number of able investigators have made studies on hallucinogens, but the results to date have been isolated findings, difficult to put together. One can't help feeling that the considerable effort needed to work out methods of study in animals would be amply repaid by the wealth of information on visual physiology in relation to behavioral control that might result.

For the rest, there has been little search for modification of sensory processes as an important mode of action of behavior-affecting drugs. Presumably people see no reason to challenge the testimony of patients that they do not see, hear, smell, or somesthetically feel things differently under the influence of drugs such as barbiturates, amphetamines, phenothiazines, and so on. Pain and its modification by analgesics may be a partial exception, but to what extent is not yet clear.

When we come to control of behavior by stimuli we find that many people have posed such questions as: does a drug affect the ability of an animal to discriminate A from B? It is much easier to start experiments designed to answer this question than it is to start to study hallucinations. We have only to get the individual to behave differently in the presence of A and B and then give the drug to see if the differential behavior is modified. If the difference between behavior in A and be-

havior in B is reduced, the discrimination is attenuated and if it is increased, discrimination is improved. In some superficial sense, such conclusions are irrefutable; but they may be trivial. The difficulty is that, of necessity, we impose a different schedule of reinforcement on the subject in the presence of stimulus A from that operating in stimulus B; that is how we get the subject to behave differently in A from in B. The effect of a drug depends on the ongoing behavior on which it is superimposed; in studying discriminatory behavior, we are necessarily studying two different ongoing patterns of behavior (it is the difference that is the evidence of discrimination): we should therefore expect the drug to affect differently behavior in the presence of the two stimuli. Such a differential effect will usually, indeed almost inevitably, affect the difference between the behaviors in the presence of the two stimuli: which has been defined as an effect on discrimination. Thompson and Schuster discuss drug effects on stimulus control in a formal manner. The following is a commentary on their position.

First, let us take an example. Suppose that under an IRT 10-sec³ schedule a pigeon maintains a fairly steady rate of responding at one response per second. Under the influence of 3 mg/kg chlorpromazine (CPZ) the rate increases to three responses per second. The same bird under a VR 30 schedule averages 10 responses per second which falls to three responses per second under 3 mg/kg CPZ. Suppose the bird is subjected to a multiple schedule in which in the presence of a blue light FR 30 is in operation and in the presence of a red light IRT 10-sec is in operation. The red and blue lights entail differential performances appropriate to the two schedules. Under the influence of 3 mg/kg CPZ, behavior in the presence of the two stimuli becomes identical. Can we say the CPZ has affected discriminatory behavior? Only in a trivial sense, since the drug is exerting its characteristic effects on the two performances and it is an accident of the selection of the schedules that makes the "discriminatory behavior" appear to be less. As a matter of fact, if we study CPZ on *mult VI EXT*, we find that the differ-

ential behavior is very little affected up to very large doses. Hence, red and blue lights can continue to control behavior in the face of behaviorally effective doses of CPZ. Can we say now that CPZ does *not* affect discriminatory behavior? No again. Stimulus control is a graded matter and if strong enough to begin with (as on *mult VI EXT*) the control may be substantially reduced without very much change in the control pattern of responding.

What emerges from the example is that it is not easy to separate, in practice, the effects of drugs on discriminatory processes from the effects on the different behaviors compliant with the different stimuli and their correlated schedules. Instead of attempting to isolate discrimination as a discrete process, which may be logically defensible but is probably biologically nonsensical, it has proved profitable to study stimulus control of behavior. Stimulus control of behavior involves simultaneous consideration of the stimuli governing and the behavior governed.

The available evidence, admittedly fragmentary, suggests that drugs affect stimulus control in a way that depends on what behavior is being controlled and how well by the stimulus, as well as on the physical characteristics of the stimuli. Thompson and Schuster refer (p. 144) to the work of Terrace, who trained pigeons in such a way that stimulus control of particular responding and of no-responding was achieved without any responses ever having been made in the presence of the S^A in the fully trained bird. He compared the effects of imipramine in birds so trained and in ordinarily trained birds, which had made many responses in S^A during training, but which had come not to respond in S^A. Although the final performances were manifestly similar, the effect of imipramine was quite different, considerable S^A responding being reinstated in the ordinarily trained birds but no S^A responding being induced in the errorless birds. The difference in drug sensitivity must have been related to the control of responding by the stimulus rather than to qualities of the stimuli or their discriminability, since these latter were absolutely identical for both groups of animals.

Stimulus control includes most of what has been discussed traditionally as a variety of different processes: sensory discrimination of

³IRT 10-sec is used instead of the more familiar DRL 10-sec because the former, but not the latter, is accurate and descriptive of the procedure.

a stimulus, perception, and paying attention, as well as cognitive control of responding. Fractionation of drug effects on stimulus control along such lines has never been achieved. The possibility must be entertained that the conceptual subdivision of stimulus control into sensation, perception, attention, and cognitive execution, may turn out to have no biological counterpart. The validity of subdivision of stimulus control into a series of processes has been discussed within psychology, of course, but of necessity the discussions have been mostly as to whose point of view makes most sense; when people are arguing about points of view the overwhelmingly most likely conclusion is to agree to differ, which is fine for friendship but not progressive for science. As a result, theories have extraordinary longevity in psychology compared to other natural sciences. Students are invited to look at the same general facts from the same points of view as the authors of the theories did often some decades before. The theory the students give allegiance to is more influenced by the tradition of the institution they attend than by consideration of the experimental evidence. One might have hoped that physiological psychology would have erupted with biological realities that would heavily weight the scale for or against particular theories. For whatever reason, this has not happened. We have high hopes for pharmacological psychology. Already pharmacological evidence seems to be weighing against theories of stimulus control comprising an attending and perceiving sprite in a sensing brain towards theories of stimulus control which regard discriminative stimuli as ingredients in the stimulus-schedule complex determining temporal patterns of responding.

Effects on Motivation

Most everybody once supposed that an important source of selective effects of drugs was the differences in behaviors of different motivations. Some still believe it. The case has been strongly urged by N. E. Miller and his colleagues (see Miller and Barry, 1960). The prejudice is so strong that Thompson and Schuster feel obliged to refer to it, though with apparent reluctance (p. 221). We hear of effects of drugs on food-maintained behavior, water-maintained behavior, on fear- or anxiety-motivated behavior or on reward-motivated

behavior and so on. Selectivity is implied, if not made explicit. That is, if we speak of a drug affecting hunger, then it is implied that behavior in relation to food is selectively affected; for example, affected by lower doses of a drug than behavior of other motivation.

Thompson and Schuster discuss the sort of evidence necessary to establish a selective drug effect in relation to a particular reinforcer (p. 142). It seems to me, however, that they miss the most direct approach. More than 10 years ago, I suggested that if a drug effect is to be attributed to an effect on, for example, hunger, then the effects of the drug should be able to be mimicked by manipulation of the state of food deprivation of the animal (Dews, 1956). Because all drugs have multiple effects, because the time relations of the drug action will hardly be identical with the time relations of manipulation of food, and for other reasons, we cannot hope exactly to duplicate a drug effect on hunger by manipulation of food. But if the effect of the drug is importantly on hunger, then hunger must be an important variable in controlling the behavior, and manipulation of food should cause large effects that bear an identifiable similarity to effects of the drug. If the effects of manipulation of food are small, then even if a drug had a large selective effect on "hunger" this could not be the basis for a large behavioral effect of the drug. In general, if we are going to account for a behavioral effect of a drug by a selective motivational effect, it must be shown that a quantitative change in the motivational factor is a sufficiently potent agent itself in the control of the behavior. Has this ever been done?

Finally, there is the old problem that when motivation is changed, when the reinforcer is changed, the schedule and the behavior are also changed almost inevitably. There are numerous studies in the literature comparing a variety of food presentation schedules with continuous or discrete avoidance procedures and purporting to show selective drug effects on avoidance or on positively reinforced behavior. Usually the schedules and the consequent temporal patterning of behavior are grossly dissimilar; the dissimilarity is entirely competent to account for the difference in the drug effects, and so the experiments tell us nothing about the difference in drug effects on behavior maintained by stimuli function-

ing aversively and stimuli functioning as positive reinforcers.

Experimental isolation as discrete independent variables of the nature of the reinforcer and motivational factors has proved so difficult that we have arrived at one of those paradoxical situations in which a little negative evidence can outweigh a great deal of positive evidence. Instead of starting with the situation of a selective drug effect associated with a difference in motivation, and then trying to divine how much of the selectivity is due to motivational differences and how much is due to differences in schedule and ensuing behavior, we can try to make schedule and behavior as nearly as possible alike under different motivations and then see how the drugs affect the performances in relation to the motivation. Thompson and Schuster refer (p. 153) to the successful attempt of Kelleher and Morse to engender similar schedules and patterns of behavior using electric shocks on the one hand and food on the other. The schedules were formally the same. The resultant patterns of responding were closely similar. And so were the drug effects. Work of Vaillant (1967) and of Weiss and Laties (1963) has a similar impact. In view of these types of findings, it seems to me that Thompson and Schuster too easily accept the view that apparently contradictory findings might be due to specific motivational effects being important in some species and procedures (p. 152). Is it not more likely that the difference in drug effects is more likely directly due to differences in minutiae of procedure? The negative evidence of no difference in drug effects according to reinforcer outweighs positive evidence and puts onus of proof clearly on claimants of motivational specificity; they must show that the apparent differences according to motivation are not secondary to differences in the behavior developed under the different motivators.

What effects have findings of this kind on psychology as a whole? Consider experiments engendered by the results. If it matters so little whether noxious stimuli or food is involved to the effects of drugs, maybe the fundamental behavioral difference between noxious stimuli and such things as food has been exaggerated; pleasure, is less than has been supposed and maybe the difference between positive and negative reinforcers, or between pain and

certainly less than antithetical. This line of questioning has led to experiments with dramatic results (Kelleher and Morse, 1968; Byrd, 1969; McKearney, 1969): large amounts of behavior over long periods can be maintained in monkeys when the only consequence of the behavior is delivery of an electric shock. The electric shock fulfills the defining criteria of a positive reinforcer. Yet there is no doubt that an electric shock can function as a negative reinforcer; legions of rats and scores of monkeys have had their behavior strengthened when its consequence was removal of actual electric shock or stimuli associated with it. The conclusion is inescapable; positivity and negativity of a reinforcer is not an absolute property of a reinforcing stimulus. Whether a stimulus will *function* as a negative or positive reinforcer depends not only on the inherent qualities of the stimulus but also on the schedule on which it is presented in relation to behavior and on the ongoing behavior in whose context the stimulus is presented.

If motivation is to be anything more than an inferred cause that is assumed *ad hoc* for every bit of behavior that actually occurs, then the involvement of schedule in determination of whether a stimulus is a positive or negative reinforcer shakes the foundations of the concept of motivation—indeed, shakes them down to earth together with all the elaborate theoretical superstructures.

It is interesting to note in passing that whereas experiments are tending to minimize the distinction between sensation, perception, and attention, the experiments just described indicate that the supposedly single reinforcing effect of a reinforcer has two components: the reinforcing effect *per se*, which strengthens responding, and a second component, which determines when the stimulus will function as a positive and when as a negative reinforcer.

In all fairness it cannot be claimed that pharmacological studies are responsible for the whole of the developments just outlined. The general psychological importance of schedules of reinforcement has, of course, been advocated by a whole group of psychologists, led by Skinner, for years. Since schedules through their control of patterns of responding have been shown incontrovertibly to be extremely important in determining the effect a drug will have on behavior, the pharmacological studies have forced us to the same con-

clusions on entirely independent evidence. The pharmacological evidence is peculiarly compelling in that within a single experimental session one can see displayed before one's eyes the preemptive effect of schedule in determining the effect of the drug. Also, the action of drug on organism is an earthy biological thing that effectively complements the arguments for the importance of schedules based on analogy, plausibility, and inspection of the affairs of society.

Effects on Learning

A trivial definition of learning makes easy the demonstration of drug effects on learning. If a drug keeps a student awake during a class through which he would otherwise have slept, and he learns something during the class, then we could say the drug had affected learning. Such a drug effect may be useful, but it is hardly a selective effect on the process of learning; it is in the latter sense that drug effects on learning will be discussed in this section.

Learning is such a dramatic phenomenon that to most people outside psychology, and many within, experimental psychology is more or less the same thing as study of learning. There is a strong disposition to attribute drug effects to effects on learning. Implicit is a pseudo-Jacksonian argument: learning is the highest and most subtle function of brain; the higher the function the more susceptible it is to modification by all sorts of influences, including drugs; ergo, learning should be the most susceptible of functions to drugs. Where a drug effect could be attributed to learning, it usually was, and everybody was satisfied even if the effect could have been attributed, on the information available, to any one or more of a host of other factors. A considerable literature on drug effects on learning has grown up on the proposition that a drug effect on behavior was due to an effect on learning until proved otherwise. Since most authors omitted the procedural details of their experiments that would have permitted their critics to point out schedule influences as a possible basis for the drug effects, they were generally safe from challenge.

The situation has changed greatly in the last few years, partly because molecular biologists have started talking about mechanisms of memory, and, of course, learning is acquisi-

tion of memory. Biochemists did not seem to know that people believed that most drug effects were on learning, so they demanded, and sometimes devised themselves, situations in which learning seemed easily recognized and measured as an uncontaminated factor. Take the situation studied by Jarvik and colleagues (1964). A mouse on a small metal platform steps down onto a larger metal platform just below. When the animal simultaneously touches both platforms an electric circuit is completed, delivering an electric shock to the mouse. If the animal is promptly removed from the situation and replaced on the smaller platform next day, a very much longer time elapses before the animal steps down, if, indeed, it does so at all within the time allowed in the experimental design. Clearly, there was learning in the first exposure to the situation. We can identify precisely when learning was in process because in the seconds following removal from the situation after the shock, subsection of the mouse to an electroconvulsive seizure effectively prevents learning. Now comes the surprise. At a time when learning is being established, we can plunge the mouse into an eventually lethal concentration of ether below 70° F; leave the mouse there until it is in Stage IV anesthesia, which is the stage at which all physiological evidence of central nervous system function is abolished, and then remove the mouse and restore it with artificial respiration. Testing next day shows evidence that learning survived the heroic treatment, since the mouse takes much longer to step down than if it had not had a shock the day before. In quite different sorts of experiments, learning has been shown to survive other drastic treatments, such as injections of puromycin sufficient to inhibit greatly protein synthesis by brain (Glassman, 1969). From the point of view of one interested in mechanisms of learning, the principal interest is in experiments in which interference with learning *has* been achieved, since these experiments are more likely to give leads as to mechanism. From the point of view of one interested in behavioral effects of drugs, the principal interest derives from the finding that learning is not the most sensitive aspect of central nervous system function to drug influences, but that it is, indeed, extraordinarily resistant to modification. At the same time as the pharmacological evidence has been accumulating

there has been increasing recognition of learning as a primitive, a "low" or gross function, of nervous tissue rather than a high and subtle function of highly evolved cognating brains. Certainly "learning" phenomena that obey the Law of Effect can be found in members of a variety of phyla from molluscs to chordates. Similarity of phenomena does not prove similarity in mechanism, of course; but in both octopus and man the same type of mechanism, using pigment to transduce light into nervous signals, is involved in vision; so why shouldn't a similar molecular mechanism of memory be used in most all species? Be that as it may, an impartial student of pharmacological psychology surveying the literature on drug effects on learning cannot help but conclude that the evidence that has been accepted in the past for a subtle drug effect being on the *process* of learning has been probably always inadequate. It follows that it is gratuitous to seek for effects on learning of clinical doses of drugs such as barbiturates, amphetamines, and phenothiazines as a significant factor in their characteristic behavioral effects. It follows that Thompson and Schuster were correct to eschew discussion of drug effects on learning.

A final comment needs to be made in this section. It is that experiments on the biology of learning and memory must go on, and pharmacological as well as other methods should be used. The experiments are interesting enough, even if they do not contribute to the understanding of the behavioral effects of the drugs most important clinically. The strictures of preceding paragraphs were cautionary rather than discouraging; a reminder that a minute change in behavior can lead to a change in the effect of drug with consequences on future behavior that could be detected as significant if good enough agricultural statistics are used. Nevertheless, future editions of this book will probably cover effects of drugs injected after short sessions—as short as one trial—on future performance, even if these effects turn out to be related to modification of reinforcement rather than learning.

So much for some of the things the book, rightly, does not cover. What it is concerned with are the big effects of drugs on behavior; about selective effects of drugs and about the kinds of behavior that are highly susceptible to drug effects. By big effects is meant big effects relative to the effects of other impor-

tant independent variables on behavior, such as deprivation and the quantitative and qualitative properties of reinforcers. By susceptibility of behavior is meant that large changes in behavior can be seen with doses of drugs whose effects are undetectable on motor capabilities or by any available physiological technique. Selectivity has two facets: one facet is that certain behavioral activities can be affected while others are unaffected, or are affected in the opposite direction. The other facet of selectivity is that the behaviors selected for modulation differ from one type of drug to another.

Before commenting on these topics, a word on nomenclature. One of the two most important chapters of the book is entitled "Drug-Environment Interaction". My dictionary defines interaction as "reciprocal action; action or influence of persons or things on each other". Now I submit that the drug does not often affect the environment nor the environment the drug; drug and environment jointly affect the subject, and the nature of the joint effect can be complex. I know where use of the term interaction came from; if you put drugs and environment and, if you want, a few more things, into an analysis of variance mill, you will come up with, *inter alia*, a term for drug $\times$ environment interaction, which, because the joint effect is generally complicated, will often be significant. Of course, there the matter will end, because you will not have any clue as to what the nature of the interaction is. I suggest this sort of nomenclature is unfortunate. What we want to know is the functional relations between salient environmental features and the effect of the drug, what determines their joint effect, and not merely that there is a statistical relationship. So let us start talking of "environmental determinants of (or influences on, or factors in) drug effects".

Big Effects of Drugs

The book abounds in examples of big effects of drugs. To someone accustomed to weak parametric dependencies, an ordinary dose-effect relationship has the impact of a revelation, so high is the slope and so unequivocal is the relationship.

Now, the emphasis on the size of these effects is not due simply to a Texan-like bias. Big effects are indeed important in their own

right. They are also important in that when we come to study small effects we must be careful that we are not dealing with diluted big effects, rather than direct effects of new variables. If a drug causes an apparent 10% change in acquisition rate, but the same drug has effects on different performances that differ by 1000%, then we must be extremely careful in inferring a drug effect on acquisition processes themselves, since a very slight difference in performances could well account for the apparent effect on acquisition.

Selectivity

The selectivity of the effects of drugs is not confined to selectivity between different general types of activity, or between behaviors of different origins and maintenance or of differences between "learning behavior" and "learned behavior" and so on. A case has been made that none of these is, in fact, a primary determinant of the selectivity of the effects of the distinctive behavior-affecting drugs. Thompson and Schuster gives instances in which in a single individual after a single dose of drug and recording only one specific response, a high degree of selectivity of the drug may be seen. It arises as follows. Even though only one response is being recorded, if the response is discrete and easily repeatable, it may occur many times during the period of observation. The pattern of occurrences of the response in time may take one of a wide variety of forms. The drug may affect some of these patterns to a different degree or even in a different direction from other patterns. Not surprisingly, the patterns of responding in time are crucially dependent on the temporal and sequential patterns of stimuli to which the individual is subjected. Programs of stimuli, especially stimuli made consequent on the responding of the individual, constitute schedules. "Schedule-controlled behavior" is thus patterned responding whose pattern is substantially dependent on the schedule in operation. Since the effects of a drug are greatly dependent on the pattern of responding and since the pattern is greatly dependent on the schedule, we frequently say briefly but not quite explicitly, that the effect of the drug depends on the schedule. There are examples of "schedule-dependent" drug effects in the book in which the training to respond and the individual responses, types of stimuli, deprivation and

reinforcer, the apparatus, the individual (and thus his genes and personality!), and even the particular dose of drug, are identical and yet the effects are grossly different as the schedule in operation changes from time to time.

Susceptibility

The large drug effects on schedule-controlled behavior, and the great dependency on the particularities of the schedule assume special importance when it is realized that schedule-type influences are always operating because all experiments (and, indeed, all unfolding life situations) must have a program, explicit or implicit, whereby they are conducted—a sequencing of stimuli, a timing of trials, a concatenating of consequences, a preassigning of probabilities. Sequencing, timing, arranging, and assigning are the essentials of scheduling.

The notion of scheduling is not immediately apparent and compelling. Some psychologists have suggested that scheduling subsumes most of experimental psychological procedures; others that it is trivial. We can take, however, a subject of particular species and strain, of particular genetic background, and we can decide to study certain responses out of the many available and we can decide on parameter values. We can make stimuli impinge on the subject through one or more of a variety of modalities. We can prepare the subject according to differing regimens of deprivation and training. We can modify the individual surgically or chemically. We can make the study in one or another environment. All of these are well recognized procedures in the experimental analysis of behavior. None of them is scheduling. The concept of scheduling is therefore not all-inclusive. When all the above matters have been settled we have still to arrange the stimuli and reinforcers in time and in relation to responses. The arrangements constitute the schedule. The arrangements have a profound effect on the consequences of administration of a drug. Therefore, scheduling is not trivial.

Comparative psychology, genetic psychology, study of the peculiar characteristics of stimuli of different modalities, and intensities and so on and so on are legitimate fields of study and some day will yield interesting chapters in behavioral pharmacology. That actual experiments in these fields involve a schedule in

their conduct means, however, that we must always take cognizance of the effects of the particular schedule chosen; especially so since a change in species, in response, in reinforcer, in stimuli almost inevitably involves a change in schedule as a corollary. We must be careful not to attribute to the difference in species, or response, or reinforcer, or stimuli those differences in the behavior that are really due to differences in the schedule operating. So we must know first about the procedural dependencies of drug effects; in concentrating on these issues at this stage of development of the subject, Thompson and Schuster are simply putting first things first.

We may notice as an aside that since the characteristics of behavior dependent on the schedule have been shown to be so important in determining drug effects on the behavior, people have been recognizing increasingly that the effects of many other variables are importantly determined by schedule-dependent characteristics of behavior. Two examples out of the many that could be cited are the studies by Falk (1961) of excessive drinking in rats determined by a schedule of food-reinforcement without manipulation of any factors that would traditionally be associated with determination of drinking and the previously mentioned studies of Morse and Kelleher on maintenance of responding solely by severe electric shocks consequent on a response, shocks that on other schedules would suppress responding. Falk found that rats with free access to water in their home cage would drink more than three times as much water during a 3-hr session under a VI schedule than the mean preexperimental 24-hr value. Thus, the VI schedule created what traditionally would have been called motivation. Kelleher and Morse (1968) found that squirrel monkeys with no history of avoidance could be trained to respond under an FI schedule when the reinforcing stimuli at the end of the interval was essentially the delivery on a response of a 15-mA electric shock to the tail of the monkey. Such a shock, on other schedules, would lead to vast amounts of behavior whose consequences was postponement of the shock, or, on still other schedules, would suppress strong behavior whose occurrence was promptly followed by the shock. The schedule can thus determine whether a given stimulus, the electric shock, will function as what traditionally

has been called a "reward", or whether it will function as an aversive stimulus, to be avoided, or whether it will function as a punishing stimulus, which suppresses behavior. That a given stimulus can function as an aversive event and as a punishing event comes as no surprise, but that it can also function as a "reward" is dramatic evidence of the crucial role of schedules in the organization and determination of behavior.

Mechanisms

Having found big effects of drugs on behavior, the next question is: what attributes of behavior is it that drugs are affecting? At least, that is what the next question should be. Historically, behavioral pharmacology has advanced to this question backwards. People have started by asking: what are the effects of drugs on motivation? on perception? on motor dexterity? on learning? and so on, rather than starting with a drug effect and finding out the nature of the effect. To start behavioral pharmacology with the nature of the drug effects prejudged is surely bad strategy. Scientific pharmacology started with people who were interested in poisons that affected animals and man and who started to analyze the effects. Behavioral pharmacology must start with behavioral effects of drugs and must then analyze the effects. What a pleasure it is, then, to find that Thompson and Schuster have made explicit for beginners just such an approach. One could bicker about the taxonomy, the examples and the analogies; but to do so would obscure the heuristic correctness of the approach.

A drug makes an individual do some things under particular circumstances at certain times that he would not have done otherwise and makes him not do some things that he otherwise would have done during a certain period. Translated into psychological terms, a drug makes some responses become more likely and other responses become less likely in the presence of particular stimuli during a certain period. Different drugs differently affect the different tendencies to make different responses. Very complicated! The problems are: first, what are the features of the patterns of responding that are changed by a given dose of a drug; how is the pattern changed, and what determines susceptibility; and what are the characteristics of the drugs

that determine whether a given pattern of responding will be changed? Included in the characteristics of the drug are dose-dependencies, how the effect varies with the dose. If we study the effect of a drug at one dose level only, then anything that is said about the drug at other dose levels is extrapolation, and usually quite unjustified extrapolation.

An example of a surprisingly simple characteristic of responding that seems to be quite generally important in determining drug effects is the rate of responding. Thompson and Schuster analogize the dependence of drug effects on control rate of responding to the familiar dependency of drug effects on physiological systems to the functional state of the system; they single out effects on blood pressure but they could equally well have chosen the dependency of the effects on propulsion in the gastro-intestinal tract on preexisting smooth muscle tone and peristalsis or of the effects on liver glycogen on the preexisting condition of carbohydrate metabolism; and so on. There is one big difference between physiological and behavioral systems they overlook. In physiological systems, in the absence of specific information we can assume values to fall within some narrow range of normality; in behavioral systems there is no comparable narrow range of "normal" rates of responding. Consistent mean rates in pigeons have been recorded at least over the range from about 0.01 to 3 responses per second, a 300-fold range that is far greater than permissible for any vital physiological system. It is therefore not surprising that the effects of drugs on behavior are grossly affected by the environmental influences that determine the rate of responding; for this reason alone, environmental influences are quantitatively much more predominant in determining behavioral effects of drugs than physiological effects of drugs.

A final aside, please, on the way in which pitfalls associated with the words depressants and stimulants are avoided in the book, although no rule seems to be given explicitly. The authors are obviously aware of the dangers; for example, stimulant appears in quotes on p. 168. The problem arises out of old sins of extrapolation. Let me illustrate. Pentobarbital is universally classed as a depressant. It is called a depressant because in sufficient doses it can produce general anesthesia and even

Stage IV anesthesia in which respiration and central vasomotor control cease. It is reasonable to call such a state "central nervous system depression", but it is better to use the more precise term general anesthesia. The trouble with the word depression is that we slip easily from saying that a drug depresses a behavioral activity to saying the drug is a depressant. We then expect a depressant to depress without regard to the behavior under study or the dose level (see Jarvik, p. 62) and we start doing experiments on depressants and stimulants like those of Eysenck (1957). But the very grossness of the characterization of a drug as a depressant is a denial of those principles of selectivity mentioned earlier—selectivity with regard to behavior and differential selectivity from drug to drug. To expect that because a drug can produce general anesthesia it will always or even usually in small doses lead to a reduction of any selected behavioral activity is a quite unjustified extrapolation. As a consequence, the terms depression and stimulation must be used only when the behavior that is depressed or stimulated is specified and then only as synonyms for decreased or increased; which are far safer words.

In conclusion, let me say to non-behavioral pharmacological readers that the impact of behavioral pharmacology will not be confined to pharmacology and clinical medicine. If the theories of behavior that enable us to make sense of the drug effects are different from traditional psychological theories, then it will behoove us to take a new look at the anatomy of psychology. Drugs are totally blind to the prestige and persuasiveness of psychological theorists and yield impartial evidence. Cherished notions and unquestioned assumptions may be expected to fall victim to the new look. The new theories, however, will be more in congruence with biology, and eventually will show their greater power in greater generality and greater ability to predict unequivocally and quantitatively. All this is happening already, and this book will serve to speed the enlightenment.

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