Pharmacology Biochemistry & Behavior, Vol. 19, pp. 1027–1029, 1983. © Ankho International Inc. Printed in the U.S.A.

Interrelationships Between Behavior and Pharmacology as Factors Determining the Effects of Nicotine

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BARRETT, J. E. *Interrelationships between behavior and pharmacology as factors determining the effects of nicotine.* PHARMACOL BIOCHEM BEHAV **19**(6) 1027–1029, 1983.—Behavioral consequences play an important role in determining subsequent behavior. The specific effects a particular consequent event will have, however, depend on many factors. Under certain conditions, the same event can produce diametrically opposite effects on behavior. Nicotine and electric shock are events which can function either as reinforcers capable of maintaining behavior, or as punishers which can suppress behavior. The reinforcing or punishing properties of consequent events depend on the prior experience of the organism and on the conditions existing at the time those events occur. The study of these pivotal events, and of those factors which contribute to their dual behavioral effects, has provided important information for developing a better understanding of general processes governing behavior. Further, the results of these studies have clarified the role of both behavioral and environmental factors in the initiation and maintenance of drug-taking behavior.

Nicotine Electric shock Behavior Pharmacology

MANY drugs have been shown to function as effective reinforcing events in laboratory animals. Often, the ability of a drug to serve as a reinforcer under such conditions has been regarded as a major factor contributing to a drug's abuse potential. Thus, compounds such as cocaine, amphetamine and morphine readily sustain substantial levels of behavior that results in their administration. These drugs are used widely, often detrimentally, and have been studied extensively using drug self-administration procedures. Many other drugs, however, although also used widely by humans, do not appear to be easily established as reinforcing events. These include some of the hallucinogenic compounds (e.g., LSD), the anti-anxiety compounds such as the benzodiazepines, and what is believed to be the major constituent of tobacco, nicotine. Perhaps different antecedent and/or current conditions are necessary for these compounds to maintain behavior than are required for other drugs.

Results from a number of studies in which electric shock has either maintained or suppressed behavior are relevant to this issue because they have helped clarify those processes which help to determine the specific effects consequent events will have on behavior. These findings with shock have general implications for developing a better understanding of the interrelationships between behavioral and pharmacological factors which contribute to the effects that drugs and other environmental influences have on behavior.

EXPERIMENTS WITH RESPONSE-PRODUCED SHOCK

Although response-produced shock has been used most frequently in studies of punishment to suppress behavior, it is now clear that the delivery of shock immediately following a response can also maintain behavior. Initial experiments with squirrel monkeys [10, 11, 14] and cats [5] demonstrated that responding could be maintained under fixed-interval schedules by response-produced shock. Stable, positively-accelerated rates and patterns of responding could be developed and maintained by shock presentation that were comparable to those occurring under similar schedules of food presentation, drug administration and other reinforcing events.

SCHEDULE OF REINFORCEMENT

The schedule under which shock was delivered was crucial in determining whether responding was maintained or suppressed. When shock was delivered under a fixed-interval schedule, performances were well-maintained; however, when in the same animals every response produced an identical electric shock, responding was suppressed [10]. Thus, shock could *both* maintain and suppress responding of the same animal at approximately the same time depending on the schedule under which it was delivered.

The general findings of these studies are summarized in Fig. 1 which provides a composite illustration of the multiple effects electric shock can have on behavior. Panel A shows responding of a squirrel monkey maintained under a 5-min fixed-interval schedule of food presentation. As is characteristic of this schedule, there is a customary early period during which little or no responding occurs, followed by a period of positively-accelerated responding that continues until food delivery. Panel B shows the rate-decreasing ef-

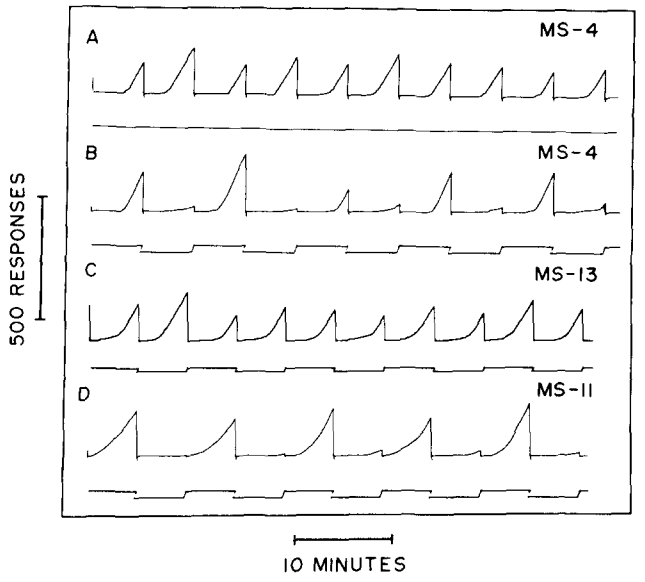

FIG. 1. Multiple effects of response-produced shock on responding. Ordinate: cumulative responses; abscissae: time. All performances were maintained under a 5-min fixed-interval schedule. The pen reset at the end of each fixed-interval interval. (A) fixed-interval food-presentation schedule; (B) *punishment:* when line beneath each record was displaced, every 30th response under the fixed-interval food-presentation schedule produced shock; (C) *reinforcement:* responding was maintained by response-produced shock when the line beneath the records was displaced; (D) *simultaneous reinforcement and punishment:* responding was maintained by shock when the line was not deflected; during alternate components every 30th response during the interval produced shock and the first response after the interval elapsed produced food. See text for more detailed explanation.

fects (i.e., punishment) of delivering a 7 mA electric shock following each 30th response during alternate components of the 5-min fixed-interval schedule of food delivery. During this time, punishment and non-punishment components of the schedule were correlated with different visual stimuli (i.e., a multiple schedule). The third cumulative record (Panel C) shows stable performances of a different monkey (MS-13) under a multiple schedule where responding under a 5-min fixed-interval schedule produced either food or shock (7 mA) depending on the prevailing stimuli. Comparable rates and patterns of responding were maintained by both events. The bottom record (Panel D) shows performances developed in a monkey where a 7 mA shock *both maintained and suppressed* responding (MS-11) depending on the schedule under which shock was delivered. During the first and then alternate components, shock was presented under a 5-min fixed-interval schedule. In the second and subsequent even-numbered components, responding produced food, also under a 5-min fixed-interval schedule. Additionally, however, each 30th response during this component (a fixed-ratio schedule) produced the same electric shock that maintained responding in the alternate component. Thus, when delivered under a fixed-interval schedule, shock maintained high rates of responding, whereas when delivered under a fixed-ratio schedule, shock suppressed responding to low levels.

In these experiments, the same noxious stimulus, electric shock, was capable of either suppressing or maintaining behavior depending on how that stimulus was scheduled. It is still not widely acknowledged that merely scheduling the same event in different ways can so profoundly determine the effects that event will have on behavior. Nevertheless, it is clear that the behavioral effects of stimuli such as shock are not intrinsic, immutable properties of those stimuli but depend to a considerable extent on environmental factors such as the manner in which they are delivered.

BEHAVIORAL HISTORY

A second factor involved in these studies with shock and, as with the schedule of reinforcement, of widespread import, is the previous experience of the animal. Performances maintained by shock depend critically on prior experience. In some studies (e.g., [5,11]) responding maintained by shock presentation was developed after initial training under a shock-postponement schedule. However, this history is not essential. Other procedures, such as a schedule of response-independent shock that elicited responding [12] or a schedule of food delivery [10] have also been sufficient to produce a level of responding that could be modulated and then eventually maintained solely by response-produced shock. Performances maintained by shock with MS-13 (shown in the third record) were developed without prior exposure to a shock-postponement schedule [1], whereas with MS-11 (Panel D), responding was established initially under a shock-postponement schedule which was subsequently replaced by the schedule of response-produced shock [3].

These studies, plus others, suggest that shock presentation acts on existing behavior, established in various ways, to produce a particular effect from which subsequent behavior then develops. The behavioral efficacy of many different environmental events depends on both a suitable behavioral history and a favorable immediate environment. Experiments with shock have re-emphasized the critical importance of interactions between historical and contemporary factors as determinants of future behavior. Further, these studies have provided a basis for developing a better understanding of the manner in which events such as drugs can produce multiple behavioral effects.

NICOTINE AND BEHAVIOR

Until recently, it has been difficult to establish reasonable levels of behavior maintained by nicotine in the laboratory. However, studies have now demonstrated reliable, moderate-to-high rates of responding maintained by nicotine self-administration [8]. Conversely, nicotine has also been shown to suppress responding and, therefore, function as a punisher [9]. As is true with electric shock, an important factor in determining whether nicotine will maintain or suppress responding is the schedule under which it is delivered. When responding of squirrel monkeys produced nicotine under a fixed-interval schedule, response rates were maintained that were well above those maintained by saline; in some cases rates of responding maintained by nicotine were comparable to those maintained by cocaine [9]. However, when responding maintained by food produced nicotine under a fixed-ratio schedule, responding was markedly suppressed. These findings are nearly identical to those discussed earlier in this paper with electric shock which were illustrated in Fig. 1.

In related studies responding has been maintained when it postponed scheduled intravenous injections of nicotine [13]. Again, these findings with nicotine parallel those shown with electric shock. Under some conditions, nicotine and electric

shock are able to maintain high levels of schedule-appropriate responding when they are response-produced; under other circumstances, however, these events will maintain responding when they are postponed and will suppress responding when produced. The multiple behavioral properties of events such as electric shock and nicotine are created by and emphasize factors other than their physical and molecular features.

Studies showing that events such as shock and nicotine can produce dual behavioral effects have been important in drawing attention away from classes of events with categorically restrictive boundaries. In doing so, these experiments have emphasized principles and processes that have been often neglected experimentally. For example, procedures which have established nicotine as a reinforcer have occasionally employed a condition where, if responding does not occur, nicotine is injected automatically, independently of whether a response occurs [8,9]. This procedure was also used to establish responding under schedules of response-produced shock [12]. These procedures may be viewed as a violation of "traditional" training procedures or, more accurately, as merely effective methods of developing performances maintained by their consequences. Different events undoubtedly require different procedures for them to be behaviorally effective. Behavior is not always (and is probably only infrequently) "shaped" or gradually developed by the method of successive approximations [6] from a relatively amorphous form to an integrated, structured performance.

Events are also frequently superimposed on behavior which has already been established. Perhaps more often, behavior is literally coerced by the environment. In both instances, the particular behavior, regardless of precipitating factors, is then modified in ways that depend on the immediate environmental consequences and the specific characteristics of the behavior that existed at the time the event occurred.

Studies with electric shock in particular have also been influential in focusing attention on the importance of behavioral history in determining both the momentary and enduring effects of different environmental interventions. A suitable behavioral history is essential for behavior to be maintained by response-produced shock. An organism's behavioral history can also play a significant role in determining the effects of drugs. For example, the behavioral effects of *d*-amphetamine and morphine can be completely different depending on behavioral experience [2,4]. The characteristic rate-decreasing effects of *d*-amphetamine and morphine on punished responding and on responding maintained under shock-avoidance schedules, respectively, can be completely reversed by interpolated exposure to a different schedule of shock delivery. Morphine and *d*-amphetamine produce different effects under these conditions even though performances are no different than those which occurred prior to the intervening experience. Further, the behavioral effects of pentobarbital can also depend on prior experience with other drugs [7].

These studies show that drugs are not substances with static and unalterable behavioral properties. The behavioral effects of drugs can depend in significant ways on experiential factors, both behavioral and pharmacological, which can alter substantially the response to a drug. If the behavioral effects produced by a drug are related to the likelihood that a drug will be used repeatedly, and possibly detrimentally abused, then variables such as prior history which can determine those effects clearly may be involved in the abuse of certain compounds.

SUMMARY

The study of behavior maintained by noxious events such as electric shock, together with the analyses of the behavioral effects of other events such as nicotine that can function in dual ways to either maintain or suppress behavior, has helped clarify and extend fundamental behavioral principles. The behavioral effects produced by events such as drugs and noxious stimuli, as well as numerous other significant environmental consequences, depend to a large extent on both antecedent behavior and current environmental conditions. Subsequent research will undoubtedly extend these principles to other types of environmental events and greatly expand our understanding of those factors involved in determining the multiple effects that consequent events can have on behavior.

ACKNOWLEDGEMENTS

Supported in part by PHS Grant DA-02873. I thank Myra J. Zimmerman for assistance in the preparation of this manuscript.

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