THE EFFECT OF AMPHETAMINE ON FORCED DRINKING IN THE RAT[1]

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Amphetamine is a sympathomimetic drug that is known to decrease the amount of food eaten daily (5). Recently, Andersson and Larsson have shown that amphetamine depresses water intake in the dog (1). They found that, even after an intravenous infusion of a hypertonic NaCl solution, dogs under the influence of amphetamine drank little or nothing when allowed free access to water. Williams and Teitelbaum have studied the drinking behavior of rats, using a technique of forcing rats to drink to postpone electric shock (10). The licking pattern in the forced-drinking situation is a stable and sensitive indicator of the rat's readiness to drink, and the pattern is different when the animal drinks less readily, as it does when it is satiated or when the fluid is unpalatable. It seemed of interest, therefore, to see whether amphetamine would have the same effect on drinking to postpone shock as it has on thirst-induced drinking. Since amphetamine depresses thirst-induced water intake (1), it was expected that water intake forced by electric shock would also be decreased after amphetamine, and that the pattern of licking would be similar to the pattern shown under the conditions in which the rat is less willing to drink to avoid shock. However, as is described below, quite the opposite effect was found: after amphetamine injection, rats in the forced-drinking situation drank water rapidly and in much larger quantities to avoid electric shock. The nature of this phenomenon was then explored more fully, by manipulating several aspects of the shock-avoidance situation.

EXPERIMENT I: THE EFFECT OF AMPHETAMINE ON ANIMALS REWARDED FOR LICKING AT A RAPID RATE

Method

Subjects. Four female rats, two brown and two Wistar albino, from the animal colony of the Harvard Psychological Laboratories were used. They were approximately six months old and weighed between 200 and 250 gm. Throughout the experiment, they were allowed free daily access to Purina laboratory chow pellets and to water.

Apparatus and procedure. The rat was placed in a cage where intermittent electric shocks were delivered through the bars that made up the floor of the cage. By licking the fluid at the end of a tube, the rat could turn off the train of shock pulses and postpone the onset of shock for a period of time. The licks were detected by a drinkometer (9) by means of which the rat completed a grid circuit between the drinking tube and the cage floor.

Shock was provided by the output of a variable transformer. During each shock pulse, the connections between the shock bars were automatically changed in order to prevent the rat from learning to stand on bars that were always of the same polarity. The duration of the shock pulse was 92 msec., and shocks were applied at 0.9-sec. intervals if the rat did not respond. The intensity of shock was varied in the different experiments between 0.5 ma. and 2 ma., but the usual setting was 0.5 ma. A train of shock pulses was used in preference to a steady shock so that the bars of the floor of the cage could serve alternately to detect the licks and to transmit the shock to the rat. During the interval between shock pulses, the bars were connected in parallel so that the rat could stand on any one and still complete the drinkometer circuit when it licked at the tube. During the shock pulse, the bars were connected separately to the shocking apparatus, and the drinkometer was switched out of the circuit to prevent the possibility that shock might be delivered through the fluid in the drinking tube. Thus, the rat could operate the drinkometer only in the interval between shock pulses and never during the shock.

The shock schedule used was modified from one described by Sidman (8). There were two response-shock postponement periods available to the rat—a short one (1 sec.) for licking once or twice, and a long one (15 sec.) for licking three or more times. When the animal was receiving shock, the first lick following a shock postponed the next shock for 1 sec. Each successive lick resulted in the same short postponement, unless there were three or more licks within 1 sec. of each other. When that occurred, the shock was postponed for 15 sec., and each successive lick during this long postponement started the postponement period over again. Thus, the rat had 15 sec. free of shock from the time of the last lick and could avoid shock indefinitely by licking at least once in 15 sec. If it did not

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respond for 15 sec., the long postponement period ended, shock came on again, and the rat again had two postponement periods available.

A light above the cage turned on when the train of shock pulses started and turned off and remained unlit whenever the animal had succeeded in postponing the shock by licking. This served in addition to the shock pulses as a signal to the animal that shock had been postponed by licking.

In order to prevent responses other than licking (e.g., pawing the tube or pressing it with the nose) from operating the drinkometer, accessibility to the drinking tube was restricted. The lower tip of the tube was set 4 mm. from a rectangular opening 5 mm. wide by 9 mm. high in the front wall of the cage through which the rat licks. The opening was 4 in. above the cage floor.

After an initial training in which the animals learned to lick at the tube in order to turn off shock (10), 5 or 6, 1-hr. sessions of forced drinking were usually adequate to produce very consistent licking behavior. Before each 1-hr. session, the water bottle was removed from the animal's living cage for 1 hr. to insure that the rat had not just drunk a large quantity of water.

In evaluating the effect of the drug, the usual procedure was to establish a control period of 15 to 20 min. of forced drinking, inject the animal, place it back in the forced-drinking situation, and observe the effect on the pattern of drinking. The animal was often forced to drink for several hours after injection until the effect wore off. At least 2 days were allowed to elapse before the animal was injected again. Usually 5 mg/kg of a solution of 20 mg/cc of dl-amphetamine sulphate (Benzedrine) in 0.9% sodium chloride solution was used. All drugs were injected subcutaneously.

Results and Discussion

As is shown at the top of Figure 1, animals in the forced-drinking situation lick in a characteristic pattern to postpone shock. They obtain the long shock-postponement period by licking three or four times, and then they wait for the next shock. When this comes, they again lick in a burst of three or four licks and wait out their shock-postponement period until the next shock. They almost never lick again during a shock-postponement period, although it is possible to avoid shock indefinitely by licking once before the end of each postponement period. In the course of 1 hr. of drinking to escape shock, they may ingest 4 to 5 ml. of water.

Within 10 min. after subcutaneous injection of 5 mg/kg dl-amphetamine, the animal's fur stood on end, its eyes bulged, and its pupils became dilated. At the same time, it began to react more violently to even a relatively weak shock by leaping around the cage and clawing at the cage door. If it was subjected to shock

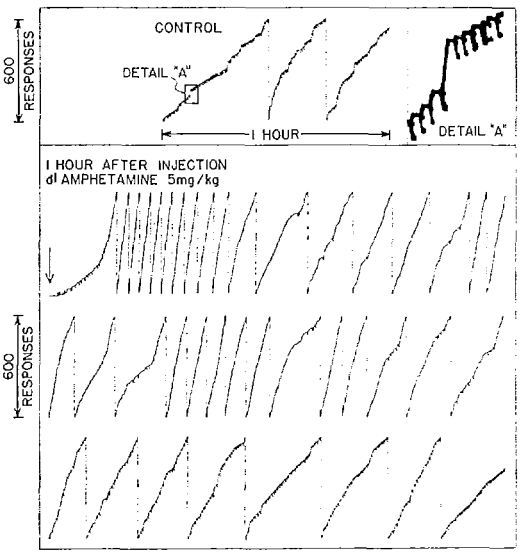

FIG. 1. Cumulative response records showing forced drinking. The pen moves upward with each lick and toward the right as time elapses. Each shock period is indicated by a small (⅛ in.) downward displacement of the pen. Control: Normal forced drinking of water, showing several licks after each shock and then the wait for the next shock. After amphetamine: The animal no longer waits for each shock before drinking but drinks very rapidly and avoids shock.

without being allowed the opportunity to escape by licking, within 10 or 15 min. its hind legs became limp and cold and it became unable to stand. It became very wet around the nose and mouth and, in the extreme, the fur on the entire underside of its body became moist. The same effect could be produced in the rat without amphetamine, but only by using a very strong shock for at least a half-hour.

As seen in Figure 1, when the rat was placed in the shock cage 1 hr. after amphetamine injection and was forced to drink, a striking change also occurred in the pattern of licking and in the amount drunk. There was a period of 2 or 3 min. during which the animal gave only single licks or refused to lick and took many shocks. This behavior then changed quite drastically: the animal began to lick in bursts more readily and then to respond during the shock-postponement period. The frequency of licking during the shock-postponement period increased until the animal was responding quite rapidly and was avoiding shock completely. This licking had a

quality of wildness, being poorly controlled and very often missing the tube entirely. The amount of fluid consumed during this period increased greatly, averaging 10 to 15 ml/hr.

When the animals were thus forced to drink hour after hour, this wild drinking behavior continued for 5 to 6 hr., during which time they consumed as much as 80 ml. of water. One animal, forced to lick for 18 consecutive hours, consumed 160 ml. of water.

After 5 to 6 hr., the licking pattern began to change back to normal, presumably as the main effects of the drug wore off. The animals began to pause longer between licks and to take shock more and more frequently, until after 6 hr. they were once again waiting for each shock, then licking three times, and waiting for the next shock.

This effect has been repeated at least twenty times with each of the four animals. Doses of 3 mg/kg or greater of dl-amphetamine produced the effect. The d-isomers of amphetamine or methamphetamine were effective in doses of 1 mg/kg. When the experiment was repeated several times with the same animal, the animal generally consumed less water than it had the first time, but it always drank more than a normal amount and always showed the characteristic change in its pattern of licking.

Since amphetamine produces a great increase in the amount of fluid drunk in the forced-drinking situation, it is clear that this result is different from the decrease in water intake after amphetamine injection in dogs reported by Andersson and Larsson (1). We did an experiment comparable to theirs, therefore, to see whether amphetamine would depress thirst-induced water intake in rats.[3] Eight female albino rats were injected with 5 mg/kg dl-amphetamine. Thirty minutes later, these rats and seven controls were injected intraperitoneally with 2 ml. of 1 M NaCl solution per 100 gm. of body weight. All the animals were allowed free access to water. The animals that had not received prior injections of amphetamine showed little bodily activity but drank an average of 6.9 ml. of water during the first 2 hr. after hypertonic salt injection and 3.3 ml. during the third hour. Rats that had been previously injected showed a great deal of bodily activity even after the hypertonic salt injection, but none of them drank any water in the half-hour following the amphetamine injection or in the 2 hr. following the hypertonic salt injection. In the third hour, they drank 0.5 ml. After 3 hr., they began to drink more water, and within the following 2 hr. had equaled or surpassed the water intake of the control animals.

Similarly, when two days of water deprivation was substituted for the hypertonic salt solution, an injection of 5 mg/kg dl-amphetamine, 30 min. prior to access to water, completely prevented the consumption of any water for 3 hr. Animals that had received no amphetamine drank 16 cc. in the first 3 hr. of access to water.

We have, therefore, verified the findings of Andersson and Larsson in showing that amphetamine will completely inhibit water intake for at least 2 hr. even in the presence of an extreme thirst stimulus. Since amphetamine produces the opposite effect on drinking when the animals are forced to drink to postpone electric shock, it seemed wise to analyze more closely the effects of amphetamine on shock-avoidance behavior.

When the four animals were trained to turn a wheel instead of to lick, the identical shock-postponement schedule produced exactly the same kind of escape behavior. The animals waited for the shock, turned the wheel three or four times, and then waited during the postponement period until the next shock. The wheel was 2 in. in diameter and 1½ in. wide, with 10 ⅛-in. spokes spaced evenly around the circumference. The administration of amphetamine produced the same kind of effect on wheel-turning as on licking: the rats no longer waited for the next shock before responding, but kept responding before the shock came again.

Furthermore, when the animals were under the influence of amphetamine and were avoiding shock by turning the wheel, if they were placed immediately in the cage where the licking response was appropriate, they would instantly begin to display licking behavior in the same avoidance pattern. If they were placed in their home living cage, however, they did not lick the water tube. There was a great

[3] We wish to thank Mark E. Molliver for his technical assistance in this experiment.

deal of bodily activity, but it was apparently not channeled into any one type of activity.

The excessive drinking after amphetamine injection in the forced-drinking situation seems, then, to be due to the fact that the licking response is effective in avoiding shock. However, one might say that amphetamine merely increases the rate of responding in any work situation, and that the change from escape to avoidance behavior is merely a by-product of the increased rate of work. Therefore, a schedule was set up in which the rat could postpone shock more effectively by responding slowly and with few responses than by many rapid responses.

EXPERIMENT II: THE EFFECT OF AMPHETAMINE ON ANIMALS REWARDED FOR LICKING AT A SLOW RATE

Method

The four rats used previously were now trained to lick according to the new schedule. This schedule was merely the inverse of the one used in the first experiment: if the rat licked once or twice, it received the 15-sec. postponement; if it licked three or more times within 3 sec., it was immediately switched over to the 1-sec. shock postponement. In order to avoid shock for long periods of time, the rat would have to turn off the train of shock pulses by licking once or twice, after which it could keep on licking during the shock-postponement period. It could extend that period indefinitely, but only by licking fewer than three times during each consecutive 3-sec. interval. The 3-sec. intervals were timed by a timer whose audible resetting served as a signal that each 3-sec. interval had elapsed.

Results and Discussion

As the middle of Figure 2 shows, before injection the rats displayed a characteristic and stable licking pattern on the slow schedule. As in the first experiment, they showed escape behavior to shock—that is, they licked once or twice to escape the train of shock pulses, and then waited without responding until the shock pulses started again at the end of the postponement period. They did not avoid by responding during the postponement period. Observations of the effects of drugs were not started until the animals were receiving the short postponement period (for licking too frequently) in less than 10% of their opportunities to turn off the train of shock pulses. Furthermore, when they reached this criterion at the standard level of shock intensity, they were made to repeat this performance at higher and very traumatic shock levels to ensure that no mere intensification of pain would disrupt their response pattern.

The middle of Figure 2 shows, in addition, the effect of subcutaneous administration of 5 mg./kg dl-amphetamine on forced drinking governed by a slow-rate schedule. Within 30 min. after the injection, the rat began to show avoidance licking. For several minutes at a time, it continually avoided shock by licking at a slow rate—that is, only once or twice in each consecutive 3-sec. interval. Then as the drug took full effect, the animal began suddenly to respond faster and with more licks, despite the fact that it now began to receive shock postponements lasting only 1 sec. and thus took many more shocks than it would have taken with only single licks. Eventually, however, the rat was licking so rapidly that even with only a 1-sec. postponement, the shock frequency decreased considerably.

On the face of it, this could be interpreted to mean that amphetamine merely acts to increase the animal's rate of responding, and that as a natural consequence of this, it responds more and more often in the shock-postponement period. Thus, though the rat seems to be changing from escape to avoidance behavior, is it just responding with shorter pauses between each lick? When, on the slow-rate schedule, the rate of licking becomes too fast and the rat receives many shocks, it does not slow its licking rate but continues to lick rapidly.

A closer analysis of the amphetamine-influenced behavior on the slow-rate schedule indicates that these hypotheses do not fully account for the behavior.

As the drug began to take effect, for periods as long as 5 to 10 min. the rats licked at a rate slow enough to avoid shock completely. The responses were not spaced uniformly within the shock-postponement period; on the contrary, they usually followed the reset timer signal very closely. Thus, the rats paused until the signal had occurred and then gave the one or two licks the schedule allowed. This slow licking served to prolong the period of successful shock avoidance. But as the effect of the drug became greater, the animals more frequently licked in bursts, despite the fact that these led to shock 1 sec. later.

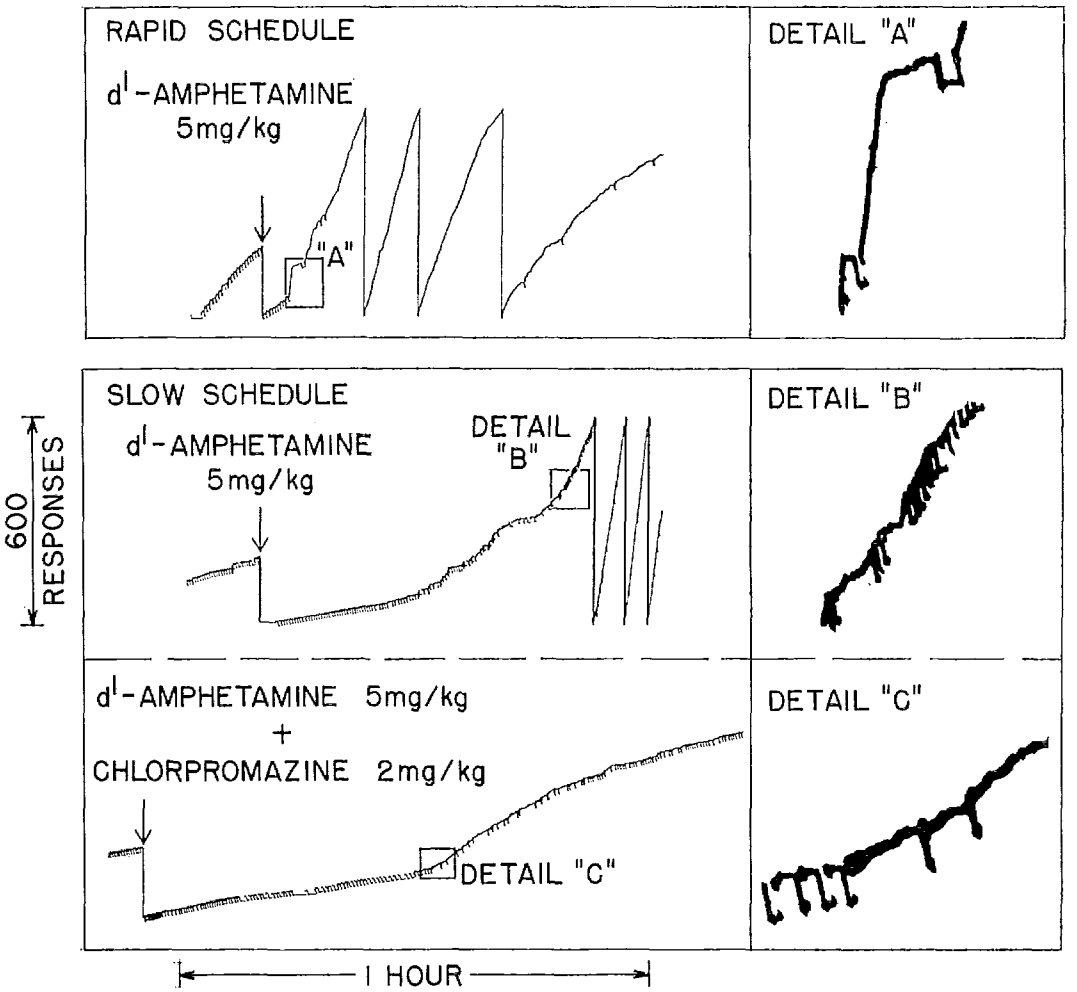

FIG. 2. Forced drinking after amphetamine on different shock-avoidance schedules. Where rapid drinking avoids shock, the animal soon drinks rapidly and avoids shock almost completely (few ⅛-in. downward displacements are seen). Where slow licking avoids shock, the animal changes from slow escape to slow avoidance licking. This soon changes further to wild, rapid licking even though many shocks are received (Detail B shows the transition). When chlorpromazine is combined with amphetamine on the slow-licking schedule, the only effect of amphetamine is to produce slow avoidance without wild, rapid licking.

In order to understand the nature of the effect of amphetamine, it is instructive also to look more closely at the typical rat's behavior when it is licking rapidly in spite of receiving more shock.

A first observation was that, when the apparatus was turned off and the cage door opened, the animal did not immediately climb out as it would have normally. Instead, it remained at the licking aperture and continued to lick steadily. If allowed to continue, it consumed as much as 10 to 15 cc. in the next hour or two, even though no shock was present. If the drinking tube was removed, the rat continued to lick steadily through the licking aperture at the empty air for several hours. If during this time it was placed in its home cage, it showed no licking behavior at all, only apparently undirected activity. When replaced in the shock cage, it immediately resumed licking through the aperture at the empty air. If it was placed in the shock cage that had a wheel in the front panel instead of a licking aperture, it began to turn the wheel and continued this activity steadily for hours.

If the animal was allowed to continue licking

at the tube when the shock and the sound and light signal of the schedule were turned off, it continued to lick for several hours before it finally stopped. If, at this point, the sound and light of the schedule were turned on but no shock was presented, the animal resumed licking and continued to show the rapid licking pattern. Gradually, this pattern changed to escape-licking, and finally the animal again stopped licking. If, at this time, usually 5 to 6 hr. after the injection, the shock was turned back on, the animal showed the normal pattern of waiting for shock before licking.

To the present *E*s, this behavior seems to indicate that when an animal under amphetamine abandons the shock-postponement schedule and shows wild, rapid licking, similar to that seen in Experiment I, it has become oblivious to many of the external events that were formerly affecting its behavior and even to the consequences of its actions. In the shock cage the rat's behavior is directed completely by the licking aperture or the wheel, both of which elicit the response that is appropriate for turning off shock. The additional shocks received for responding too fast on the slow-rate schedule seem merely to goad the animal to respond even faster.

When the dose of amphetamine is decreased in the slow-licking situation, it is possible to produce various degrees of the entire phenomenon described above. Doses of 3 mg/kg or greater of dl-amphetamine were sufficient to produce the slow avoidance licking and then the wild, rapid licking. Doses of 1 to 3 mg/kg were sufficient to produce the slow avoidance licking without the breakdown of the discrimination of the shock schedule. Less than 1 mg/kg seemed to have little or no consistent effect on the change from escape to avoidance.

The wild, rapid licking seems to have resulted from an interaction of shock and amphetamine. When the dose of amphetamine used produced slow avoidance but not wild licking, it was often possible to precipitate the rapid licking by subjecting the animal to a period of strong shock. Indeed, very strong shock for prolonged periods, even without amphetamine, produced some wild, rapid licking in addition to many of the same stress symptoms that appeared with amphetamine. But in order to produce these effects without amphetamine, such strong shock was needed that the animals soon appeared stunned or numbed and were unable to respond for prolonged periods of time. Conversely, in trained animals, the wild, rapid licking could be produced without any shock at all by using a massive dose of amphetamine. The animal was injected with 10 mg/kg dl-amphetamine and was placed in the shock cage, but the apparatus was not turned on. In a few minutes the rat began to show restless behavior and to claw violently at the cage door, the way they do when they are trying to escape from the cage. Finally, it went over to the licking aperture and began to lick rapidly at the tube, and behaved in every respect as it had when shock and amphetamine were combined. As always, it did not lick when it was placed in its home living cage, but when it was placed in the shock cage with the wheel, it turned the wheel steadily.

The fact that, after a massive dose of amphetamine, just being in the shock cage is sufficient to produce the avoidance behavior without any shock at all being present, indicates that the rat is responding more strongly than before to the mere threat of shock presentation. Without amphetamine, this kind of behavior does not occur. The rat never starts to lick before shock is presented, and it ceases whenever the shock is turned off. Since amphetamine in huge doses has often been reported to produce extreme apprehension in human beings (7), it is possible that a somewhat similar effect is being produced in the rats in the shock cage.

It is possible that if amphetamine produced increased emotionality, it might be counteracted by a tranquilizing drug. It has been reported by Lasagna et al. (6) that mice placed together in groups of three may be killed by doses of amphetamine one-eighth as great as what is lethal when they are alone. These *E*s found that chlorpromazine nullified almost completely the extra danger present in the group situation and reduced the mortality to the level found for the solitary mouse. They suspected that the increased mortality in the group situation was due to the increased excitement and stress produced by fighting and other interaction among the amphetamine-treated mice. For this reason, the present

experiment was carried out to see whether chlorpromazine could counteract the effects of amphetamine on forced drinking.

Amphetamine in a dose of 5 mg/kg always produced the slow avoidance which then turned into the wild, rapid licking. By using 2 mg/kg chlorpromazine in various time relations with the amphetamine, it was possible to produce various degrees of the effect of the 5 mg/kg dose of the amphetamine or to counteract it completely. By itself, chlorpromazine within a half-hour produced a slight decrease in the readiness with which the rat would respond to turn off the train of shock pulses. Usually it responded after the first or second shock. After chlorpromazine it often waited until it had received 20 or 30 shocks. This effect lasted for about 1 hr. But other than in this decrease in the rate at which the rat responded to turn off the shock, there seemed to be no other change in the animal after this dose of chlorpromazine. As is shown in the bottom section of Figure 2, when rats were injected simultaneously with chlorpromazine and amphetamine, only slow avoidance licking appeared without any breakdown of the discrimination of the shock schedule and without the accompanying rapid licking. Furthermore, it seemed that the slow avoidance was maintained longer and with more control over the licking with the double injection than with a weak dose of amphetamine alone. With amphetamine alone, the animal often seemed to control its licking poorly, in that it licked inaccurately and often missed the tube as the drug took greater effect. With the addition of chlorpromazine, the lick seemed more precisely directed at the tube, and it missed much less often. Chlorpromazine injected 1 hr. before amphetamine completely prevented any change in the normal pattern of licking. The animal continued to show the escape pattern of licking, and the only change that occurred was that the animal responded immediately after the first shock without waiting for several shocks as it had been doing under chlorpromazine alone. If amphetamine was injected first, and chlorpromazine administered as soon as the wild licking was demonstrated, the effect of the amphetamine could be cut short.

In each of the experiments described above, the change from escape to avoidance behavior under amphetamine is always accompanied by an increase in the rate at which the animal gives the required response. A final experiment was therefore set up to see whether an animal under amphetamine could avoid shock by ceasing to respond.

EXPERIMENT III: THE EFFECT OF AMPHETAMINE ON PUNISHMENT

An experiment was set up in which responding was maintained by food reward, but during a fixed interval after the onset of a signal the animal was required to stop work in order to avoid electric shock. This schedule is similar to one previously described by Azrin (2). Four different rats were trained in this manner.

Method

A Skinner box was constructed in which the animal had to press a Plexiglas panel (4, p. 16) with its nose in order to receive a small quantity of a liquid diet. The rat pressed the panel through a 1-in. circular aperture in the front wall of the cage, 1½ in. above the floor. When the reward was delivered, a light went on at the top of the cage, and an opening in the rear wall of the cage, 11.5 in. from the front wall, was uncovered for a period of 4 sec. By licking at a drinking tube through this rear opening, the rat could obtain approximately 0.1 ml. of the liquid diet. The floor of the cage was made of ⅛-in. steel bars ½ in. apart through which shock could be delivered. The entire cage was set in a picnic icebox to prevent the animal from being distracted by visual and auditory stimuli extraneous to the work situation.

First the animal was allowed to receive food each time it pressed the panel; then it was put on a schedule in which the time intervals between rewarded responses were varied in a fixed irregular order so that the average time interval was approximately 60 sec. When the rat had established a uniform rate of pressing on this schedule, a buzzer signal was introduced. After each 3½ min. in which the animal was allowed to work for food, the buzzer signal came on for 2 min. The animal could receive food on the same variable-interval schedule during the first 1½ min. of the 2-min. signal period. However, if it pressed the panel during the last 30 sec. of the signal period, no food was delivered, but instead the rat immediately received an electric shock, 0.5 ma. in intensity and 0.75 sec. in duration, and the signal terminated. If it did not respond during the last 30 sec. of the signal period, it avoided shock, and the signal terminated on schedule. Whenever the signal terminated, the cycle began again in which the animal was allowed to press for food without the threat of shock.

Results and Discussion

After several hours of training on this schedule, the animals established a clear discrimination of the possibility of shock during the signal period. As seen in the upper half of Figure 3, they maintained a high and fairly uniform rate of work when the signal was not on. When the signal was on, there was a clearly perceptible decrease in the rate at which the rat pressed the panel, and it usually avoided shock by not responding during the critical 30-sec. period. Occasionally, it received a shock for a response during that period, but that seemed not to affect it greatly, for it would immediately begin to work again at the higher rate characteristic of the signal-free period.

In this experiment d-amphetamine was used instead of dl-amphetamine. When the dose was moderate, the rat worked at a high rate and still it avoided shock quite successfully.

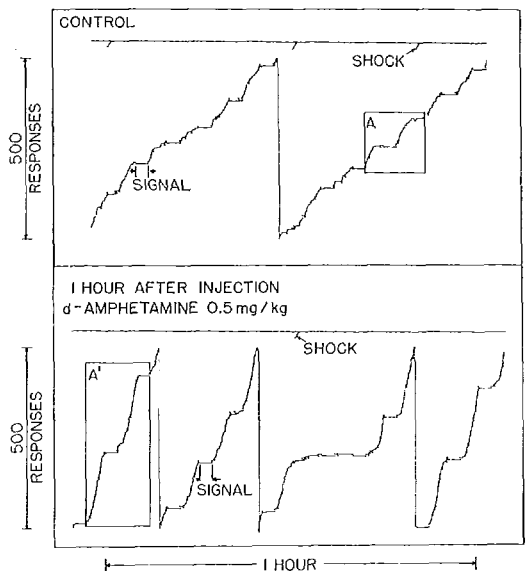

FIG. 3. Effect of amphetamine on rate of working for food where a response during the last 30 sec. of a signal is punished by electric shock. Shock is indicated by short marks in each upper horizontal line. Food reward is indicated by short downward displacements of the pen during the signal-free period and short upward displacements during the signal. Frames *A* and *A'* show comparable time cycles. After amphetamine, the animal works at a higher rate for food, yet still refrains from responding and avoids shock during most signal periods. If it receives a shock, this now causes the animal to cease work almost entirely for several minutes before it goes back to work.

The bottom half of Figure 3 shows the effect of 0.5 mg/kg d-amphetamine 1 hr. after injection. The rate of responding increased greatly during the signal-free period. But as soon as the signal began to sound, the rat abruptly ceased almost completely. When the signal ended, the rat went back to work again at the very high rate. From this sequence of behavior, it is clear that, even though amphetamine is causing the rate of responding to increase, the rat can stop all work completely if this is required for the avoidance of shock. This finding agrees well with the findings of Brady (3) that, under amphetamine, the animals' free rate of responding for water went up, but, when a signal that had been paired with inescapable shock was sounded, the animals ceased work almost completely.

The bottom half of Figure 3 shows another effect of amphetamine. The animals usually avoided shock very successfully and received it only infrequently. The few shocks they did receive, however, affected them much more than shocks received when they were not under amphetamine. As Figure 3 shows, immediately after the shock the rat decreased markedly the number of times it pressed the panel, even in the signal-free period. This decrease lasted for 5 or 10 min., after which the rat again began to work at a high rate.

If one watched an animal under amphetamine working in this situation, one could see clear-cut signs of conflict in its behavior. When there was no signal, it pressed rapidly and vigorously at the panel. When the signal sounded, however, it backed quickly away from the panel. During the entire duration of the signal, the animal showed marked approach-avoidance behavior toward the panel. The conflict was especially noticeable because the food and the panel were at opposite ends of the cage. The rat approached the panel slowly and paused with its nose a short distance from it. Then as it inched closer, it might suddenly yank its head back and leap violently backward to the rear of the cage. This sequence might be repeated several times during each 2-min. signal period, during which time the cumulative record showed no responses at all. The rat sometimes seemed to resolve the conflict by lying down at the very rear of the cage until the signal was over. Then it leaped up and went back to work.

When a larger dose (1 mg/kg) of d-amphetamine was administered, a phenomenon similar to what was seen in the forced-drinking situation occurred. After an hour or so, the animal could be seen pressing the panel at a rather high rate during the signal period as well as during the signal-free period. When it received shock, it leaped backward to the rear of the cage but instantly returned to the panel and began to work again. When food reinforcement was presented—that is, when the light went on and the cover receded from the food aperture—the rat did not respond to this, but continued to press rapidly at the panel. Normally, or after a smaller dose of amphetamine, the animal responded instantly to the light by running to the food aperture and licking at the drinking tube. Now, even if the apparatus was turned off, the animal continued to press the panel, regardless of whether or not food was presented. Indeed, if *E* attempted to remove it from the cage, or placed it at the open food aperture for free access to food, it did not lick the tube but instead scrambled back to the panel and began pressing again. Again, as in the forced-drinking situation, an animal that had received a large dose of amphetamine seemed no longer to discriminate many of the environmental events that ordinarily affect it. On the other hand, it seemed strongly impelled to continue the behavior appropriate in the work situation.

Amphetamine seems to have a much more variable effect on behavior maintained by food reward than on behavior directed toward escaping shock. When a rat is working for food, the same dose of amphetamine may on one day completely depress all responding, and on another day cause a great increase in the rate of work. When, however, the animal is responding in order to escape shock in the forced-drinking situation, a particular dose of amphetamine seems to produce similar results on different occasions and even in different rats. This may be due to the fact that the shock in the forced-drinking situation is an extremely compelling stimulus, in contrast with the food-reward situation, in which the animal's rate of work depends on its degree of food deprivation. Food deprivation is difficult to keep constant from day to day and is a much less well defined stimulus to activity than is electric shock. Another factor in the variability of results with food reward is the possibility that large doses of amphetamine may directly affect the appetite for food and thus the rate of working for it.

Amphetamine obviously has multiple and diverse effects which interact in determining behavior in a given situation. It has powerful effects on food intake, water intake, and bodily activity, and, in addition, generalized effects on organs governed by the sympathetic nervous system. But from these experiments, it seems clear that one important effect of amphetamine is to influence the way the animal is affected by electric shock and the way it will work to avoid that shock. Despite the fact that amphetamine ordinarily depresses water intake, when the response required to escape shock is that of licking the fluid in a tube, the animal will change from escape to avoidance behavior and will in the process ingest a great deal of fluid. When, under amphetamine, a rat is required to respond slowly or to cease responding in order to avoid shock, it does so unless the dose is too great. When too much amphetamine is given, the animal responds in a manner appropriate to the work situation but no longer appears to discriminate many of the stimuli that previously influenced it.

SUMMARY

Amphetamine depresses thirst-induced water intake in the rat. However, when rats were forced to drink water to escape electric shock, injection of amphetamine caused them to increase greatly the amount of water they drank. Simultaneously, they changed their response pattern from escape from shock to avoidance of shock by licking very rapidly.

In a schedule that called for slow licking to avoid shock, rats that had received moderate doses of amphetamine avoided shock successfully. When the dose was too large, however, the rats no longer responded to the shock schedule; they licked very rapidly, even though this resulted in more shocks. When they were licking thus rapidly, it was possible to demonstrate that they were no longer discriminating the shock schedule or even the consequences of their responses, but were still performing the response that was appropriate to avoiding shock.

There appeared to be an interaction between

the intensity of shock used and the amount of amphetamine needed to produce the rapid licking. The effect of amphetamine could be counteracted by chlorpromazine.

Rats were trained to press a panel for food but were punished by electric shock if they responded during a signal period. A moderate dose of amphetamine caused the rats to increase their rate of working for food, but simultaneously they successfully avoided shock by ceasing to respond during the critical signal period.

These results seem to indicate that one important effect of amphetamine is to influence the way in which the animal is affected by electric shock and the way in which it will work to avoid shock.

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