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Simultaneous Brightness Discrimination and Reversal: The Effects of Amphetamine Administration in the Two Stages

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WEINER, I., J. FELDON AND O. BEN-SHAHAR. *Simultaneous brightness discrimination and reversal: The effects of amphetamine administration in the two stages.* PHARMACOL BIOCHEM BEHAV **25**(5) 939–942, 1986.—Rats were trained in a Y-maze on a two-choice simultaneous brightness discrimination with light as S+ and dark as S− (Stage 1), and were then switched to reversal, where the reinforcement contingencies of the original training were reversed (Stage 2). d-Amphetamine, 1 mg/kg, was administered in a 2×2 design, i.e., drug-no drug in Stage 1 and drug-no drug in Stage 2. The administration of the drug in Stage 1 improved the acquisition of the initial brightness discrimination and facilitated reversal learning independently of the drug administered in Stage 2. In addition, the administration of the drug in Stage 2 only improved performance towards the end of reversal training. The results indicate that amphetamine enhances the attention to, or the associability of, the discriminative stimuli, leading to a rapid learning to these stimuli under changed contingencies of reinforcement.

d-Amphetamine Simultaneous brightness discrimination Reversal Rat

RECENTLY, we showed that the administration of 1 mg/kg d-amphetamine dramatically enhanced reversal learning of a Y-maze simultaneous brightness discrimination [29,30]. The drug had either no effect or enhanced the acquisition of the original discrimination, and had no effect on nonreversal shift. These results are of considerable interest for several reasons. First, they provide one of the few reported improvements in discrimination learning produced by d-amphetamine in animals [3, 4, 13], as opposed to the typically obtained disruption of discrimination performance (e.g., [1, 7, 9, 11, 12, 14, 20, 21]. Moreover, since we used a two-choice discrete-trial procedure and measured percent of correct choices, this facilitation was not confounded with the effects of the drug on response rate or pattern [8, 9, 12]. Second, the transfer to a reversal shift enabled us to elucidate the mechanism of drug action underlying the observed facilitation. Thus, the facilitation of reversal was due to a rapid shift of animals' choices to the new S+, indicating that the drug enhanced the associability of, or the attention to, the discriminative stimuli, without affecting their associative strengths [16, 17, 28]. Third, the facilitatory effect of amphetamine on attentional processes may have interesting implications for the animal-amphetamine model of schizophrenia (e.g., [10, 26, 27]), since overly active attentional mechanism has been emphasized in the human schizophrenia literature as a central characteristic of the disorder (e.g., [15, 18, 19, 22]).

In our previous experiments, the drug was administered throughout the original discrimination learning and the reversal shift. However, if facilitated reversal indeed stems from the effect of amphetamine on the associability of the discriminative stimuli, then the administration of the drug only during the original discrimination should suffice to enhance reversal, independently of drug administration in the reversal stage. The present experiment was designed to answer this question. Animals were trained on a simultaneous brightness discrimination and switched to reversal. d-Amphetamine, 1 mg/kg, was administered in a 2×2 design, i.e., drug-no drug in Stage 1 (original discrimination) and drug-no drug in Stage 2 (reversal).

METHOD

Subjects

The subjects were 16 female Long-Evans rats (Tel-Aviv University Medical School, Israel), approximately 3 months old. They were housed one to a cage under reverse cycle lighting and given water for 30 min a day, about 15 min after the daily session.

Apparatus

The rats were tested in a Y-maze made of opaque Plexiglas. The floor consisted of a metal grid composed of equally spaced rods. The walls were 17.5 cm high. The startbox was

27 cm long and 10 cm wide, with a manually operated black guillotine door. The choice section was pentagonal, with 10 cm long sides. The two goal arms were 14 cm long and 10 cm wide. The arms were set at an angle of 90 degrees to one another. Each arm entrance was fitted with a manually operated, Perspex, side-opening door. The startbox and choice section had clear Perspex lids, and the goal arms had white, opaque Perspex lids. Each goal arm contained an automated Campden Instruments dipper mechanism attached to the outside of the rear wall, which delivered 0.15 ml water into the box. A 24 V electric bulb, located above each dipper, 12.5 cm from the floor, provided the light serving as S+ or S−.

Procedure

All animals were handled for a week and given 5 days of pretraining. On each day, each animal was placed in the Y-maze for 10–15 min. All Y-maze doors were open and water was available in both arms. The experimenter ensured that the animal drank from the cup before being removed from the maze. Following pretraining, animals were randomly divided into two drug conditions, amphetamine and placebo, with 8 animals per group. Both groups were trained on a simultaneous dark-light discrimination, with light serving as the S+. They were run for 10 trials a day. Upon the termination of each trial, the animal was immediately taken out of the arm and replaced into the startbox. On each daily session, S+ was in the right arm of the maze on 5 trials and in the left arm on the other 5 trials. The position of S+ and S− was randomly determined with the provision that they did not remain in the same arm of the maze for more than 2 consecutive trials. The criterion of learning was at least 17 correct responses in 20 consecutive trials on two consecutive daily sessions. Animals in each drug condition (amphetamine or saline), were divided into two groups of 4 animals each: one group was switched to reversal learning under amphetamine and the second, to reversal under saline, creating 4 groups: Placebo-Placebo (PP), Amphetamine-Placebo (AP), Placebo-Amphetamine (PA) and Amphetamine-Amphetamine (AA).

For reversal training, animals were trained on the same discrimination with the former S− (dark side) now S+. The criterion for learning was the same as in the initial discrimination.

Drug Injections

The appropriate drug, either 1 mg/kg d-amphetamine sulfate dissolved in 1 ml of saline, or an equivalent volume of saline, was administered IP 10 min prior to the daily session.

The data were analyzed using ANOVAs with repeated measurement factors of blocks and days.

RESULTS

Stage 1—Initial Discrimination

Figure 1 presents the mean percent of correct choices in the initial brightness discrimination for the Placebo and Amphetamine groups. As can be seen, amphetamine-treated animals acquired the original discrimination faster than placebo controls. This was supported by 2×13×2 ANOVA with a main factor of drug in Stage 1 and repeated measurement factors of blocks and days performed on the data which yielded a main effect of Drug which approached significance, $F(1,14)=3.89$, $p<0.07$, and a significant Drug × Blocks interaction, $F(12,168)=1.88$, $p<0.05$, as well as a significant quadratic component of this interaction, $F(1,168)=12.21$, $p<0.01$.

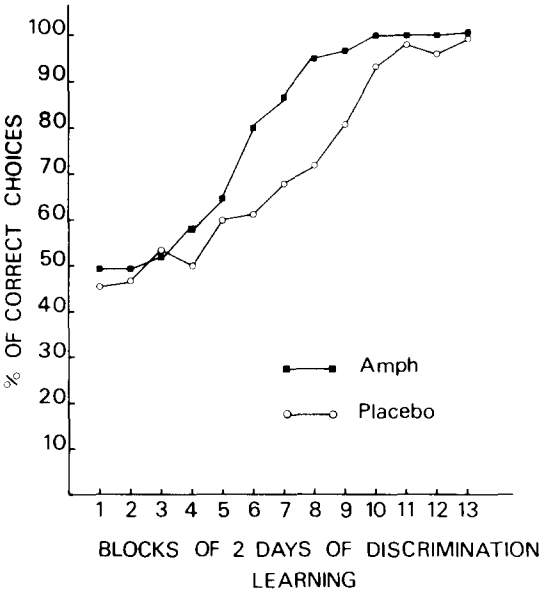

FIG. 1. Mean percent correct choices during the initial brightness discrimination in the Placebo and Amphetamine groups.

Stage 2—Reversal

Figure 2 presents the mean percent of correct choices in reversal for the Placebo-Placebo, Placebo-Amphetamine, Amphetamine-Placebo and Amphetamine-Amphetamine groups. A 2×2×17×2 ANOVA, with main factors of drug in Stage 1 and drug in Stage 2, and repeated measurements factors of blocks and days, yielded a significant main effect of Drug in Stage 1, $F(1,12)=6.98$, $p<0.03$, as well as a significant interaction of Drug in Stage 1 × Blocks, $F(16,192)=1.68$, $p<0.05$. As can be seen in Fig. 2, these results reflect the fact that animals which received amphetamine in the original discrimination (Amphetamine-Placebo and Amphetamine-Amphetamine) exhibited facilitated reversal learning as compared to animals which acquired the original discrimination under saline (Saline-Saline and Saline-Amphetamine). In addition, the linear component of the Drug in Stage 2 × Blocks interaction was significant, $F(1,192)=12.93$, $p<0.001$. This trend reflects the fact that animals which received amphetamine in reversal only, showed improvement of performance towards the end of reversal training as compared to animals reversed under saline.

DISCUSSION

In our previous experiments [29,30], the administration of 1 mg/kg d-amphetamine during both the acquisition of simultaneous brightness discrimination and its reversal, facilitated reversal learning. The present experiment replicates these findings and demonstrates that this facilitation is due to the administration of the drug in the original discrimination, independently of the drug (amphetamine or saline) administered in reversal. In addition, the administration of am-

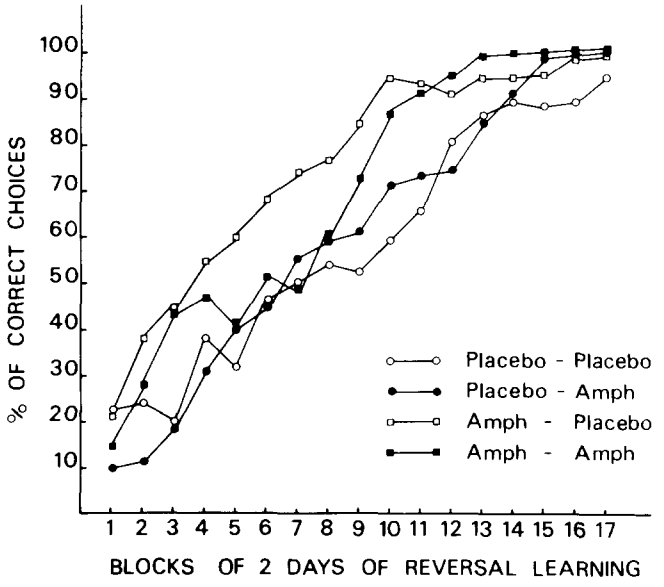

FIG. 2. Mean percent of correct choices during reversal training in the Placebo-Placebo, Placebo-Amphetamine, Amphetamine-Placebo and Amphetamine-Amphetamine groups.

phetamine improved the acquisition of the original discrimination.

The large majority of studies investigating the effects of amphetamine on discrimination learning have concluded that this drug disrupts stimulus control (e.g., [1, 9, 11, 12, 14, 21, 23, 24]), although there are exceptions (e.g., [2, 5, 6]). Actual facilitation of discrimination by amphetamine has been reported in very few studies [3, 4, 13]. Evenden and Robbins [4] argued that the improvement of discrimination performance under amphetamine was due to the fact that the task requirements in their experiment were compatible with the changes in performance produced by the drug. These authors suggested that such a compatibility also accounts for other instances in which amphetamine improves performance. However, our results rule out this explanation. Amphetamine not only facilitated the acquisition of the original discrimination task but also the subsequent reversal, which involved a change of the previously acquired response. Furthermore, this facilitation persisted in the *absence* of the drug in the reversal stage. Thus, our results appear to provide a demonstration of a genuine enhancement of stimulus control by amphetamine. Moreover, the course of reversal learning of amphetamine-treated animals clarifies the mechanism underlying this enhancement.

Reversal learning is assumed to involve two processes: (1) extinction of the original discriminative response, as indicated by the number of trials on which animals continue to select the former S+ at the outset of reversal; and (2) the acquisition of the new discriminative response, reflected in rapidity of the animals in shifting their choices to the new S+ as reversal continues. The first process is assumed to reflect the difference in the associative values of the original S+ and S−, i.e., the approach and avoidance tendencies to the discriminative stimuli. Increase in the excitatory strength of S+ and the inhibitory strength of S− will lead to greater persistence in selecting the former S+ at the outset of reversal. The second process is considered to reflect the extent of attention to, or the associability of, the relevant stimuli. An increase in the associability of the relevant stimuli will lead to a more rapid shift of choices to the new S+ (for a detailed exposition of the above analysis, see [16, 17, 28]).

As can be seen in Fig. 2, animals trained initially under amphetamine shifted their choices to the new S+ much more rapidly than controls from the very outset of reversal. According to the analysis of reversal learning presented above, this pattern of results indicates that amphetamine does not affect the associative values of S+ and S−. In contrast, the drug enhances the attention to, or the associability of, these stimuli, i.e., their rate of conditioning under changed contingencies of reinforcement. It should be noted that the rapid switch to the new S+ occurred in spite of the fact that amphetamine enhanced original discrimination, which would be expected to lead to a greater persistence in choosing the former S+ at the outset of reversal. This suggests that although animals under amphetamine acquire stimulus-response associations rapidly, in fact, more so than normal animals, these associations are not "stamped in" as effectively as in normal animals. Thus, whereas in normal animals the original discriminative stimuli continue to exert control over behavior upon transfer to reversal, amphetamine-treated animals exhibit a rapid switch of responding according to the changed contingencies of reinforcement. As we suggested elsewhere [29,30], this phenomenon may have interesting implications for the animal amphetamine model of schizophrenia.

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