Differential effects of d-amphetamine in classical discrimination conditioning of rabbits[1]

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D-Amphetamine was administered to rabbits performing a "difficult" and an "easy" classical discrimination task. The drug had no significant effect on overall nictitating membrane responding whereas it debilitated heart rate responding. Heart rate discrimination was debilitated for both tasks; however, amphetamine facilitated nictitating membrane discrimination for the "difficult" task while having no effect on the "easy" task. The results are discussed in terms of support for the "cue-monitoring" interpretation of amphetamine facilitation and the observed divergence of response systems in the rabbit.

The literature indicates that a wide range of behavior, both animal and human, can be enhanced by amphetamine under certain conditions. Such facilitation has usually been considered due merely to the drug increasing the level of motor activity, but Cole (1967) has suggested that such increased performance may be due to the drug facilitating the monitoring of cues. Studies by Hauty, Payne, & Bauer (1957) and Payne, Hauty, & Moore (1957) have provided additional support for such an interpretation of amphetamine facilitation.

Studies which have found no evidence of amphetamine facilitation may have used a task not requiring a high degree of alertness or a discrimination task so easy that little facilitation could take place. A discrimination task of greater difficulty requiring considerable attention and cue-monitoring ability by S might be more sensitive to amphetamine facilitation. The present study employed two discrimination tasks of different levels of difficulty to test this cue-monitoring interpretation of amphetamine facilitation.

METHOD

The Ss were 40 New Zealand albino rabbits weighing 4.2-6.0 lbs. Each S was caged individually and had free access to food and water.

During training Ss were restrained in a Plexiglas box which was placed in a ventilated sound attenuated chamber. The nictitating membrane (NM) response was recorded by using a loop suture through the NM attached to a strain gage. Respiration rate (RR) was recorded by means of a thermocouple attached to a cup placed over S's snout. [For a detailed account of the technique used to transduce NM and RR responses, see Yehle (1968).] Two stainless steel safety pins were inserted into the skin of each S to record heart rate (HR).

The CSs were tones presented to S through a 6-in. speaker located 4 in. above S. The US was a 3-mA electric shock of .3-sec duration, administered through two stainless steel hooks which held S's right eyelid open. The CS duration was .75 sec and the offset of the CS was coincident with the onset of the US on CS+ trials. The intertrial interval was 3 min.

The Ss were randomly assigned to 1 of 10 groups of four Ss each. A 2 by 5 factorial design using two levels of discrimination difficulty and five levels of drug dosage constituted the 10 cells. The "easy" discrimination employed tone CSs of 700 Hz and 1900 Hz, while the "difficult" discrimination used tone CSs of 700 Hz and 1300 Hz. Dosage levels were 3.0, 1.5, 1.0, and .5 mg/kg of d-amphetamine and a saline control, injected subcutaneously into the back of each S 30 min prior to conditioning.

Conditioning consisted of one day of adaptation and five days of classical discrimination training. During each daily session Ss received 20 trials with the CS+ and 20 trials with the CS– randomly presented with the restriction of no more than two similar trials in succession. Trials 9 and 10, 19 and 20, 29 and 30, and 39 and 40 were designated as test trials and used to assess HR responding to the CS+ and the CS– by measuring the distance between 15 successive heart beats prior to CS onset and comparing this with the measurement of 15 successive heart beats immediately following CS onset. A per cent change from baseline was then calculated and used as a measure of HR-CRs. The NM responding was measured on every trial and 2-mm pen deflection with a latency less than .75 sec was used as a criterion for a conditioned NM response.

RESULTS

Compared to the saline controls, drug effects were consistent, but the effects of different dosage levels showed considerable variability among Ss. Therefore, the results of all amphetamine groups were combined and averaged before comparing with the saline controls.

To assess overall drug effects on NM and HR conditioning, the response to both CS+ and CS– were added together for each daily session. It can be seen in Fig. 1 that total NM responding for all groups was quite similar and this was confirmed by Mann-Whitney U tests which indicated no significant differences.

Total HR responding (sum of CS+ and CS– responses) showed a significant debilitating effect of amphetamine on the easy task ($p < .008$) and a slight but nonsignificant debilitating effect of amphetamine on the difficult task. In addition the difficult task itself resulted in decreased HR responding for the saline ($p < .004$) and the amphetamine ($p < .048$) groups. Figure 2 portrays these effects.

To assess discrimination, the difference between CS+ and CS– responses was divided by the sum of CS+ and CS– responses and a score calculated for both the HR and NM measures. Mann-Whitney U tests were used to indicate discrimination differences between the various groups.

Figure 1 indicates the facilitory effect of amphetamine on NM discrimination for the difficult task ($p < .014$) and little effect on the NM discrimination for the easy task ($p < .443$). A significant discrimination difference between the "easy" and the "difficult" saline groups is also clearly indicated ($p < .014$).

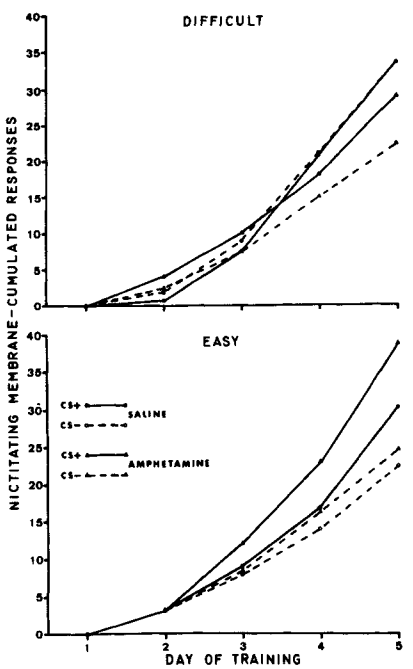

Fig. 1. Mean NM responses to CS+ and CS– for the average S in each group cumulated over days of training.

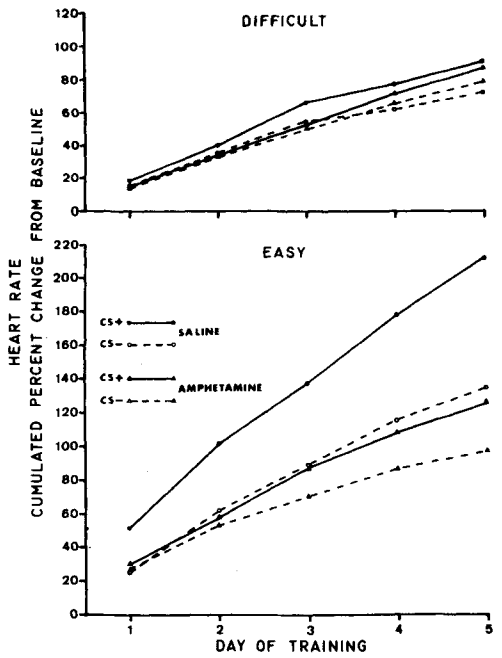

Fig. 2. Mean HR responses to CS+ and CS– for the average S in each group cumulated over days of training. Per cent changes represent HR decelerations.

The HR discrimination portrayed in Fig. 2 shows the debilitating effect of amphetamine on both the easy ($p < .048$) and the difficult ($p < .048$) tasks. In addition, the effects of task difficulty were also significant for the amphetamine group ($p < .048$) and the saline controls ($p < .028$).

DISCUSSION

Responding

The effects of amphetamine are apparently very complex ranging from facilitation to debilitation depending on the response system and the task involved. Physiologically, the direct action of d-amphetamine is on the sympathetic portion of the autonomic nervous system and not on the skeletal motor system. Increased motor activity as a result of amphetamine administration is an indirect manifestation of the drug's direct effects on the cortex and the reticular activating system (Goodman & Gilman, 1966). Total NM CRs were not affected although spontaneous and random responses may have been.

The HR-CR, however, is the consequence of both sympathetic and parasympathetic impulses and is a phasic deceleration in the rabbit. Increased sympathetic activation by amphetamine via the cardiac acceleratory nerve would increase HR and thus partially suppress deceleratory HR CRs, as the results have indicated.

A significant decrease in HR responding was also demonstrated as a result of task difficulty. The tendency for the HR-CRs to decrease in amplitude as a discrimination task becomes more difficult has been previously noted by the authors in other studies and is presently under investigation.

The debilitating effect of amphetamine on overall HR responding was significant for the "easy" task but not for the difficult group. Presumably with the already low responding in the "difficult" group there was less opportunity for the amphetamine to evidence a debilitating effect.

Discrimination

The discrimination results portrayed in Figs. 1 and 2 clearly confirm the difference in task difficulty for both the NM and the HR discriminations. Amphetamine, however, affected the two response systems in opposite directions. The facilitation of the NM discrimination on the "difficult" task without increasing overall NM responding lends support to Cole's (1967) cue-monitoring or alertness concept of amphetamine, whereby increased activation of some CNS area results in greater attention and hence a better discrimination. It seems reasonable that differential effects of amphetamine on NM discrimination are due to the opportunity to evidence a facilitation on the "difficult" task which was virtually insoluble by the saline control group, and to evidence no effect on the "easy" task in which the saline control group was able to achieve a good discrimination.

The debilitating effect of amphetamine on HR discrimination for both tasks is somewhat puzzling; and is apparently a result of the direct sympathetic action of amphetamine on HR responding coupled with its effect on some CNS area affecting the translation of the discrimination to the HR response system. In addition, heart arrhythmias, known to occur as a result of amphetamine administration (Goodman & Gilman, 1966) were more likely responsible for the decreased differential HR responding.

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NOTE

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