FACILITATION OF AVOIDANCE BEHAVIOUR BY LSD-25 AND MESCALINE IN HAMSTERS

Mario Sansone, Claudio Castellano and Patrizia Messeri
Laboratorio di Psicobiologia e Psicofarmacologia, C.N.R.
1, via Reno - 00198 Roma, Italy

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SUMMARY Golden hamsters were subjected to ten daily 50-trial avoidance sessions in the shuttle-box. Control animals showed low levels of avoidance responding. LSD-25 and mescaline significantly improved performances. The role of brain moanoamines in the effect of the two psychotomimetic agents has been discussed by considering previous findings indicating the importance of an adrenergic mechanism in the facilitating effects of some stimulating drugs on avoidance behaviour of hamsters.

INTRODUCTION Researches by Babbini & Davis (1967) and Matalka & Bunnel (1968) demonstrated that hamsters are characterized by low avoidance levels in experimental situations requiring a running response. Afterwards it has been observed that difficulties exhibited by this animal species in shuttle-box avoidance responding can be overcome by administration of centrally acting drugs, such as amphetamine (Sansone & Renzi, 1970; 1971), methylphenidate (Sansone & Renzi, 1971), and monoamine oxidase inhibitors (Sansone, Renzi & Messeri, 1972). More recently several central stimulating agents have been tested and the results seem to account for the hypothesis that only those drugs which act on adrenergic mechanisms may improve avoidance behaviour in hamsters (Castellano, Sansone, Renzi & Annecker, 1973). Facilitation of avoidance responding by methamphetamine has been also evidentiated in a lever-press situation, in which hamsters show difficulty in the acquisition of avoidance behaviour as in the shuttle-box (Sansone, Renzi & Castellano, in

press).

The above findings indicate, on the whole, that avoidance behaviour of hamsters can be considered a useful tool in the study of centrally acting drugs. In the present research the effects of two psychotomimetic agents, Lysergic acid diethylamide (LSD-25) and mescaline, have been studied.

METHODS The technique was the same previously described for avoidance training of hamsters (Sansone & Renzi, 1970; 1971). Eight automated shuttle-boxes were used, each one divided into two 24x21 cm compartments connected by a 7x7 cm opening. A light (two 10 W lamps) was switched on alternately in the two compartments and used as conditioned stimulus (CS). The CS preceded the onset of the unconditioned stimulus (US) by 15 sec and overlapped it for 45 sec. The US was a pulsed electric shock applied to the grid floor (250 V delivered through a 500,000 ohms resistance). The intertrial interval was 60 sec. A conditioned response was recorded when the animal avoided the US by running into the dark compartment within 15 sec after the onset of the CS. If animals failed to avoid the shock, they could escape it by crossing during the US. Spontaneous crossings were punished and recorded as intertrial responses.

The subjects were naive male golden hamsters (85-110 g) randomly assigned to the experimental groups. All groups were subjected to ten daily 50-trial avoidance sessions in two weeks (from Monday to Friday).

Drug treatment consisted in the administration of saline (2.0 ml/kg) in one group, LSD-25 in three groups at the doses of 0.05, 0.1, and 0.2 mg/kg respectively, and mescaline hydrochloride in two groups at the doses of 5 and 10 mg/kg respectively. Drugs were injected intraperitoneally 15 min before each of the ten sessions.

The control group consisted of 16 animals, while other groups included eight subjects.

RESULTS Performances of the six experimental groups are expressed in Fig. 1 (saline and LSD-25) and Fig. 2 (saline and mescaline) as mean percent avoidances for each 50-trial session. Table 1 reports the mean percent avoidances in blocks of five 50-trial sessions (one block for each experimental week).

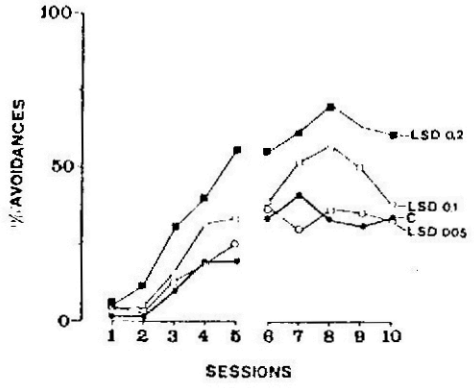

Fig. 1 Mean percent avoidances in each of the ten daily 50-trial sessions. The experiment was carried out in two weeks, from Monday to Friday.
C = control group (saline); LSD 0.05, LSD 0.1 and LSD 0.2= LSD-25 at the doses of 0.05, 0.1 and 0.2 mg/kg respectively.

As previously observed in similar experimental conditions (Matalka & Bunnel, 1968; Sansone & Renzi, 1970; 1971; Sansone et al., 1972; Castellano et al., 1973), control animals showed poor ability in the acquisition of the avoidance behaviour. The low level of avoidance responsing, however, was not accompanied by absence of escape responses, which on the contrary were always at the 100% level.

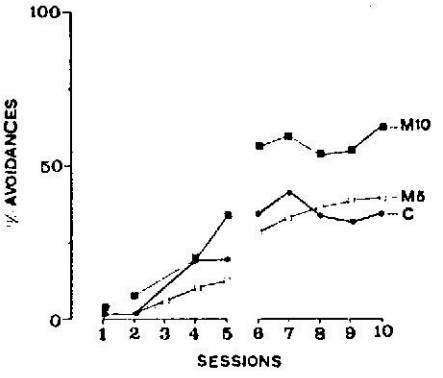

Fig. 2 Mean percent avoidances in each of the ten daily 50-trial sessions. The experiment was carried out in two weeks, from Monday to Friday.
C = control group (saline). M5 and M10 = mescaline hydrochloride at the doses of 5 and 10 mg/kg respectively.

Table 1

Mean percent avoidances (± S.E.) in blocks of five 50-trial sessions Significances between drug and saline treatments were based on the Student *t* test.

Treatments	SESSIONS 1 - 5		SESSIONS 6 - 10	
	Avoidances	Signif. level	Avoidances	Signif. level
Saline	11.60 ± 2.17	-	34.72 ± 6.11	-
LSD 0.05 mg/kg	13.00 ± 3.17	n.s.	33.95 ± 6.73	n.s.
LSD 0.1 mg/kg	16.55 ± 3.43	n.s.	48.15 ± 6.27	n.s.
LSD 0.2 mg/kg	22.56 ± 5.08	$P < 0.01$	62.15 ± 7.50	$P < 0.05$
Mescaline 5 mg/kg	6.30 ± 1.98	n.s.	34.85 ± 7.12	n.s.
Mescaline 10 mg/kg	15.30 ± 3.81	n.s.	56.60 ± 8.60	$P < 0.05$

LSD-25 was ineffective at the dose of 0.05 mg/kg, while at the two higher doses it improved performances in comparison to the saline control group. An avoidance improvement, in fact, appeared evident in the second experimental week following the administration of LSD-25 at the dose level of 0.1 mg/kg. The dose of 0.2 mg/kg produced avoidance improvements more evident and statistically significant (Fig. 1 and Table 1).

Mescaline was ineffective at the dose of 5 mg/kg, while it increased avoidance responding at the dose of 10 mg/kg (Fig. 2 and Table 1).

Intertrial responses, under drug tratments as in the control group, were present at some extent in the first two sessions (2-5%) but seldom appeared in the other sessions.

DISCUSSION The findings reported above demonstrate that the two psychotomimetic agents tested in the present experiment, LSD-25 and mescaline, facilitate avoidance responding in hamsters. A similar effect has been recently evidentiated by Bignami (1972) following the administration of LSD-25 to rats subjected to a two-way avoidance training. This Author has also reported and widely discussed previous researches concerning the often contrasting effects of LSD-25 on avoidance behaviour.

As concerns the effects of mescaline, Smythies & Sykes (1964) found that in trained rats this drug exerted a biphasic effect, since a depression of avoidance responding was followed by a prolonged excitatory phase. Bridger & Mandel (1972) observed that mescaline, if administrated before learning, improves shuttle-box avoidance behaviour by facilitating performance rather than acquisition.

Such an interpretation can be probably given also to the faci-

litating effects observed in the present experiment. In a previous research, in fact, it has been demonstrated that amphetamine and methylphenidate improve shuttle-box avoidance responding of hamsters by affecting performance rather than learning (Sansone & Renzi, 1971). The same conclusion was later reached for the effects of other drugs (Sansone et al., 1972; Castellano et al., 1973).

An explanation of the avoidance facilitation by LSD-25 and mescaline must certainly consider the alerting properties of the psychotomimetic agents (see review by Brawley & Duffield, 1972). However it has been recently put forward the hypothesis that only those central stimulating agents which act on adrenergic mechanism improve avoidance behaviour of hamsters (Castellano et al., 1973). In this regard the action of mescaline, which is similar in structure to amphetamine, undoubtedly implicates an adrenergic mechanism, since the drug possesses various sympathomimetic activities (Taeschler, 1967). The action of LSD-25, instead, has been prevalently linked to brain serotonin (5-HT), but its mechanism has not jet been well clarified (see review by Brawley & Duffield, 1972). A possible antagonism of 5-HT by LSD-25 in the central nervous system could explain the facilitating effect of the drug on avoidance behaviour, since it seems that 5-HT exerts inhibitory functions in the CNS (Brodie & Reid, 1968; Jouvet, 1969). Moreover p-chlorophenylalanine, a serotonin depletor, enhances sensitivity to LSD-25 (Appel, Lowell & Freedman, 1970) and facilitates active avoidance behaviour (Schlesinger & Schreiber, 1968; Tenen, 1967).

Anyway, whatever its influences on brain 5-HT may be, LSD-25 exerts, like mescaline, a variety of sympathomimetic effects (Taeschler, 1967). Furthermore, in a study on the behavioural effects

of LSD-25 in the rat, Dixon (1968) obtained results supporting the concept that the drug acts, at least partly, through catecholamine mediation.

In conclusion, even if different interpretations may be given in relation to the mechanism of action of psychotomimetic drugs, an adrenergic mechanism can be supposed in the facilitating effects induced by the drugs used in this study. The effects of LSD and mescaline, in fact, appear quite similar to those exerted by amphetamine and other central adrenergic stimulants on avoidance behaviour of hamsters.

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