

Influence of CNS Stimulants and Hallucinogens on Rats in Special Circumstances

P. C. Dandiya, B. D. Gupta, M. L. Gupta

Department of Pharmacology and Physiology, S.M.S. Medical College, Jaipur

A variety of drugs are known to produce behavioural changes that lead to psychotic disorders in humans. The CNS stimulant drugs could be classified into hallucinogens, analeptics, and the antidepressants. Although, these groups of drugs differ in their mechanism of action, each one of these individually produces psychotic behavioural pattern when given in adequate doses. If it is true, the present pharmacological classification of CNS stimulant drugs does not have a direct relationship with the behavioural effects of these drugs. It is, therefore, necessary to determine whether drugs in these pharmacological groups differ significantly in their action on various behavioural components. To this end, the known representative drugs of these pharmacological groups have been compared with each other on two components of Open Field performance of rats.

Methods

Subject – The subjects were naive male albino rats of *Haffkines'* strain weighing between 100 to 150 g. The experimental design was composed of 45 cells (9 drugs $\times$ 5 doses of each drug); each cell containing 5 subjects. Thus, in all 225 rats were subjected to Open Field Test with a pretreatment of either of the drugs administered i.p.

Apparatus – The apparatus used for the "Open Field Test" was similar to that used by *Holland* and *Gupta* (1966). Briefly, it consisted of a circular open arena made up of wood measuring $32\frac{3}{4}$ inches in diameter, enclosed by a sunmica wall $12\frac{1}{2}$ inches high. The floor, which had a sunmica surface, was marked out in three concentric circles divided into segments by lines radiating from the floor centre. The wall was fixed on the outermost of these circles. The markings provided 25 floor units of approximately equal size and were used to score the ambulation of the animal moving around in the arena during the test. The placement by the rat of all four of its limbs in a segment was taken as one unit of ambulation. In the "Open Field Test" two types of stimuli were presented to the animal: white noise with an intensity of 78 dB was presented by an oscillator through 5 loudspeakers, and light of 165 foot candles intensity was produced by five photographic lamps. A translucent glass screen enclosed the arena from all the sides, the front side having a glass door through which the subject was placed in the arena and the experimenter observed the rat under test. By the side of the arena there was a small table on which three hand-operated counters were fixed to record the number of ambulation, rearing and preening responses. There was a clock

on the table for recording the testing period. The ambulation response was defined as a "walking around" score derived from the number of radial segments of the arena which were crossed by the subject. Rearing response was defined by the number of times the rat stood on its hind legs during the test.

Table 1 shows the drugs and their doses and their latencies. Each subject was tested only for 2 minutes in the Open Field Test and the scores on ambulation and rearing were recorded for analysis.

Discussion

It has been shown earlier in this laboratory by Dandiya et al. (1969) that ambulation response in the Open Field Test may be a stereotyped response on which hallucinatory drugs produce an enhancing effect. Gupta and Gregory (1967) have shown that rearing may be a behavioural response to a higher level of cortical excitation, a facilitation

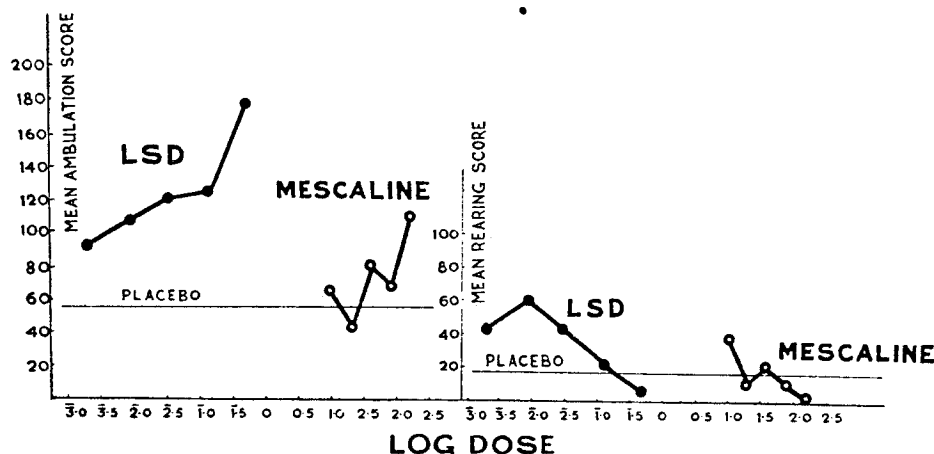


Fig. 1

of which is a positive function of increasing doses of amphetamine. Thus, the present results indicate that LSD, iproniazid and mescaline facilitate ambulation of stereotyped nature with a simultaneous inhibition of a comparatively complex response of rearing (Fig. 1, 3). In other words, such drugs augment the action of those nervous loci which operate in simple stereotyped activities while reduce the activity of those which control the complex behavioural processes by maintaining a higher degree of muscular coordination and discriminatory functions. An opposite effect is produced by amphetamine and methyl phenidate which augment the action of those nervous loci operating on the complex behavioural processes (Fig. 2). Amphetamine has been shown to increase cortical arousal (Gupta 1967). Thus, it can be suggested that for a complex response of rearing, cortical arousal is necessary which is clearly a function of amphetamine. On the contrary, for the simple stereotyped response of ambulation those nervous loci may determine the activity which is a positive function of LSD like drugs. In other words,

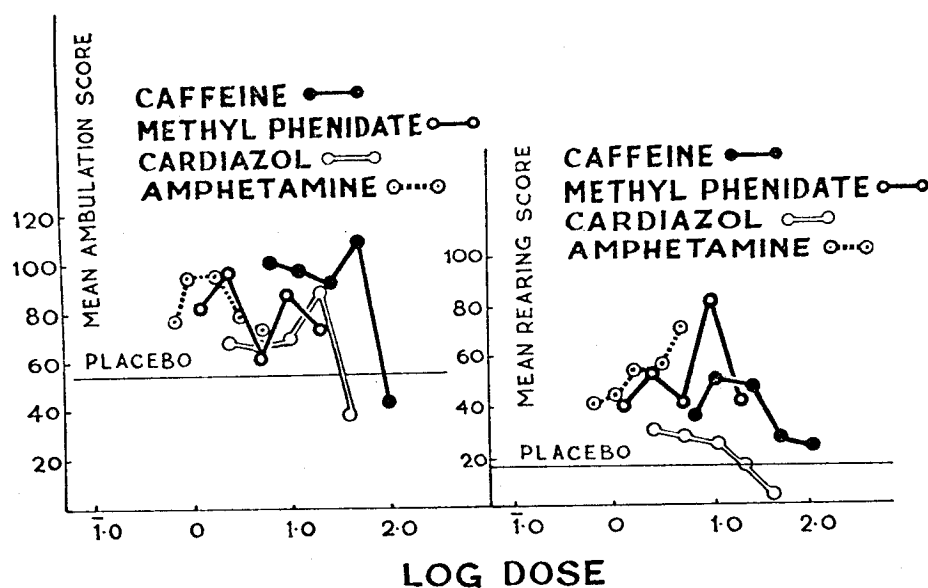


Fig. 2

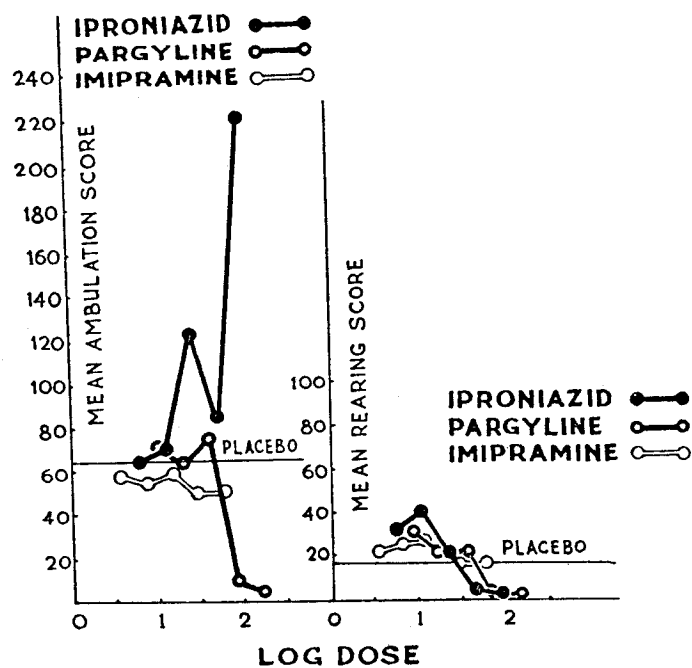


Fig. 3

Table 1 Drugs doses in Mgs and the latency period.

No.	Drug	I	II	III	IV	V	Latency between drug and test in hours
1	LSD	0.002	0.008	0.032	0.136	0.5	0.4
2	Mescaline	10.0	20.0	40.0	80.0	160.0	2.5
3	Amphetamine	0.65	1.1	1.8	3.0	5.0	1.0
4	Meth. Phen.	1.25	2.5	5.0	10.0	20.0	0.33
5	Caffeine	6.25	12.5	25.0	50.0	100.0	0.5
6	Cardiazol	2.5	5.0	10.0	20.0	40.0	0.5
7	Iproniazid	6.25	12.5	25.0	50.0	100.0	*
8	Pargyline	10.0	20.0	40.0	80.0	160.0	3.0
9	Imipramine	3.8	7.5	15.0	30.0	60.0	4.0

* Iproniazid was divided into 3 equal parts, the first part was given 28 hours, second part 24 hours and the last part 20 hours before the test.

Table 2 Ambulation scores in Open Field Test. t-Test table for drug group mean differences. Each drug group was composed of 25 rats divided into 5 subgroups, each of these subgroups was given a different dose of the drug. The mean response (in 25 rats) due to the drugs was compared with one another. The relevant t-values between any pair of drugs are given against that pair. For example in column 7, 2nd row 5.78 is the t-value between the mean responses due to 5 different doses of mescaline and 5 different doses of drug No. 7, i.e. iproniazid. The values which are asterisked are statistically significant. One, two and three asterisks show significance at 0.1%, 1% and 5% levels respectively.

Drug group	2	3	4	5	6	7	8	9
LSD (124.48)	7.41 ¹	6.94 ¹	6.38 ¹	5.24 ¹	8.50 ¹	1.62	11.65 ¹	10.13 ¹
Mescaline (74.08)		1.45	1.02	2.17 ³	1.08	5.78 ¹	4.24 ¹	2.72 ²
Amphetamine (84.04)			0.44	0.70	2.55 ³	4.31 ¹	5.70 ¹	4.18 ¹
Meth. Phen. (81.04)				1.14	2.11 ³	4.75 ¹	5.26 ¹	3.74 ¹
Caffeine (88.84)					3.25 ¹	3.59 ¹	6.41 ¹	4.89 ¹
Cardiazol (66.68)						6.87 ¹	3.15 ²	1.63
Iproniazid (113.40)							10.02 ¹	5.50 ¹
Pargyline (45.24)								1.51
Imipramine (55.56)								

¹ 0.1% ² 1% ³ 5%.

Table 3 Rearing scores in Open Field Test. t-Test table for drug group mean differences. Each drug group was composed of 25 rats divided into 5 subgroups, each of these subgroups was given a different dose of the drug. The mean responses due to the drugs were compared with one another. The relevant t-values between any pair of drugs is given against that pair for example in column 6, third row 8.08 is the t-value between the mean responses due to 5 different doses of amphetamine with 5 different doses of drug No. 6, i.e. cardiazol. The values which are asterisked were statistically significant. Single and double asterisks show significance at 0.1 and 1% respectively.

Drug group	2	3	4	5	6	7	8	9
LSD (34.92)	4.73 ¹	4.78 ¹	4.74 ¹	0.59	3.80 ¹	3.85 ¹	5.05 ¹	3.26 ²
Mescaline (16.12)		9.52 ¹	9.48	5.33 ¹	1.44	0.87	0.31	1.47
Amphetamine (53.92)			0.04	4.19 ¹	8.08 ¹	8.64 ¹	9.83 ¹	8.05 ¹
• Meth. Phen. (53.76)				4.15 ¹	8.04 ¹	8.60 ¹	9.80 ¹	8.01 ¹
Caffeine (37.28)					3.88 ¹	4.45 ¹	5.64 ¹	3.85 ¹
Cardiazol (21.84)						0.56	1.75	0.00
Iproniazid (19.60)							1.18	0.59
Pargyline (14.88)								1.78
Imipramine (21.95)								

increasing doses of amphetamine increase muscular coordination and discriminatory functions which determine the degree of rearing response, whereas, increasing doses of LSD, iproniazid or mescaline reduce these functions (Table 4). *Lat* (1965) has suggested that with increasing dose frequency of stereotypy increases and the form becomes more simple. This was in connection with amphetamine. While we would like to say that this statement is true for hallucinogenic drugs and iproniazid, if ambulation is simple stereotypy and rearing a more complicated one. With amphetamine and to some extent methyl phenidate the opposite is true.

Table 4 Reclassification of the drugs on the basis of present study.

Drug group	Effect of increasing doses on Open Field parameters	
	(I) Ambulation	(II) Rearing
LSD, Iproniazid, Mescaline	↑	↓
Amphetamine, Met. phen.	↓	↑
Caffeine, Cardiazol and Pargyline	↓	↓
Imipramine	No definite trends	

Summary

It was planned to make a critical psychological analysis of the Open Field performance and a appreciation of the differential and/or common features of a number of CNS stimulant and hallucinogenic drugs belonging to various groups. The results indicated a differential distribution of the drugs and their optimal effect-producing doses on ambulation, rearing, and preening responses. Psychotic drugs like LSD and iproniazid were differentiated on the stereotyped ambulation responses in contrast to the cortical stimulant drugs such as amphetamine which were found discriminated on the CNS-excitation determined rearing performance; on the other hand, anti-depressant drugs like imipramine, failing to show any definite similarity with either of the groups. The possibility of the exploitation of the Open Field Test for differentiating the finer effects of individual drugs is discussed.

Zusammenfassung

Es sollte eine kritische psychologische Analyse des Open Field-Verhaltens durchgeführt werden. Außerdem sollten verschiedene bzw. gemeinsame Wirksamkeitseigenschaften einer Reihe von zentralnervösen Stimulantien und halluzinogener Verbindungen erörtert werden. Die festgestellten Ergebnisse weisen auf eine unterschiedliche Verteilung der Drogen und der die Laufaktivität, das Aufrichten und Putzverhalten beeinflussenden Dosen hin. Psychotomimetika wie LSD und Iproniazid wurden anhand stereotypisierter Laufreaktionen differenziert, während kortikal wirksame Stimulantien wie Amphetamin das durch eine zentralnervöse Exzitation bedingte Aufrichten auf den Hinterbeinen beeinflussten. Antidepressiva wie Imipramin ließen keine Ähnlichkeiten mit den genannten Pharmakagruppen erkennen. Die Möglichkeiten der Auswertung des Open Field-Tests für die Differenzierung subtilerer Effekte der einzelnen Präparate werden diskutiert.

Literature

- Dandiya, P. C., B. D. Gupta, M. L. Gupta, S. K. Patni: Effects of LSD on open field performance in rats. *Psychopharmacologia (Berl.)* 15 (1969), 333-349
- Gupta, B. D.: An examination of the effects of stimulant and depressant drugs on escape (avoidance conditioning in rats selectively bred for emotionality) non emotionality. Ph.D. Thesis, London University 1967
- Gupta, B. D., Keir Gregory: The effect of drugs and their combinations on the rearing response in two strains of rats. *Psychopharmacologia (Berl.)* 11 (1967) 365-371
- Holland, H. C., B. D. Gupta: Some correlated measures of activity and reactivity in two strains of rats selectively bred for differences in the acquisition of a conditioned avoidance response. *Anim. Behav.* 14 (1966), 574-580
- Lat, J.: The spontaneous exploratory reactions as a tool for psychopharmacological studies. A contribution towards a theory of contradictory results in psychopharmacology. *Pharmacology of conditioning, learning and retention. Proc. of 2nd Intern. Pharmacological Meeting, 22-23 August, 1963. Czechoslovak Med. Press, Praha 1963, 47-66*

P. C. Dandiya, M. Pharm., M.Sc., Ph.D., Professor of Pharmacology, S.M.S. Medical College, Jaipur-4, India