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The Discriminative Stimulus Properties of 2,5-Dimethoxy-4-Methylamphetamine (DOM): Differentiation from Amphetamine

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Abstract. Rats were trained in a two-lever operant procedure to discriminate either 1.0 mg/kg (+)amphetamine or 1.5 mg/kg DOM from saline. Rats trained to discriminate DOM from saline showed generalization with the DOM training condition when tested with mescaline or 2,5-dimethoxy-4-ethylamphetamine (DOET), but not when tested with (+)amphetamine or methylphenidate. Both isomers of DOM generalized with racemic training compound, the (–)isomer being more potent. The DOM stimulus was completely blocked by the serotonin (5-HT) antagonists cinanserin and methysergide, but not by the peripheral 5-HT antagonist xylamidine nor the dopamine antagonist haloperidol. Rats trained to discriminate (+)amphetamine from saline generalized with the amphetamine training condition when tested with methylphenidate but not when tested with mescaline, DOET, racemic DOM, or either isomer of DOM. The amphetamine stimulus was blocked by pretreatment with haloperidol but not by cinanserin, methysergide, or xylamidine. The results show that, despite their structural similarity, amphetamine and DOM induce pharmacologically distinct stimuli.

Key words: Drug discrimination – 2,5-Dimethoxy-4-methylamphetamine (DOM or STP) – Amphetamine – Haloperidol – Serotonin antagonists

Clinical studies of 2,5-dimethoxy-4-methylamphetamine (DOM), following its identification as the street drug STP, showed it to be a potent hallucinogen with LSD-like effects (Snyder et al., 1967, 1968; Hollister, 1969). Additionally, low doses of DOM induce a mild euphoria in the absence of perceptual distortion (Snyder et al., 1968). Comparison of the subjective effects of a low dose of DOM with those induced by (+)amphetamine showed similarity in some respects, but the overall effects were clearly distinguishable. In animal studies, low doses of DOM produce some behavioral effects like those produced by (+)amphetamine, e.g., increments in locomotor activity, conditioned avoidance responding (CAR), and food reinforced operant responding (Yamamoto and Ueki, 1975; Beaton et al., 1969; Tilson et al., 1975a).

While drug discrimination procedures have been useful for classifying drugs into distinct groups (Barry, 1974; Lal, 1977), the results of discrimination studies involving DOM are inconsistent. Huang and Ho (1974) found that rats trained to discriminate (+)amphetamine from saline made responses appropriate for the saline condition when tested with DOM, i.e., DOM did not generalize with (+)amphetamine. On the other hand, Tilson et al. (1975b) obtained generalization from (+)amphetamine to (–)DOM and vice versa. In rats trained to discriminate mescaline from saline, DOM generalized with mescaline while amphetamine and cocaine did not (Winter, 1975a). Browne and Ho (1975) and Winter (1975b) showed that the discriminative stimulus induced by mescaline could be blocked by pretreatment with serotonin (5-HT) antagonists. Winter (1978) subsequently found that the generalization of DOM with mescaline could be blocked in the same manner. Blockade of DOM generalization with mescaline by 5-HT antagonists does not mean that the DOM stimulus itself can be blocked in this manner. DOM may have stimulus properties in addition to those that are mescaline-like (e.g., DOM may also have amphetamine-like attributes).

The discrimination data thus suggest that DOM is similar to mescaline, and may or may not be similar to amphetamine. In only one of the studies cited above was DOM used as the training drug (Tilson, 1975b) and neither generalization with other hallucinogens nor susceptibility to antagonists was tested. The purpose of

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the present work was to examine more closely the discriminative stimulus properties of DOM and compare them with those of (+)amphetamine.

Materials and Methods

Subjects. Forty male Sprague-Dawley rats (200–240 g) (Simonsen Labs, Gilroy, California) served as subjects. They were housed individually and had unlimited access to drinking water. Subjects were maintained at about 80% of their expected free-feeding weights by adjusted feedings of Wayne Lab Blox after each session and on weekends.

Drugs. (+)Amphetamine sulfate (Sigma), cinanserin [2′-(3,3-dimethylaminopropyl)thiocinnamanilide] HCl (Nutritional Biochemical), haloperidol (Haldol, McNeil), and mescaline HCl (Aldrich) were purchased from the indicated commercial sources. Methylphenidate HCl (Ritalin, Ciba Pharmaceutical), methysergide maleate (Sansert, Sandoz Pharmaceuticals), and xylamidine tosylate (Wellcome Research Laboratories) were generous gifts of the manufacturers. (–)DOM HCl, (+)DOM HCl, and psilocybin (base) were supplied by the National Institute on Drug Abuse. Racemic, DOM, DOET, 4-methylamphetamine, and 2,5-dimethoxyamphetamine (all HCl salts) were synthesized in the Neurochemistry/Neuropharmacology Research Section of the Texas Research Institute of Mental Sciences.

In all experiments, drugs were administered IP in 1 ml/kg saline except for haloperidol, which was administered as an aqueous dilution of the commercial preparation. Doses refer to the salts.

Pretraining. In daily 30-min sessions, subjects were trained to bar press for food reinforcement. During pretraining, only one lever was operable and the operable lever was alternated daily. In the first five sessions the response criterion for reinforcement was raised from one (continuous reinforcement) (CRF) to five (fixed-ratio 5) (FR5). In sessions six and seven, a variable interval of 15 s (VI15 s) separated opportunities for reinforcement on the FR5 schedule. This variable interval was increased to an average of 30 s beginning in session eight, resulting in the tandem VI30 s FR5 schedule used in training.

Training. Training sessions were conducted 5 days per week and were of 20-min duration. During training sessions both levers were operable. At 15 min prior to each session subjects were injected IP with drug or saline. For one group of animals ($N = 30$) the drug injection was 1.0 mg/kg (+)amphetamine sulfate. For the other group of animals ($N = 10$) the drug injection was 1.5 mg/kg DOM HCl.

For half the animals in each group, the drug injection was paired with availability of reinforcement for responses on the right lever; saline injection was paired with the left lever. For the other half of each group, the pairings were the opposite. Prior to the thirteenth training session, responses on the incorrect lever were counted but had no consequences. Beginning with the thirteenth session, responses on the incorrect lever during the ratio portion of the schedule reset the ratio requirement. Thus, after the variable interval had elapsed, five consecutive responses on the appropriate lever were required to obtain a reinforcer. The order of sessions was random except that no more than two consecutive sessions were in the same condition.

Acquisition Tests. Two or three training sessions per week began with a 3-min extinction period. Following this period, the session continued as a normal training session. The percentage of drug-appropriate responses (number responses on drug lever/total responses) emitted during the extinction period was determined for each subject, and the mean of these scores was plotted to produce an acquisition (learning) curve.

Generalization Tests. Following acquisition (at least 80% appropriate responding in each training condition) sessions were conducted in the order saline, drug, drug, saline, test. One drug and one saline session each week began with a 5-min extinction period. Scores obtained from these extinction periods were used in comparison with test day scores. On test days subjects were injected 15 min prior to the session with a compound or dosage not used in training. These test sessions consisted solely of a 5-min extinction period. The percentage of drug-appropriate responses was calculated for each subject. Scores for subjects making fewer than ten responses in the test period were discarded. At least five subjects from the DOM-trained and (+)amphetamine-trained groups were tested with each dose of a compound under consideration. Assignment of subjects to test conditions was arbitrary with the restriction that no subject was tested twice in the same condition. In this manner, dose-response curves and cross dose-response curves for the training compounds were determined. Similarly, generalization tests were conducted for the separate isomers of DOM and for mescaline, 4-methylamphetamine, 2,5-dimethoxyamphetamine, DOET, psilocybin, and methylphenidate.

Antagonist Tests. Tests of antagonists were conducted by pretreating subjects with a 5-HT antagonist or haloperidol, then injecting either saline or the training drug 15 min before the 5-min extinction test. Antagonists, at the indicated doses, were injected at the following times pretest: Cinanserin (15.0 mg/kg) at 30 min; methysergide (5.0 mg/kg) at 45 min; and xylamidine (1.0 mg/kg) and haloperidol (0.5 mg/kg) at 90 min.

Statistics. Three scores were obtained for each subject each week, one in each training condition and one in the test condition. Scores for subjects receiving the same generalization test were analyzed with a repeated measures analysis of variance followed by a Newman-Keuls procedure ($\alpha = 0.05$). Scores for the antagonist tests were compared with the scores for the appropriate training condition by means of a paired Student's *t*-test. No statistic was calculated if the majority of animals failed to emit at least ten responses under the test condition.

Results

The acquisition of the amphetamine and DOM discrimination are shown in Figure 1. The order of drug and saline administrations were the same for both groups and the acquisition curves appear to be quite similar, suggesting that the training doses chosen were approximately equipotent as discriminative stimuli. Subjects in both groups averaged greater than 90% correct responses in both training conditions from the end of the acquisition period to the end of the study.

Results of generalization tests are shown in Tables 1 and 2. Tests with the two training drugs did not show cross-generalization. At 0.75 mg/kg, (+)amphetamine induced saline-appropriate responding in DOM animals and drug-appropriate responding in amphetamine animals. Higher doses of (+)amphetamine induced responding significantly different from either training condition in DOM animals. At 0.5 mg/kg, DOM induced drug-appropriate responding in DOM animals and saline-appropriate responding in amphetamine animals. Higher doses of DOM induced responding significantly different from either training condition in

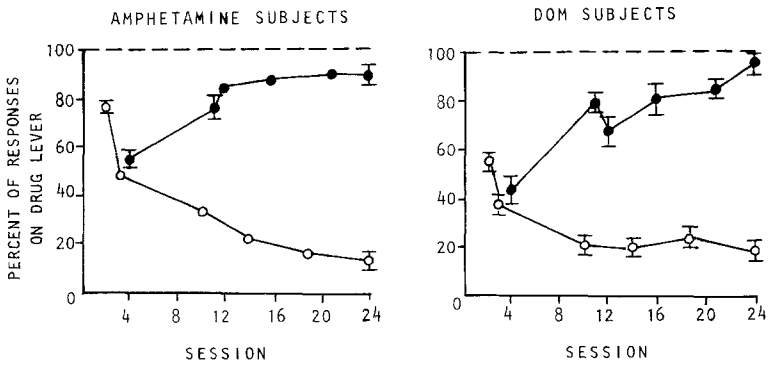

Fig. 1
Acquisition curves for discrimination of 1.0 mg/kg (+)amphetamine sulfate (left) and 1.5 mg/kg DOM HCl (right) from saline. Filled symbols are mean (± SEM) scores for drug sessions and open symbols are the same for saline sessions. For amphetamine discrimination, $N = 30$ and for DOM discrimination, $N = 10$

Table 1. Dose-response and cross dose-response effects for the training drugs. Subjects emitting fewer than ten responses were considered to be not responding. No statistical test was performed where a majority of subjects failed to respond

Test drug	Dose (mg/kg)	Amphetamine subjects			DOM subjects		
		N	Percent responding	Percent drug responses[a]	*N*	Percent responding	Percent drug responses[a]
(+)Amphetamine	0.25	10	100	22 ± 5 **			
	0.5	10	100	58 ± 9 ***			
	0.75	10	100	83 ± 5 *	6	100	23 ± 11 **
	1.5				10	90	60 ± 8 ***
	2.25				10	80	57 ± 6 ***
(±)DOM	0.25				7	100	17 ± 8 **
	0.5	6	100	12 ± 5 **	7	100	76 ± 11 *
	0.75	10	100	33 ± 7 ***			
	1.0	10	70	48 ± 10 ***	7	100	81 ± 11 *
	1.5	15	73	64 ± 5 ***			
	2.0	5	20	20			

[a] Mean ± SEM
* $P < 0.05$ different from saline
** $P < 0.05$ different from training drug
*** $P < 0.05$ different from both training conditions

amphetamine animals. At the highest dose of DOM tested (2.0 mg/kg), only one of five amphetamine animals responded at all.

Mescaline (15 mg/kg) generalized to the DOM training condition but not to amphetamine. With 22.5 mg/kg mescaline, DOM subjects responded exclusively on the lever paired with DOM, but only two of five animals responded; only one of five amphetamine subjects responded at this dose of mescaline and did so exclusively on the saline-appropriate lever.

Both isomers of DOM were capable of producing the DOM stimulus, but the (−)isomer appeared to be considerably more potent. Neither isomer generalized to amphetamine.

DOET generalized with DOM but not with amphetamine. Methylphenidate generalized with amphetamine but not with DOM. Both 2,5-dimethoxyamphetamine and psilocybin showed greater similarity to DOM than to amphetamine, although neither generalized completely with DOM. 4-Methylamphetamine induced no generalization with either training compound.

The effects of the 5-HT antagonists cinanserin, methysergide, and xylamidine, and the dopamine antagonist haloperidol on DOM and amphetamine discrimination are shown in Table 3. None of the treatments had a significant effect on saline responding in either group of subjects. Cinanserin and methysergide effectively eliminated the DOM cue while having no significant effect on the amphetamine cue. The peripheral 5-HT antagonist xylamidine had no effect on either group. Haloperidol significantly antagonized the amphetamine cue but had no effect on the DOM cue.

In the amphetamine subjects, 0.5 mg/kg (+)amphetamine and 1.5 mg/kg DOM resulted in comparable performance, i.e., about 60% drug-appropriate responding. Pretreatment with cinanserin significantly reduced drug-appropriate responding following DOM, but did not significantly change responding following amphetamine (Table 4).

Table 2. Results of generalization tests with structurally related compounds. Subjects emitting fewer than ten responses were considered to be not responding. No statistical test was performed where a majority of subjects failed to respond

Test drug	Dose (mg/kg)	Amphetamine subjects			DOM subjects		
		N	Percent responding	Percent drug responses[a]	*N*	Percent responding	Percent drug responses[a]
Mescaline	7.5	5	100	4 ± 3 **	5	100	26 ± 9 **
	12.0	5	80	33 ± 14 ***	5	100	51 ± 7 ***
	15.0	10	80	37 ± 12 ***	10	100	86 ± 4 *
	22.5	5	20	0	5	40	100 ± 0
R(−)DOM	0.25	6	83	30 ± 14 **			
	0.38	6	67	44 ± 15 ***	6	100	40 ± 14 ***
	0.5	6	83	34 ± 11 ***			
	0.75	6	33	52 ± 18	6	100	94 ± 5
S(+)DOM	0.75	6	100	5 ± 2 **	5	100	0 ± 0 **
	1.5	6	67	28 ± 4 ***	6	100	53 ± 10 ***
	2.25	6	67	39 ± 9 ***	6	100	84 ± 5 *
4-Methylamphetamine	1.0	5	100	20 ± 3 ***	5	100	39 ± 17 ***
	2.0	5	80	42 ± 6 ***	5	100	40 ± 14 ***
	3.0	5	0	–	5	20	12
2,5-Dimethoxy-amphetamine	1.0	5	100	14 ± 7 **			
	2.0	5	100	5 ± 1 **			
	4.0	5	100	24 ± 10 **	5	100	51 ± 16 ***
	8.0	10	80	21 ± 8 **	10	100	72 ± 7 ***
DOET	0.25	5	100	19 ± 6 ***	5	100	36 ± 12 ***
	0.5	5	40	10 ± 2	5	100	78 ± 4 ***
	0.75				5	80	83 ± 13 *
Psilocybin	0.5	5	100	23 ± 6 ***	5	100	10 ± 7 **
	1.0	10	90	50 ± 9 ***	10	100	74 ± 9 ***
	1.5	6	0	–	10	100	71 ± 6 ***
Methylphenidate	2.5	15	100	54 ± 8 ***	5	100	20 ± 10 ***
	5.0	11	100	92 ± 7 *	5	100	32 ± 11 ***

[a] Mean ± SEM
* $P < 0.05$ different from saline
** $P < 0.05$ different from training drug
*** $P < 0.05$ different from both training conditions

Discussion

The data show that the stimuli induced by DOM and (+)amphetamine are not the same. First, the training compounds did not generalize with one another. Second, differences are apparent in tests of generalization to structurally related compounds. Finally, DOM and (+)amphetamine are differentially affected by 5-HT and dopamine receptor blockade.

Low doses of DOM induced saline-appropriate responding in amphetamine-trained subjects. Higher doses resulted in responding significantly different from either training condition along with a number of failures to meet the response criterion. Similarly, in DOM-trained subjects, the lowest dose of (+)amphetamine tested induced saline-appropriate responding and higher doses were different from either training condition. While showing that the stimuli are not the same, the results of the cross dose-response tests do not rule out the possibility that DOM and (+)amphetamine share some common stimulus attributes. Thus, these data are not totally contradictory to either those of Huang and Ho (1974) or Tilson et al. (1975b), although greater similarity to the former is apparent. In that study, rats trained to discriminate (+)amphetamine from saline did not generalize with (+)amphetamine when tested with DOM. However, at 1.0 mg/kg (±)DOM not all subjects responded and higher doses were not tested. Similar results were obtained here, but only at higher (and sometimes disruptive) doses was any similarity of DOM and (+)amphetamine observed. In the Tilson et al. study (1975b), generalization between (+)amphetamine and (−)DOM was obtained. The difference in their results and ours may be attributed to procedural differences. In any event, Tilson et al. (1975b) contended only that DOM and amphetamine stimuli showed some similarity, not that they

Table 3. Effect of serotonin antagonists and haloperidol on discrimination of (+)amphetamine and DOM

Pretreatment (mg/kg)	Treatment	Amphetamine subjects			DOM subjects		
		N	Percent responding	Percent drug responses[a]	*N*	Percent responding	Percent drug responses[a]
None	Saline			10 ± 3			10 ± 3
Cinanserin (15)	Saline	10	100	16 ± 3	10	100	6 ± 3
None	Drug			91 ± 4			93 ± 2
Cinanserin (15)	Drug	10	100	94 ± 2	10	100	16 ± 7*
None	Saline			4 ± 1			1 ± 0
Methysergide (5)	Saline	10	100	6 ± 1	10	100	6 ± 3
None	Drug			97 ± 2			95 ± 2
Methysergide (5)	Drug	10	100	95 ± 2	10	100	11 ± 4*
None	Saline			10 ± 3			14 ± 5
Xylamidine (1)	Saline	5	100	10 ± 4	5	100	9 ± 3
None	Drug			92 ± 6			88 ± 5
Xylamidine (1)	Drug	9	100	96 ± 1	10	100	92 ± 3
None	Saline			3 ± 1			0 ± 0
Haloperidol (0.5)	Saline	10	90	6 ± 1	5	100	5 ± 2
None	Drug			99 ± 0			97 ± 1
Haloperidol (0.5)	Drug	10	100	19 ± 5*	10	90	92 ± 4

[a] Mean ± SEM
* $P < 0.001$ different from no pretreatment

Table 4
Effect of cinanserin pretreatment on drug-appropriate responding induced by 1.5 mg/kg DOM or 0.5 mg/kg (+)amphetamine in (+)amphetamine-trained subjects

Pretreatment (dose in mg/kg)	Test drug (dose in mg/kg)	*N*	Percent responding	Percent drug responses (mean ± SEM)
None	Amphetamine (0.5)	10	100	58 ± 9
Cinanserin (15)	Amphetamine (0.5)	10	100	78 ± 8
None	DOM (1.5)	15	73	64 ± 5
Cinanserin (15)	DOM (1.5)	11	91	7 ± 4 *

* $P < 0.001$ different from no pretreatment

were the same. This contention cannot be disputed on the basis of the cross dose-response data presented here.

Results of generalization tests with structurally or functionally related compounds demonstrate important differences in the DOM and (+)amphetamine stimuli. DOET induces a state of euphoria virtually identical to that induced by low doses of DOM (Snyder et al., 1971). DOET generalized with DOM but not (+)amphetamine, suggesting that this prehallucinogenic state is not stimulant-like. Mescaline generalized with DOM, just as DOM and DOET have been shown to generalize with mescaline (Winter, 1975a). Psilocybin and 2,5-dimethoxyamphetamine did not show complete generalization with DOM, but showed greater similarity to DOM than to (+)amphetamine. 2,5-Dimethoxyamphetamine shows 'marked amphetamine-like action' on CAR in rats (Smythies et al., 1969) but is, in fact, hallucinogenic (Shulgin et al., 1969). The psychomotor stimulant methylphenidate generalized completely with (+)amphetamine, as demonstrated in an earlier study (Huang and Ho, 1974). Methylphenidate showed no generalization with DOM. 4-Methylamphetamine, which reportedly has potent stimulant effects on CAR (Beaton et al., 1968) and locomotor activity (Mantegazza et al., 1970), was unlike either training compound and disrupted behavior completely at 3.0 mg/kg. Taken together, the results of these generalization tests show that the DOM stimulus is like that of other hallucinogens and differentiable from psychomotor stimulants.

Neither isomer of DOM generalized with (+)amphetamine. This is inconsistent with results showing generalization of (−)DOM with (+)amphetamine (Tilson et al., 1975b). We can presently offer no definite reason for this discrepancy. In the present study, the separate isomers of DOM appeared, in fact, to have less

similarity to (+) amphetamine than did the racemic mixture. Others have found that the behavioral effects of racemic 3,4-dimethoxyamphetamine (Barfknecht and Nichols, 1972) and racemic DOM (Harris et al., 1977) are not totally predictable from the activities of the separate isomers.

Of particular interest is the finding that both isomers of DOM generalized with (±)DOM. The fact that (–)DOM, which is of *R* absolute configuration, was the more potent isomer is consistent with a theoretical model in which the asymmetric α-carbon of DOM corresponds to the asymmetric 5-carbon of LSD which is also of *R* absolute configuration (Clothia and Pauling, 1969). The present result is also consistent with other behavioral data (Benington et al., 1973; Harris et al., 1977) showing the (–)isomer to have greater activity. Stereoselectivity of the ethyl analog of DOM, DOET, has also been demonstrated. (–)DOET was shown to be three to four times more potent than (+)DOET both in inducing subjective effects in man (Snyder et al., 1974) and in displacing labeled LSD from its binding sites in rat brain preparations (Bennett and Snyder, 1975). The stereoselectivity of these compounds is the opposite of that for amphetamine, where *S*(+)amphetamine is the more potent isomer. What is surprising in our data is the demonstration that (+)DOM shows good generalization with racemic DOM in rats. Unlike (+)DOET, (+)DOM was found to have neither hallucinogenic nor stimulant activity in man (Shulgin, 1973). The correspondence between 'hallucinogenic stimulus' in rats and in man, as discussed by Winter (1975a), thus remains open to question.

Results of the antagonist tests were clear. 5-HT antagonists did not reduce the discriminability of (+)amphetamine. The DOM stimulus was effectively eliminated by the centrally active 5-HT antagonists. In this regard, DOM is like mescaline (Browne and Ho, 1975). DOM has been shown to generalize with 5-methoxy-N,N-dimethyltryptamine (5-OMe DMT), and the stimulus induced by 5-OMe DMT is blocked by the 5-HT antagonist BC-105 (Glennon et al., 1979). A recent study shows that the LSD stimulus in rats is also blocked by 5-HT antagonists (Kuhn et al., 1978), although this finding is at variance with an earlier study (Hirschhorn and Rosecrans, 1974). Pretreatment with 5-HT antagonists, but not with the 5-HT synthesis inhibitor *p*-chlorophenylalanine, was shown to block both the gross behavioral and EEG effects of DOM in cats (Wallach et al., 1972). Direct receptor activity for DOM is thus suggested. DOM has been shown to effectively compete for LSD binding sites in rat brain preparations, a property not shared with (+)amphetamine (Bennett and Snyder, 1975). Classical 5-HT antagonists also compete for LSD binding sites and, in fact, have greater affinity for LSD than 5-HT binding sites (Bennett and Snyder, 1976). Apparently, activity at this site is a necessary feature of the DOM stimulus.

The peripherally active 5-HT antagonist xylamidine did not block the DOM stimulus, suggesting a central locus for the DOM stimulus. We have obtained more direct evidence for this contention using intraventricular administration of DOM (unpublished data). Haloperidol, at a dose which blocked the (+)amphetamine stimulus, had no effect on DOM discriminability. The ability of dopamine antagonists to block stimulant stimuli is well established (Silverman and Ho, 1977) and failure to antagonize DOM suggests that any amphetamine-like properties of DOM are not important for DOM discriminability. Our preliminary data showing that α-methyl-*p*-tyrosine did not affect DOM discriminability supports this contention.

In addition to blocking the DOM stimulus itself, cinanserin pretreatment eliminated the amphetamine-appropriate responding induced by DOM in amphetamine-trained subjects. Cinanserin pretreatment did not block a similar level of performance induced by a low dose of (+)amphetamine. Thus, any stimulant-like effects of DOM appear to be mediated via a different mechanism from that of stimulants themselves. Any action of DOM on catecholamine systems may first require activity at the LSD binding site, i.e., the activities may be sequential rather than parallel.

The prehallucinogenic state induced by low doses of DOM and other methoxylated phenylisopropylamine hallucinogens is not unique by any means. The ability of LSD to induce such a state is well described (Katz et al., 1968) and was in fact the basis of 'psycholytic therapy' (Abramson, 1967). The effect of low doses of DOM in rat and man may then better be described as 'LSD-like' rather than 'amphetamine-like'. DOM, DOET, and related compounds may merely have a less steep dose-response curve than does LSD.

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References

Abramson, H. A.: The use of LSD in psychotherapy and alcoholism. Indianapolis: Bobbs Merrill 1967

Barfknecht, C. F., Nichols, D. E.: Effects of *S*-(+)- and *R*-(–)-3,4-dimethoxyphenylisopropylamines in the rat. J. Med. Chem. **15**, 109–110 (1972)

Barry, H., III: Classification of drugs according to their discriminable effects in rats. Fed. Proc. **33**, 1814–1824 (1974)

Beaton, J. M., Smythies, J. R., Benington, F., Morin, R. D., Clark, L. C.: Behavioural effects of some 4-substituted amphetamines. Nature **220**, 800–801 (1968)

Beaton, J. M., Smythies, J. R., Benington, F., Morin, R. D.: The behavioural effects of 2,5-dimethoxy-4-methylamphetamine (DOM) in rats. Commun. Behav. Biol. **3**, 81–84 (1969)

Benington, F., Morin, R. D., Beaton, J., Smythies, J. R., Bradley, R. J.: Comparative effects of stereoisomers of hallucinogenic amphetamines. Nature **242**, 185–186 (1973)

Bennett, J. P., Snyder, S. H.: Stereospecific binding of D-lysergic acid diethylamide (LSD) to brain membranes: Relationship to serotonin receptors. Brain Res. **94**, 523–544 (1975)

Bennett, J. P., Snyder, S. H.: Serotonin and lysergic acid diethylamide binding in rat brain membranes: Relationship to postsynaptic serotonin receptors. Mol. Pharmacol. **12**, 373–389 (1976)

Browne, R. G., Ho, B. T.: The role of serotonin in the discriminative stimulus properties of mescaline. Pharmacol. Biochem. Behav. **3**, 429–435 (1975)

Clothia, C., Pauling, P.: On the conformation of hallucinogenic molecules and their correlation. Proc. Natl. Acad. Sci. **63**, 1063–1070 (1969)

Glennon, R. A., Rosecrans, J. A., Young, R., Gaines, J.: Hallucinogens as a discriminative stimuli: Generalization of DOM to a 5-methoxy-N,N-dimethyltryptamine stimulus. Life Sci. **24**, 993–998 (1979)

Harris, R. A., Snell, D., Loh, H. H.: Stereoselective effects of 1-(2,5-dimethoxy-4-methylphenyl)-2-aminopropane (DOM) on schedule-controlled behavior. Pharmacol. Biochem. Behav. **7**, 307–310 (1977)

Hirschhorn, I. D., Rosecrans, J. A.: A comparison of the stimulus effects of morphine and lysergic acid diethylamide (LSD). Pharmacol. Biochem. Behav. **2**, 361–366 (1974)

Hollister, L. E., Macnicol, M. F., Gillespie, H. K.: An hallucinogenic amphetamine analog (DOM) in man. Psychopharmacologia **14**, 62–73 (1969)

Huang, J. T., Ho, B. T.: Discriminative stimulus properties of *d*-amphetamine and related compounds in rats. Pharmacol. Biochem. Behav. **2**, 669–673 (1974)

Katz, M. M., Waskow, I. E., Olsson, J.: Characterizing the psychological state produced by LSD. J. Abnormal Psychol. **73**, 1–14 (1968)

Kuhn, D. M., White, F. J., Appel, J. B.: The discriminative stimulus properties of LSD: Mechanisms of action. Neuropharmacology **17**, 257–263 (1978)

Lal, H., ed.: Discriminative stimulus properties of drugs. New York: Plenum 1977

Mantegazza, P., Müller, E. E., Naimzada, M. K., Riva, M.: Studies on lack of correlation between hyperthermia, hyperactivity and anorexia induced by amphetamine. In: Amphetamines and related compounds, E. Costa, S. Garratini, eds., pp. 559–575. New York: Raven 1970

Shulgin, A. T., Sargent, T., Naranjo, C.: Structure-activity relationships of one-ring psychotomimetics. Nature **221**, 537–541 (1969)

Shulgin, A. T.: Stereospecific requirements for hallucinogenesis. J. Pharm. Pharmacol. **25**, 271–272 (1973)

Silverman, P. B., Ho, B. T.: Characterization of discriminative response control by psychomotor stimulants. In: Discriminative stimulus properties of drugs, H. Lal, ed., pp. 107–119. New York: Plenum 1977

Smythies, J. R., Johnston, V. S., Bradley, R. J.: Behavioural models of psychosis. Br. J. Psychiatry **115**, 55–68 (1969)

Snyder, S. H., Faillace, L., Hollister, L.: 2,5-Dimethoxy-4-methylamphetamine (STP): A new hallucinogenic drug. Science **158**, 669–670 (1967)

Snyder, S. H., Faillace, L. A., Weingartner, H.: DOM (STP), a new hallucinogenic drug, and DOET: Effects in normal subjects. Am. J. Psychiatry **125**, 357–364 (1968)

Snyder, S. H., Weingartner, H., Faillace, L. A.: DOET (2,5-dimethoxy-4-ethylamphetamine), a new psychotropic drug: Effects of varying doses in man. Arch. Gen. Psychiatry **24**, 50–55 (1971)

Snyder, S. H., Unger, S., Blatchley, R., Barfknecht, C. F.: Stereospecific actions of DOET (2,5-dimethoxy-4-ethylamphetamine) in man. Arch. Gen. Psychiatry **31**, 103–106 (1974)

Tilson, H. A., Baker, T. G., Chamberlain, J. H., Marquis, W. J., Rech, R. H.: Behavioral and neuropharmacological analysis of amphetamine and 2,5-dimethoxy-4-methylamphetamine in rats. Psychopharmacologia **44**, 229–239 (1975a)

Tilson, H. A., Baker, T. G., Gylys, J. A.: A comparison of the discriminative stimulus properties of R-2,5-dimethoxy-4-methylamphetamine (R-DOM) and S-amphetamine in the rat. Psychopharmacologia **44**, 225–228 (1975b)

Wallach, M. B., Friedman, E., Gershon, S.: 2,5-Dimethoxy-4-methylamphetamine (DOM), a neuropharmacological examination. J. Pharmacol. Exp. Ther. **182**, 145–154 (1972)

Winter, J. C.: The effects of 2,5-dimethoxy-4-methylamphetamine (DOM), 2,5-dimethoxy-4-ethylamphetamine (DOET), *d*-amphetamine, and cocaine in rats trained with mescaline as a discriminative stimulus. Psychopharmacologia **44**, 29–32 (1975a)

Winter, J. C.: Blockade of the stimulus properties of mescaline by a serotonin antagonist. Arch. Int. Pharmacodyn. Ther. **214**, 250–253 (1975b)

Winter, J. C.: Stimulus properties of phenethylamine hallucinogens and lysergic acid diethylamide: The role of 5-hydroxytryptamine. J. Pharmacol. Exp. Ther. **204**, 416–423 (1978)

Yamamoto, T., Ueki, S.: Behavioral effects of 2,5-dimethoxy-4-methylamphetamine (DOM) in rats and mice. Eur. J. Pharmacol. **32**, 156–162 (1975)

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