*Pharmacology Biochemistry & Behavior*, Vol. 15, pp. 711–715, 1981. Printed in the U.S.A.

# Serotonergic and Dopaminergic Effects on Yawning in the Cat[1]

JAMES L. MARINI[2]

*Department of Psychiatry, Yale University School of Medicine and Connecticut Mental Health Center 34 Park Street, New Haven, CT 06508*

Received 6 June 1981

MARINI, J. L. *Serotonergic and dopaminergic effects on yawning in the cat.* PHARMAC. BIOCHEM. BEHAV. 15(5) 711–715, 1981.—The serotonergic agents LSD (0.01–0.05 mg/kg) and lisuride (0.025 and 0.05 mg/kg) elicited a high frequency of limb flicking in the cat after IP doses; LSD, but not lisuride, elicited a significantly increased frequency of yawning as well. In combination, LSD plus lisuride (0.025 mg/kg each) gave additive frequencies of limb flicking, but the frequency of yawning was half that after LSD alone. The dopamine agonist apomorphine had no significant effect on either yawning or limb flicking over the dose range 0.006 to 3.2 mg/kg. Pretreatment of cats with 1.0 mg/kg of apomorphine (but not with 0.05 mg/kg) significantly reduced the frequency of yawning elicited by 0.01 or 0.025 mg/kg of LSD, but had no effect on limb flicking. The dopamine antagonist haloperidol had no effect on limb flicking at doses from 0.008 to 0.512 mg/kg, but produced a significantly increased frequency of yawning at 0.256 mg/kg, an effect antagonized by lisuride administration. Given that lisuride has more potent dopamine agonist properties than LSD, these results are consistent with serotonergic elicitation of yawning, dopaminergic inhibition of yawning, and with their concomitant interaction in the expression of drug-induced yawning in the cat. The behavioral pharmacologies of limb flicking and yawning are different in this species.

Yawning Cats Serotonin Dopamine LSD Lisuride Limb flicking

RECENT pharmacological studies of yawning in the rat have shown that in this species the behavior is affected by cholinergic, dopaminergic, and serotonergic agents, and to some extent by glutamate [8]. The cholinergic drugs physostigmine and pilocarpine (PILO) elicit yawning [21,28] by a mechanism involving muscarinic, but not nicotinic, cholinergic receptors in the central nervous system [21,28]. The frequency of such cholinergically-elicited yawning is greatest in rats less than 10 days of age [21]. There is also evidence that a dopaminergic mechanism inhibits yawning in the rat. For instance, fluphenazine, which blocks dopamine (DA) receptors, potentiates physostigmine-induced yawning [28], and yawning is induced by doses of the DA agonist, apomorphine (APO), that inhibit dopamine-firing [2, 15, 28]. It has been proposed that cholinergic activation and dopaminergic inhibition act concomitantly in the expression of yawning in rats [2,28].

A serotonergic mechanism also affects the behavior, although it has been less thoroughly studied. For example, citalopram (Lu-10-171), an inhibitor of serotonin (5HT) reuptake, strongly potentiates physostigmine-induced yawning in rats [2,22], and the effect of citalopram is antagonized by metergoline, which blocks 5HT receptors [22]. Because administration of citalopram alone was without effect on yawning, the action of 5HT was assumed to be "modulatory" [22], that is, to require ongoing (cholinergic?) activity or tone for its expression. This proposal is consistent with the results of studies of the application of 5HT to motor neurons in anesthetized rats [12–14, 16, 23, 25] and cats [25], and to neurons in the myenteric plexus of the guinea pig [26,27], all of which indicate a modulatory effect of 5HT on neuronal activity in these systems.

Hallucinogens with 5HT-agonist properties, including *d*-lysergic acid diethylamide (LSD) and N,N-dimethyltryptamine (DMT), have also been reported to modulate motor neuron activity [13]. DMT elicits yawning in monkeys [13], and these and other LSD-like hallucinogens have been reported to produce increased frequencies of yawning in cats [7,20]; data on this subject have been published only for the 5HT agonist 5-methoxy-N,N-dimethyltryptamine [20].

During studies [9–11] of the specificity of a cat behavior model for hallucinogens [5–7, 19], I observed that LSD elicited a high frequency of yawning. Since LSD is a potent serotonergic agent (e.g., [18]) which also possesses dopaminergic properties (e.g., [4]), and since both 5HT and DA have been implicated in yawning, I used LSD-elicited yawning as a starting point for a study of the roles of serotonergic and dopaminergic mechanisms in the behavior. In addition to its relevance to the pharmacology of yawning and the behavioral pharmacology of LSD, the study was intended as a preliminary investigation of yawning as a behavioral index of serotonergic and dopaminergic properties

[1]Supported by Research Grant MH 26446 from the National Institute of Mental Health, and by the State of Connecticut.
[2]Present address: 36 West Shore Drive, Clinton, CT 06413.

of drugs. Since 5HT mechanisms appear to increase, and DA mechanisms decrease, the frequency of occurrence of yawning, drug-elicited yawning may provide a simple system for studying the interactions of serotonergic and dopaminergic drugs, or for investigating the concomitant expression of 5HT- and DA-related properties of a drug with "mixed" effects. For purposes of comparison, I also scored limb flicking, a well-studied feline behavior which is not obviously related to yawning, and is elicited by many drugs [10, 11, 24], including LSD and related hallucinogens [5, 6, 9, 24].

## METHOD

### *Animals*

Twelve healthy adult mongrel cats (5 females, 2.6–4.0 kg; 7 males, 3.5–7.5 kg) were employed. They were housed in standard stainless steel cages for at least two months prior to these studies, in a temperature-controlled room on a 12-hr light-dark cycle (lights on: 7 a.m. to 7 p.m.). Food (Purina Cat Chow) and water were always available. Routine daily cage maintenance was performed by the Division of Animal Care, Yale University School of Medicine. All animals had received LSD and lisuride [9,10], and seven had received methysergide [10], prior to these experiments.

### *Drugs*

Saline (control) and drugs dissolved in saline were administered by the intraperitoneal (IP) route in all cases; injection volume was 1 ml/kg except for pilocarpine (0.25 ml/kg). For experiments not reported in Table 1, the numbers of animals and doses employed are given below. Doses of LSD (as bitartrate, National Institute on Drug Abuse, NIDA) were prepared by dilution of a 0.10 mg/ml stock solution in saline, stored in the dark at room temperature. Lisuride (LIS, as hydrogen maleate, Schering AG) solutions were prepared daily. Apomorphine (APO, as hydrochloride, Merck) solutions were prepared daily, except in one or two cases in which solutions were stored refrigerated for no more than 3 days. No APO solution used showed evidence of decomposition (development of a green color darker than that of a fresh solution). Eleven APO doses were employed, 10 based on consecutive doubling of 0.00625 mg/kg to 3.2 mg/kg, and 1.0 mg/kg. Four cats were tested at each dose, except for 0.10 mg/kg, for which N=7. Pilocarpine (PILO, as hydrochloride, Sigma) solutions were prepared daily. Four cats were tested at 0.125, 0.25, and 1.0 mg/kg; six were tested at 0.5 mg/kg. Haloperidol (HAL, McNeil) solutions were prepared by dilution of the injectible preparation (5 mg/ml) with HCl-acidified saline (pH=4.3), and were stored for no more than 4 days. The maximum HAL concentration used was 0.512 mg/ml in saline (pH=3.2, lower than saline's due to buffers in the injectible preparation), all other HAL solutions were made by dilution of this concentration with acidified saline, and none showed precipitation of drug upon visual examination. (HAL precipitated from solution when prepared in this way for a nominal concentration of 2 mg/ml.) Two–four cats were scored at 0.008–0.064 mg/kg, and six at 0.128, 0.256, and 0.512 mg/kg.

TABLE 1

FREQUENCIES OF DRUG-ELICITED YAWNING AND LIMB FLICKING IN CATS

| | | Mean Occurrences per 90 min ± S.E. | | | |
|---|---|---|---|---|---|
| | | Drug Treatments | | Saline (Control) | |
| (N) | Drugs and Dose, mg/kg | Yawns | Limb Flicks | Yawns | Limb Flicks |
| (6) | LSD, 0.01 | 7.8 ± 2.4§ | 41 ± 12§ | 0.3 ± 0.2 | 2.5 ± 1.5 |
| (9) | LSD, 0.025 | 6.2 ± 1.4# | 53 ± 9.3# | 0.3 ± 0.2 | 1.7 ± 1.0 |
| (7) | LSD, 0.050 | 5.6 ± 1.5¶ | 44 ± 11¶ | 0.4 ± 0.2 | 1.3 ± 0.77 |
| (8) | LIS, 0.025 | 0.1 ± 0.1 | 19 ± 6.3§ | 1.0 ± 0.53 | 0.9 ± 0.5 |
| (9) | LIS, 0.05 | 0.3 ± 0.4 | 33 ± 13‡ | 0.3 ± 0.2 | 0.4 ± 0.3 |
| (5) | LIS + LSD, 0.025* | 2.6 ± 1.3 | 42 ± 21 | 0.8 ± 0.2 | 1.2 ± 0.65 |
| (5) | LSD, 0.025* | 5.0 ± 2.7 | 22 ± 7.4‡ | 0.4 ± 0.3 | 1.0 ± 0.71 |
| (5) | LIS, 0.025* | 1.0 ± 0.35 | 19 ± 13 | 0.2 ± 0.2 | 1.4 ± 0.76 |
| (6) | LSD, 0.025 | 6.5 ± 1.9¶ | 73 ± 14§ | 0 | 0.8 ± 0.9 |
| (6) | LSD + APO, 0.05 | 6.5 ± 1.2¶ | 70 ± 16¶ | | |
| (6) | LSD + APO, 1.0 | 1.8 ± 0.59¶ | 70 ± 23‡ | | |
| (5) | LSD, 0.01† | 5.8 ± 1.1¶ | 46 ± 12§ | 0.4 ± 0.3 | 3.0 ± 1.7 |
| (5) | LSD + APO, 0.05† | 4.0 ± 1.5‡ | 39 ± 12‡ | | |
| (6) | LSD, 0.01 | 7.8 ± 2.4§ | 41 ± 12§ | 0.3 ± 0.2 | 2.5 ± 1.5 |
| (6) | LSD + APO, 1.0 | 0.8 ± 0.6 | 38 ± 11 | | |

LSD=*d*-lysergic acid diethylamide; LIS=lisuride; APO=apomorphine.

*Data are for 60 min.

†One of six animals tested is omitted because it received an incorrect APO dose.

‡$p<0.05$; §$p<0.025$, ¶$p<0.01$; #$p<0.001$. Underscored values=Yawning frequencies significantly different by at least $p<0.05$.

*Scoring and Experimental Design*

Limb flicking and yawning were scored in 15-min epochs for 90 min immediately following drug administration except in the LSD + LIS combination experiments, which were scored for 60 min (a 90-min scoring protocol had not been adopted when the combination experiments were performed). At least 6 days elapsed between consecutive experiments with each animal, animals were scored in their home cages, and each was tested at the same time of day (10 a.m. to 4 p.m.). The behaviors were scored by criteria previously described [5,10]. In cats, yawning is often preceeded by jaw movements and partial jaw opening, usually accompanied by chop licking. Such jaw movements, whether associated with frank yawning or not, were never scored as yawns.

Scoring after saline, LSD, LIS, LSD + LIS, and HAL + LIS, was performed with a knowledge of drugs and doses; in the latter case, HAL was administered 15 min before LIS, and scoring commenced immediately after the LIS injection. The behavioral activities of LSD [5,6] and LIS [9,24] were originally scored by raters blind to dose. Since LSD and LIS can readily be distinguished from saline, and since no hypothesis about the quantitative relationship of dose to response were being tested, blind rating was not employed when these drugs were tested alone. APO doses from 0.006 to 0.05 mg/kg were scored blind to dose; because neither these doses not 1.0 mg/kg appeared behaviorally active, the other APO doses were scored non-blind. In APO + LSD experiments, APO was given 15 min before LSD, and scoring commenced immediately after the LSD injection. In the first of these experiments to be performed (LSD, 0.025 mg/kg), animals were tested during three consecutive weeks, with cats receiving LSD every week. Each week, two cats received only LSD, and four received APO (either 0.05 or 1.0 mg/kg, two cats at each APO dose) in addition. The scorer was aware of drugs and doses in this experiment. In the second (LSD, 0.01 mg/kg), all cats received a reference LSD dose during the same week. Subsequently, they were tested on two consecutive weeks, during both of which they received LSD and one of the two APO doses. In this experiment the scorer was blind to the APO dose received. All HAL and PILO experiments were scored blind to dose, except for 0.50 mg/kg of PILO [11].

*Statistics*

Comparisons of experimental with reference conditions are made with the two-tailed paried $t$-test. The measure of variance reported here is ± the standard error of the mean. $p<0.05$ is the criterion for statistical significance.

## RESULTS

The control data in Table 1 show that both yawning and limb flicking occurred infrequently after saline injections; no sex differences were found. LSD (0.01–0.05 mg/kg, Table 1) elicited a significantly increased frequency of yawning at all doses. Every animal yawned at least once after LSD. Excluding one male cat with an unusually high frequency of yawning after LSD (18 and 14 per 90 min at 0.01 and 0.025 mg/kg, respectively), the mean frequencies of occurrence of yawning for males (4–7 per 90 min) were similar to those for females (4.5–6.5 per 90 min).

As expected, these doses of LSD also elicited limb flicking, and every animal limb flicked at least 7 times after LSD. For comparison with other published reports, which used 60-min scoring periods [5–7, 9, 19, 24], the mean frequencies of LSD-elicited limb flicking in the 60 min following injection of 0.01, 0.025, and 0.05 mg/kg were: 21±6.2, 35±6.1, and 30±6.3, respectively.

Table 1 presents data showing that, while LIS doses of 0.025 and 0.05 mg/kg were comparable to LSD in eliciting limb flicking, they had no effect on yawning. Previously reported experiments also showed no effect of LIS on yawning at these doses, or at 0.006, 0.013, and 0.10 mg/kg [9]. For comparison with other published data, based on a 60-min scoring period [9,24], the mean frequencies of behaviors in the 60 min following injection of 0.025 and 0.05 mg/kg of lisuride were: Yawns, 0.1±0.1 and 0.3±0.4; limb flicks, 10±3.2 and 22±9.4, respectively.

In five cats given 0.025 mg/kg of both LSD and LIS simultaneously, the hourly frequency of limb flicking was additive compared to the frequencies when the drugs were given singly (Table 1), but the frequency of yawning was about 50% less than after LSD alone (difference not statistically significant).

APO had no significant effect on yawning or limb flicking when given at doses in the range 0.006–3.2 mg/kg (Yawns: median frequency across all doses, 0.5; range, 0–1.0; saline: median, 0.15; range, 0–0.3. Limb flicks: median, 0.9; range, 0–3.3; saline: median, 0.3; range, 0–1.3). The maximum frequency of yawning was found at 0.10 mg/kg ($N=7$, 1.0±0.47; saline, 0). No yawns were observed in four cats tested at both 1.6 and 3.2 mg/kg of APO, although they were observed to yawn in other experiments. At 3.2 mg/kg, one cat emitted 12 limb flicks. At the highest (1.6 and 3.2 mg/kg) APO doses, three cats showed stereotyped behaviors, consisting of repetitive head and forelimb movements with perseverative fixed attention, that persisted for about 45 min after drug administration. Urination, defecation, and sialorrhea were seen in some cats at these doses, and two to three animals vomited.

Pretreatment of animals with 0.05 or 1.0 mg/kg of APO had no effect on the frequency of limb flicking after either 0.01 or 0.025 mg/kg of LSD, but the higher APO dose significantly reduced the frequency of yawning in both cases (Table 1).

HAL had no significant effect on limb flicking at doses from 0.008 to 0.512 mg/kg (median, 2.6; range, 0–3; saline: median, 0.9; range, 0.5–2.8). HAL significantly increased the mean frequency of occurrence of yawning only at 0.256 mg/kg ($N=6$, 1.2±0.34; saline, 0.3±0.2; $t=5$, $p<0.01$; 5/6 cats yawned one or two times at this dose); yawning scores were close to those after saline for all other HAL doses (median, 0.3; range, 0–1.0; saline: median, 0.3; range, 0–0.5). No weakness, incoordination or ataxia were observed on handling the animals immediately after every HAL experiment, and the doses used produced no marked effects except for a wakeful, quiet restlessness at 0.256 and 0.512 mg/kg.

Four of the five cats which received 0.256 mg/kg of HAL and which yawned at that dose (mean, 1.3±0.29 yawns per 90 min) were pretreated with LIS (one animal each at 0.006 and 0.0125 mg/kg; two at 0.025 mg/kg) 15 min before receiving HAL. None of the cats yawned in the subsequent 90 min (mean yawning, HAL + LIS, 0; comparison with HAL alone: $t(3)=5$, $p<0.02$); limb flicking was observed in two of them.

PILO, 0.125–1.0 mg/kg, had no effect on yawning, but significantly increased the frequency of limb flicking at doses greater than 0.125 mg/kg, which also produced pronounced parasympathomimetic signs [11].

## DISCUSSION

As mentioned in the introduction, serotonin appears to play a role in yawning in several species. Hallucinogenic 5HT agonists have been reported to elicit yawning in the cat [7,20], and the present work shows that, in addition to limb flicking, LSD reliably elicits a significantly increased frequency of yawning. LSD has been much studied in the cat with respect to its elicitation of limb flicking [5–7, 9, 10, 19, 24], in which behavior 5HT mechanisms are important (see e.g., [20]). In an earlier study it was shown that pretreatment of cats with methysergide, which blocks some types of 5HT receptors (14), significantly antagonized both yawning and limb flicking elicited by LSD in cats, and moreover, that methysergide produced cross tolerance to both of these behaviors when it was administered 24 hr before LSD [10]. Taken together, these results provide consistent evidence that yawning has a serotonergic component in the cat,and that LSD-elicited yawning involves a serotonergic mechanism.

Unlike the case of the cat, LSD-like hallucinogens do not appear to elicit yawning in the rat. For example, doses of 0.025 or 0.10 mg/kg of LSD (subcutaneously) do not elicit yawning in hooded rats (J. L. Marini, unpublished observations), and LSD, 5-methoxy-N,N-dimethyltryptamine, and similar agents do not do so at doses producing marked effects on acoustic startle in albino rats (M. Davis, personal communication). The recent literature on the "serotonin syndrome" following LSD and similar agents in the rat does not report yawning as a sign or side effect of hallucinogen treatment.

Like LSD, LIS has potent serotonomimetic properties [17,18] and elicits limb flicking in the cat (Table 1, present work; see also [9,24]); LIS-elicited limb flicking is also antagonized by methysergide [10]. However, the present work shows that LIS does not elicit yawning, demonstrating that serotonomimetic potency is not a sufficient condition for drug-induced yawning. LIS appears to have more potent dopamine agonist properties than LSD [3,4]. By analogy with the work in the rat showing inhibition of yawning by a DA mechanism [2,28], the frequencies of yawning after LSD and LIS may be hypothesized to reflect both 5HT-mediated facilitation and DA-mediated inhibition, with the latter effect predominating in the case of LIS, the more potent dopaminergic agent. This hypothesis is supported by the results of the LSD + LIS experiment, since LIS appeared to reduce the frequency of LSD-elicited yawning. Since combining LSD and LIS did not reduce the occurrence of limb flicks, the drugs' interaction with respect to yawning is relatively specific.

The hypothesis was directly tested by using the DA agonist, APO. The 1.0 mg/kg APO dose significantly reduced LSD-elicited yawning, as would be expected from stimulation of DA receptors that mediate inhibition of yawning. The elicitation of yawning by 0.256 mg/kg of the DA-receptor blocking agent, HAL, is also consistent with the hypothesis. However, the hypothesis cannot explain why a higher HAL dose did not increase yawning. The result with HAL at 0.256 mg/kg may therefore reflect a statistical artifact, or the intervention of a mechanism unaccounted for by the simple hypothesis. Reversal of HAL-elicited yawning by LIS is consistent with the hypothesis, but must be interpreted cautiously given the preceding remarks.

Although a dose of 1 mg/kg of PILO increased yawning in infant rats [21], it had no effect on yawning in the cats used in these studies. In the rat, the maximum effect of PILO was seen at 2–4 mg/kg, doses I did not employ in cats because of the drug's pronounced parasympathomimetic activity [11]. APO has been reported to elicit a significantly increased frequency of limb flicking in cats at doses of 2 and 4 mg/kg when animals are observed in a scoring chamber [24], but I did not find uniformly increased limb flicking at similar doses (1.6 and 3.2 mg/kg). Since the environment in which cats are observed has been shown to affect their responses to at least some drugs [24], and since I scored cats in their home cages, the difference in scoring environment may explain the different observations after high APO doses.

The results of this study show that limb flicking and yawning have different behavioral pharmacologies in the cat, and that the frequency of limb flicking elicited by LSD is insensitive to DA agonists. They also suggest that serotonergic facilitation and dopaminergic inhibition can act concomitantly in the expression of drug-elicited yawning in the cat. If this proves to be the case, it would provide a useful system for studying such interactions.

## ACKNOWLEDGEMENTS

I wish to thank S. P. Williams for excellent technical support, and her and Mark Kleber for help in scoring the APO studies. I wish to acknowledge supplies of lisuride (Schering AG), methysergide (Sandoz) and LSD (NIDA). M. H. Sheard was the recipient of MH 26446, and I want to thank him for encouraging this and related independent work that I carried out in his laboratory.

## REFERENCES

1. Brewster, J. M., R. K. Siegel, C. A. Johnson and M. E. Jarvik. Observational determination of dose-response curves in hallucinogen-treated monkeys. *Int. Pharmacopyschiat.* **11:** 102–108, 1976.
2. Holmgren, B. and R. Urba-Holmgren. Interaction of cholinergic and dopaminergic influences on yawning behavior. *Acta neurobiol. exp.* **40:** 633–642, 1980.
3. Horowski, R. and H. Wachtel. Direct dopaminergic actions of lisuride hydrogen maleate, an ergot derivative, in mice. *Eur. J. Pharmac.* **36:** 373–383, 1976.
4. Horowski, R. Differences in the dopaminergic effects of the ergot derivatives bromocriptine, lisuride and *d*-LSD as compared with apomorphine. *Eur. J. Pharmac.* **51:** 157–166, 1978.
5. Jacobs, B. L., M. E. Trulson and W. C. Stern. An animal behavior model for studying the action of LSD and related hallucinogens. *Science* **194:** 741–743, 1976.
6. Jacobs, B. L., M. E. Trulson and W. C. Stern. Behavioral effects of LSD in cats: Proposal of an animal behavior model for studying the actions of hallucinogenic drugs. *Brain Res.* **132:** 301–314, 1977.
7. Jacobs, B. L. , M. E. Trulson, A. D. Stark and G. R. Christoph. Comparative effects of hallucinogenic drugs on behavior of the cat. *Communs Psychopharmac.* **1:** 243–254, 1977.
8. Lanthorn, T. H. and R. L. Isaacson. Stretching and yawning: A role of glutamate. *Psychopharmacology* **65:** 317–318, 1979.
9. Marini, J. L., B. L. Jacobs, M. H. Sheard and M. E. Trulson. Activity of a non-hallucinogenic ergoline derivative, lisuride, in an animal behavior model for hallucinogens. *Psychopharmacology* **73:** 328–331, 1981.
10. Marini, J. L. and M. H. Sheard. On the specificity of a cat behavior model for the study of hallucinogens. *Eur. J. Pharmac.* **70:** 479–487, 1981.

11. Marini, J. L. Pilocarpine, a non-hallucinogenic cholinergic agonists, elicits lamb flicking in cats. *Pharmac. Biochem. Behav.*, in press, 1981.
12. McCall, R. B. and G. K. Aghajanian. Serotonergic facilitation of facial motoneuron excitation. *Brain Res.* **169:** 11–27, 1979.
13. McCall, R. B. and G. K. Aghajanian. Hallucinogens potentiate responses to serotonin and norepinephrine in the facial motor nucleus. *Life Sci.* **26:** 1149–1156, 1980.
14. McCall, R. B. and G. K. Aghajanian. Pharmacological characterization of serotonin receptors in the facial motor nucleus: A microiontophoretic study. *Eur. J. Pharmac.* **65:** 175–183, 1980.
15. Mogilnicka, E. and V. Klimek. Drugs affecting dopamine neurons and yawning behavior. *Pharmac. Biochem. Behav.* **7:** 303–305, 1977.
16. Parry, O. and M. H. T. Roberts. The responses of motoneurons to 5-hydroxtryptamine. *Neuropharmacology* **19:** 515–518, 1980.
17. Pieri, L., H. H. Keller, W. Burkard and M. DaPrada. Effects of lisuride and LSD on cerebral monoamine systems and hallucinosis. *Nature* **272:** 278–280, 1978.
18. Rogawski, M. A. and G. K. Aghajanian. Response of central monoaminergic neurons to lisuride: Comparison with LSD. *Life Sci.* **24:** 1289–1298, 1979.
19. Trulson, M. E. and B. L. Jacobs. Usefulness of an animal behavior model in studying the duration of action of LSD and the onset and duration of tolerance to LSD in the cat. *Brain Res.* **132:** 315–326, 1977.
20. Trulson, M. E. and B. L. Jacobs. Effects of 5-methoxy-N,N-dimethyltryptamine on behavior and raphe unit activity in freely moving cats. *Eur. J. Pharmac.* **54:** 43–50, 1979.
21. Urba-Holmgren, R., R. M. Gonzalez and B. Holmgren. Is yawning a cholinergic response? *Nature* **267:** 261–262, 1977.
22. Urba-Holmgren, R., B. Holmgren, R. Rodriquez and R. M. Gonzalez. Serotonergic modulation of yawning. *Pharmac. Biochem. Behav.* **11:** 371–372, 1979.
23. VanderMaelen, C. P. and G. K. Aghajanian. Intracellular studies showing modulation of facial motoneuron excitability by serotonin. *Nature* **287:** 346–347, 1980.
24. White, F. J., A. M. Holohean and J. B. Appel. Lack of specificity of an animal behavior model for hallucinogenic drug action. *Pharmac. Biochem. Behav.* **14:** 339–343, 1981.
25. White, S. R. and R. S. Neuman. Facilitation of spinal motoneurone excitability by 5-hydroxytryptamine and noradrenaline. *Brain Res.* **188:** 119–127, 1980.
26. Wood, J. D. and C. J. Mayer. Slow synaptic excitation mediated by serotonin in Auerbach's Plexus. *Nature* **276:** 836–837, 1978.
27. Wood, J. D. and C. J. Mayer. Serotonergic activation of tonic-type enteric neurons in guinea pig small bowel. *J. Neurophysiol.* **42:** 582–593, 1979.
28. Yamada, K. and T. Furukawa. Direct evidence for involvement of dopaminergic inhibition and cholinergic activation in yawning. *Psychopharmacology* **67:** 39–43, 1980.