*Pharmacology Biochemistry & Behavior*, Vol. 33, pp. 501–505. © Pergamon Press plc, 1989. Printed in the U.S.A. 0091-3057/89 $3.00 + .00

# D1 and D2 Dopamine Receptor Interactions With Pilocarpine-Induced Oral Activity in Rats

EDWARD D. LEVIN,[1] GAYLORD D. ELLISON, RONALD E. SEE, DAVID SOUTH AND EUGENE YOUNG

*Department of Psychology, University of California, Los Angeles*

Received 5 July 1988

LEVIN, E. D., G. D. ELLISON, R. E. SEE, D. SOUTH AND E. YOUNG. *D1 and D2 dopamine receptor interactions with pilocarpine-induced oral activity in rats*. PHARMACOL BIOCHEM BEHAV **33**(3) 501–505, 1989.—To investigate the relationship between dopamine (DA) and acetylcholine (ACh) systems in the control of oral movement, we studied the effects of specific D1 and D2 drugs on vacuous chewing movements induced by the muscarinic ACh agonist, pilocarpine. In previous experiments we found that when given alone, the D1 agonist SKF 38393 increased vacuous chewing and the D1 antagonist SCH 23390 decreased it, while both the D2 agonist LY 171555 (quinpirole) and the D2 antagonist sulpiride decreased vacuous chewing. In the present experiment, the effects of the D1 drugs had similar effects in rats concurrently given pilocarpine. In contrast, the effects of both of the D2 drugs were altered by pilocarpine. Surprisingly, the actions of D2 agonist and antagonist were affected in opposite ways. The effect of sulpiride in reducing oral movement activity was eliminated by pilocarpine, while the effect of LY 171555 in reducing oral movement was enhanced by pilocarpine.

D1 D2 Pilocarpine SKF 38393 LY 171555 SCH 23390 Sulpiride Dopamine Acetylcholine Oral movement Rats

THERE is both clinical (3, 8, 14) and experimental (23,30) evidence that dopamine (DA) and acetylcholine (ACh) operate in a functional balance in the control of oral movement. Several studies have found that vacuous chewing movements (VCMs) can be induced by the ACh agonists pilocarpine and physostigmine (20–22, 27). These oral movements consist of rapid bursts of purposeless chewing behavior accompanied by tongue protrusions, yawning and gaping. Rupniak *et al.* (20) found these movements to be behaviorally indistinguishable from VCMs seen in rats after months of chronic neuroleptic administration. The latter has been touted as a model of tardive dyskinesia, while the former has been recently proposed as a model of dystonia (27). The similarity in behavioral manifestation of these two syndromes and the intimate association between cholinergic and dopaminergic systems in the control of oral movement suggests that examination of dopaminergic influences on pilocarpine-induced oral movements might elucidate basic mechanisms underlying tardive dyskinesia and dystonia.

Stewart *et al.* (27) have provided some interesting data concerning cholinergic-dopaminergic relationships in the control of oral movement. Although they found no significant effects of dopaminergic antagonists on pilocarpine-induced oral movements, they did find that apomorphine, a DA agonist, was effective in reversing the oral chewing movements induced by pilocarpine. One critical area for this interaction may be the striatum, a region important in the generation of oral movement that is innervated by both of these transmitters. ACh release in the striatum has been found to be directly regulated by DA input from the substantia nigra either via DA synapses on ACh cell bodies (15) or terminals (16). However, some DA effects in the striatum do not appear to be mediated by actions on ACh neurons. Much of the innervation of the striatum by DA bypasses ACh cells and has effects directly on other, probably GABAergic, neurons (16).

The discovery that DA receptors can be divided into D1 and D2 subtypes (13) raises the question as to whether these two subtypes of DA receptors interact differently with ACh systems. Scatton (24,25) has uncovered neuropharmacological evidence using D1 and D2 antagonists that striatal ACh cells receive D2 but not D1 input. The present experiment was designed to see if a differential relationship between ACh systems and D1 and D2 receptors could also be seen behaviorally.

Previously, we had found that the D1 agonist SKF 38393 and antagonist SCH 23390 had opposite effects on spontaneous VCMs and jaw tremor (12,19), with SKF 38393 increasing these oral behaviors and SCH 23390 decreasing them. With D2 drugs, we found that both the agonist LY 171555 (quinpirole) and antagonist sulpiride decreased spontaneous VCMs and jaw tremor (12,19). In the present study we examined the effectiveness of these drugs in

[1]Requests for reprints should be addressed to Dr. Edward D. Levin, Nicotine Research Lab (151), VA Medical Center, 508 Fulton St., Durham, NC 27705.

reversing VCMs induced by the muscarinic agonist pilocarpine.

## METHOD

This study consisted of two experiments. Experiment 1 examined the interaction of the muscarinic acetylcholine receptor agonist, pilocarpine, and a range of doses of the D1 agonist, SKF 38393, and the D1 antagonist, SCH 23390. Experiment 2 examined the interaction of pilocarpine and a range of doses of the D2 agonist, LY 171555, and the D2 antagonist, sulpiride.

The subjects were 38 (20 in Experiment 1 and 18 in Experiment 2) female Sprague-Dawley rats (Simonsen, Gilroy, CA) with an initial weight of 200–250 g. They were housed singly in rat colony rooms under a reversed light-dark cycle. All behavioral testing took place during the dark portion of the cycle. No anticholinesterase insecticides were used in the colony room during the present experiment. Before the onset of testing, all rats were habituated to being placed in plastic restraining tubes (5.7 cm diameter, 19 cm length). At one end of the tube was a 3.3 cm hole through which the rat's head protruded. At the other end there was a plug to keep the rat from backing out. Each animal was given at least five 6-minute habituation sessions over a period of three weeks.

### *Human Observer Scoring*

During each 6-minute testing session the rat was placed in the testing tube which rested inside a soundproof chamber. This chamber was illuminated only by a 6-watt ultra-violet light bulb placed in front of and below the rat's mouth. The profile of the rat's head was observed via a closed circuit TV camera with a close-up lens. The observer watched this image and recorded each instance of oral behavior by pressing keys on a computer-linked keyboard. The oral behaviors recorded were:
*Jaw Tremor:* Rapid oscillations of the masseter muscles;*Vacuous Chewing Movement:* Repetitive mouth opening and closing.
Directed oral movements, such as licking or biting at surfaces, did not occur during the experiment because the physical set-up of the tube prevented the rat from mouthing any objects. The number of times that the rat was observed to engage in these behaviors during a 6-minute session was used as the dependent measure for statistical analysis.

### *Computerized Scoring*

The same sort of computerized scoring system was used in this study as has proven to be useful in several of our previous studies (5,18). On the upper and lower jaws of the rat, small spots were painted using an ultraviolet-sensitive dye. A closed circuit TV camera with a close-up lens and an ultraviolet filter was positioned 22 cm in front of the rat's mouth. The output from this camera was fed to a computer with a movement detection circuit (the "MM" board from Biotronic Designs, Tarzana, CA). This circuit calculated the distance (number of TV rasters) between the upper and the lower spots, and stored these data, together with the human observer's reports, in the computer memory 60 times per second. Each raster of change represented 0.3 mm of movement. The computer records of the direct measurements of the mouth movements were analyzed by first detecting individual "movelets," which were defined as individual openings or closings of the mouth as reflected by progressive increases or decreases in distance between the two spots. A movelet was defined as at least two rasters of change in the size of mouth opening. A movelet terminated when the direction of movement reversed. The movelets were divided into five different amplitude categories according to how many rasters were covered by the movelet (2, 3, 4–5, 6–9, $\geq$10). These categories correspond to the following amount of actual movement: 0.4–0.8 mm, 0.8–1.2 mm, 1.2–1.6 mm, 1.6–2.8 mm and >2.8 mm. The average slope of movelets in each category was calculated by dividing the amplitude of each movelet in rasters by the duration of each movelet in 60ths of a second.

### *Statistics*

All data were evaluated using repeated measures analyses of variance. For the observer-scored data, analyses were conducted for each of the three behaviors described above, using drug dose as a repeated measure. Specific contrasts were made between saline and pilocarpine alone and between pilocarpine alone and pilocarpine plus each of the doses of the DA agonists and antagonists. For the computer-scored data, analyses of variance of the same design were run for each amplitude category.

### *Experiment 1: Pilocarpine-D1 Interactions*

Each of the 20 rats were given eight drug treatments in a counterbalanced order. The drugs were given by IP injections twice a week and 20 minutes before testing. The conditions were: saline, 1.0 mg/kg of pilocarpine alone, this dose of pilocarpine with an additional injection of one of three doses (0.3, 1.0 and 3.0 mg/kg) of the selective D1 agonist, SKF 38393, and this dose of pilocarpine with an additional injection of one of three doses (0.01, 0.05, 0.25 mg/kg) of the selective D1 antagonist, SCH 23390. These were the same doses of D1 agonists and antagonists we have previously used in dose-response studies (12,19).

### *Experiment 2: Pilocarpine-D2 Interactions*

Each of the 18 rats were given eight drug treatments in a counterbalanced order. The drugs were given by IP injections twice a week 20 minutes before testing. The conditions were: saline, 1.0 mg/kg of pilocarpine alone, this dose of pilocarpine with an additional injection of one of three doses (0.03, 0.1 and 0.3 mg/kg) of the selective D2 agonist, LY 171555, and this dose of pilocarpine with an additional injection of one of three doses (4, 20, 100 mg/kg) of the selective D2 antagonist, sulpiride. As in Experiment 1 these were the same doses of agonists and antagonists we have previously used in dose-response studies (12,19).

## RESULTS

### *Experiment 1: Pilocarpine-D1 Interactions*

Drug treatment caused a significant effect, $F(7,133) = 11.87$, $p<0.0001$, on observer-scored vacuous chewing movement (Fig. 1a). The specific comparisons showed that pilocarpine caused a significant increase over saline ($p<0.01$). The addition of the 0.05 mg/kg and 0.25 mg/kg doses of the D1 antagonist, SCH 23390, significantly attenuated the effect of pilocarpine ($p<0.0001$). The addition of the 1.0 mg/kg dose of SKF 38393 to pilocarpine also significantly attenuated the effect of pilocarpine ($p<0.05$). The lowered frequency of vacuous chewing seen with the 1.0 mg/kg dose of SKF 38393 did not reflect a true decrease in chewing, but rather an increase in the length of each chewing episode. The total duration of vacuous chewing duration a session was not changed by this dose. This was the only treatment in both experiments where the effect on frequency of vacuous chewing did not agree with the effect on the total duration of vacuous chewing.

There was a significant effect of drug treatment with duration of tremor, $F(7,133) = 5.84$, $p<0.0001$. The only significant comparison was between pilocarpine and pilocarpine plus the 3.0

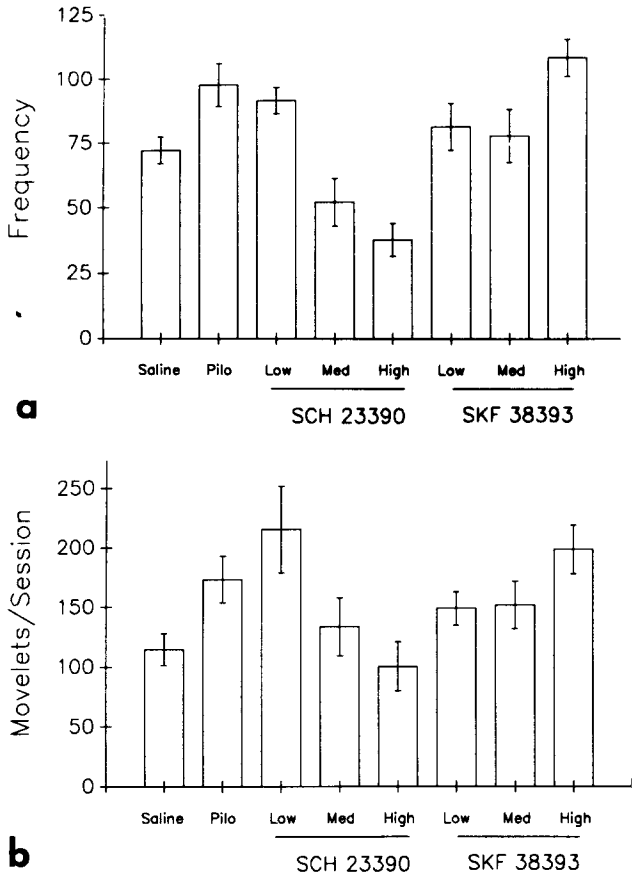


FIG. 1. (a) Experiment 1: Frequency of vacuous chewing (mean ± standard error). $p<0.01$ saline vs. pilocarpine; $p<0.05$ pilocarpine vs. 1.0 mg/kg SKF 38393 + pilocarpine; $p<0.0001$ pilocarpine vs. 0.05 mg/kg SCH 23390 + pilocarpine; $p<0.0001$ pilocarpine vs. 0.25 mg/kg SCH 23390 + pilocarpine. (b) Experiment 1: Frequency of computer-scored movelets, amplitude category 6–9 (mean ± standard error). $p<0.05$ saline vs. pilocarpine; $p<0.05$ pilocarpine vs. 0.05 mg/kg SCH 23390 + pilocarpine; $p<0.05$ pilocarpine vs. 0.25 mg/kg SCH 23390 + pilocarpine.

mg/kg dose of SKF 38393 ($p<0.0001$). This resulted from the 3.0 mg/kg dose of SKF 38393 increasing tremor (see Table 1).

In terms of computer-scored movement, significant main effects of drug treatment were seen in the number of movelets in all amplitude categories except the next to the smallest (amplitude of 3). Pilocarpine caused a significant ($p<0.05$) increase of movelets over saline only in the amplitude category of 6–9 (Fig. 1b). This category corresponds best with the vacuous chewing movements scored by the human observer. The addition of the 0.25 mg/kg dose of SCH 23390 caused significant decreases ($p<0.05$) in movelets of all amplitude categories except the smallest (amplitude of 2). The 0.05 mg/kg dose of SCH 23390 caused significantly ($p<0.05$) fewer movelets than pilocarpine alone with the amplitude of 6–9 category (Fig. 1b). No significant effects of the 0.01 mg/kg dose of SCH 23390 were detected. None of the doses of SKF 38393 significantly changed the number of movelets in any category.

Examination of the slope (amplitude/duration) for each movelet category showed a significant main effect only for movelets in the ≥10 category, $F(7,133)=4.39$, $p<0.0005$. Specific contrasts with this category detected a significant decrease in slope caused by the addition of the 0.25 mg/kg dose of SCH 23390 to pilocarpine. No effects of SKF 38393 on slope were seen.

TABLE 1

EXPERIMENT 1: SECONDS OF JAW TREMOR (MEAN ± STANDARD ERROR)

| Experiment 1: | Tremor Duration (sec) |
|---|---|
| Saline | 3.69 ± 2.23 |
| Pilocarpine 1.0 mg/kg | 1.10 ± 0.54 |
| Pilo + SCH 0.01 mg/kg | 2.81 ± 1.59 |
| Pilo + SCH 0.05 mg/kg | 0.95 ± 0.85 |
| Pilo + SCH 0.25 mg/kg | 0.08 ± 0.06 |
| Pilo + SKF 0.3 mg/kg | 0.73 ± 0.68 |
| Pilo + SKF 1.0 m/kg | 4.73 ± 2.19 |
| Pilo + SKF 3.0 mg/kg | 13.51 ± 4.11 |

$p<0.0001$ pilocarpine vs. 3.0 mg/kg of SKF 38393 + pilocarpine.

*Experiment 2: Pilocarpine-D2 Interactions*

With observer-scored movements, significant main effects of drug treatment were seen for the frequency of vacuous chewing (Fig. 2a), $F(7,119)=15.10$, $p<0.0001$, and head movement, $F(7,119)=9.22$, $p<0.0001$. As in Experiment 1, pilocarpine caused a significant increase in chewing ($p<0.005$). Sulpiride did not attenuate the pilocarpine-induced increases in chewing, but all three doses of LY 171555 caused significant declines in chewing ($p<0.001$). There were no significant drug effects on the duration of tremor in this experiment.

With the number of computer-scored movelets, significant main effects ($p<0.0005$) of drug treatment were seen in every amplitude category except for the smallest (amplitude of 2). Specific contrasts showed significant pilocarpine-induced increases in movelets in the 4–5, 6–9 (Fig. 2b) and ≥10 categories ($p<0.05$). Significant decreases ($p<0.05$) were seen with all doses of LY 171555 in all amplitude categories except the smallest. With the slope of computer-scored movelets, significant main effects of drug treatment ($p<0.025$) were seen at the two largest categories (6–9 and ≥10). Specific comparisons at these two categories showed that all three doses of LY 171555 caused significantly shallower slopes than pilocarpine alone ($p<0.0005$) in the 6–9 category and only the 0.1 mg/kg dose of LY 171555 caused significantly shallower slopes ($p<0.025$) in the ≥10 category.

## DISCUSSION

The pilocarpine-induced oral movements were reversed by two treatments in this study: the D1 antagonist SCH 23390 and the D2 agonist LY 171555. Both of these treatments were previously seen to reduce spontaneous oral movements in the same testing paradigm (12,19). The D1 antagonist, SCH 23390, decreased pilocarpine-induced VCMs with roughly the same potency as its effect on spontaneous VCMs (19). On the other hand, the effect of LY 171555 seemed to be enhanced. The D2 antagonist sulpiride was ineffective at reducing pilocarpine-induced oral movements in the present study despite our previous finding using the same testing paradigm that it was effective at reducing spontaneous VCMs. The D1 agonist, SKF 38393, did not attenuate pilocarpine-induced VCMs, but rather added to this effect by increasing tremor.

As in the present study, Stewart *et al.* (27) found that

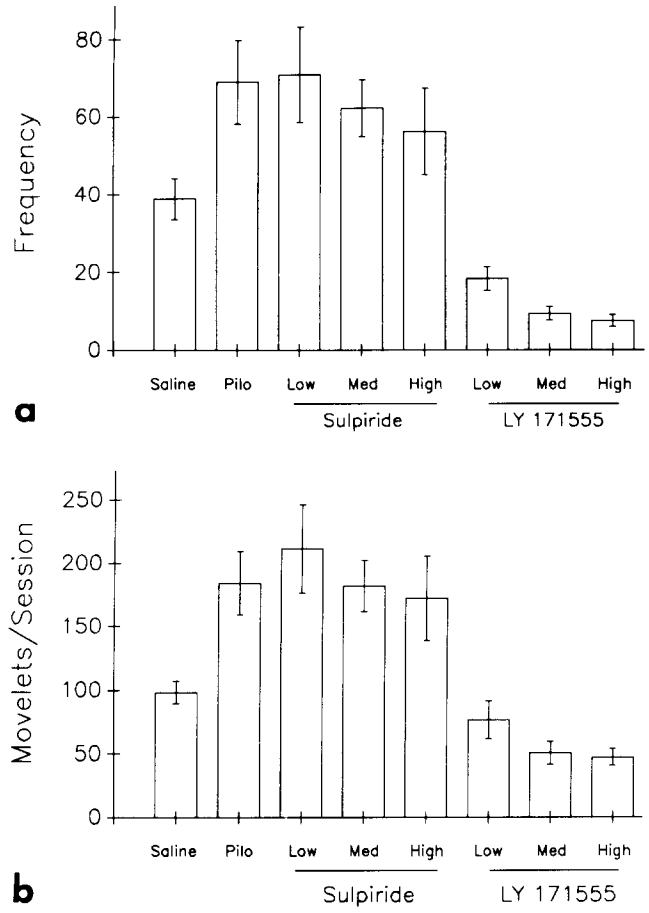


FIG. 2. (a) Experiment 2: Frequency of vacuous chewing (mean ± standard error). $p<0.005$ saline vs. pilocarpine; $p<0.0001$ pilocarpine vs. 0.03 mg/kg LY 171555 + pilocarpine; $p<0.0001$ pilocarpine vs. 0.1 mg/kg LY 171555 + pilocarpine; $p<0.0001$ pilocarpine vs. 0.3 mg/kg LY 171555 + pilocarpine. (b) Experiment 2: Frequency of computer-scored movelets, amplitude category 6–9 (mean ± standard error). $p<0.05$ saline vs. pilocarpine; $p<0.05$ pilocarpine vs. 0.03 mg/kg LY 171555 + pilocarpine; $p<0.05$ pilocarpine vs. 0.1 mg/kg LY 171555 + pilocarpine; $p<0.05$ pilocarpine vs. 0.3 mg/kg LY 171555 + pilocarpine.

pilocarpine-induced chewing movements were not reversed by sulpiride. However, in contrast to the present study, they found that the D1 antagonist SCH 23390 was ineffective at reversing pilocarpine-induced VCMs. This may have resulted from the higher dose of pilocarpine (4 mg/kg) that was used in their study. Also, the single dose of SCH 23390 that they used was below the doses (0.05 and 0.25 mg/kg) that we found to be effective in reversing the pilocarpine-induced chewing. With DA receptor stimulation they found that the nonspecific DA agonist apomorphine reversed pilocarpine-induced chewing. The results of the current study show that selective D2 stimulation is sufficient for this reversal. The selective D1 agonist SKF 38393 provided no evidence for reversing the pilocarpine-induced VCMs.

The differential relationship of D1 and D2 receptors to the stimulation of postsynaptic cAMP may be crucial to the understanding of DA-ACh relationships in the control of oral movement. In the present study, two of the dopaminergic drugs, SCH 23390 and LY 171555, were effective in reducing the pilocarpine-induced VCMs. The ability of these drugs to overcome the pilocarpine-induced increase in VCMs may be related to their ability to decrease the activity of cAMP. Stimulation of the D1 receptor has been related to an increase in postsynaptic cAMP activity (13). Therefore, the D1 antagonist, SCH 23390, should serve to decrease cAMP activity. On the other hand, stimulation of the D2 receptor has been related to a increase or no change in cAMP activity (13). Therefore, the D2 agonist, LY 171555, may also serve to decrease cAMP activity. In contrast, the two drugs that had no effect in reducing pilocarpine-induced VCMs do not have cAMP reducing actions.

Differential effects of these D1 and D2 drugs on pilocarpine-induced VCMs is in some respects is paralleled by their differential effects on ACh release in the striatum. Stimulation of D2 receptors, which inhibits pilocarpine-induced VCMs, has also been found to inhibit striatal ACh release (9, 24, 25). D1 blockade with SCH 23390, which in the present study reduced pilocarpine-induced VCMs, has also been found to inhibit striatal ACh release (6). In contrast, Gorell and co-workers (9,10) found that this compound increased ACh release, but these results may be explained by the biphasic dose-effect function of SCH 23390 (10). D1 stimulation which was found which in the present study to have no effect in reducing pilocarpine-induced VCMs but rather added to oral movement by increasing tremor, has been found to have either no effect (25) or increase ACh release (9,10). The only substantial discrepancy comes with D2 blockade which in the present study was ineffective in reversing pilocarpine-induced VCMs but has been found to be effective in enhancing ACh release in the striatum (1, 2, 24).

This apparent discrepancy may be due an incomplete understanding of the complex nature of D2 receptors. There is behavioral and neuropharmacological evidence suggesting that sulpiride and LY 171555 are not acting in opposite fashions on the same receptor population. These drugs have been found to have similar, not opposite effects in terms of decreasing VCMs (12,19) and locomotor activity (17,29). There is neuropharmacological evidence that the binding site for sulpiride may be different from other neuroleptics such as spiperone, that also bind to D2 receptors. Substituted benzamide neuroleptics like sulpiride preferentially bind to a subpopulation of D2 receptors located presynaptically on cortical fibers innervating the striatum (26), whereas D2 receptors preferentially binding nonbenzamide D2 ligands like spiperone are located on intrinsic striatal neurons (2). The benzamide-binding sites are distinguishable from D2 receptors located on intrinisic striatal cells not only by their preferential binding of benzamides, but also because of their lower sensitivity to GTP (5) and requirement for sodium for receptor binding (11,28). The predominant activities of sulpiride and LY 171555 may be mediated through these different types of D2 receptors.

ACKNOWLEDGEMENTS

This study was supported by NIH grant No. MH 39961. Edward Levin was supported by NIH grant No. MH 15795 and a grant from the Swedish Medical Research Council.

## REFERENCES

1. Boireau, A.; Chambry, J.; Dubedat, P.; Farge, G.; Carruette, A. M.; Zundel, A. M.; Blanchard, J. C. Enhancing effect of dopamine blockers on evoked acetylcholine release in rat striatal slices: A classical D-2 antagonist response? Eur. J. Pharmacol. 128:93–98; 1986.
2. Bridge, S.; Christie, M. J.; Beart, P. M. No change in neostriatal D-2 dopamine receptors after NMDA lesions of rat prefrontal cortex. Pharmacol. Biochem. Behav. 24:1829–1832; 1986.

3. Casey, D. E.; Denney, D. Pharmacological characterization of tardive dyskinesia. Psychopharmacology (Berlin) 54:1–8; 1977.
4. Creese, I.; Usdin, T.; Snyder, S. H. Guanine nucleotides distinguish between two dopamine receptors. Nature 278:577–578; 1979.
5. Ellison, G. D.; See, R. E.; Levin, E. D.; Kinney, J. Tremorous mouth movements in rats administered chronic neuroleptics. Psychopharmacology (Berlin) 92:122–126; 1987.
6. Fage, D.; Scatton, B. Opposing effects of D-1 and D-2 receptor antagonists on acetylcholine levels in the rat striatum. Eur. J. Pharmacol. 129:359–362; 1986.
7. Gerlach, J.; Kistrup, K.; Korsgaard, S. Effect of selective D1 and D2 dopamine antagonists and agonists in Cebus monkeys: Implications for acute and tardive dyskinesia. Psychopharmacology (Berlin) Suppl. 3:236–242; 1987.
8. Gerlach, J.; Reisby, N.; Randrup, A. Dopaminergic hypersensitivity and cholinergic hypofunction in the pathophysiology of tardive dyskinesia. Psychopharmacologia 34:21–35; 1974.
9. Gorell, J. M.; Czarnecki, B. Pharmacologic evidence for direct dopaminergic regulation of striatal acetylcholine release. Life Sci. 38:2239–2246; 1986.
10. Gorell, J. M.; Czarnecki, B.; Hubbell, S. Functional antagonism of D-1 and D-2 dopaminergic mechanisms affecting striatal acetylcholine release. Life Sci. 38:2247–2254; 1986.
11. Jenner, P.; Marsden, C. D. Multiple dopamine receptors in brain and the pharmacological actions of substituted benzamide drugs. Acta Psychiatr. Scand. 69(Suppl. 311):109–123; 1985.
12. Johansson, P.; Levin, E. D.; Ellison, G. D.; Gunne, L. Opposite effects of a D1 and a D2 agonist on oral movements in rats. Eur. J. Pharmacol. 134:83–88; 1987.
13. Kebabian, J. W.; Calne, D. B. Multiple receptors for dopamine. Nature 277:93–96; 1979.
14. Klawans, H.; Rubovits, R. Effect of cholinergic and anticholinergic agents on tardive dyskinesia. J. Neurosurg. Psychiatry 27:941–947; 1974.
15. Kubota, Y.; Inagaki, S.; Shimada, S.; Kito, S.; Eckenstein, F.; Tohyama, M. Neostriatal cholinergic neurons receive direct synaptic inputs from dopaminergic axons. Brain Res. 413:197–184; 1987.
16. Lehmann, J.; Langer, S. Z. The striatal cholinergic interneuron: Synaptic target of dopaminergic neurons? Neuroscience 10:1105–1120; 1983.
17. Levin, E. D.; Bowman, R. E. Effects of the dopamine D-2 receptor agonist, LY 171555, on radial arm maze performance in rats. Pharmacol. Biochem. Behav. 25:1117–1119; 1986.
18. Levin, E. D.; Galen, D. M.; Ellison, G. D. Chronic haloperidol effects on oral movements and radial-arm maze performance in rats. Pharmacol. Biochem. Behav. 26:1–6, 1987.
19. Levin, E. D.; See, R. E.; Johansson, P.; South, D.; Gunne, L. M.; Ellison, G. D. Effects of the D1 and D2 antagonists, SCH 23390 and sulpiride, on oral movement in rats. Soc. Neurosci. Abstr. 13:451; 1987.
20. Rupniak, N. M.; Jenner, P.; Marsden, C. D. Cholinergic manipulation of perioral behaviour induced by chronic neuroleptic administration to rats. Psychopharmacology (Berlin) 79:226–230; 1983.
21. Rupniak, N. M.; Jenner, P.; Marsden, C. D. Pharmacological characterisation of spontaneous or drug-associated purposeless chewing movements in rats. Psychopharmacology (Berlin) 85:71–79; 1985.
22. Salamone, J. D.; Lalies, M. D.; Channell, S. L.; Iversen, S. D. Behavioral and pharmacological characterization of mouth movements induced by muscarinic agonists in the rat. Psychopharmacology (Berlin) 88:467–471; 1986.
23. Saligaut, C.; Daoust, M.; Chadelaud, M.; Moore, N.; Chretien, P.; Boismare, F. Oxotremorine-induced cholinergic syndrome: Modifications by levodopa and/or oral cytidine diphosphocholine. Methods Find. Exp. Clin. Pharmacol. 7:5–8; 1985.
24. Scatton, B. Effect of dopamine agonists and neuroleptic agents on striatal acetylcholine transmission in the rat: Evidence against dopamine receptor multiplicity. J. Pharmacol. Exp. Ther. 220:197–202; 1982.
25. Scatton, B. Further evidence for the involvement of D2 but not D1 dopamine receptors in dopaminergic control of striatal cholinergic transmission. Life Sci. 31:2883–2890; 1982.
26. Sokoloff, P.; Redouane, K.; Brann, M.; Martres, P.; Schwartz, J. $^3$H-(−)DO 710 discriminates guanine nucleotide sensitive and insensitive dopamine receptor binding sites. Naunyn Schmiedbergs Arch. Pharmacol. 329:236–243; 1985.
27. Stewart, B. R.; Jenner, P.; Marsden, C. D. The pharmacological characterisation of pilocarpine-induced purposeless chewing behaviour in the rat. Psychopharmacology (Berlin) 96:55–62; 1988.
28. Theodorou, A. E.; Hall, M. D.; Jenner, P.; Marsden, C. D. Cation regulation differentiates specific binding of [$^3$H]spiperone to rat striatal preparations. J. Pharm. Pharmacol. 32:441–444; 1980.
29. Ungerstedt, U.; Herrera-Marschitz, M.; Stahle, L.; Tossman, U.; Zetterstrom, T. Functional classification of different dopamine receptors. Psychopharmacology (Berlin) Suppl. 2:19–40; 1985.
30. Yamada, K.; Furukawa, T. Direct evidence for dopaminergic inhibition and cholinergic activation of yawning. Psychopharmacology (Berlin) 67:39–43; 1980.