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# Role of dopamine D1 receptors in the striatal and cortical fos expression induced by the muscarinic agonist pilocarpine

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**Abstract**

Injections of the muscarinic cholinergic receptor agonist pilocarpine (50 mg/kg) induced pronounced expression of the immediate early gene (IEG) product Fos in the striatum and cortex of rats. Pretreatment with the dopamine D1 receptor antagonist 7-chloro-8-hydroxy-3-methyl-1-phenyl-2,3,4,5-tetrahydro-*H*-3-benzazepine hydrochloride (SCH-23390; 0.2–2.0 mg/kg) drastically attenuated the pilocarpine response in the striatum, but had no effect in the cortex. In contrast, the muscarinic receptor antagonist scopolamine (0.75–3.00 mg/kg) virtually abolished the Fos response at both sites. These results suggest that stimulation of dopamine D1 receptors may mediate the effects of muscarinic agonists on Fos expression in the striatum, but not the cortex.


*Keywords:* Immediate early gene; c-fos; Striatum; Caudate; Acetylcholine; Dopamine D1 receptor

## 1. Introduction

Many studies have now shown that examination of the expression of immediate early genes (IEGs) provides a powerful tool for studying the effects of various pharmacological agents on cells in the striatal complex (Robertson et al., 1991; Hughes and Dragunow, 1995). Dopaminergic agents have been by far the most studied compounds in this regard, but the striatum also contains very high levels of a number of other neurotransmitters including acetylcholine, which is localized to a small population of large, aspiny interneurons (Graybiel, 1990). Several studies have shown that nonselective muscarinic cholinergic receptor agonists, like pilocarpine and oxotremorine, are able to induce robust expression of the IEG product Fos (Bernard et al., 1993; MacGibbon et al., 1995; Hughes and Dragunow, 1993; Cook and Wirtshafter, 1998; Miwa et al., 2000), but the exact mechanism underlying these effects remains to be determined. The available evidence suggests that dopamine is not involved in the effects of muscarinic agonists on Fos expression, a finding which is surprising given that the striatal IEG expression induced by most known methods can be powerfully influenced by dopaminergic systems. Thus, Bernard et al. (1993) have found that the induction of Fos expression by muscarinic agonists cannot be prevented by pretreatment with the dopamine depleting agent reserpine. This result, however, may need to be interpreted with some caution since no "positive controls" for the efficacy of the depletions were examined and it is possible that dopamine levels were not sufficiently reduced to produce an effect. For example, in pilot studies we have found that reserpine, given according to the exact protocol used by these authors, does not significantly attenuate the Fos expression induced by the dopamine uptake blocker cocaine, even though the response to this drug is undoubtedly mediated through dopaminergic mechanisms (unpublished observations). Bernard et al. (1993) also found that the muscarinic response was not blocked by 6-hydroxydopamine lesions, but these results may also need to be treated cautiously since no independent measure of the effectiveness of the lesions was presented. On the other hand, we have observed that pilocarpine-induced Fos expression can be blocked by injections of the dopamine D2 receptor agonist quinpirole (Cook and Wirtshafter, 1998), a drug which would be expected to reduce dopamine release through an action on autoreceptors. It would seem, therefore, that the issue of dopamine involvement in

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the effects of muscarinic receptor agonists cannot be regarded as closed. Since the ability of dopamine to induce Fos expression is dependent on stimulation of dopamine D1 receptors, a more direct way to examine dopamine involvement in the effects of cholinergic agonists would be to investigate whether the actions of these drugs can be blocked by administration of dopamine D1 receptor antagonists. In the current experiments we therefore investigated the effects of pretreatment with the dopamine D1 receptor antagonist SCH-23390 on pilocarpine-induced Fos expression. We examined Fos expression in both the striatum and the cerebral cortex, in order to determine whether any actions of SCH-23390 are global or are restricted to certain brain regions, and also studied the effects of the muscarinic receptor antagonist scopolamine in order to verify the effects of pilocarpine were indeed mediated through cholinergic receptors.

## 2. Methods

### 2.1. Subjects

Subjects were 36 adult, male Sprague–Dawley derived rats obtained from a colony maintained by the Psychology Department of the University of Illinois at Chicago. Rats were housed in individual wire mesh cages and handled daily for several days prior to testing.

### 2.2. Drugs

7-Chloro-8-hydroxy-3-methyl-1-phenyl-2,3,4,5-tetrahydro-1*H*-3-benzazepine hydrochloride (pilocarpine; mol. wt. = 244.7) and scopolamine hydrobromide (mol. wt. = 384.3) were obtained from Sigma (St. Louis, MO, USA) and 7-chloro-8-hydroxy-3-methyl-1-phenyl-2,3,4,5-tetrahydro-*H*-3-benzazepine hydrochloride (SCH-23390; mol. wt. = 324.1) was obtained from Research Biochemicals (Natick, NJ, USA). All drugs were dissolved in saline and administered in a volume of 1 ml/kg. The pilocarpine dose used in these studies (50 mg/kg) was chosen based on previous investigations of pilocarpine-induced striatal Fos expression (Bernard et al., 1993; MacGibbon et al., 1995; Hughes and Dragunow, 1993; Cook and Wirtshafter, 1998), and is at the low end of the dose range typically employed in studies of cataleptic behavior (e.g., Mason et al., 1978; Klemm, 1987). Pilocarpine treated subjects salivated profusely, and were inactive behaviorally, but displayed no signs of convulsions which have been reported after treatment with much higher doses of pilocarpine (e.g., Millan et al., 1986; Turski et al., 1986).

### 2.3. Drug treatments

Four groups of three to seven subjects were used to study the effects of SCH-23390 on pilocarpine-induced Fos expression. These animals received s.c. injections of SCH-

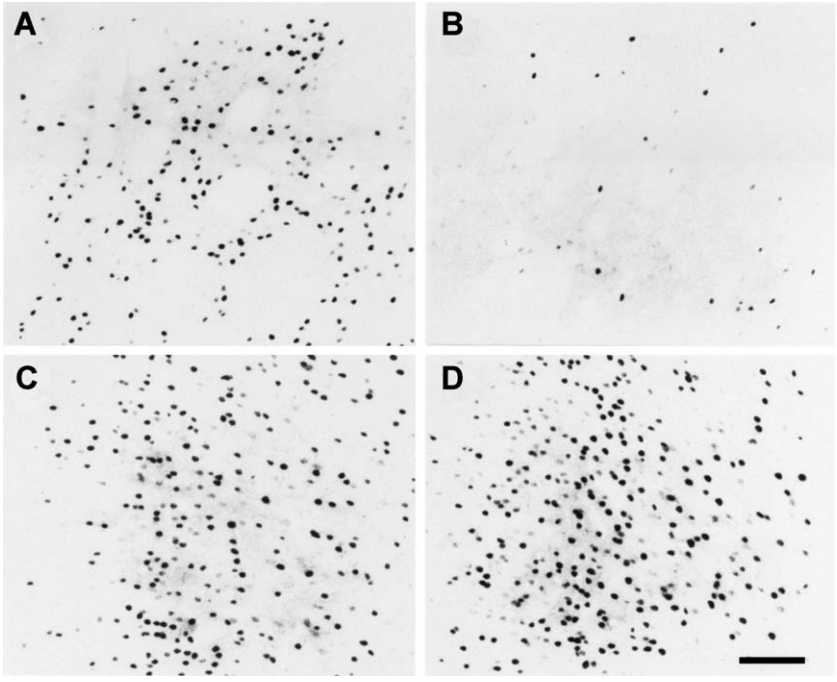


Fig. 1. Photomicrographs illustrating the effects of SCH-23390 on the Fos-like immunoreactivity induced by pilocarpine in the medial striatum (top row, panels A and B) and the anterior cingulate cortex (lower row, panels C and D.) The left-hand column (panels A and C) shows tissue from animals injected with saline followed by pilocarpine (50 mg/kg), whereas the right-hand column (panels B and D) shows tissue from animals injected with SCH-23390 (2 mg/kg) followed by pilocarpine. Scale bar = 100 μm.

223390 at doses of 0.2, 1.0 or 2.0 mg/kg or of its saline vehicle. Thirty minutes later, all subjects were injected with pilocarpine (50 mg/kg i.p.). Three groups of three to four animals were used to examine the effects of scopolamine; these subjects were injected with saline or with scopolamine (0.75 or 3.00 mg/kg s.c.) 30 min prior to injections of pilocarpine. All of these animals were sacrificed 90 min following pilocarpine injections, as described below. Three additional control animals received two injections of saline separated by 30 min and three others an injection of SCH-23390 followed by an injection of saline. These animals were sacrificed 90 min following the second injection.

### 2.4. Perfusion and immunocytochemistry

Animals were deeply anesthetized with sodium pentobarbital (100 mg/kg) and then rapidly perfused at room temperature with normal saline followed by 500 ml of a 10% solution of formalin prepared in phosphate buffer. Brains were then removed from the skulls and post fixed in the formalin solution for 2 h at 4 °C. The tissue was then transferred to a solution of phosphate-buffered saline (PBS) containing 20% sucrose where it was stored at 4 °C until the next day. Cryostat sections were then cut through the rostral striatum at a thickness of 35 μm and processed using standard immunocytochemical methods we have described in detail previously (Wirtshafter and Asin, 2001). The primary antibody was a rabbit anti-c-Fos serum (Oncogene Sciences/Calbiochem, Cambridge, MA, AB5, 25,000 ×) and antigenic sites were visualized using a Vectastain Elite ABC kit (Vector Laboratories, Burlingame, CA) employing nickel-intensified diaminobenzadine as the chromagen. In control sections in which the primary antibody was omitted or replaced by nonimmune rabbit serum, no stained nuclei were seen.

### 2.5. Quantitative analysis

Fields in the medial striatum measuring 1.15 × 1.52 mm (width × height) were digitally captured using a Quantimet Q500 image analysis system at a level similar to that we have documented in previous publications (Wirtshafter and Asin, 1994). Fields through the anterior cingulate cortex measuring 0.94 × 0.72 mm, the medial edges of which were aligned with the outer boundary of cortical lamina II, were also captured on the same sections. Fields were edited, when necessary, to remove obvious artifacts and immunoreactive nuclei within these fields were then automatically counted based on their intensity of staining relative to background, size and aspect ratio, as determined in extensive preliminary investigations.

## 3. Results

Almost no immunoreactive cells were seen in the dorsal striatum of animals treated with saline or SCH-23390 alone. In contrast, treatment with pilocarpine induced intense Fos-like immunoreactivity which was maximal in the medial region of the striatum (Fig. 1A) and appeared slightly patchy, especially in regions where the overall staining was not too intense.

Pretreatment with SCH-23390 markedly attenuated the striatal response to pilocarpine (Figs. 1A,B and 2). Analysis of the quantitative data shown in Fig. 2A by means of a one-way, four-level analysis of variance (ANOVA) indicated a highly significant effect of SCH-23390 dose [$F(3,13)=34.8$; $P<0.001$] and post hoc comparisons conducted using the Tukey technique demonstrated that all doses of SCH-23390 produced a significant suppression ($P<0.001$). A small number of cells could, however, still be observed after even the highest dose of SCH-23390 and these, again, tended to be distributed in a somewhat patchy pattern.

Pilocarpine also produced very marked staining in the anterior cingulate cortex, as well as other cortical regions, which was not obviously affected by pretreatment with SCH-23390 (Fig. 1C,D). Analysis of the quantitative data shown in Fig. 2B by means of a one way ANOVA failed to demonstrate a significant effect of the D1 antagonist at this site ($F<1$).

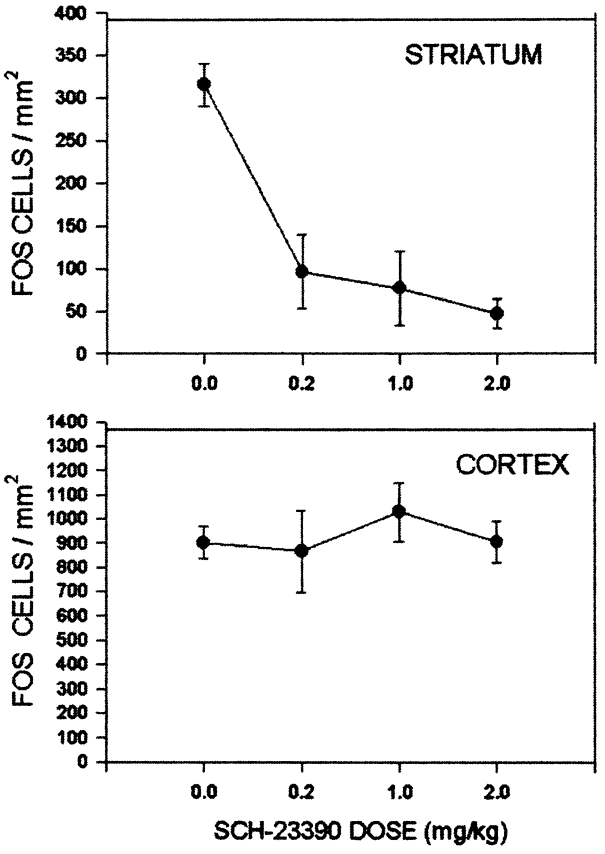


Fig. 2. Effects of SCH-23390 pretreatment on the mean density (± S.E.M.) of cells displaying Fos-like immunoreactivity following pilocarpine treatment (50 mg/kg) in the striatum and anterior cingulate cortex.

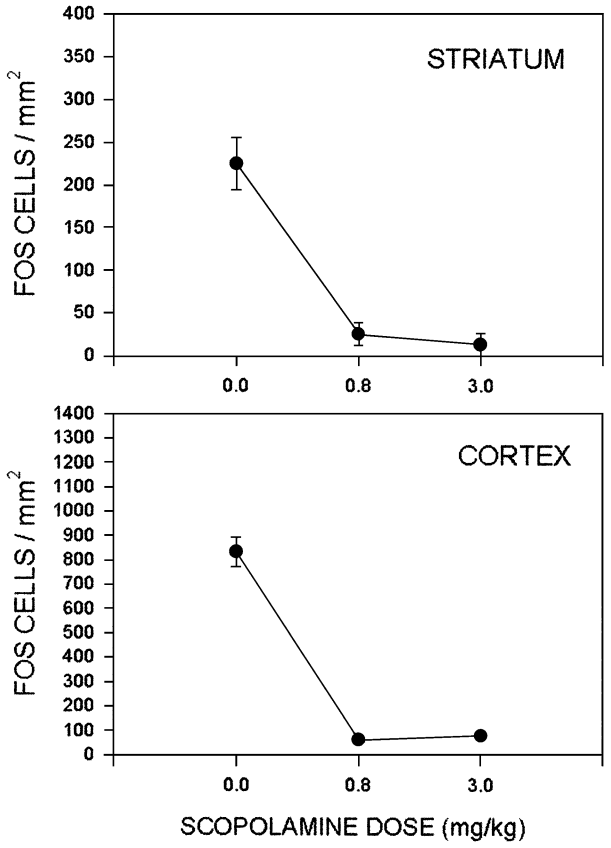


Fig. 3. Effects of scopolamine pretreatment on the mean density ( ± S.E.M.) of cells displaying Fos-like immunoreactivity following pilocarpine treatment (50 mg/kg) in the striatum and anterior cingulate cortex.

Fig. 3 demonstrates that pretreatment with scopolamine drastically attenuated the response to pilocarpine in both the striatum [$F(2,7)=24.4$; $P<0.001$] and the cortex [$F(2,7)=83.4$; $P<0.001$], and Tukey tests indicated that the suppression was significant in both structures at both the high and low doses of scopolamine ($P<0.002$).

## 4. Discussion

The current results agree with previous reports that muscarinic receptor agonists are able to induce intense Fos-like immunoreactivity in both the striatum and cerebral cortex (Bernard et al., 1993; MacGibbon et al., 1995; Hughes and Dragunow, 1993; Cook and Wirtshafter, 1998; Miwa et al., 2000). Both of these effects could be markedly antagonized by scopolamine, further suggesting that they were mediated by stimulation of muscarinic receptors. In other studies, we have found that blockade of peripheral muscarinic receptors with methyscopolamine is unable to attenuate the pilocarpine response, demonstrating that it results from stimulation of central receptors (unpublished observations).

The primary result of the present experiments was the finding that the selective dopamine D1 receptor antagonist SCH-23390 was able to dramatically attenuate pilocarpine-induced Fos expression in the striatum, but not the cerebral cortex. This result strongly supports a role for D1 receptors in the mediation of the pilocarpine effect in the striatum. As discussed in the introduction, it is possible that previous studies which concluded that dopamine was not involved in the effects of muscarinic receptor agonists (Bernard et al., 1993) may not have sufficiently disrupted the function of this transmitter to have allowed for the demonstration of an effect. It is also possible that although the response to acetylcholine receptor agonists can be attenuated by an acute disruption of dopaminergic function, such as that employed here, compensatory mechanisms may make it more difficult to detect the effects of longer term alterations, such as those produced by 6-hydroxydopamine lesions or reserpine treatment. A role for dopamine in the response to muscarinic receptor agonists is also suggested by our previous report that pilocarpine-induced striatal Fos expression can be antagonized by the dopamine D2/D3 receptor agonist quinpirole (Cook and Wirtshafter, 1998). This effect might reflect an action of quinpirole on release-inhibiting dopamine autoreceptors, although it is also possible that quinpirole may have acted directly on striatal cells to inhibit Fos expression.

Although there are some exceptions (al-Tajir and Starr, 1993), many studies have indicated that muscarinic receptor agonists can act directly on the striatum to increase dopamine release at this site (Marchi et al., 1992; Raiteri et al., 1984; Kemel et al., 1992; Bymaster et al., 1994; Smolders et al., 1997). Muscarinic receptor agonists may also be able to excite the cell bodies of dopaminergic neurons in the substantia nigra, again resulting in increased striatal dopamine release (Hernandez-Lopez et al., 1992). It is well established that dopamine acts in the striatum to increase Fos expression and this effect appears to be dependent on activation of dopamine D1 receptors (Robertson et al., 1991). The simplest explanation of the current results, then, is that pilocarpine induces Fos expression in the striatum at least partially as a consequence of its ability to increase dopamine release at this site. It is also possible that the actions of pilocarpine may be mediated through mechanisms other than alterations in dopamine release (Calabresi et al., 2000), but that stimulation of dopamine receptors plays a permissive role in this effect.

Although SCH-23390 greatly attenuated the response to pilocarpine, it did not completely abolish it. The residual response appeared to be distributed in a patchy pattern reminiscent of that seen following costimulation of D1 and D2 dopamine receptors (Wirtshafter and Asin, 1994), although not nearly as pronounced. It is quite possible that the failure to produce a total abolition of staining may have been the result of dose or time course factors. It is also possible, however, that pilocarpine may induce Fos expression by several different mechanism, or in several different classes of neurons, which are differentially dependent on dopamine D1 receptor activation. For example,

muscarinic agonists have been shown to induce Fos expression both in striatal neurons containing substance P and in those containing enkephalin (Bernard et al., 1993). Since dopamine D1 receptors appear to be largely concentrated in substance P containing neurons (Gerfen, 1992; Le Moine et al., 1991), it is possible that SCH-23390 might selectively disrupt pilocarpine-induced Fos expression in this population of cells. It is possible that, in contrast, effects on enkephalin containing cells might result from a direct action on muscarinic receptors located on these neurons (Di Chiara and Morelli, 1994). This notion is consistent with reports that anticholinergics attenuate neuroleptic induced Fos expression, which occurs primarily in enkephalinergic neurons (Guo et al., 1992 Hussain et al., 2002). It should be noted, however, that this result has not been obtained under all conditions (MacGibbon et al., 1995; Merchant and Dorsa, 1993; Gerfen and Kitai, 1997; Hussain et al., 2002) suggesting that cholinergic neurons do not form an obligatory link mediating the effects of neuroleptics on enkephalinergic cells. Although further work will be needed to investigate these possibilities, it is clear that muscarinic synapses must be able to exert a variety of different effects within the striatum. For example, agonists selective for the m2 and m4 muscarinic receptors have been found to inhibit dopamine agonist induced striatal Fos expression (Fink-Jensen et al., 1988; Kane and Wirtshafter, 2002), an effect opposite to the excitatory effects seen here with a nonselective agonist. An inhibitory effect of muscarinic receptor activation is also suggested by reports that muscarinic receptor antagonists are able to potentiate dopamine D1 receptor mediated striatal Fos expression (Wang and McGinty, 1996; Wirtshafter and Asin, 2001). It is possible that these various effects may reflect actions on different receptor subtypes or be mediated through different classes of striatal cells, but the diversity of the responses produced by manipulations of acetylcholine certainly highlight the complexity of the role of this transmitter within the striatum.

In marked contrast to its effects in the striatum, SCH-23390 was unable to attenuate pilocarpine-induced Fos expression in the anterior cingulate cortex. As scopolamine was able to antagonize the effects of pilocarpine at this site, this finding demonstrates that SCH-23390 could not have been directly interfering with muscarinic transmission. The finding of differential antagonism of pilocarpine's effects in the striatum and cortex also indicates that the actions of pilocarpine at the two sites must have been mediated through different mechanisms with dopamine D1 receptors playing a critical role at the former, but not the latter, site. Since the firing rate of many cortical neurons can be influenced by iontophoretic application of acetylcholine receptor agonists (McCormick, 1992), it seems likely that the effects of systemic pilocarpine on cortical Fos expression were mediated through a direct action on local muscarinic receptors, although actions in other brain regions, such as the thalamus, may also play a role.

Although recent studies have suggested that activation of striatal dopamine D1 receptors can have a powerful effect on cortical activity (Steiner and Kitai, 2000), the current findings suggest that the effects of pilocarpine on Fos expression in the cortex cannot be a reflection of alterations in striatal dopamine $D_1$ receptor stimulation. Indeed, since dopamine agonists have been shown to increase cortical acetylcholine release (Day and Fibiger, 1992), it is possible that dopaminergic effects on cortical Fos expression may be mediated at least partly through cholinergic mechanisms. This possibility is supported by observations that scopolamine is able to attenuate the cortical IEG expression produced by injections of either amphetamine (unpublished observations) or of the dopamine D1 receptor agonist SKF-82958 (Wang and McGinty, 1996). Further studies will be necessary to clarify the mechanisms through which dopamine receptor activation can influence cortical immediate early gene expression, but the current studies are certainly consistent with the possibility that cholinergic mechanisms may play a critical role in this process.

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## References

al-Tajir, G., Starr, M., 1993. Disordered dopamine neurotransmission in the striatum of rats undergoing pilocarpine-induced generalized seizures, as revealed by microdialysis. J. Neural Transm., Parkinson's Dis. Dement. Sect. 5, 89–100.

Bernard, V., Dumartin, B., Lamy, E., Bloch, B., 1993. Fos immunoreactivity after stimulation or inhibition of muscarinic receptors indicates anatomical specificity for cholinergic control of striatal efferent neurons and cortical neurons in the rat. Eur. J. Neurosci. 5, 1218–1225.

Bymaster, F.P., Wong, D.T., Mitch, C.H., Ward, J.S., Calligaro, D.O., Schoepp, D.D., Shannon, H.E., Sheardown, M.J., Olesen, P.H., Suzdak, P.D., Swedberg, D.B., Sauerberg, P., 1994. Neurochemical effects of the M1 muscarinic agonist xanomeline (LY246708/NNC11-0232). J. Pharmacol. Exp. Ther. 269, 282–289.

Calabresi, P., Centonze, D., Gubellini, P., Pisani, A., Bernardi, G., 2000. Acetylcholine-mediated modulation of striatal function. T.I.N.S. 23, 120–126.

Cook, D.F., Wirtshafter, D., 1998. Quinpirole attenuates striatal c-fos induction by serotonin, opioid and muscarinic receptor agonists. Eur. J. Pharmacol. 349, 41–47.

Day, J., Fibiger, H.C., 1992. Dopaminergic regulation of cortical acetylcholine release. Synapse 12, 281–286.

Di Chiara, G., Morelli, M., 1994. Acetylcholine, dopamine and NMDA transmission in the caudate–putamen: their interactions and function as a striatal modulatory system. In: Percheron, G., McKenzie, J.S., Feger, J. (Eds.), The Basal Ganglia, vol. IV. Plenum, New York, pp. 491–505.

Fink-Jensen, A., Kristensen, P., Shannon, H.E., Calligaro, D.O., Delapp, N.W., Whitesitt, C., Ward, J.S., Thomsen, C., Rasmusseen, T., Sheardown, M.J., Jeppesen, L., Sauerberg, P., Bymaster, F.P., 1988. Mus-

carinic agonists exhibit functional dopamine antagonism in unilaterally 6-OHDA lesioned rats. NeuroReport 9, 3481–3486.
Gerfen, C.R., 1992. The neostriatal mosaic: multiple levels of compartmental organization. J. Neural Transm., Suppl. 36, 43–59.
Gerfen, C.R., Kitai, S.T., 1997. Intrastriatal administration of the muscarinic antagonist scopolamine: effects on D2 dopamine receptor antagonist-induced behavior and gene expression in striatal neurons. Abstr. - Soc. Neurosci. 23, 745.
Graybiel, A.M., 1990. Neurotransmitters and neuromodulators in the basal ganglia. T.I.N.S. 13, 244–254.
Guo, N., Robertson, G.S., Fibiger, H.C., 1992. Scopolamine attenuates haloperidol-induced c-fos expression in the striatum. Brain Res. 588, 164–167.
Hernandez-Lopez, S., Gongora-Alfaro, J.L., Martinez-Fong, D., Aceves, J., 1992. A cholinergic input to the substantia nigra pars compacta increases striatal dopamine metabolism measured by in vivo voltammetry. Brain Res. 598, 114–120.
Hughes, P., Dragunow, M., 1993. Muscarinic receptor-mediated induction of Fos protein in rat brain. Neurosci. Lett. 150, 122–126.
Hughes, P., Dragunow, M., 1995. Induction of immediate-early genes and the control of neurotransmitter-regulated gene expression within the nervous system. Pharmacol. Rev. 47, 133–178.
Hussain, N., Flumerfelt, B.A., Rajakumar, N., 2002. Muscarinic, adenosine A2 and histamine H3 receptor modulation of haloperidol-induced C-FOS expression in the striatum and nucleus accumbens. Neuroscience 112, 427–438.
Kane, M.C., Wirtshafter, D., 2002. The m2/m4 muscarinic receptor agonist BuTAC attenuates dopamine agonist-induced behaviors. Abstr. - Soc. Neurosci., 682.9.
Kemel, M.L., Gauchy, C., Desban, M., Krebs, M.O., Glowinski, J., 1992. Control of dopamine release by acetylcholine and dynorphin in the striosomal and matrix compartments of the cat caudate nucleus. Neurochem. Int. 20, 111s–114s (Suppl.).
Klemm, W.E., 1987. Experimental catalepsy is both enhanced and disrupted by apomorphine. Psychopharmacology 87, 12–15.
Le Moine, C., Normand, E., Bloch, B., 1991. Phenotypical characterization of the rat striatal neurons expressing the D1 dopamine receptor gene. Proc. Natl. Acad. Sci. U. S. A. 88, 4205–4209.
MacGibbon, G.A., Lawlor, P.A., Hughes, P., Young, D., Dragunow, M., 1995. Differential expression of inducible transcription factors in basal ganglia neurons. Mol. Brain Res. 34, 294–302.
Marchi, M., Volpe, G., Augliera, A., Codignola, A., Lunardi, G., Raiteri, M., 1992. Cholinergic modulation of dopamine release in corpus striatum and substantia nigra of the rat. Neurochem. Int. 20, 271S–274S (Suppl.).
Mason, S.T., Roberts, D.C.S., Fibiger, H.C., 1978. Noradrenergic influences on catalepsy. Psychopharmacology 60, 53–57.
McCormick, D.A., 1992. Neurotransmitter actions in the thalamus and cerebral cortex. J. Clin. Neurophysiol. 9, 212–223.
Merchant, K.M., Dorsa, D.M., 1993. Differential induction of neurotensin and c-fos gene expression by typical versus atypical antipsychotics. Proc. Natl. Acad. Sci. U. S. A. 90, 3447–3451.
Millan, M.H., Patel, S., Meldrum, B.S., 1986. Olfactory bulbectomy protects against pilocarpine-induced motor limbic seizures in rats. Brain Res. 398, 204–206.
Miwa, H., Nishi, K., Fuwa, T., Mizuno, Y., 2000. Differential expression of c-Fos following administration of two tremorgenic agents: harmaline and oxotremorine. NeuroReport 11, 2385–2390.
Raiteri, M., Leardi, R., Marchi, M., 1984. Heterogeneity of presynaptic muscarinic receptors regulating neurotransmitter release in the rat brain. J. Pharmacol. Exp. Ther. 228, 209–214.
Robertson, H.A., Paul, M.L., Moratalla, R., Graybiel, A.M., 1991. Expression of the immediate early gene c-fos in basal ganglia: induction by dopaminergic drugs. Can. J. Neurol. Sci. 19, 380–383.
Smolders, I., Bogaert, L., Ebinger, G., Michotte, Y., 1997. Muscarinic modulation of striatal dopamine, glutamate, and GABA release, as measured with in vivo microdialysis. J. Neurochem. 68, 1942–1948.
Steiner, H., Kitai, S.T., 2000. Regulation of rat cortex function by D1 dopamine receptors in the striatum. J. Neurosci. 20, 5449–5460.
Turski, L., Cavalheiro, E.A., Sieklucka-Dziuba, M., Ikonomidou-Turski, C., Czuczwar, S.Z., Turski, W.A., 1986. Seizures produced by pilocarpine: neuropathological sequelae and activity of glutamate decarboxylase in the rat forebrain. Brain Res. 398, 37–48.
Wang, J.Q., McGinty, J.F., 1996. Scopolamine augments c-fos and zif/268 messenger RNA expression induced by the full D1 dopamine receptor agonist SKF-82958 in the intact rat striatum. Neuroscience 72, 601–616.
Wirtshafter, D., Asin, K.E., 1994. Interactive effects of stimulation of D1 and D2 dopamine receptors on Fos-like immunoreactivity in the normosensitive rat striatum. Brain Res. Bull. 35, 85–91.
Wirtshafter, D., Asin, K.E., 2001. Comparative effects of scopolamine and quinpirole on the striatal Fos expression induced by stimulation of D1 dopamine receptors in the rat. Brain Res. 893, 202–214.