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Prefrontal, accumbal [shell] and ventral striatal mechanisms in jaw movements and non-cyclase-coupled dopamine D1-like receptors

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Abstract

The effect on jaw movements of intracerebral injections of the dopamine D1-like receptor agents SK&F 83959 (3-methyl-6-chloro-7,8-dihydroxy-1-[3-methylphenyl]-2,3,4,5-tetrahydro-1*H*-3-benzazepine), SK&F 38393 ([*R*]-7,8-dihydroxy-1-phenyl-2,3,4,5-tetrahydro-1*H*-3-benzazepine) and SCH 23390 ([*R*]-3-methyl-7-chloro-8-hydroxy-1-phenyl-2,3,4,5-tetrahydro-1*H*-3-benzazepine) and of injections of the dopamine D2-like receptor agonist quinpirole into the ventrolateral striatum, accumbens shell or prefrontal cortex were studied. SK&F 38393 and SK&F 83959 injected into the ventrolateral striatum synergised with i.v. quinpirole; in the shell of accumbens, SK&F 38393 evidenced weaker synergism with quinpirole, while SK&F 83959 did not synergise with it; neither agent synergised with quinpirole in the prefrontal cortex. Co-injection of SCH 23390 or SK&F 83959 into the prefrontal cortex antagonised jaw movements induced by injection of SK&F 83959 into the ventrolateral striatum in combination with i.v. quinpirole. Injection of SK&F 83959 + quinpirole into the ventrolateral striatum, but not into the accumbens shell, resulted in synergism. These findings indicate a primary, but not exclusive, role for ventral striatal, non-cyclase-coupled dopamine D1-like receptors in the induction of jaw movements. These processes appear to require tonic activity of prefrontal cyclase-linked dopamine D1A [and/or D1B] receptors.

Keywords: Dopamine D1-like receptor; Adenylyl cyclase; Dopamine D1-like receptor, non-cyclase-coupled; Cortex, prefrontal; Striatum, ventrolateral; Accumbens, shell; Dopamine D1-like:D2-like receptor synergism; Jaw movement; SK&F 83959; (Rat)

1. Introduction

Though there is now substantial evidence for an important role of the dopamine D1-like [D1A/D1, D1B/D5] receptor family in the regulation of orofacial movements, particularly via functional interactions with its counterpart dopamine D2-like [D2L/S, D3, D4] receptor family (Rosengarten et al., 1986; Collins et al., 1991; Koshikawa et al., 1991; Waddington et al., 1995, 2001; Tomiyama et al., 2001, 2002; Niznik et al., 2002), it is not clear which dopaminergically innervated brain region(s) participate in the induction/expression of these effects. Also, while dopamine D1-like receptors have been defined conventionally in terms of their linkage to the stimulation of adenylyl cyclase, neurochemical, neurophysiological and behavioural evidence indicates the existence of a dopamine D1-like receptor coupled to a transduction system other than/additional to adenylyl cyclase, with phosphoinositide hydrolysis being the most widely entertained candidate (Mahan et al., 1990; Undie and Friedman, 1990; Undie et al., 1994, 2000; Waddington et al., 1995, 1998; Niznik et al., 2002).

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We have reported (Adachi et al., 1999) the synergistic induction of characteristic jaw movements in rats by i.v. co-administration of the selective dopamine D1-like receptor agents SK&F 83959 or SK&F 38393 with the selective dopamine D2-like receptor agonist quinpirole, and these responses were sensitive to antagonism by i.v. administration of the selective dopamine D1-like receptor antagonists SCH 23390 and BW 737C. However, unlike SK&F 38393, SK&F 83959 fails to stimulate adenylyl cyclase and inhibits the cyclase stimulation induced by dopamine, thus showing the defining neurochemical characteristics of a selective dopamine D1-like receptor antagonist; it also stimulates phosphoinositide hydrolysis. Hence, SK&F 83959 appears to have at least two actions on dopaminergic function with different affinities, i.e. antagonism at cyclase-coupled dopamine D1A [and D1B] receptors, like SCH 23390, and agonism at non-cyclase-coupled dopamine D1-like receptors, like SK&F 38393 (Arnt et al., 1992; Undie et al., 1994; Deveney and Waddington, 1995; Gnanalingham et al., 1995; Waddington et al., 1995, 1998; Andringa et al., 1999; Panchalingam and Undie, 2001; Niznik et al., 2002).

In individual brain regions, one action might predominate. Therefore, in a second study (Hasegawa et al., 2001), injection of SCH 23390 or SK&F 83959 into the ventrolateral striatum blocked jaw movements induced by i.v. SK&F 38393 plus quinpirole, while only SCH 23390 blocked the action of i.v. SK&F 83959 plus quinpirole. Conversely, SCH 23390 injected into the accumbens shell was less effective than SCH 23390 injected into the ventrolateral striatum, and SK&F 83959 was ineffective in blocking this response, while neither SCH 23390 nor SK&F 83959 blocked the effect of i.v. SK&F 83959 plus quinpirole. This implies an important role for non-cyclase-coupled dopamine D1-like receptor sites as well as dopamine D1A [or D1B] receptors in the regulation of jaw movements via dopamine D1-like:D2-like receptor synergism, particularly in the ventrolateral striatum.

However, not just the ventrolateral striatum and the accumbens shell are implicated in the dopamine-dependent induction/expression of jaw movements (Koshikawa et al., 1989, 1996; Delfs and Kelley, 1990; Cools et al., 1995); dopamine function in the prefrontal cortex influences these subcortical dopaminergic terminal fields, usually in an inverse manner (Pycock et al., 1980; Louilot et al., 1989; Kolachana et al., 1995; King et al., 1997; Cools et al., 2002). Therefore, it is not clear what combination of regional effects might subserve the induction of jaw movements following i.v. drug administration. To help clarify these issues, we compared: (i) the effects of intracerebral injections of SK&F 38393 or SK&F 83959 into each of these three regions together with i.v. quinpirole; (ii) the effects of SCH 23390 or SK&F 83959 injected into the prefrontal cortex on responsivity to injections of SK&F 83959 into the ventrolateral striatum or accumbens shell together with i.v. quinpirole; (iii) the effects of SK&F 38393 or SK&F 83959 co-injected with quinpirole into the ventrolateral striatum or accumbens shell (Table 1).

Table 1
Overall plan of experiments combining i.v. and intracerebral administration of quinpirole, SK&F 38393, SK&F 83959 and SCH 23390 into the ventrolateral striatum (VLS), shell of the nucleus accumbens (NAC) and prefrontal cortex (PFC)

Experiment	Combination of drug and site
1a	quinpirole i.v. + SK&F 38393 into VLS vs. NAC vs. PFC
1b	quinpirole i.v. + SK&F 83959 into VLS vs. NAC vs. PFC
2a	quinpirole i.v. + SK&F 83959 into VLS + SCH 23390 into PFC
2b	quinpirole i.v. + SK&F 83959 into VLS + SK&F 83959 into PFC
2c	quinpirole i.v. + SK&F 83959 into NAC + SK&F 83959 into PFC
3a	quinpirole into VLS; SK&F 38393 into VLS; SK&F 38393 + quinpirole into VLS
3b	quinpirole into VLS; SK&F 83959 into VLS; SK&F 83959 + quinpirole into VLS
3c	quinpirole into NAC; SK&F 83959 into NAC; SK&F 83959 + quinpirole into NAC

2. Materials and methods

2.1. Surgical procedures

Male Sprague–Dawley rats weighing 238–320 g were housed in cages (27 × 45 × 20 cm) that were held in a temperature (24 ± 2 °C)- and humidity (55 ± 5%)-controlled environment under a 12-h light/dark cycle (lights on at 07:00 h), with free access to food and water.

Rats were anaesthetised with halothane (0.5–4.0%), supplemented with ketamine HCl (10.0 mg/kg i.p.). The surgical and recording procedures were as described previously (Adachi et al., 1999; Hasegawa et al., 2001). After cannulation of the right external jugular vein, a small light-emitting diode was fixed to the mandible. The animal was then placed in a stereotactic frame so that the head was kept in constant relation to a light-sensitive transducer which detected the vertical and lateral movements of the diode. After surgery, the animals received ketamine (10.0 mg/kg i.p.) continuously; this dose is in the range that fails to influence either jaw movements elicited by co-activation of dopamine D1-like and D2-like receptors or dopamine metabolism in the striatum (Koshikawa et al., 1988). Lignocaine (2.0% gel) was applied to all incisions to ensure complete analgesia. Rectal temperature was maintained at 37.0 °C with a thermostatically controlled heating pad. Monitored concentrations of expired O_2 and CO_2 during experiments were 19–21% and 2.0–2.5%, respectively. Jaw movements were recorded on a tape recorder (RD-180T; TEAC) for off-line analysis. Recordings were analysed automatically, using a spike trigger that counted jaw movements per 5 min.

The movements detected consisted of jaw openings and closings in the vertical plane. Though perioral movements often described as 'vacuous chewing', defined as episodes of vertical jaw movements in the absence of any chewable material in rats' mouth, are also induced by long-term treatment with antipsychotic drugs (Waddington, 1990), the extent to which such movements might involve mechanisms similar to or different from those studied here is less well understood (Ikeda et al., 1999; Tomiyama et al., 2002). In this context, we have previously demonstrated that enhanced 'vacuous chewing' induced by haloperidol (1.0 mg/kg, twice daily for 4 weeks), observed visually in freely moving rats, could not be detected by the method used in this study (Ikeda et al., 1999), i.e. a light-sensitive transducer system in ketamine-anaesthetised rats. To clarify this methodological issue, we have recently developed a new automated jaw movement measuring system using a magnet-sensing transducer that allows measurement of orofacial movements qualitatively and quantitatively in freely moving rats (Lee et al., in press). With this system, the mechanisms involved in 'vacuous chewing' induced by antipsychotic drugs can be analysed better in the future.

Guide cannulas (external diameter 0.5 mm, internal diameter 0.3 mm) were implanted bilaterally into the brain according to previously described procedures (Koshikawa et al., 1996; Hasegawa et al., 2001). Coordinates based on the atlas of Paxinos and Watson (1986) were, for ventrolateral striatum: anterior = 8.6 mm from interaural line, vertical = 3.0 mm from interaural line, lateral = 4.0 mm from midline; for the shell of the accumbens: anterior = 10.6 mm, vertical = 2.0 mm, lateral = 0.7 mm, with cannulas angled 21° from the midsagittal plane to avoid the ventricular system; for prefrontal cortex: anterior = 11.2 mm, vertical = 7.0 mm, lateral = 1.0 mm, with cannulas angled 20° from the midsagittal plane to allow their attachment proximal to the midline. For simultaneous injections into the accumbens shell and prefrontal cortex, cannulas in the prefrontal cortex were also angled 20° forward from the coronal plane to accommodate the proximity of cannulas for these sites. The injection volume was 0.2 μl per side and was delivered over a 20-s period with the needle left in situ for an additional 20-s period after completion of the injection to allow diffusion. Damage to the target site was minimised by implanting the tips of guide cannulas 1.6 mm (ventrolateral striatum), 2.0 mm (shell) or 1.0 mm (prefrontal cortex) above the desired injection site. Wire stylets were placed in the guide cannulas to prevent occlusion.

These experiments were approved by the Animal Experimentation Committee of Nihon University School of Dentistry. They were performed in accordance with institutional guidelines for the care and use of experimental animals, which are in compliance with the UK Animals Scientific Procedures Act 1986.

2.2. Histology

At the end of each experiment, rats were deeply anaesthetised with pentobarbitone (80 mg/kg i.p.) and perfused transcardially with 10% formalin. Brains were removed, sectioned at 50 μm and stained with Cresyl violet to visualise injection sites (Fig. 1); only data from animals in which the injections were correctly placed were included in subsequent analyses.

2.3. Drugs

The drugs used were SK&F 83959 (3-methyl-6-chloro-7,8-dihydroxy-1-[3-methylphenyl]-2,3,4,5-tetrahydro-1*H*-3-benzazepine; Research Biochemicals International/NIMH Chemical Synthesis program, USA); [*R*]-SK&F 38393 ([*R*]-7,8-dihydroxy-1-phenyl-2,3,4,5-tetrahydro-1*H*-3-ben-

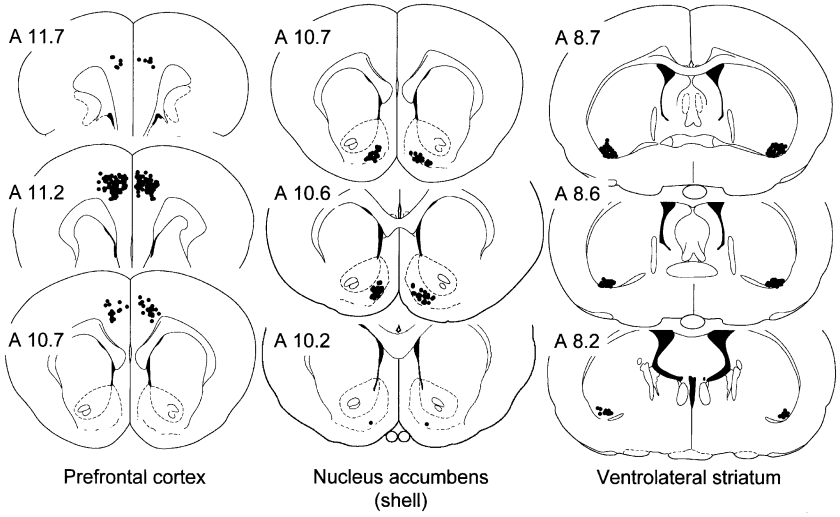

Fig. 1. Location of injection sites in the prefrontal cortex (left), shell of the accumbens (centre) and ventrolateral striatum (right). Planes are modified from the atlas of Paxinos and Watson (1986); approximate coordinates indicated are mm anterior to the interaural line for each plane.

zazepine; Sigma, St. Louis, USA); SCH 23390 ([*R*]-3-methyl-7-chloro-8-hydroxy-1-phenyl-2,3,4,5-tetrahydro-1*H*-3-benzazepine; Sigma); and quinpirole (Sigma); all were dissolved in saline. In combination experiments, i.v. quinpirole was followed 30 min later by intracerebral injections of SK&F 38393 or SK&F 83959 into the ventrolateral striatum, accumbens shell or prefrontal cortex; i.v. quinpirole was followed 30 min later by intracerebral injections of SCH 23390 or SK&F 83959 into the prefrontal cortex and 5 min later by intracerebral injections of SK&F 83959 into the ventrolateral striatum or accumbens shell; co-administration of SK&F 38393 or SK&F 83959 with quinpirole into the ventrolateral striatum or into the accumbens shell was with a single injection volume of 0.2 μl.

2.4. Data analysis

All data are expressed as means ± S.E.M. and analysed using a one-way analysis of variance (ANOVA) or two-way ANOVA (group × time), followed by a post-hoc Student's *t*-test where appropriate. A probability value of $P < 0.05$ was considered statistically significant.

3. Results

3.1. Responsivity to SK&F 38393 vs. SK&F 83959 injected into ventrolateral striatum, accumbens shell or prefrontal cortex in combination with i.v. quinpirole

When given following i.v. quinpirole (1.0 mg/kg), 5 μg SK&F 38393 injected into the ventrolateral striatum synergised with it and, after a latency of approximately 30–40 min, induced jaw movements which then continued for over 240 min. After a latency of 60–90 min, a similar response was seen following injection of 50–500 ng SK&F 83959 into the ventrolateral striatum (Fig. 2). SK&F 38393 (5 μg) injected into the accumbens shell showed reduced synergism with i.v. quinpirole, after a longer latency of 90–120 min, whereas SK&F 83959 (100 ng) was without effect. When injected into the prefrontal cortex, neither 5 μg SK&F 38393 nor 100 ng SK&F 83959 synergised with i.v. quinpirole.

3.2. Effect of SCH 23390 or SK&F 83959 injected into prefrontal cortex on responsivity to SK&F 83959 into ventrolateral striatum or accumbens shell in combination with i.v. quinpirole

Injection of 100–1000 ng SCH 23390 into the prefrontal cortex antagonised jaw movements induced by injection of 100 ng SK&F 83959 into the ventrolateral striatum in combination with i.v. quinpirole (1 mg/kg). Injection of 50–100 ng SK&F 83959 into the prefrontal cortex antagonised this response similarly (Fig. 3). The lack of synergism between 100 ng SK&F 83959 injected into the accumbens shell and i.v. quinpirole (1 mg/kg) was unaltered following additional injection of 100 ng SK&F 83959 into the prefrontal cortex (data not shown).

3.3. Effect of SK&F 38393 or SK&F 83959 and quinpirole injected alone and in combination into ventrolateral striatum and accumbens shell

When injected alone into the ventrolateral striatum, neither 5 μg SK&F 38393, 100 ng SK&F 83959 nor 10

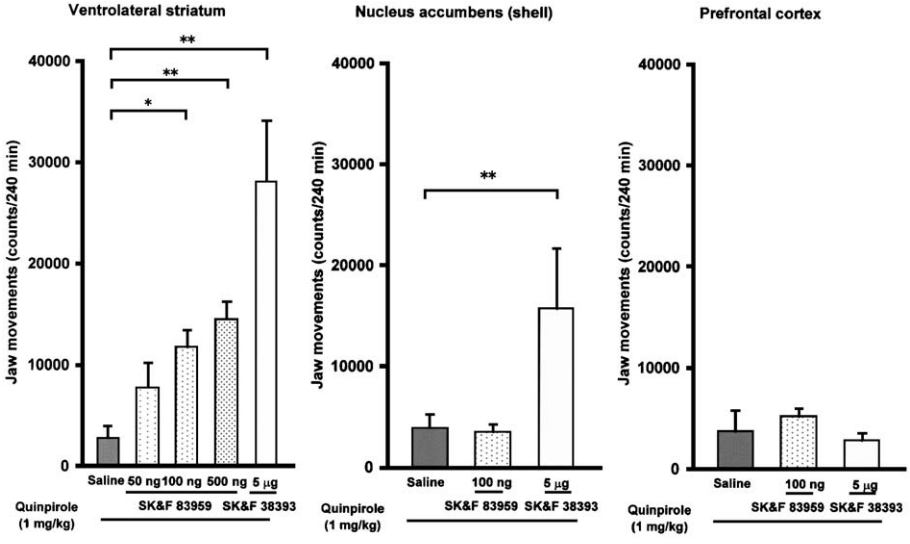

Fig. 2. Jaw movements following injection of vehicle, 5 μg SK&F 38393 or 50–500 ng SK&F 83959 into the ventrolateral striatum (left); vehicle, 5 μg SK&F 38393 or 100 ng SK&F 83959 into the shell of the accumbens (centre); and vehicle, 5 μg SK&F 38393 or 100 ng SK&F 83959 into the prefrontal cortex (right). All intracerebral injections were made in a volume of 0.2 μl, 30 min following i.v. co-administration of 1.0 mg/kg quinpirole. Data are mean counts ± S.E.M. from $n = 6–16$ animals per group over a total period of 240 min. $^{**}P < 0.01$, $^{*}P < 0.05$ vs. vehicle.

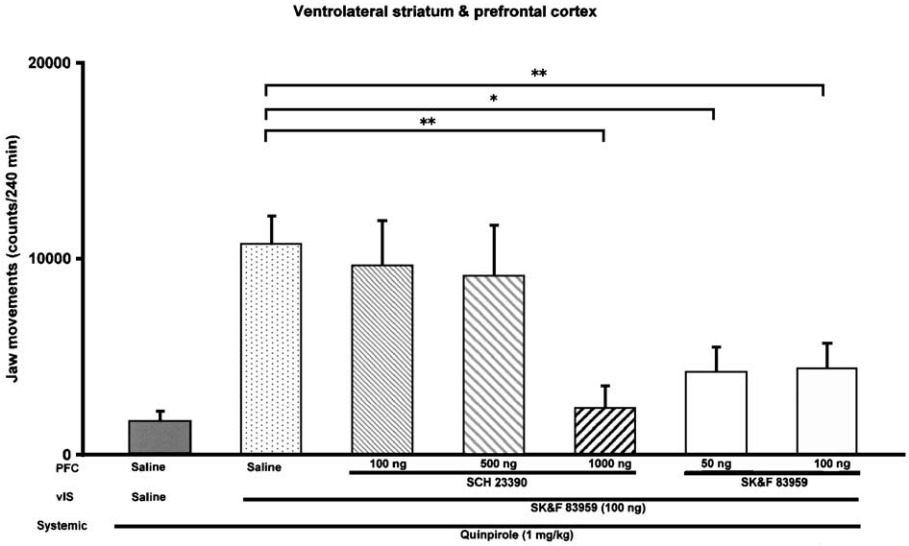

Fig. 3. Effect of injection of vehicle, 100–1000 ng SCH 23390 or 50–100 ng SK&F 83959 into the prefrontal cortex on jaw movements induced by injection of vehicle or 100 ng SK&F 83959 into the ventrolateral striatum. All intracerebral injections were made in a volume of 0.2 μl, 30 min following i.v. co-administration of 1.0 mg/kg quinpirole. Data are mean counts ± S.E.M. from $n = 6–7$ animals per group over a total period of 240 min. $^{**}P < 0.01$, $^{*}P < 0.05$ vs. SK&F 83959 in the ventrolateral striatum.

μg quinpirole induced jaw movements; however, jaw movements were readily induced following co-injection of 5 μg SK&F 38393 with 10 μg quinpirole and, similarly, following co-injection of 50–100 ng SK&F 83959 with 10 μg quinpirole into the ventrolateral striatum (Fig. 4). There was no synergistic induction of jaw movements following co-injection of 100 ng SK&F 83959 with 10 μg quinpirole into the accumbens shell (data not shown).

4. Discussion

The induction of jaw movements by i.v. co-administration of SK&F 38393 or SK&F 83959 with i.v. quinpirole, in accordance with well-described cooperative/synergistic dopamine D1-like:D2-like receptor interactions (Waddington et al., 1994; Adachi et al., 1999), was reproduced readily by co-administration of SK&F 38393 or SK&F 83959 into the ventrolateral striatum with i.v. quinpirole.

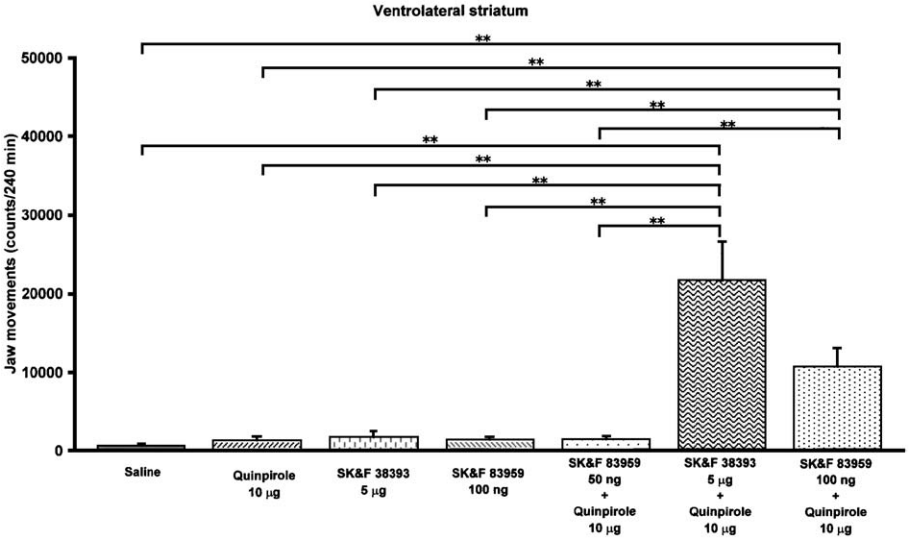

Fig. 4. Jaw movements following injection of vehicle, 5 μg SK&F 38393, 100 ng SK&F 83959, 10 μg quinpirole, 5 μg SK&F 38393 + 10 μg quinpirole and 50–100 ng SK&F 83959 + 10 μg quinpirole into the ventrolateral striatum. All intracerebral injections were made in a volume of 0.2 μl. Data are mean counts ± S.E.M. from $n = 6–7$ animals per group over a total period of 240 min. $^{**}P < 0.01$ vs. vehicle.

This indicates that dopamine D1-like receptors in the ventrolateral striatum are critical for the induction of jaw movements by i.v. SK&F 38393 or SK&F 83959 plus i.v. quinpirole and supports our recent finding that SCH 23390 injected into the ventrolateral striatum antagonised the induction of such jaw movements by the same i.v. drug combinations (Hasegawa et al., 2001).

Also, these results indicate that the effects of SK&F 38393 and SK&F 83959 in the ventrolateral striatum are likely to involve a common dopamine D1-like mechanism. As SK&F 38393 and SK&F 83959 have agonist and antagonist effects at dopamine D1A [and D1B] receptors linked to adenylyl cyclase, respectively, but share an agonist action at dopamine D1-like receptors linked to phosphoinositide hydrolysis (Arnt et al., 1992; Undie et al., 1994; Deveney and Waddington, 1995; Gnanalingham et al., 1995; Waddington et al., 1995, 1998; Andringa et al., 1999; Panchalingam and Undie, 2001; Niznik et al., 2002), an action involving stimulation of dopamine D1-like receptors not linked to adenylyl cyclase is implicated in the *induction* of such jaw movements.

However, SCH 23390 and SK&F 83959 injected into the ventrolateral striatum shared a common action to antagonise the induction of jaw movements by i.v. co-administration of quinpirole together with SK&F 38393 (which stimulates dopamine D1-like receptors linked to adenylyl cyclase), while SCH 23390 but not SK&F 83959 injected into the ventrolateral striatum antagonised the induction of jaw movements by i.v. co-administration of quinpirole and SK&F 83959 (which does not stimulate dopamine D1-like receptors linked to adenylyl cyclase) (Hasegawa et al., 2001). This could suggest some regulatory role for ventral striatal dopamine D1A [and/or D1B] receptors linked to adenylyl cyclase in the *expression*, as distinct from the putative role of dopamine D1-like receptors not linked to adenylyl cyclase in the *induction* of such jaw movements. Mechanistically, these distinct profiles for SCH 23390 and SK&F 83959 may reflect differences in their actions to antagonise ventral striatal dopamine D1-like receptors linked to adenylyl cyclase: SCH 23390 may block both tonic [dopamine] and phasic [SK&F 38393] stimulation, while SK&F 83959 may be less effective in blocking tonic as opposed to phasic stimulation of adenylyl cyclase. The K_i of SK&F 83959 to inhibit dopamine-sensitive adenylyl cyclase appears to be less than that of SCH 23390 (Arnt et al., 1992). Alternatively, there may be complex interactions between adenylyl cyclase-coupled and non-adenylyl cyclase-coupled dopamine D1-like receptors in the ventrolateral striatum.

A different profile of results was apparent following injections into the accumbens shell, where SK&F 38393 synergised less prominently with i.v. quinpirole and SK&F 83959 did not evidence synergism. This indicates that the role of the accumbens shell in the *induction* of jaw movements (Cools et al., 1995) is both less critical than, and mechanistically different from, that of the ventrolateral striatum and supports our recent finding that injection of SCH 23390 into the accumbens shell is less effective than into the ventrolateral striatum in antagonising the induction of such jaw movements by i.v. co-administration of SK&F 38393 and quinpirole (Hasegawa et al., 2001). That SK&F 83959, which does not stimulate dopamine-sensitive adenylyl cyclase, failed to synergise with quinpirole in this region could suggest that cyclase-coupled rather than non-cyclase-coupled dopamine D1-like receptors may be more important in the accumbens shell than in the ventrolateral striatum for the *induction* of jaw movements.

Though neither SK&F 38393 nor SK&F 83959 injected into the prefrontal cortex synergised with i.v. quinpirole, the body of evidence supporting the prefrontal cortex dopaminergic regulation of subcortical dopaminergic function (Pycock et al., 1980; Louilot et al., 1989; Kolachana et al., 1995; King et al., 1997; Cools et al., 2002) made it necessary to explore any such processes using antagonists. The synergistic action between SK&F 83959 injected into the ventrolateral striatum and i.v. quinpirole in the induction of jaw movements was antagonised by SCH 23390 and by SK&F 83959 injected into the prefrontal cortex. This suggests a shared action of SCH 23390 and SK&F 83959 to block dopamine D1-like receptors and therefore implies their common antagonism of cyclase-coupled dopamine D1A [and/or D1B] receptors. Prefrontal dopamine D1-like receptors might antagonise the *expression* of jaw movements without appearing to play a role in their *induction* if the level of tonic activity through these receptors is high such that agonists result in little further increase in activation while antagonists reduce such activation. This would indicate an important 'enabling' or 'permissive' regulatory role of prefrontal cyclase-coupled dopamine D1A [and/or D1B] receptors in the mediation of jaw movements induced primarily by ventral striatal non-cyclase-coupled dopamine D1-like receptors. The action of SCH 23390 and SK&F 83959 to block cyclase-coupled prefrontal dopamine D1-like receptors may also be the basis of their antagonism of the synergistic induction of jaw movements via non-cyclase-coupled ventrolateral striatal dopamine D1-like and D2-like receptors following i.v. co-administration of SK&F 38393 or SK&F 83959 with quinpirole (Adachi et al., 1999).

While it has been proposed that the antagonism of prefrontal cyclase-coupled dopamine D1-like receptors by agents such as SK&F 83959 should enhance subcortical dopamine release, due to an inverse relationship between these regions (see Cools et al., 2002), the present results are indicative of a facilitatory rather than an inverse effect of the prefrontal cortex on jaw movements induced via non-cyclase-coupled dopamine D1-like receptors in the ventral striatum. It is possible that the subcortical mechanisms regulating jaw movements are distinct from those identified as regulating dopamine release, and that they are therefore influenced differently following antagonism of prefrontal cyclase-coupled dopamine D1-like receptors.

These considerations relate to the site(s) of action of SK&F 38393 and SK&F 83959 in synergising with i.v. quinpirole in the induction of jaw movements but leave open the site(s) of action of quinpirole in these processes. When SK&F 83959 and quinpirole were co-injected into the ventrolateral striatum, synergism was evident in a manner similar to that seen after their i.v. co-administration or the injection of SK&F 83959 into the ventrolateral striatum with i.v. quinpirole; however, when SK&F 83959 and quinpirole were co-injected into the accumbens shell, no such synergism was apparent. This indicates that the synergistic induction of jaw movements by dopamine D1-like:D2-like receptor interactions (Waddington et al., 1994; Adachi et al., 1999) occurs in the ventrolateral striatum, where primarily non-cyclase-coupled dopamine D1-like receptors participate in local cooperative/synergistic interactions with their dopamine D2-like counterparts.

Taken together, these findings suggest a primary role for ventral striatal, non-cyclase-coupled dopamine D1-like receptors in the *induction* of jaw movements by dopamine D1-like receptor agonists in combination with dopamine D2-like receptor agonists. Additionally, cyclase-coupled dopamine D1A [and/or D1B] receptors in the accumbens shell appear to play a lesser role in the *induction*, while those in the ventral striatum play a greater role in the *expression*, of such jaw movements. Importantly, these processes appear to be 'enabled' by the tonic activity of prefrontal cyclase-linked dopamine D1A [and/or D1B] receptors. More precise details regarding the neuronal circuitry subserving these effects will require further study.

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