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Topographical assessment and pharmacological characterization of orofacial movements in mice: dopamine D_1-like vs. D_2-like receptor regulation

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Abstract

A novel procedure for the assessment of orofacial movement topographies in mice was used to study, for the first time, the individual and interactive involvement of dopamine D_1-like vs. D_2-like receptors in their regulation. The dopamine D_1-like receptor agonists A 68930 ([1*R*,3*S*]-1-aminomethyl-5,6-dihydroxy-3-phenyl-isochroman) and SK&F 83959 (3-methyl-6-chloro-7,8-dihydroxy-1-[3-methylphenyl]-2,3,4,5-tetrahydro-1*H*-3-benzazepine) each induced vertical jaw movements with tongue protrusions and incisor chattering. The dopamine D_1-like receptor antagonists SCH 23390 ([*R*]-3-methyl-7-chloro-8-hydroxy-1-phenyl-2,3,4,5-tetrahydro-1*H*-3-benzazepine) and BW 737C ([*S*]-6-chloro-1-[2,5-dimethoxy-4-propylbenzyl]-7-hydroxy-2-methyl-1,2,3,4-tetrahydroisoquinoline) antagonised these responses, while the dopamine D_2-like receptor antagonist YM 09151-2 (*cis-N*-[1-benzyl-2-methyl-pyrrolidin-3-yl]-5-chloro-2-methoxy-4-methylaminobenzamide) attenuated those to SK&F 83959 and released horizontal jaw movements. These findings suggest some role for a dopamine D_1-like receptor that is coupled to a transduction system other than/additional to adenylyl cyclase, and for dopamine D_1-like:D_2-like receptor interactions, in the regulation of individual orofacial movement topographies in the mouse. This methodology will allow the use of knockout mice to clarify the roles of individual dopamine receptor subtypes in their regulation.

Keywords: Dopamine D_1-like and D_2-like receptor; Orofacial movement topography; Dopamine D_1-like receptor, non-cyclase-coupled; Dopamine D_1-like:D_2-like receptor interaction; A 68930; SK&F 83959; (Mouse)

1. Introduction

It is recognised from several studies, confined essentially to rats, that both the dopamine D_1-like [$D_{1A/1}$, $D_{1B/5}$] and D_2-like [$D_{2L/S}$, D_3, D_4] families of receptor subtypes are involved in the regulation of orofacial movements. Current theory, deriving from the use in rats of agonists and antagonists that distinguish *between* but not *within* these families, posits a greater primary role for dopamine D_1-like than for D_2-like receptors in the genesis of such movements; these studies also indicate oppositional dopamine D_1-like:D_2-like receptor interactions in their regulation (Rosengarten et al., 1983, 1986; Murray and Waddington, 1989; Koshikawa et al., 1989; Collins et al., 1991; Daly and Waddington, 1993; Deveney and Waddington, 1995; Waddington et al., 1995, 1998; Adachi et al., 1999; Niznik et al., 2001). However, the roles of individual family members in these processes are poorly understood in the absence of agonists and antagonists able to discriminate between them.

One fundamental approach to clarifying these issues involves mice having ablation of individual family members by targeted gene deletion [knockout] (Sibley, 1999; Waddington et al., 2001). However, systematic assessment of orofacial movement topography in mice has yet to be undertaken, because of practical issues: mice are considerably smaller and their orofacial movements more rapid, making for problems in resolution and quantification, while their generally heightened level of overall behaviour is an

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additional complication to their naturalistic assessment; furthermore, there is little general consensus as to how orofacial movements in rodents should be defined phenomenologically and resolved empirically (Waddington, 1990; Waddington et al., 1998). We have developed a novel procedure for the observation, categorisation and quantification of orofacial movement topographies in mice. This has then been applied in studies challenging mice with the dopamine D_1-like receptor agonist A 68930, the anomalous dopamine D_1-like receptor agent SK&F 83959 and the dopamine D_2-like receptor agonist RU 24213, following pretreatment with the dopamine D_1-like receptor antagonists SCH 23390 and BW 737C and the dopamine D_2-like receptor antagonist YM 09151-2 (see Deveney and Waddington, 1995; Adachi et al., 1999). This now allows, and provides a pharmacological background on which to interpret, subsequent studies in dopamine receptor subtype knockouts.

2. Materials and methods

2.1. Animals

Young adult female or male C 57BL/6 mice [BRF, RCSI, Dublin] were used. They were housed in groups of five, with food and water available ad libitum, and maintained at 21 ± 1°C on a 12 h/12 h (0900 on/2100 off) light/dark schedule. These studies were approved by the Research Committee of the Royal College of Surgeons in Ireland and the Higher Education Authority of Ireland, and conducted under licence from the Department of Health in accordance with EU regulations for the care and use of experimental animals.

2.2. Assessment system

The system consisted of a 'restrictor', by which mice were lightly restrained around the neck by a clear perspex

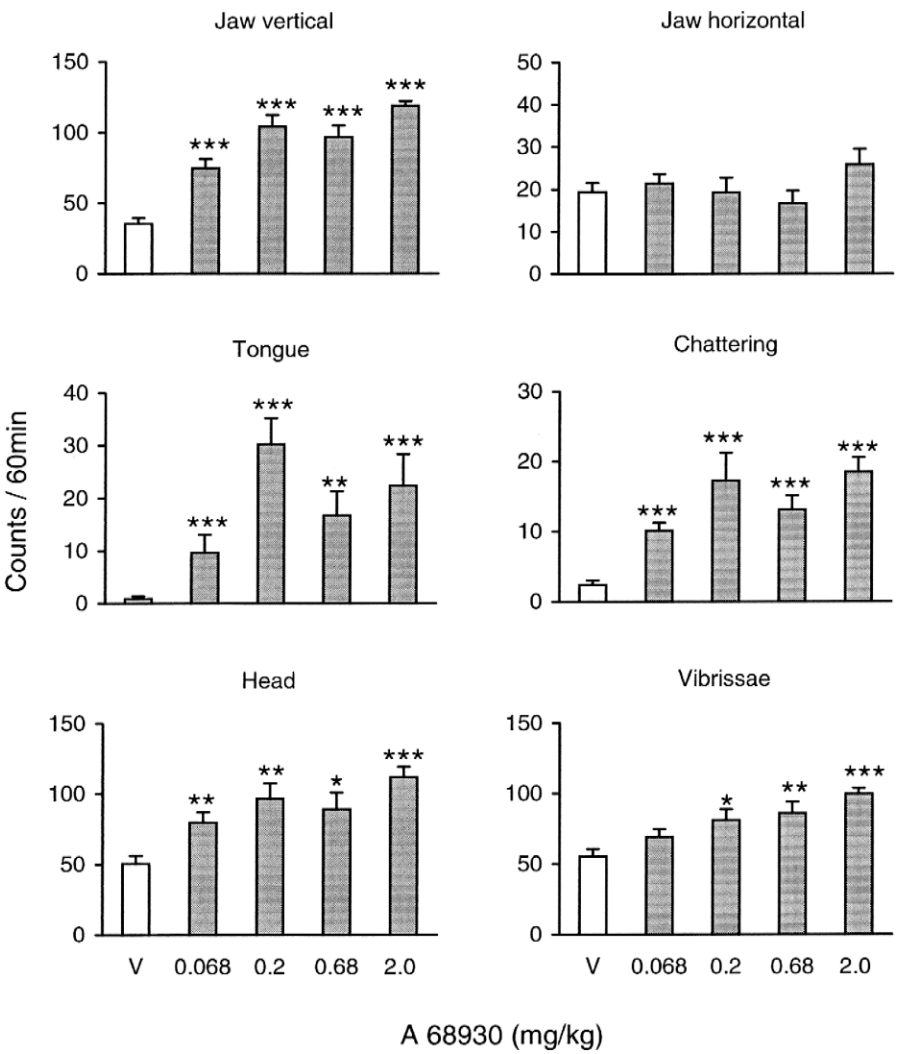

Fig. 1. Behavioural counts for orofacial movement topographies in response to vehicle or 0.068–2.0 mg/kg A 68930 over a 1-h period. Data are mean counts ± S.E.M. of $n = 8$ female mice per group. $^{*}P < 0.05$, $^{**}P < 0.01$, $^{***}P < 0.001$ vs. vehicle (V).

collar attached to a horizontal platform; this allowed visual observation to be focussed onto the orofacial region with minimal disturbance to movements other than locomotion, rearing and grooming. Circular collars were composed of two semicircular elements: one fixed to the platform and constituting a trough into which the neck was positioned; the other, inserted from above, completed light enclosure of the neck. Both the diameter of the collar and its height above the platform were adjustable according to body size, to allow a comfortable posture to be maintained. A piece of absorbent paper was spread over the platform of the restrictor. To facilitate observation of the orofacial region, small mirrors were fixed in inclined positions just under the snout of each mouse and lighting directed appropriately to illuminate the head and mouth. For each experimental session, five mice were placed individually into identical 'restrictors', each separated by cardboard dividers to minimize visual and auditory disruption. The observer viewed each animal through slits in a cardboard screen in front of the array of 'restrictors'; these slits were positioned optimally in relation to the head and mouth, mirrors and illumination.

2.3. Behavioural assessment

On the basis of their natural repertoire of behaviours at an ethological level, orofacial movements of mice were categorised into the following seven topographies: vertical jaw movements; horizontal [lateral] jaw movements; tongue protrusions; chattering [high-frequency rhythmical jaw movements with incisor tapping]; head movements; vibrissae movements; stillness [motionless, with no behaviour evident]. Following a 3-h period of habituation to 'restrictors' and subsequent treatment with drug(s) or vehicle(s) as indicated, a rapid time-sampling behavioural checklist technique, used previously to resolve topographies of general mouse behaviour in an unrestricted paradigm (Clifford et al., 1998, 1999, 2000), was applied similarly to resolve the above elements of orofacial movement: each of five mice was observed sequentially for 5-s periods at 25-s intervals over a total period of 1 h; for each mouse, the

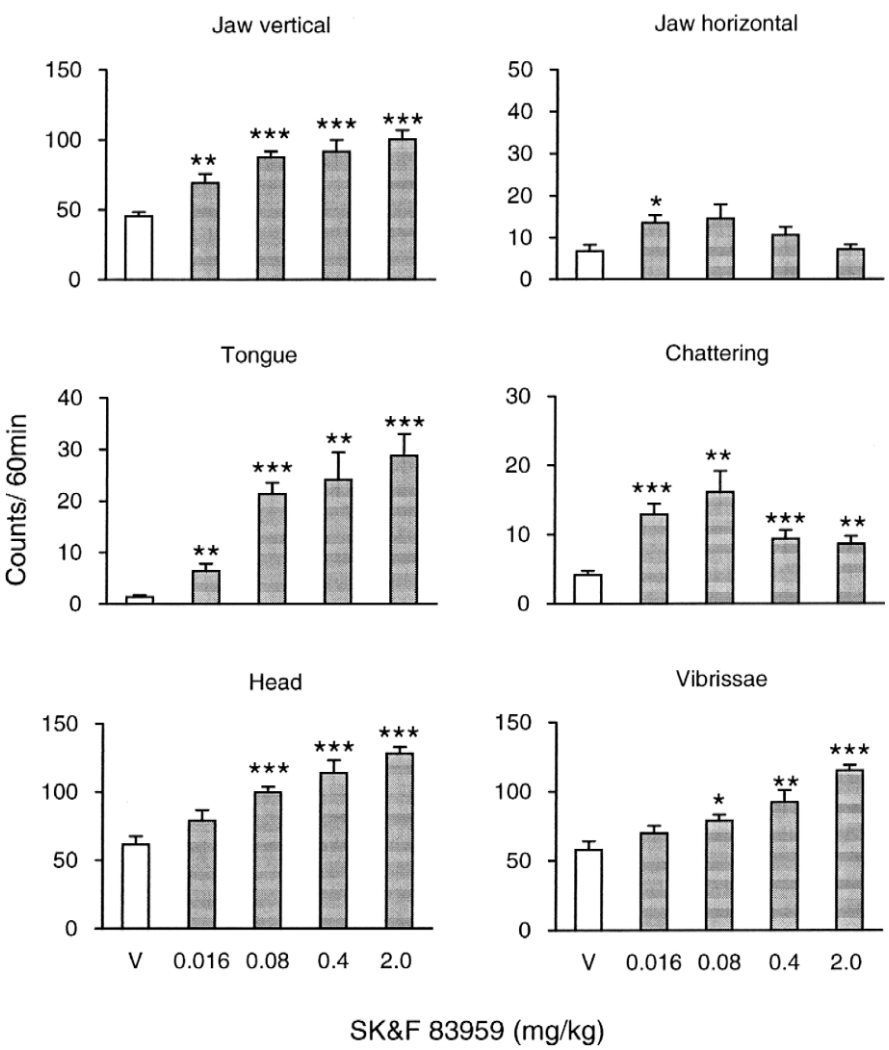

Fig. 2. Behavioural counts for orofacial movement topographies in response to vehicle or 0.016–2.0 mg/kg SK&F 83959 over a 1-h period. Data are mean counts ± S.E.M. of $n = 8$ female mice per group. $^{*}P < 0.05$, $^{**}P < 0.01$, $^{***}P < 0.001$ vs. vehicle (V).

presence or absence of each individual pattern of orofacial movement (occurring alone or in any combination) was determined in each of the 144 periods of 5 s constituting this 1-h period. Mice were used on two occasions only, separated by a drug-free interval of at least 1 week, with random allocation to one of the various treatments in each instance. All assessments were made by an observer who was unaware of the treatment given to each animal.

2.4. Drugs

The drugs used were: A 68930 ([1*R*,3*S*]-1-aminomethyl-5,6-dihydroxy-3-phenyl-isochroman; Abbott, USA); SK & F 83959 (3-methyl-6-chloro-7,8-dihydroxy-1-[3-methyl-phenyl]-2,'3, 4, 5-tetrahydro-1*H*-3-benzazepine; Research Biochemicals International/NIMH Chemical Synthesis Program, USA); RU 24213 (*N*-*n*-propyl-*N*-phenyl-*p*-3-hydroxyphenylethylamine; Hoechst-Marion-Roussel, France); SCH 23390 ([*R*]-3-methyl-7-chloro-8-hydroxy-1-phenyl-2, 3, 4, 5-tetrahydro-1*H*-3-benzazepine; Research Biochemicals International); BW 737C ([*S*]-6-chloro-1-[2,5-dimethoxy-4-propylbenzyl]-7-hydroxy-2-methyl-1,2,3,4-tetrahydroisoquinoline; Glaxo-Wellcome, UK); YM 09151-2 (*cis*-*N*-[1-benzyl-2-methyl-pyrrolidin-3-yl]-5-chloro-2-methoxy-4-methylaminobenzamide; Yamanouchi, Japan). SK&F 83959, RU 24213, SCH 23390 and BW 737C were dissolved in distilled water; A 68930 was dissolved in dilute acetic acid and made up to volume with distilled water; YM 09151-2 was dissolved in 0.1 N HCl and made up to volume with distilled water. All drugs and their respective vehicles were injected subcutaneously into the flank in a volume of 2 ml/kg, with antagonists or their vehicles given 30 min before agonists in combination experiments.

2.5. Data analysis

From application of the behavioural checklist, the total 'counts' for each individual orofacial movement were determined as the number of 5-s observation windows in which a given behaviour was evident, summed over the 1-h period, and expressed as means ± S.E.M.. These data were then analysed using analysis of variance (ANOVA) followed by Student's *t*-test or, in instances where data

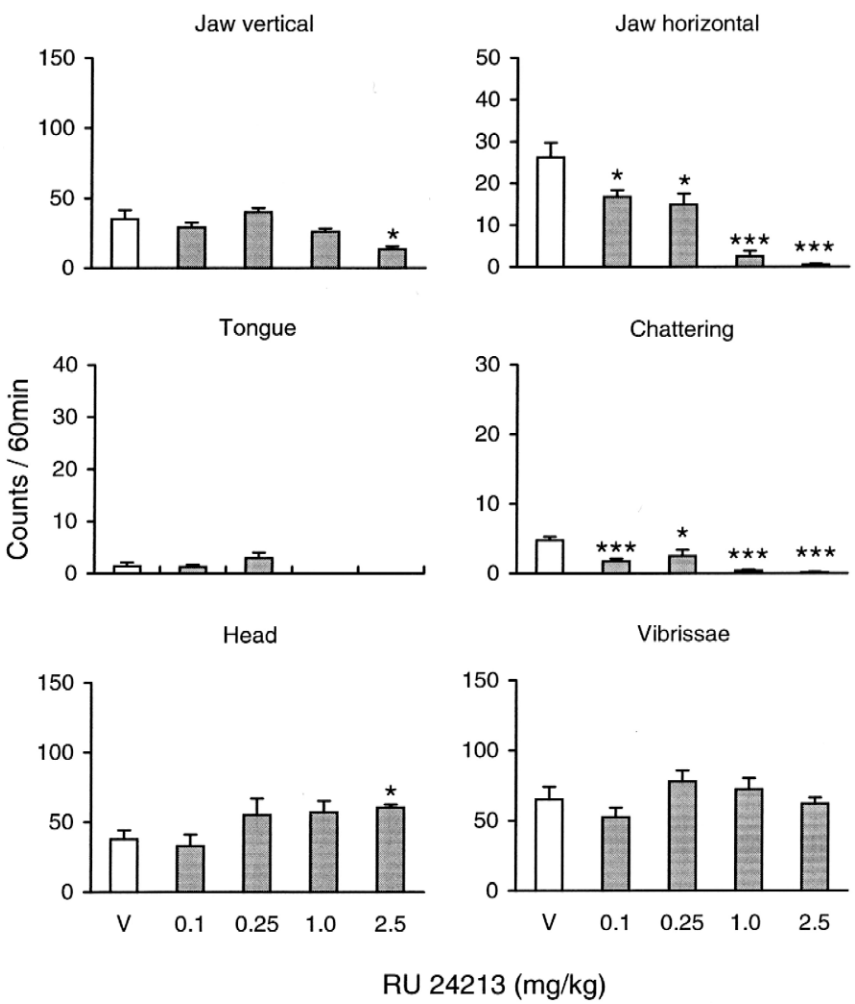

Fig. 3. Behavioural counts for orofacial movement topographies in response to vehicle or 0.1–2.5 mg/kg RU 24213 over a 1-h period. Data are mean counts ± S.E.M. of $n = 8$ male mice per group. $^{*}P < 0.05$, $^{***}P < 0.001$ vs. vehicle (V).

distribution deviated from normality, using the Kruskal–Wallis non-parametric ANOVA followed by Mann–Whitney *U*-test.

3. Results

3.1. Effects of A 68930, SK&F 83959 and RU 24213 given alone

When given alone, both A 68930 (0.068–2.0 mg/kg; Fig. 1) and SK&F 83959 (0.016–2.0 mg/kg; Fig. 2) each induced prominent, dose-dependent increases in vertical jaw movements, accompanied by tongue protrusions and incisor chattering, together with head and vibrissae movements; there were only modest or no effects on horizontal jaw movements, while stillness, reflecting the absence of any of the above orofacial movements, was essentially abolished by both drugs. Conversely, RU 24213 (0.1–2.5 mg/kg; Fig. 3) resulted in a modest decrease in baseline levels of vertical jaw movements, together with more marked decreases in horizontal jaw movements and incisor chattering; there were only modest or no effects on tongue protrusions and on head and vibrissae movements, while episodes of stillness were increased.

3.2. Effects of SCH 23390 and BW 737C on responsivity to A 68930 and SK&F 83959

SCH 23390 (0.005–0.125 mg/kg) dose-dependently antagonised vertical jaw movements ($P < 0.001$), tongue protrusions ($P < 0.05$) and incisor chattering ($P < 0.001$) induced by A 68930 (0.2 mg/kg), with modest attenuation ($P < 0.05$) of head and vibrissae movements but no effect on horizontal jaw movements (data not shown); the effects of SCH 23390 on responsivity to SK&F 83959 (0.08 mg/kg) were generally similar, though little antagonism of incisor chattering was evident (Fig. 4). BW 737C (0.08–0.2 mg/kg) also dose-dependently antagonised vertical jaw movements ($P < 0.05$), tongue protrusions ($P < 0.01$) and incisor chattering ($P < 0.01$) induced by A 68930, with some attenuation of head ($P < 0.01$) but less so of vibrissae movements, and no effect on horizontal jaw movements; the effects of BW 737C on responsivity to SK&F 83959 were similar (data not shown).

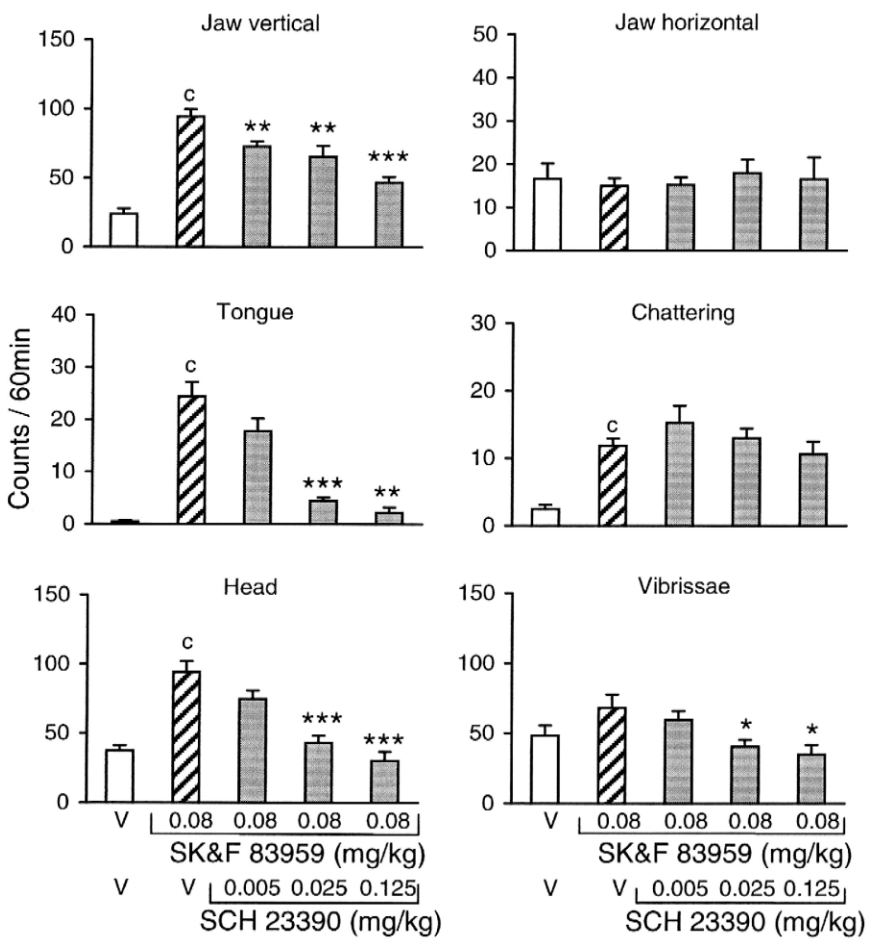

Fig. 4. Behavioural counts for orofacial movement topographies in response to vehicle or 0.08 mg/kg SK&F 83959 over a 1-h period, 30 min following pretreatment with 0.005–0.125 mg/kg SCH 23390. Data are mean counts ± S.E.M. of $n = 5–8$ female mice per group. $^{c}P < 0.001$ vs. vehicle (V); $^{*}P < 0.05$, $^{**}P < 0.01$, $^{***}P < 0.001$ vs. SK&F 83959.

3.3. Effects of YM 09151-2 on responsivity to A 68930 and SK&F 83959

YM 09151-2 (0.005–0.125 mg/kg) did not influence vertical jaw movements, tongue protrusions or incisor chattering induced by A 68930 (0.2 mg/kg), while attenuating head ($P < 0.01$) and vibrissae movements ($P < 0.05$) but not horizontal jaw movements (data not shown). However, YM 09151-2 attenuated vertical jaw movements, tongue protrusions, head and vibrissae movements but not incisor chattering induced by SK&F 83959 (0.08 mg/kg), and released horizontal jaw movements (Fig. 5).

4. Discussion

In preliminary studies, mice were immobilized in a plastic tube to expose only the snout and exclude all other forms of movement, but the resultant level of stress and soiling was both inappropriate and a confound to psychopharmacological studies. The final form of 'restrictor' was considerably less stressful, and enabled mice to maintain a more comfortable posture with freedom of trunk movement without soiling; this allowed resolution and quantification of a range of individual orofacial movement topographies more extensive than has been possible previously, even in the rat.

The full efficacy-cyclase-stimulating, selective dopamine D_1-like receptor agonist A 68930 and the selective dopamine D_1-like receptor agent SK&F 83959, which inhibits the stimulation of adenylyl cyclase, induced similar profiles of orofacial movement topography; thus, such movements may be mediated at least in part by a putative D_1-like receptor that is linked to a transduction system other than/additional to adenylyl cyclase, possibly to phosphoinositide hydrolysis (Mahan et al., 1990; Undie and Friedman, 1990, 1994; Arnt et al., 1992; Deveney and Waddington, 1995; Rosengarten and Friedhoff, 1998; Adachi et al., 1999; Niznik et al., 2001). The distinct profile induced by the selective dopamine D_2-like receptor

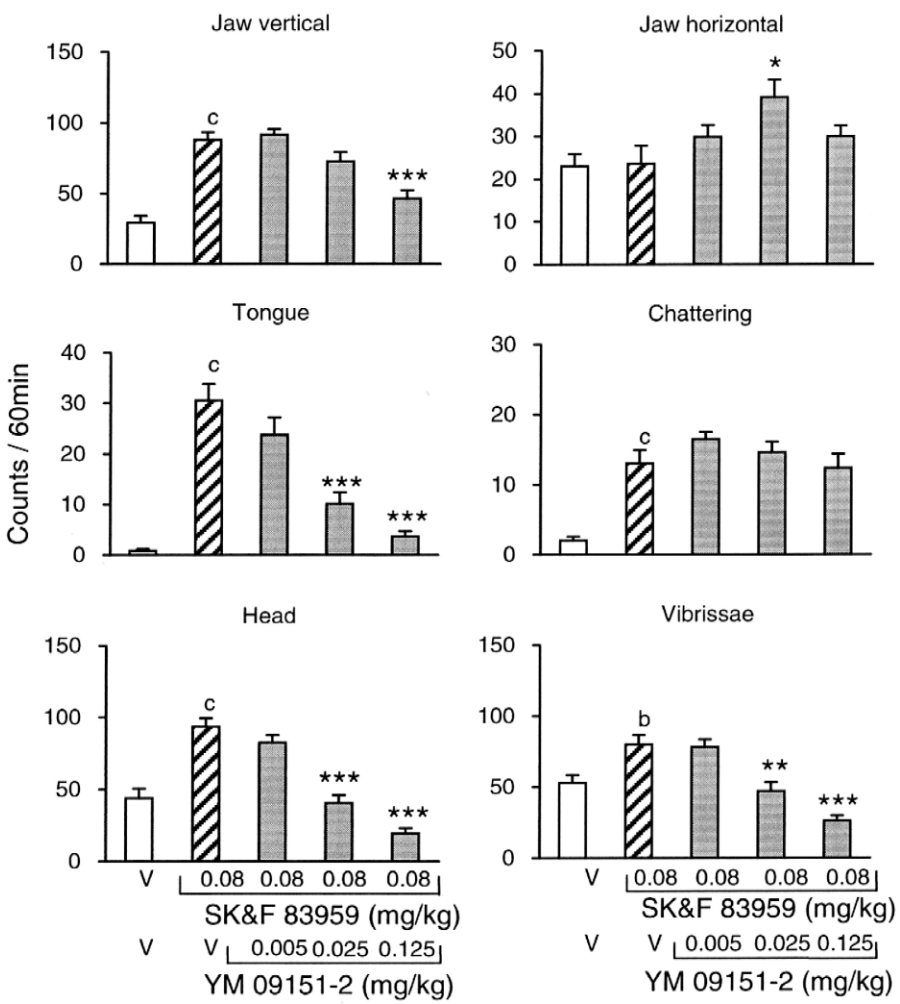

Fig. 5. Behavioural counts for orofacial movement topographies in response to vehicle or 0.08 mg/kg SK&F 83959 over a 1-h period, 30 min following pretreatment with 0.005–0.125 mg/kg YM 09151-2. Data are mean counts ± S.E.M. of $n = 8$ female mice per group. $^{b}P < 0.01$, $^{c}P < 0.001$ vs. vehicle (V); $^{*}P < 0.05$, $^{**}P < 0.01$, $^{***}P < 0.001$ vs. SK&F 83959.

agonist RU 24213 indicates that the functional role of dopamine D_2-like receptors in these processes appears to be at least in part opposite to that of their D_1-like counterparts. These findings elaborate importantly on those deriving from studies in rats by indicating that dopamine D_1-like receptor agonism influences jaw movements primarily in the vertical plane, together with excursive tongue movements and incisor chattering.

Orofacial movement responses to A 68930 and to SK&F 83959 were readily blocked in a generally similar manner by each of SCH 23390 and BW 737C. However, only BW 737C antagonised incisor chattering induced by SK&F 83959. We (Daly and Waddington, 1993; Deveney and Waddington, 1996) and others (Sugamori et al., 1998) have previously offered evidence that BW 737C appears to interact with dopamine D_1-like receptor family members in a manner different from SCH 23390. Thus, the present findings might indicate also a differential involvement of specific dopamine D_1-like receptor family members in relation to incisor chattering as opposed to vertical jaw movements with tongue protrusions. The selective dopamine D_2-like receptor antagonist YM 09151-2 exerted little effect on responsivity to A 68930, but attenuated vertical jaw movements and tongue protrusions, and released horizontal jaw movements in response to SK&F 83959. This might indicate some involvement of a novel D_1-like receptor in the regulation of orofacial movement topography by oppositional D_1-like:D_2-like interactions (Rosengarten et al., 1986; Murray and Waddington, 1989; Waddington et al., 1994; Niznik et al., 2001).

Functional roles for individual members of the dopamine D_1-like and D_2-like receptor families can now be studied directly using mice in which individual subtypes have been knocked out by targeted gene deletion (Sibley, 1999; Waddington et al., 2001). We have recently applied ethologically based techniques to the topographical assessment of behavioural phenotype in mutant mice lacking D_{1A} (Clifford et al., 1998, 1999), D_2 (Clifford et al., 2000, 2001) and D_3 (McNamara et al., 2000) receptors. The present model and findings constitute a paradigm for clarifying similarly their roles in the regulation of orofacial movement topography.

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References

Adachi, K., Ikeda, H., Hasegawa, M., Nakamura, S., Waddington, J.L., Koshikawa, N., 1999. SK&F 83959 and non-cyclase-coupled dopamine D_1-like receptors in jaw movement via dopamine D_1-like/D_2-like receptor synergism. Eur. J. Pharmacol. 367, 143–149.

Arnt, J., Hyttel, J., Sanchez, C., 1992. Partial and full dopamine D_1 receptor agonists in mice and rats: relation between behavioural effects and stimulation of adenylate cyclase activity in vitro. Eur. J. Pharmacol. 213, 259–267.

Clifford, J.J., Tighe, O., Croke, D.T., Sibley, D.R., Drago, J., Waddington, J.L., 1998. Topographical evaluation of the phenotype of spontaneous behaviour in mice with targeted gene deletion of the D_{1A} dopamine receptor: paradoxical elevation of grooming syntax. Neuropharmacology 37, 1595–1602.

Clifford, J.J., Tighe, O., Croke, D.T., Kinsella, A., Sibley, D.R., Drago, J., Waddington, J.L., 1999. Conservation of behavioural topography to dopamine D_1-like receptor agonists in mutant mice lacking the D_{1A} receptor implicates a D_1-like receptor not coupled to adenylyl cyclase. Neuroscience 93, 1483–1489.

Clifford, J.J., Usiello, A., Vallone, D., Kinsella, A., Borrelli, E., Waddington, J.L., 2000. Topographical evaluation of behavioural phenotype in a line of mice with targeted gene deletion of the D_2 dopamine receptor. Neuropharmacology 39, 382–390.

Clifford, J.J., Kinsella, A., Tighe, O., Rubinstein, M., Grandy, D.K., Low, M., Croke, D.T., Waddington, J.L., 2001. Comparative, topographically-based evaluation of behavioural phenotype and specification of D_1-like:D_2-like interactions in a line of incipient congenic mice with D_2 dopamine receptor 'knockout'. Neuropsychopharmacology (in press).

Collins, P., Broekkamp, C.L.E., Jenner, P., Marsden, C.D., 1991. Drugs acting at D-1 and D-2 receptors induce identical purposeless chewing in rats which can be differentiated by cholinergic manipulation. Psychopharmacology 103, 503–512.

Daly, S.A., Waddington, J.L., 1993. Behavioural evidence for 'D-1-like' dopamine receptor subtypes in rat brain using the new isochroman agonist A 68930 and isoquinoline antagonist BW 737C. Psychopharmacology 113, 45–50.

Deveney, A.M., Waddington, J.L., 1995. Pharmacological characterisation of behavioural responses to SK&F 83959 in relation to "D_1-like" dopamine receptors not linked to adenylyl cyclase. Br. J. Pharmacol. 116, 2120–2126.

Deveney, A.M., Waddington, J.L., 1996. Evidence for dopamine D_1-like receptor subtypes in the behavioural effects of two new selective antagonists, LY 270411 and BW 737C. Eur. J. Pharmacol. 317, 175–181.

Koshikawa, N., Aoki, S., Hiruta, M., Tomiyama, K., Kobayashi, M., Tsuboi, Y., Iwata, K., Sumino, R., Stephenson, J.D., 1989. Effects of intrastriatal injections of selective dopamine D-1 and D-2 agonists and antagonists on jaw movements of rats. Eur. J. Pharmacol. 163, 227–236.

Mahan, L.C., Bush, R.M., Monsma Jr., F.J., Sibley, D.R., 1990. Expression of striatal D_1 dopamine receptors coupled to inositol phosphate production and Ca^{2+} mobilization in *Xenopus oocytes*. Proc. Natl. Acad. Sci. U. S. A. 87, 2196–2200.

McNamara, F.N., Clifford, J.J., Kinsella, A., Accili, D., Fuchs, S., Drago, J., Croke, D.T., Waddington, J.L., 2000. Topographically based specification of behavioural phenotype in congenic mice with targeted gene deletion of the D_3 dopamine receptor. Br. J. Pharmacol. 131, (Suppl.), 4 p.

Murray, A.M., Waddington, J.L., 1989. The induction of grooming and vacuous chewing by a series of selective D-1 dopamine receptor agonists: two directions of D-1:D-2 interaction. Eur. J. Pharmacol. 160, 377–384.

Niznik, H.B., Sugamori, K.S., Clifford, J.J., Waddington, J.L., 2001. D_1-like dopamine receptors: molecular biology and pharmacology. In:

Di Chiara, G. (Ed.), Handbook of Experimental Pharmacology: Dopamine in the CNS. Springer, Heidelberg (in press).

Rosengarten, H., Friedhoff, A.J., 1998. A phosphoinositide-linked dopamine D_1 receptor mediates repetitive jaw movement in rats. Biol. Psychiatry 44, 1178–1184.

Rosengarten, H., Schweitzer, J.W., Friedhoff, A.J., 1983. Induction of oral dyskinesia in naïve rats by D-1 stimulation. Life Sci. 33, 2471–2482.

Rosengarten, H., Schweitzer, J.W., Friedhoff, A.J., 1986. Selective dopamine D-2 receptor reduction enhances a D-1 mediated oral dyskinesia in rats. Life Sci. 39, 29–35.

Sibley, D.R., 1999. New insight into dopaminergic receptor function using antisense and genetically altered animals. Ann. Rev. Pharmacol. Toxicol. 39, 313–341.

Sugamori, K.S., Hamadanizadeh, S.A., Scheideler, M.A., Hohlweg, R., Vernier, P., Niznik, H.B., 1998. Functional differentiation of multiple dopamine D_1-like receptors by NNC 01-0012. J. Neurochem. 71, 1685–1693.

Undie, A.S., Friedman, E., 1990. Stimulation of a dopamine D_1 receptor enhances inositol phosphate formation in rat brain. J. Pharmacol. Exp. Ther. 253, 987–992.

Undie, A.S., Friedman, E., 1994. Inhibition of dopamine agonist-induced phosphoinositide hydrolysis by concomitant stimulation of cyclic AMP formation in brain slices. J. Neurochem. 63, 222–230.

Waddington, J.L., 1990. Spontaneous orofacial movements induced in rodents by very long-term neuroleptic drug administration: phenomenology and putative relationship to tardive dyskinesia. Psychopharmacology 101, 431–447.

Waddington, J.L., Daly, S.A., McCauley, P.G., O'Boyle, K.M., 1994. Levels of functional interaction between D_1-like and D_2-like dopamine receptor systems. In: Niznik, H.B. (Ed.), Dopamine Receptors and Transporters: Pharmacology, Structure and Function. Marcel-Dekker, New York, pp. 511–537.

Waddington, J.L., Daly, S.A., Downes, R.P., Deveney, A.M., McCauley, P.G., O'Boyle, K.M., 1995. Behavioural pharmacology of 'D_1-like' dopamine receptors: further subtyping, new pharmacological probes and interactions with 'D_2-like' receptors. Prog. Neuro-Psychopharmacol. Biol. Psychiatry 19, 811–831.

Waddington, J.L., Deveney, A.M., Clifford, J.J., Tighe, O., Croke, D.T., Sibley, D.R., Drago, J., 1998. D_1-like dopamine receptors: regulation of psychomotor behaviour, D_1-like: D_2-like interactions and effects of D_{1A} targeted gene deletion. In: Jenner, P., Demirdama, R. (Eds.), Dopamine Receptor Subtypes: From Basic Science to Clinic. IOS Press, Amsterdam, pp. 45–63.

Waddington, J.L., Clifford, J.J., McNamara, F.N., Tomiyama, K., Koshikawa, N., Croke, D.T., 2001. The psychopharmacology-molecular biology interface: exploring the behavioural roles of dopamine receptor subtypes using targeted gene deletion ['knockout']. Prog. Neuro-Psychopharmacol. Biol. Psychiatry (in press).