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The superior colliculus contains a discrete region involved in the control of jaw movements: role of $GABA_A$ receptors

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Abstract

The role of $GABA_A$ receptors in the superior colliculus in the production of rat repetitive jaw movements was examined, as this nucleus receives tonic GABAergic inhibitory inputs from the dorsolateral part of the substantia nigra pars reticulata and the entopeduncular nucleus. Both regions are also connected with the ventrolateral striatum where stimulation of either dopamine or acetylcholine receptors has been found to elicit distinct types of jaw movements in rats. The $GABA_A$ receptor antagonist bicuculline (50 and 150 ng/0.2 μl per side) dose-dependently produced repetitive jaw movements only when injected bilaterally into a circumscribed region (A 3.0) of the lateral deeper layers of the superior colliculus; this region is known to receive input predominantly from the dorsolateral part of the substantia nigra pars reticulata. The effects of bicuculline were $GABA_A$ receptor specific because the effects were abolished by muscimol, a $GABA_A$ receptor agonist, given into the same site. The bicuculline-induced jaw movements differed qualitatively from those elicited by injection of a mixture of (±)-6-chloro-7,8-dihydroxy-3-allyl-1-phenyl-2,3,4,5-tetrahydro-1*H*-3-benzazepine-7,8-diol (SKF 82958; 5 μg) and quinpirole (10 μg), agonist at dopamine D1 and D2 receptors, respectively, or carbachol (2.5 μg), an acetylcholine receptor agonist, into the ventrolateral striatum. Nevertheless, injection of muscimol into the lateral deeper layers of the superior colliculus (A 3.0) inhibited jaw movements evoked by the dopamine D1/D2 receptor stimulation. Conversely, the jaw movements evoked by acetylcholine receptor stimulation were enhanced by injection of muscimol into the superior colliculus. In conclusion, $GABA_A$ receptor blockade in a circumscribed region (A 3.0) of the lateral deeper layers of the superior colliculus elicits characteristic repetitive jaw movements, and the $GABA_A$ receptors in that region modulate the dopamine D1/D2 receptor-mediated and acetylcholine receptor-mediated jaw movements in an opposite manner.

Keywords: Jaw movement; Superior colliculus; Ventrolateral striatum; $GABA_A$ receptor; Dopamine receptor; Acetylcholine receptor; (Rat)

1. Introduction

Stimulation of dopamine or acetylcholine receptors in the ventrolateral part of the striatum has been found to elicit repetitive jaw movements in rats (Kelley et al., 1989; Delfs and Kelley, 1990), each of these marked by its own movement profile (Kikuchi de Beltrán et al., 1992). Recently, we have provided additional evidence that these dopamine-receptor-mediated and acetylcholine-receptor-mediated jaw movements are indeed two distinct types of jaw movements that are differentially funnelled via separate γ-aminobutyric acid (GABA)ergic output channels (Adachi et al., 2002), namely striato-nigral (Von Krosigk et al., 1992; Iwata et al., 1996; Parent et al., 2000) and striato-entopeduncular (Parent, 1990; Takada et al., 1994; Parent et al., 2000) pathways, to the parvicellular reticular formation (Von Krosigk and Smith, 1991; Yasui et al., 1992; Von Krosigk et al., 1992; Takada et al., 1994; Iwata et al., 1996), a region that is directly connected with the orofacial motor nuclei.

Until now, it is not clear whether or not the deeper layers of the superior colliculus play any role in the transmission of these jaw movements. Such a role can be expected in view of the fact that it is known for a long time that the superior

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colliculus is involved in the control of dopamine-dependent oral stereotypy (Redgrave et al., 1980; Dean et al., 1982) and other oral behaviours in rats (Redgrave et al., 1981; Taha et al., 1982; Scheel-Krüger, 1986). More precisely, it has been found that a lesion of the superior colliculus attenuates apomorphine-induced oral stereotypy and oral behaviour that is elicited by nigral injection of the $GABA_A$ receptor agonist muscimol into the deeper layers of the superior colliculus of rats (Redgrave et al., 1980; Taha et al., 1982). In addition, it has been reported that microinjections of the $GABA_A$ receptor antagonist picrotoxin into the superior colliculus elicits gnawing (Redgrave et al., 1981), while similar injections of muscimol attenuates apomorphine-induced oral stereotypy (Dean et al., 1982). Indeed, both the dorsolateral part of the substantia nigra pars reticulata and the entopeduncular nucleus send GABAergic projection fibres to the caudal respectively rostral parts of the lateral region of the deeper layers of the superior colliculus (Redgrave et al., 1992; Takada et al., 1994; Yasui et al., 1995), a region that in turn sends an excitatory output to the parvicellular reticular formation, predominantly at the contralateral side (Murray and Coulter, 1982; Redgrave et al., 1990; Yasui et al., 1994). However, detailed inspection of the precise striato-entopedunculo-collicular and striato-entopedunculo-bulbar pathways reveals that the striato-entopedunculo-collicular pathway has its origin in the dorsal part of the striatum, a region that is primarily involved in the control of eye-head movements, whereas the striato-entopedunculo-bulbar pathway has its origin in the ventrolateral part of the striatum, a region that is primarily involved in the control of orofacial movements (Takada et al., 1994). A similar differentiation holds true for the striato-nigro-collicular pathway and the striato-nigro-bulbar pathway: the former has its origin in the dorsal part of the striatum, in contrast to the latter which has its origin in the ventrolateral part of the striatum (Takada et al., 1994). On the basis of these data, it is hypothesised that the superior colliculus does not funnel jaw movements elicited by stimulation of dopamine or acetylcholine receptors in the ventrolateral striatum. In contrast, the superior colliculus is hypothesised to modulate these jaw movements because it sends an excitatory output to the parvicellular reticular formation (Murray and Coulter, 1982; Redgrave et al., 1990; Yasui et al., 1994), namely a region that itself is innervated by striato-entopedunculo-bulbar and striato-nigro-bulbar fibres (see above).

In the present study, we utilised muscimol and the $GABA_A$ receptor antagonist bicuculline to activate and inhibit, respectively, $GABA_A$ receptors in the superior colliculus. According to our hypothesis, jaw movements that differ from those elicited by stimulation of dopamine or acetylcholine receptors in the ventrolateral part of the striatum are elicited. According to the studies of Redgrave et al. (1980, 1981), Dean et al. (1982) and Taha et al. (1982), it is predicted that bicuculline, but not muscimol, is effective in eliciting jaw movements. Like in our previous studies (Adachi et al., 2002), we used electromyography and a phototransduction system to characterise the pattern of jaw movements induced by injections of GABAergic drugs into the superior colliculus in order to compare these with those elicited by injections of dopamine and acetylcholine receptor agonists into the ventrolateral striatum (Adachi et al., 2002). Once the nature of the behavioural response to collicular injections of GABAergic drugs was established, we constructed a dose-response curve and studied the specificity of the response using muscimol and/or bicuculline. Because the rostro-caudal extension of the deeper layers of the superior colliculus is heterogeneous in terms of its afferents (see above; Redgrave et al., 1992; Yasui et al., 1994; Takada et al., 1994), special attention was paid to the presence of a site specificity of the behavioural response to GABAergic drugs.

To analyse the role of the deeper layers of the superior colliculus in the jaw movements that are elicited by stimulation of dopamine or acetylcholine receptors in the ventrolateral part of the striatum, muscimol was injected bilaterally into the deeper layers of the lateral superior colliculus of rats treated with bilateral injections into the ventrolateral striatum of a mixture of the dopamine D1 receptor agonist, (±)-6-chloro-7,8-dihydroxy-3-allyl-1-phenyl-2,3,4,5-tetrahydro-1*H*-3-benzazepine-7,8-diol (SKF 82958; 5 μg), and the dopamine D2 receptor agonist, quinpirole (10 μg), or the acetylcholine receptor agonist, carbachol (2.5 μg); the latter dopaminergic and cholinergic treatments have been found to be highly effective to elicit the above-mentioned dopamine receptor-mediated and acetylcholine receptor-mediated jaw movements (Kikuchi de Beltrán et al., 1992; Adachi et al., 2002).

2. Materials and methods

2.1. Surgical procedures

Male Sprague–Dawley rats weighing 260–330 g were housed in cages (27 × 45 × 20 cm) that were kept at constant room temperature (23 ± 2 °C) and relative humidity (55 ± 5%) under a 12 h light/dark cycle (lights on at 0700 h), with free access to food and water.

Rats were anaesthetised with halothane (0.5–4.0% when appropriate) and supplemented with ketamine HCl (10.0 mg/kg, i.p.). The surgical and recording procedures were as described previously (Koshikawa et al., 1989, 1990a,b, 1991; Cools et al., 1995). After cannulation of the right external jugular vein, a small light-emitting diode was fixed to the mandible. The animal was placed in a stereotactic frame so that the head was kept in constant relation to a light-sensitive transducer, which detected the vertical movements of the diode. Bipolar electrodes were placed into the masseter and digastric muscles to record electromyographic (EMG) activity. After surgery, the animals continuously received ketamine in a dose (10.0 mg/kg, i.v.) unable to influence either the jaw movements under study (Koshikawa et al., 1989) or dopamine metabolism in the striatum

(Koshikawa et al., 1988). Lignocaine HCl (2% 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 the experiment were 19–21% and 2.0–2.5%, respectively. The jaw movements and EMG activity were recorded on an eight-channel tape recorder (RD-180T; TEAC) for offline analyses according to previously described procedures (Adachi et al., 2002). Thus, the recordings were analysed automatically, using a spike trigger that counted vertical jaw movements per 5 min. The recording period lasted 60 or 120 min. Moreover, to conduct more precise analysis of jaw movement pattern, ''duration of cycle'', defined as duration between successive points of maximum closure, and ''duration of opening phase'', defined as duration between point of maximum closure and point of maximum jaw opening, were calculated for a 5-min recording period around their peak effects.

Guide cannulas (0.5 mm o.d., 0.3 mm i.d., 6.0 or 3.0 mm length) were implanted bilaterally into the brain according to previously described procedures (Koshikawa et al., 1989). The coordinates based on the atlas of Paxinos and Watson (1986) were: anterior = 2.6–3.4 mm from interaural line, vertical = 4.0–4.5 mm from interaural line, lateral = 1.5–2.0 mm from midline (superior colliculus); anterior = 3.0 mm, vertical = 3.0 mm, lateral = 2.0 mm (site adjacent but ventral to superior colliculus); anterior = 8.6 mm, vertical = 3.0 mm, lateral = 4.0 mm (ventrolateral striatum). The injection was made slowly in a volume of 0.2 μl per side over 20 s, and the needle was left in situ for an additional 20-s period after completion of the injection. Damage to the target site was minimised by implanting the tips of the guide cannulas 1.5 mm (ventrolateral striatum or superior colliculus) or 2.5 mm (site adjacent but ventral to superior colliculus) 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, and were performed in accordance with Institutional guidelines for the care and use of experimental animals that were in compliance with the UK Animals Scientific Act 1986.

2.2. Drugs

The animals ($n = 6–9$ per experiment) received bilateral injections of the full dopamine D1 receptor agonist, SKF 82958 (5 μg; (±)-6-chloro-7,8-dihydroxy-3-allyl-1-phenyl-2,3,4,5-tetrahydro-1*H*-3-benzazepine-7,8-diol hydrobromide, Sigma, St. Louis, MO), and the dopamine D2 receptor agonist, quinpirole (10 μg; Sigma), combination (cocktail) or the nonselective acetylcholine receptor agonist, carbachol (2.5 μg; carbamylcholine, Sigma), into the ventrolateral striatum. The $GABA_A$ receptor agonist, muscimol (50 or 100 ng; 5-aminomethyl-3-hydroxyisoxazole, Sigma), or the antagonist, (−)-bicuculline methbromide (50 or 150 ng; Sigma), was injected into the superior colliculus immediately before the injection of the mixture of SKF 82958 and quinpirole or carbachol into the ventrolateral striatum; muscimol was injected 15 min before carbachol or bicuculline, where appropriate. All drugs were dissolved in saline immediately before use. Doses employed were based on previously published studies (Koshikawa et al., 1990a; Kikuchi de Beltrán et al., 1992; Cools et al., 1995; Adachi et al., 2002). The animals were used only once.

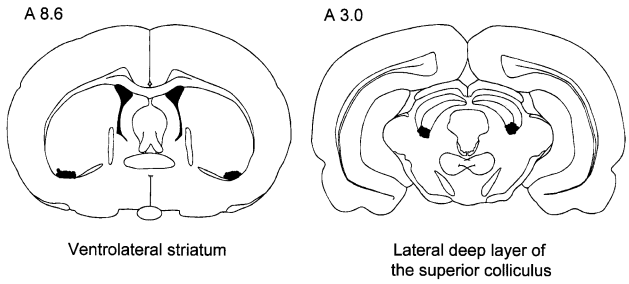

Fig. 1. Location of injection sites in the ventrolateral striatum (vlS, left) and lateral deeper layers of the superior colliculus (ldSC, right). Planes are modified to a series of two or three sections for each brain area from the atlas of Paxinos and Watson (1986); approximate coordinates indicated are in mm anterior to the interaural line.

2.3. Histology

At the end of each experiment, the rats were deeply anaesthetised with sodium pentobarbitone (80 mg/kg, i.p.) and perfused transcardially with 10% formalin. The brains were removed, sectioned at 50 μm and stained with Cresyl violet to visualise the injection site; only data from animals in which the injections were correctly placed were included in subsequent analyses. Fig. 1 gives a survey of the injection sites located in the ventrolateral striatum, and lateral deeper layers of the superior colliculus.

2.4. Data analysis

All values are expressed as means ± S.E.M. and analysed using one-way analysis of variance (ANOVA) or two-way ANOVA (group × time), followed by a post hoc Dunnett's test where appropriate. In addition, a Student's *t*-test was used to analyse jaw movement pattern (duration of opening phase and duration of cycle). A probability value of $P < 0.05$ was considered statistically significant.

3. Results

3.1. Pattern of jaw movements elicited by bilateral injections of GABAergic drugs into the superior colliculus

Muscimol alone had no effects. In contrast, bicuculline was highly effective in eliciting jaw movements. Fig. 2 shows the results of the averaged EMG activity recorded

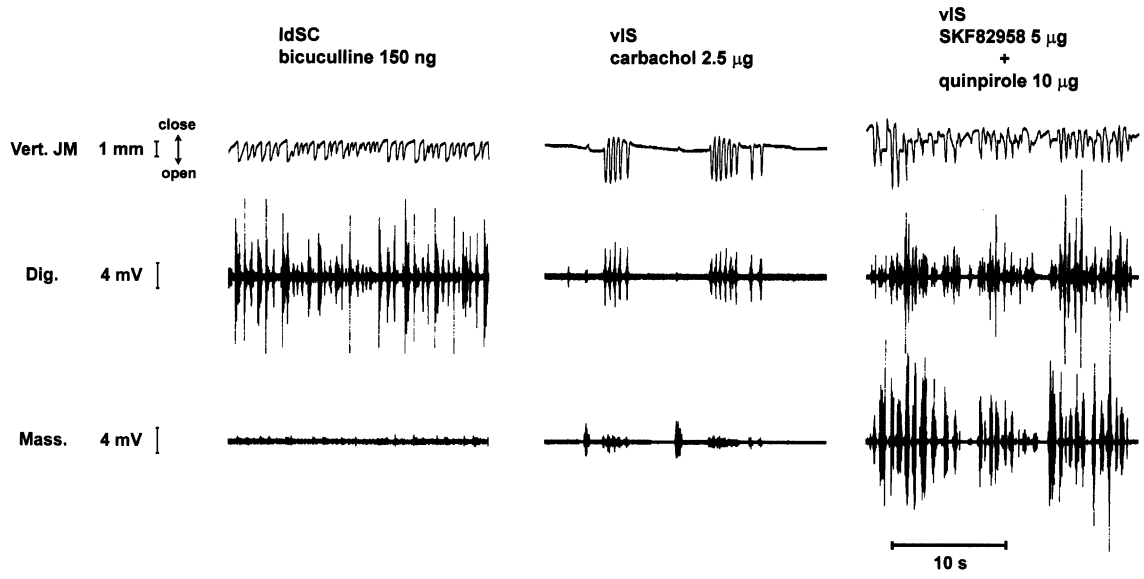

Fig. 2. Pattern of jaw movements elicited 10 min after bilateral injections of bicuculline (150 ng) into the lateral deeper layers of the superior colliculus (ldSC, left part). For the sake of comparison, the pattern of jaw movements elicited 10 min after bilateral injections of carbachol (2.5 μg, middle part) and 60 min after bilateral injections of the cocktail of SKF 82958 (5 μg) and quinpirole (10 μg) into the ventrolateral striatum (right part) are included. Vertical component of jaw movements (Vert. JM) and associated electromyographic activity recorded from digastric (Dig.) and masseter (Mass.) muscles are shown.

from digastric and masseter muscle and the vertical component of jaw movements. Bilateral injections of bicuculline into the superior colliculus (Fig. 2, left part) increased EMG activity in the digastric muscle that was associated with the movement of jaw opening, but did not change the stable moderate tone of the EMG activity in the masseter muscle during jaw movements (digastric type). This characteristic feature was unique in the sense that it did not match the patterns elicited by stimulation of dopamine or acetylcholine receptors in the striatum (Fig. 2, middle and right parts), although it shared some features with the pattern elicited by bilateral injections of carbachol (2.5 μg) into the ventrolateral striatum. However, detailed analysis of the vertical jaw movement pattern, using the peak effects measured in bicuculline-treated rats and carbachol-treated rats during a 5-min observation period, revealed that the duration of cycle of bicuculline-induced jaw movements was approximately two times longer than that of carbachol-induced jaw movements [0.580 ± 0.014 s ($n = 391$) vs. 0.252 ± 0.003 s ($n = 161$); $P < 0.001$, Student's t-test], and that the duration of opening phase of bicuculline-induced jaw movements was approximately half of that of carbachol-induced jaw movements [0.056 ± 0.002 s ($n = 391$) vs. 0.107 ± 0.001 s ($n = 161$); $P < 0.001$, Student's t-test].

3.2. Dose-dependent, site-specific and GABA-specific effects of bicuculline within the superior colliculus

Bilateral injections of bicuculline (50 ng; $n = 7$; 150 ng; $n = 7$) into the superior colliculus elicited jaw movements in a dose-dependent manner (overall: $F(2,17) = 21.07$, $P < 0.0001$; 50 ng vs. saline: $P > 0.05$; 150 ng vs. saline: $P < 0.01$, Dunnett's test). The time-dependent effects of bicuculline, shown in Fig. 3, clearly illustrates that the effect started nearly immediately after injection, reached its peak around 10 min and vanished about 30 min after injection. Injections of saline ($n = 6$) into the superior colliculus did not elicit repetitive jaw movements (Fig. 3).

Injection site of bicuculline (150 ng; $n = 32$) were plotted onto four serial coronal sections (A 2.7, A 3.0, A 3.2 and A 3.4) to analyse the site specificity of the bicuculline response (Fig. 4, left panel). Only injections correctly made into the lateral deeper layers of the superior colliculus at level A 3.0 elicited prominent jaw movements, whereas injections made into the other sites and the site adjacent, but 1.0 mm ventral to the superior colliculus at level A 3.0, remained without any effect (Fig. 4, right panel). Therefore, only the effects of

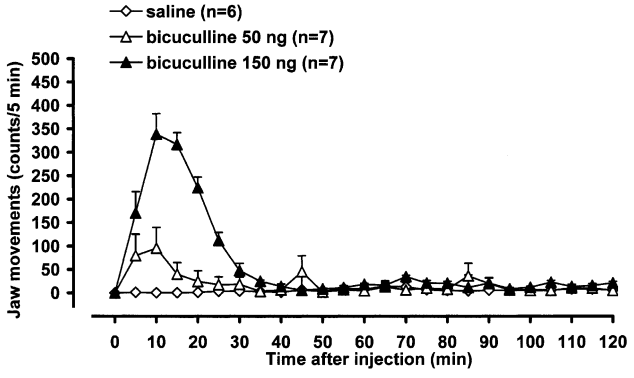

Fig. 3. The time-dependent effects of bilateral injections of saline (0.2 μl per side) and bicuculline (50 and 150 ng per side) into the lateral deeper layers of the superior colliculus in a coronal section at A 3.0 on production of jaw movements. The data are expressed as the mean number of jaw movements occurring in 5-min observation periods ($n = 6–7$). Vertical bars indicate S.E.M.

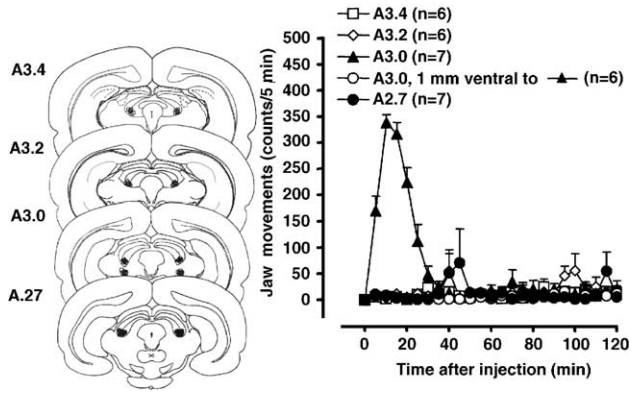

Fig. 4. Site-specific effects of bicuculline (150 ng per side) injections within the lateral deeper layers of the superior colliculus on production of jaw movements (right part). The injection sites are indicated on the drawings modified to a series of two to three sections for each injection from the atlas of Paxinos and Watson (1986); coordinates are indicated in mm anterior to the interaural line (left part). The data are expressed as the mean number of jaw movements occurring in 5-min observation periods ($n=6-7$). Vertical bars indicate S.E.M.

injections that were correctly placed at level A 3.0 were incorporated in the analysis presented below.

The effects of bicuculline at level of A 3.0 ($n=7$) were completely abolished by muscimol (50 ng; $n=6$; $F(1,264)=93.23$, $P<0.001$) injected into the same site: muscimol (50 ng; $n=6$) alone did not elicit any jaw movement (Fig. 5).

3.3. Effects of bilateral injections of muscimol into the superior colliculus on jaw movements elicited by administration of SKF 82958 and quinpirole mixture into the ventrolateral striatum

The time-dependent effects of the mixture of SKF 82958 and quinpirole are shown in Fig. 6. This figure illustrates that the jaw movements occurred initially at low levels but subsequently increased markedly and then declined over the

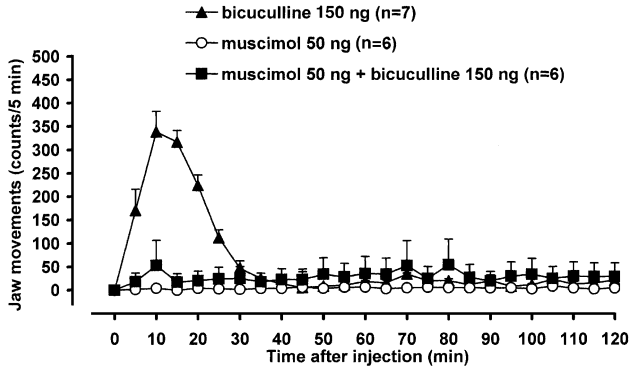

Fig. 5. Antagonism by muscimol (50 ng per side) of jaw movements induced by bicuculline (150 ng per side) injected into the lateral deeper layers of the superior colliculus in a coronal section at A 3.0. The data are expressed as the mean number of jaw movements occurring in 5-min observation periods ($n=6-7$). Vertical bars indicate S.E.M.

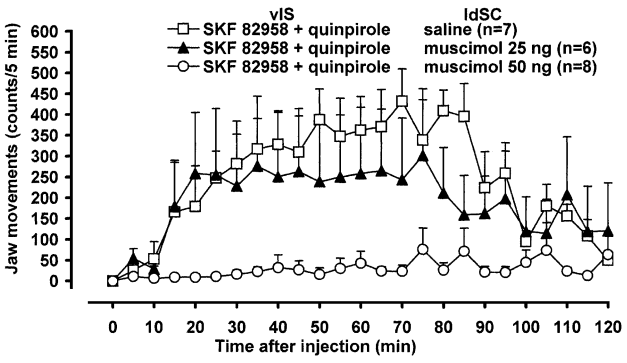

Fig. 6. Effects of muscimol (25 and 50 ng per side) injection into the lateral deeper layers of the superior colliculus in a coronal section at A 3.0 on production of jaw movements induced by the mixture of SKF 82958 (5 μg) and quinpirole (10 μg) given into the ventrolateral striatum. The data are expressed as the mean number of jaw movements occurring in 5-min observation periods ($n=6-8$). Vertical bars indicate S.E.M.

120-min observation period. When given into the superior colliculus, muscimol produced a dose-dependent inhibition of the number of jaw movements elicited by the mixture of SKF 82958 and quinpirole injected into the ventrolateral striatum [overall: $F(2,18)=4.04$, $P<0.05$; 25 ng ($n=6$) vs. control ($n=7$): $P>0.05$; 150 ng ($n=8$) vs. control ($n=7$): $P<0.05$, Dunnett's test] (Fig. 6). However, the pattern of jaw movements and the associated muscle activity were not altered by muscimol.

3.4. Effects of bilateral injections of muscimol into the superior colliculus on jaw movements elicited by administration of carbachol into the ventrolateral striatum

The time-dependent effects of carbachol are shown in Fig. 7. This figure clearly illustrates that the effect started nearly immediately after injection, reached its peak around 10 min and vanished about 30 min after injection. When given into the superior colliculus, muscimol significantly

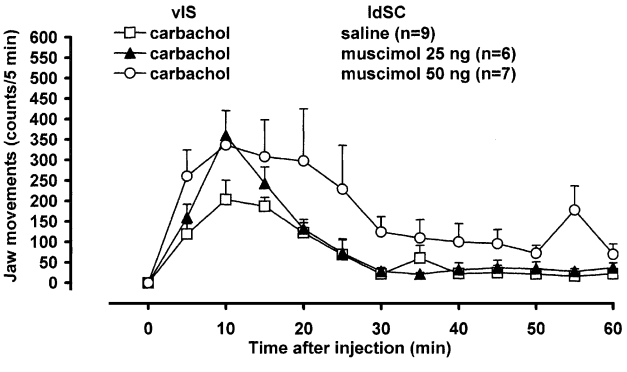

Fig. 7. Effects of muscimol (25 and 50 ng per side) injection into the lateral deeper layers of the superior colliculus in a coronal section at A 3.0 on production of jaw movements induced by carbachol (2.5 μg) given into the ventrolateral striatum. The data are expressed as the mean number of jaw movements occurring in 5-min observation periods ($n=6-9$). Vertical bars indicate S.E.M.

enhanced the number of jaw movements elicited by injections of carbachol into the ventrolateral striatum [overall: $F(2,19)=5.64$, $P<0.05$; 25 ng ($n=6$) vs. control ($n=9$): $P>0.05$; 50 ng ($n=7$) vs. control ($n=9$): $P<0.01$, Dunnett's test] (Fig. 7). However, the pattern of jaw movements and the associated muscle activity were not altered by muscimol.

4. Discussion

The present study demonstrates that bilateral injections of the $GABA_A$ receptor antagonist bicuculline produced characteristic repetitive jaw movements when injected into the superior colliculus. The behavioural response to bicuculline was dose-dependent (Fig. 3), and it was specific for $GABA_A$ receptors, because the $GABA_A$ receptor agonist muscimol inhibited this response (Fig. 5).

There appeared to be a hot spot for the $GABA_A$-receptor-specific response to bicuculline, because the effective injections of 150 ng bicuculline were concentrated in the deeper layers of lateral portion of the superior colliculus at level A 3.0 (Fig. 4). This spot fully matches the target area of the nigro-collicular pathway described by Redgrave et al. (1992), Yasui et al. (1994) and Takada et al. (1994), opening the perspective that the nigro-colliculo-bulbar pathway is involved in the bicuculline-induced jaw movements. Neither the sites adjacent, but 1 mm ventral to the lateral superior colliculus at level A 3.0, nor the sites more anterior of the lateral deeper layers of the superior colliculus (A 3.2–3.4) were sensitive to bicuculline. Because the latter ineffective sites are concentrated in a spot that encompasses the region innervated by the entopedunculo-collicular pathway (cf. Takada et al., 1994), it is suggested that the entopedunculo-colliculo-bulbar pathway is not involved in the control of the bicuculline-induced jaw movements.

As illustrated in Fig. 2, the site-specific and $GABA_A$-receptor-mediated jaw movements are characterised by a dominant digastric activity during jaw opening without any significant change in masseter activity during jaw closing (digastric type), namely a pattern that fully differs from the patterns elicited by stimulation of either dopamine or acetylcholine receptors in the ventrolateral part of the striatum. In view of this data, it is concluded that the superior colliculus is not a station that transmits jaw movements elicited by stimulation of dopamine or acetylcholine receptors in the striatum (see also Jaspers et al., 1989). This conclusion fully fits in with the finding that the ventrolateral portion of the striatum, namely the region that is primarily involved in the control of orofacial movements, funnels its information via striato-entopedunculo-bulbar and striato-nigro-bulbar pathways, but not striato-entopedunculo-colliculo-bulbar and striato-nigro-colliculo-bulbar pathways, to the parvicellular reticular formation (see Introduction).

The mechanism that gives rise to the bicuculline-induced movements is unknown. However, it is evident that removal of the GABAergic inhibitory tone that is exerted by nigro-collicular neurons (cf. Hikosaka and Wurtz, 1985) can disinhibit collicular neurons that terminate in the reticular region around the motor trigeminal nucleus and parvicellular reticular formation of the medulla oblongata (Murray and Coulter, 1982; Redgrave et al., 1990; Yasui et al., 1994), where many premotor neurons for the orofacial motor nuclei are present.

As mentioned in the Introduction, the superior colliculus is hypothesised to modulate jaw movements that are elicited by stimulation of dopamine or acetylcholine receptors in the ventrolateral portion of the striatum, because it sends an excitatory output to the parvicellular reticular formation (Murray and Coulter, 1982; Redgrave et al., 1990; Yasui et al., 1994), namely a region that itself is innervated by striato-entopedunculo-bulbar and striato-nigro-bulbar fibres (see above). The present study shows that muscimol injections into the deeper layers of the superior colliculus inhibited the jaw movements elicited by stimulation of dopamine receptors in the ventrolateral striatum, but enhanced the jaw movements elicited by stimulation of acetylcholine receptors in the ventrolateral part of the striatum. The finding that muscimol inhibited the jaw movements elicited by stimulation of striatal dopamine receptors is understandable in view of the fact that muscimol was given into a collicular spot that sends neurons to a region in the parvicellular reticular formation that itself is innervated by nigral neurons that project to the collicular region under study: thus, muscimol inhibited the colliculo-bulbar input that controls the nigro-bulbar pathway at the level of the parvicellular reticular formation. The finding that muscimol enhanced the jaw movements elicited by stimulation of striatal acetylcholine receptors is less understandable. However, muscimol was given into a collicular spot that does not receive an entopedunculo-collicular input, excluding thereby the possibility that it indirectly influenced the region in the parvicellular reticular formation that receives a direct input of the entopeduncular nucleus. A possible explanation for the effect of muscimol upon the jaw movements elicited by stimulation of striatal acetylcholine receptors might be the following. It is known that the superior colliculus contains an extensive intrinsic circuitry, encompassing interneurons that provide a substrate for mutual inhibition (Behan and Kime, 1996). Given the presence of such a circuitry, it is postulated that muscimol inhibited interneurons that connect the caudal region that receives a nigral input, with the rostral region that receives a entopeduncular input: in this way, muscimol given into the caudal region might have disinhibited the collicular neurons that have their origin in the rostral region and project to the portion in the parvicellular reticular formation that itself is innervated by direct entopeduncular-bulbar neurons. Accordingly, it facilitated the jaw movements elicited by stimulation of striatal acetylcholine receptors. Future research is required to validate this hypothesis. Anyhow, both sets of data clearly reveal that $GABA_A$ receptors in the

superior colliculus do modulate the jaw movements that can be elicited by stimulation of dopamine or acetylcholine receptors in the ventrolateral portion of the striatum.

In conclusion, the present study demonstrates that a $GABA_A$ receptor blockade in a discrete region (A 3.0) of the lateral deeper layers of the superior colliculus elicits a characteristic type of repetitive jaw movements that fully differs from those elicited by stimulation of either dopamine or acetylcholine receptors in the ventrolateral portion of the striatum. Furthermore, evidence is provided that collicular $GABA_A$ receptors control ventrolateral striatum-specific dopamine D1/D2-receptor-mediated and acetylcholine-receptor-mediated jaw movements in an opposite manner: it inhibits the former type of movements, but enhances the latter type of movements.

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