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Role of excitatory amino acids in the direct and indirect presynaptic regulation of dopamine release from nerve terminals of nigrostriatal dopaminergic neurons

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Summary. In vivo experiments carried out in halothane-anaesthetized cats implanted with push-pull cannulae demonstrated that glutamate (GLU) released from corticostriatal fibers triggers the release of dopamine (DA), even in the absence of activity in nigral DA cells. As shown in vitro, using rat striatal slices or synaptosomes or in vivo in the cat, both NMDA and AMPA receptors subtypes are involved in the GLU-induced release of DA. Beside this direct regulation, GLU also exert several indirect facilitatory and inhibitory controls on DA release, particularly through cholinergic and GABAergic striatal neurons. Indeed, as shown by numerous authors, the GLU-evoked release of DA is markedly reduced in the presence of tetrodotoxin, bicuculline or atropine or by previous kainate- or ibotenate-induced lesion of striatum. Differences in the presynaptic regulation of DA release in striosomal and matrix compartments have also been found with NMDA and acetylcholine. The effect of acetylcholine was of shorter duration in the matrix than in the striosomal-enriched areas. Two opposite indirect regulations of DA release could be demonstrated: one is facilitatory and involves nicotinic receptors, the other is inhibitory, involves muscarinic receptors and mediated, at least in the matrix by dynorphin containing neurons. The NMDA-evoked responses are of larger amplitude and more sensitive to tetrodotoxin in the matrix than in the striosomes. In conclusion, GLU released from corticostriatal fibers, is able to control the release of DA from terminals of nigrostriatal neurons through direct facilitatory mechanisms (NMDA and AMPA receptors), but also through indirect facilitatory and inhibitory local circuits involving cholinergic and GABAergic neurons.

Keywords: Amino acids – Excitatory amino acids – Dopamine release – Rat striatal synoptosomes – Presynaptic mechanisms

Introduction

Several interactions between mesencephalic dopamine (DA) neurons and striatal neurons have been demonstrated. Besides electrophysiological studies indicating that DA either inhibits or stimulates the activity of striatal cells (Akaike et al., 1987; Carlson et al., 1987; Hu et al., 1988; Williams et al., 1990), anatomical investigations have shown that, the main target cells of DA neurons are the medium size spiny neurons which represent about 95% of the total population of striatal neurons innervating the substantia nigra and/or the globus pallidus (Bolam, 1984; Gerfen, 1984; Smith and Bolam, 1990). Biochemical evidences have been also obtained for a control by DA cells of striatal neurons rich in GABA and containing either met-enkephalin or tachykinins and dynorphin (Besson et al., 1984; Young et al., 1986; Gerfen et al., 1990; Graybiel, 1990). Moreover, it is well established that the nigro-striatal DA neurons exert a tonic inhibitory presynaptic regulation of acetylcholine (ACh) release from the large cholinergic interneurons (Stadler et al., 1973; Guyenet et al., 1975; Lehmann and Langer, 1983) and interactions between DA cells and somatostatin/NPY interneurons have been also described (Salin et al., 1990a, 1990b). Although this list is not limitative, DA neurons have also been shown to control presynaptically the release (or transport) of GLU (Mitchell and Doggett, 1980; Rowlands and Roberts, 1980; Nieoullon et al., 1982, 1983; Godukin et al., 1984) from nerve terminals of cortical cells innervating monosynaptically striatal output neurons and cholinergic interneurons (Bolam, 1984; Smith and Bolam, 1990).

Reciprocally, striatal interneurons and output neurons (through their collaterals) regulate presynaptically the release of DA either directly through receptors located on DA nerve terminals (tetrodotoxin- (TTX) resistant process) or indirectly through receptors located on non-DA neurons (TTX-sensitive process). Several studies made in vitro on slices and occasionally on synaptosomes from the rat striatum have revealed indeed that most transmitters found in the striatum regulate presynaptically either directly or indirectly the release of DA (Chesselet et al., 1984). This applies as well to GLU which as shown first in vitro, stimulates the release of DA through a TTX-resistant process, this effect being antagonized by diethyl ester glutamic acid and reproduced by kainic acid and several other excitatory amino acids (Giorguieff et al., 1977a; Roberts and Sharif, 1978; Roberts and Anderson, 1979).

In the present review, we will discuss briefly data indicating that: 1) cortico-striatal GLU neurons facilitate presynaptically the release of DA in halothane-anaesthetized cats; 2) receptors of the quisqualate/kainate and NMDA subtypes are involved in the direct TTX-resistant facilitatory effect of GLU on DA release as shown both in vivo in the cat and in vitro in the rat; 3) apart from its direct presynaptic control of DA release, GLU exerts also indirect effects on DA release through local circuits; 4) as observed particularly with NMDA and ACh, differences exist in the presynaptic control of DA release in striatal striosomal and matrix areas.

Role of the cortico-striatal glutamatergic projection in the presynaptic control of DA release in the cat caudate nucleus

Evidence in favor of the intervention of cortico-striatal glutamatergic neurons in the presynaptic control of DA transmission was obtained in halothane-anaesthetized cats implanted with push-pull cannulae by examining the local effects of GLU and the influence of direct or indirect activation of cortico-striatal glutamatergic neurons.

Confirming in vitro observations, when applied locally into the caudate nucleus, GLU stimulated the release of newly synthesized ^{3}H-DA through a calcium-dependent and TTX-resistant process. This effect was seen with a concentration as low as 10^{-8} M and was found concentration-dependent in the presence of TTX (Chéramy et al., 1986) (Fig. 2).

The unilateral electrical stimulation of the peri-cruciate cortex (Nieoullon et al., 1978) and the application of GABA (10^{-5} M) into thalamic motor nuclei (Romo et al., 1984) induced a marked and prolonged increase in the release of DA (Fig. 1). These effects were seen in both caudate nuclei and contralateral responses were prevented by acute section of the corpus callosum. Confirming that the cortico-striatal neurons are activated by the application of GABA (10^{-5} M) into thalamic motor nuclei (as expected GABA 10^{-3} M inhibited the activity of thalamic cells), parallel bilateral increases in GLU release were observed in caudate nuclei and the contralateral response was also abolished by the acute section of the corpus callosum (Barbeito et al., 1989). The stimulatory effects on DA release of either GLU or activation of the thalamo-cortico-striatal loop were antagonized by the local application of PK 26124 (a compound which prevents glutamatergic transmission) into the caudate nucleus (Chéramy et al., 1986; Romo et al., 1986b). This treatment also antagonized the stimulatory effect on DA release in the ipsilateral caudate nucleus of the nigral application of substance P (Fig. 1) but not of neurokinin A (NKA) (Baruch et al., 1988). These observations suggest that the two tachykinins released from striato-nigral neurons act by two distinct processes, NKA stimulating the activity of nigral DA cells and substance P activating a nigro-thalamo-cortico-striatal neuronal loop also involved in the presynaptic control of DA release. Confirming these statements, similar results were obtained in the rat by Ungerstedt and his colleagues (Reid et al., 1991a, 1991b). In addition, these authors reported that the nigral application of substance P (but not that of NKA) stimulates the release of GLU in the ipsilateral striatum (Reid et al., 1991b).

Two other observations indicated that the changes in DA release evoked by the activation of the thalamo-cortical-striatal loop are due to presynaptic processes and not to modifications of the firing rate of DA cells: 1) as determined simultaneously by extracellular recording of nigral identified DA neurons, changes in DA release evoked by the unilateral application of GABA (10^{-5} M) into thalamic motor nuclei occurred in spite of an inhibition of the firing rate of DA cells (Romo et al., 1986a); 2) this evoked release of DA was still observed ipsilaterally following the acute transection of the nigro-striatal DA pathway, a procedure which decreases markedly the spontaneous release of DA by interrupting the propagation of nerve impulse flow (Romo et al., 1986a).

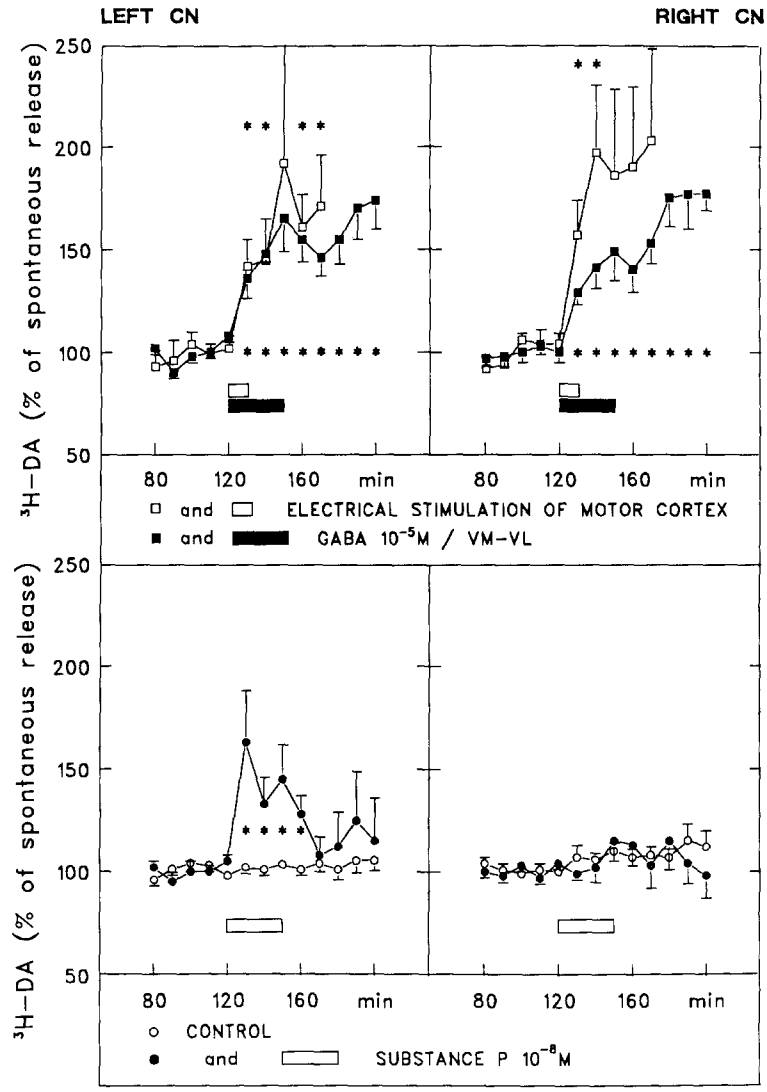

Fig. 1. In vivo effects of various unilateral treatments on the release of ^{3}H-dopamine in both caudate nuclei of the cat. In halothane-anaesthetized cats, an artificial CSF containing ^{3}H-tyrosine was delivered continuously to push-pull cannulae implanted into the left and right caudate nuclei (*CN*). ^{3}H-dopamine (^{3}*H-DA*) was estimated in successive 10 min superfusate fractions. Upper panels, open squares: Effect of the electrical stimulation of the left motor cortex performed through a pair of electrodes using trains of square pulses (train duration: 100 msec; shock duration: 0.5 msec; shock frequency: 300 Hz; train frequency: 0.2 Hz; 4–6V) during 10 min (open bars) (5 animals). Upper panels, closed squares: Effect of the application of GABA (10^{-5} M, 30 min, hatched box) made through a third push-pull cannula inserted into the left ventralis medialis or ventralis lateralis (*VM-VL*) thalamic nuclei (6 animals). Lower panels, closed circles; Effect of the application of substance P (10^{-8} M, 30 min, hatched box) made through a third push-pull cannula inserted into the left substantia nigra (7 animals). Individual data were expressed as a percentage of the average spontaneous release calculated from the 5 fractions collected before the treatment. Results are the mean ± SEM of data obtained in groups of N animals. $^*p < 0.05$ when compared to corresponding control experiments (lower panels, open circles, $N = 7$)

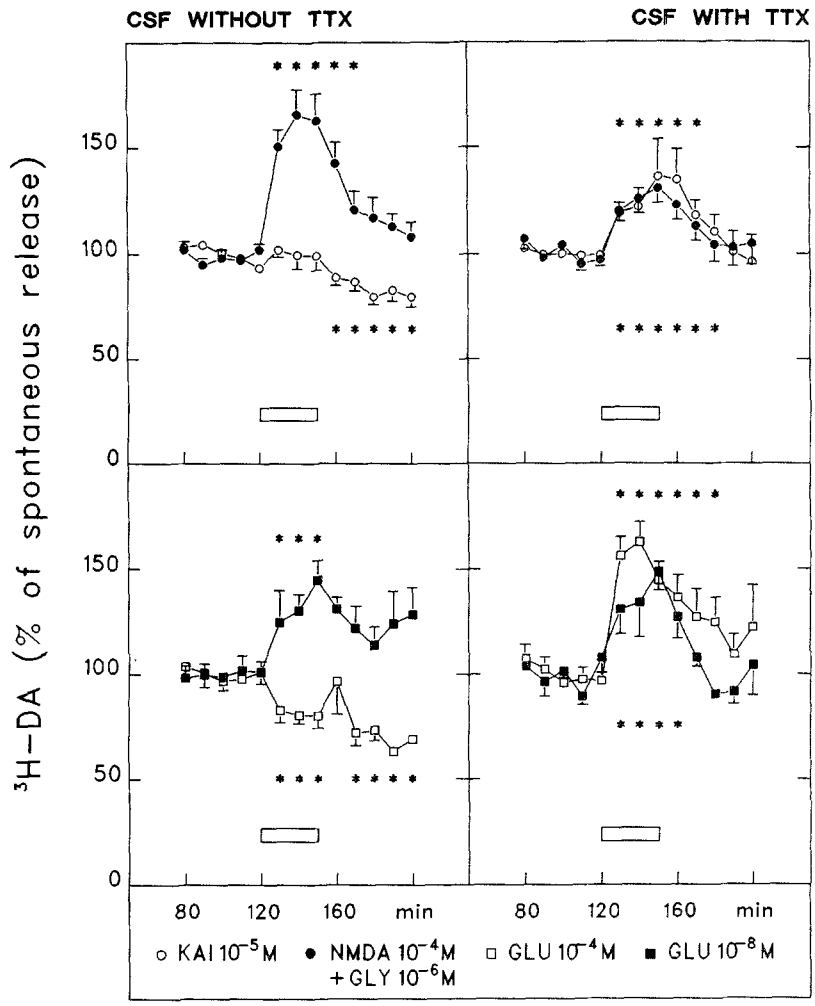

Fig. 2. In vivo effects of the local application of kainate, N-methyl-D-aspartate and glutamate in the absence or presence of tetrodotoxin on the release of ^{3}H-dopamine in the cat caudate nucleus. An artifical CSF containing ^{3}H-tyrosine without (left panels) or with (right panels) tetrodotoxin (*TTX*, 10^{-6} M) was delivered continuously through a push-pull cannula implanted into the left caudate nucleus. ^{3}H-dopamine (*^{3}H-DA*) was estimated in 10 min fractions of superfusates. Either kainate (*KAI*, 10^{-5} M) or N-methyl-D-aspartate (*NMDA*, 10^{-4} M) plus glycine (*GLY*, 10^{-6} M) or L-glutamate (*GLU*, 10^{-4} M or 10^{-8} M) were added for 30 min into the CSF delivered to the caudate nucleus, 2 hours after the onset of superfusion. In experiments in which NMDA was tested, the CSF was magnesium-free and contained also strychnine (10^{-6} M). Results are expressed as a percentage of the average spontaneous release estimated before the drug application. The mean ± SEM of data obtained in the absence or presence of TTX, from respectively 8, and 10 KAI-treated, 15 and 14 NMDA-treated, 4 and 8 GLU 10^{-4} M, 7 and 4 GLU 10^{-8} M-treated animals were calculated. *$p < 0.05$ when compared to corresponding control animals (not shown)

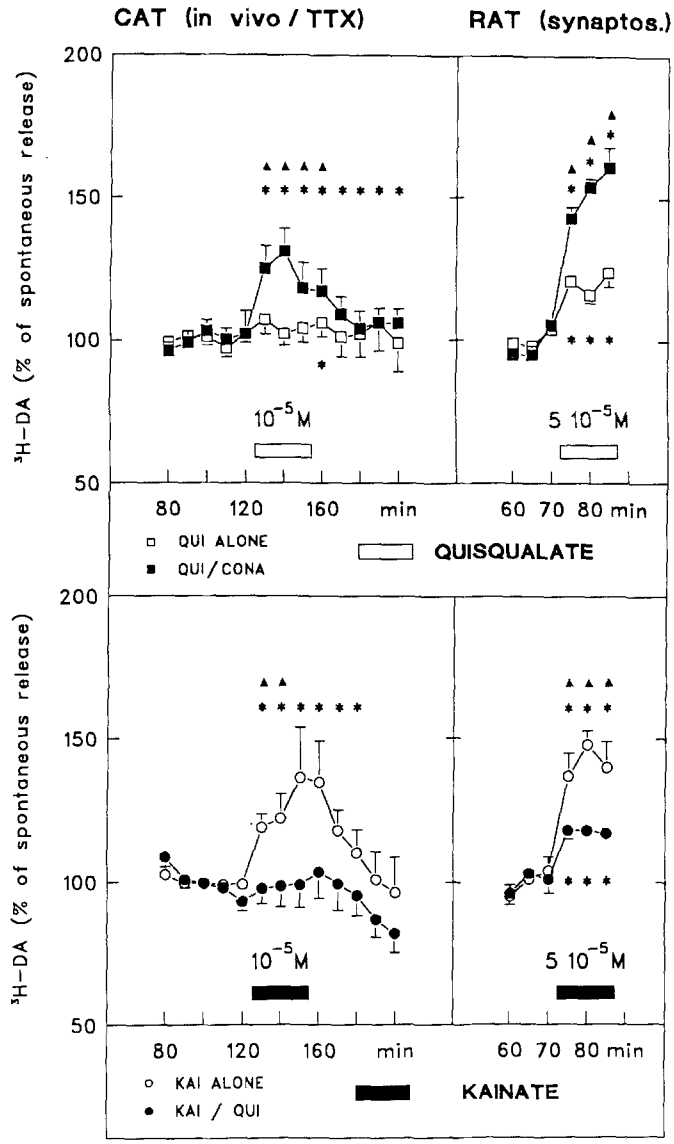

Fig. 3. Desensitization by quisqualate of the quisqualate/kainate receptors involved in the direct presynaptic regulation of ^{3}H-dopamine release. Experiments were performed either in vivo (left panels) in the cat caudate nucleus as described in fig. 1, using a push-pull cannula supplied with a TTX containing CSF or in vitro (right panels) using rat striatal synaptosomes prepared on Percoll gradients. In both cases, the artificial CSF was enriched in ^{3}H-tyrosine. ^{3}H-dopamine (^{3}*H-DA*) was estimated in 10 min (cat) or 5 min (rat) fractions of superfusates

Upper Panels: Effects on the release of ^{3}H-DA of the local application of quisqualate (*QUI*, open box, 10^{-5} M, 30 min in vivo or 10^{-5} M, 15 min in vitro) in the absence (open squares) or presence (closed squares) of concanavalin A (*CONA*, 10^{-7} M delivered continuously during all the experiment). Results are expressed as a percentage of the average spontaneous release estimated before QUI application. The mean ± SEM of individual data obtained in the absence or presence of CONA, from respectively 11 and 11 (in vivo) or 4 and 6 (in vitro) experiments were calculated. $*p < 0.05$ when compared to corresponding control experiments with TTX, but without or with CONA, not shown). Black triangles: $*p < 0.05$ when data obtained with CONA were compared to corresponding data obtained without CONA

Finally, there is some evidence indicating that the cortico-striatal neurons involved in the presynaptic control of DA release contain GLU but not aspartate. For instance, the release of GLU but not that of aspartate was enhanced in the striatum following either the application of GABA (10^{-5} M) into thalamic motor nuclei of the cat (Barbeito et al., 1989) or the nigral application of substance P in the rat (Reid et al., 1990a). In addition, the electrical stimulation of the substantia nigra in the rat enhanced selectively the release of GLU in the striatum and this response was abolished in animals with an electrolytic lesion of the ventralis medialis (VM) thalamic nucleus (Girault et al., 1986).

Kainate/quisqualate and NMDA receptors are involved in the direct presynaptic control of DA release by cortico-striatal glutamatergic fibers

In the in vivo cat preparation, as observed with GLU, a TTX-resistant evoked release of DA was seen also with kainate (10^{-5} M) (Fig. 2) but not quisqualate (10^{-5} M) (Barbeito et al., 1990) (Fig. 3). The stimulatory effects of GLU and kainate were both antagonized not only with PK 26124 (Riluzole) (10^{-5} M) but also with glutamate diethyl ester (10^{-5} M) or gamma-D-glutamyl-glycine (10^{-5} M) (Barbeito et al., 1990). Quisqualate seems to desensitize rapidly the kainate-sensitive receptors. Indeed, concanavalin A, a lectin which prevents the quisqualate-induced desensitization of GLU receptors on striatal neurons in primary culture (Pin et al., 1989) allowed the detection of the quisqualate excitatory effect on DA release (Barbeito et al., 1990) (Fig. 3). In addition, in the absence of concanavalin A, prior application of quisqualate (10^{-5} M) prevented the TTX-resistant stimulatory effects on DA release of both GLU (10^{-4} M) and kainate (10^{-5} M) (Barbeito et al., 1990) (Fig. 3). Confirming the existence of receptors of the quisqualate/kainate subtype (AMPA receptors) on DA nerve terminals, similar results have been also recently observed on purified synaptosomes from the rat striatum (Fig. 3) (Desce et al., 1991).

A part from quisqualate/kainate receptors, NMDA receptors are also involved in the presynaptic control of DA release. Using a new superfusion procedure allowing the estimation of the release of newly synthesized ^{3}H-DA in discrete areas of rat striatal slices we have shown indeed that NMDA (5×10^{-5} M) stimulates the release of ^{3}H-DA in the absence of Mg^{2+} and that this response is blocked by adding either Mg^{2+} or MK 801, the well known powerful antagonist of NMDA receptors (Krebs et al., 1989). In addition, the NMDA-evoked release of ^{3}H-DA was potentiated by glycine (10^{-6} M) acting on strych-

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Lower panels: Effects on the release of ^{3}H-DA of the local application of kainate (*KAI*, hatched box, 10^{-5} M, 30 min in vivo or 10^{-5} M, 15 min in vitro) in the absence (open circles) or presence (closed circles) of QUI (10^{-5} M delivered continuously starting 15 min before the KAI treatment). Results are expressed as a percentage of the average spontaneous release estimated before KAI application. The mean ± SEM of individual data obtained in the absence or presence of QUI, from respectively 10 and 8 (in vivo) or 4 and 4 (in vitro) experiments were calculated. *$p < 0.05$ when compared to corresponding control experiments with TTX, but without or with QUI, not shown). Black triangles: $p < 0.05$ when data obtained with QUI were compared to corresponding data obtained without QUI

nine-resistant sites and this potentiation was reversed by kynurenate (Krebs et al., 1989). Part of the NMDA receptors involved in the presynaptic regulation of DA release are located on DA nerve terminals since, in agreement with data obtained by other workers (Roberts and Anderson, 1979; Snell and Johnson, 1987; Clow and Jhamandas, 1989), NMDA-evoked responses could be observed in both the presence or absence of TTX. Confirming this statement, the stimulatory effect of NMDA on DA release, its potentiation by glycine and its blockade by either Mg^{2+} or MK 801 were also shown on purified synaptosomes from the rat striatum (Krebs et al., 1990a).

In the absence of Mg^{2+} and the presence of both glycine and strychnine, a high concentration of NMDA (10^{-4} M) stimulated also the in vivo release of ^{3}H-DA in the cat caudate nucleus and this response was seen both in the presence or absence of TTX (Galli et al., 1990). It remains to determine whether, besides quisqualate/kainate receptors, NMDA receptors contribute as well to the facilitation of DA release resulting from the direct or indirect activation of cortico-striatal glutamatergic neurons.

Indirect presynaptic modulation of DA release by glutamate and some other excitatory amino acids

Preliminary evidence for the existence of an indirect presynaptic regulation of DA release by either GLU or agonists of GLU receptors were obtained in vivo in the cat. In the absence of TTX, when used in high concentration (10^{-4} M), GLU decreased the spontaneous release of ^{3}H-DA (Chéramy et al., 1986). This effect was prevented by PK 26124 (Riluzole) but more interestingly by bicuculline. Therefore, GABA containing neurons seem to be involved in this indirect inhibitory control of DA transmission. This is not surprising since the medium size spiny GABA containing neurons, the main target cells of the cortico-striatal glutamatergic neurons, possess numerous collaterals. In contrast to that observed in the presence of TTX, as GLU, kainate (10^{-5} M) did not stimulate the release of ^{3}H-DA release but exerted a slight inhibitory effect (Fig. 2) (Barbeito et al., 1990). These results differ from those obtained with NMDA since, as already indicated, ^{3}H-DA release is stimulated by a high concentration of NMDA (10^{-4} M) (in the absence of Mg^{2+}) in the presence or absence of TTX, this response being even of larger amplitude in the latter case (Galli et al., 1990) (Fig. 2). Although this has to be further explored, these results already suggest that a population of NMDA receptors implicated in the indirect presynaptic regulation of DA release are located on cells which do not possess kainate/quisqualate receptors. These neurons could be the striatal cholinergic neurons since, as discussed below, ACh facilitates presynaptically the release of DA through a direct process (Giorguieff et al., 1976, 1977b).

Differences in the presynaptic regulation of DA release in striosomal and matrix compartments as shown with NMDA and acetylcholine

Striatal compartments can be distinguished not only by their content in several biochemical markers but also by their afferent fibers and efferent neurons

(Gerfen and Young, 1988; Gerfen, 1989; Graybiel, 1990). In addition, studies made in the cat and the rat have indicated that distinct populations of DA neurons innervate these compartments (Gerfen et al., 1987; Jimenez-Castellanos and Graybiel, 1987). Indeed, although a large population of cells from the A9 group project to both compartments, those located in the so-called denso-cellular zone of the pars compacta innervate selectively the striosomes. In addition, the matrix receives projections from the A10 and A8 DA cell groups. These important anatomical findings led us to look for the eventual existence of differences in the presynaptic control of DA release in these two striatal compartments. Using acetylcholinesterase (AChE) staining as a marker of the matrix in the cat, and ^{3}H-naloxone binding for the autoradiographic visualization of striosomes in the rat, striosomes maps were made in the striatum of both species on sagittal as well as on frontal sections. Thanks to these maps, a tridimensional reconstruction of the striosomal compartment could be made in the cat (Desban et al., 1989) and in addition a good reproducibility of the localization of a large proportion of striosomal areas was found. This allowed us to device a new in vitro superfusion procedure with which the release of newly synthesized ^{3}H-DA can be studied in striosomal or matrix enriched areas of small sizes (Kemel et al., 1989).

Using this sensitive approach either on frontal or sagittal brain sections, the effects of ACh and NMDA on DA release were compared in both striatal compartments either in the cat (ACh) (Kemel et al., 1989) or in the rat (NMDA) (Krebs et al., 1989) (Fig. 4). These agonists were selected for several reasons: 1) the striosomes are particularly rich in muscarinic (M1) receptors (Nastuk and Graybiel, 1988); 2) the cell bodies of the large cholinergic interneurons are mainly located in the matrix and it has been suggested that these neurons which send some of their neurites in striosomes could contribute to the transfer of signals from one compartment to the other (Graybiel et al., 1986); 3) although cortico-striatal glutamatergic neurons project to both compartments, cholinergic neurons present in the matrix are rich in NMDA receptors (Scatton and Lehmann, 1982; Lehmann and Langer, 1983); 4) as already indicated (Krebs et al., 1990a) and also found by others (Roberts and Anderson, 1979; Snell and Johnson, 1987; Carter et al., 1988; Clow and Jhamandas, 1989) the TTX-sensitive component of the NMDA-evoked release of DA is relatively important suggesting important indirect effects. We will briefly summarize our main findings which have been recently described elsewhere (Kemel et al., 1989; Krebs et al., 1989; Gauchy et al., 1991).

Experiments made in the presence of TTX have revealed first that ACh and NMDA (in the absence of Mg^{2+} and the presence of strychnine) stimulate the release of ^{3}H-DA in both striosomal-and matrix-enriched superfused areas, the effects of each agonist being of similar amplitude and duration in both compartments (Fig 4). As indicated by experiments made with atropine, the cholinergic receptors involved in the TTX-resistant ACh-evoked responses are muscarinic (Kemel et al., 1989). On the other hand NMDA-evoked responses are mediated in all cases by receptors exhibiting classical pharmacological characteristics of the NMDA type (Krebs et al., 1989). On these basis, it can be already concluded that in both compartments, DA nerve terminals possess muscarinic

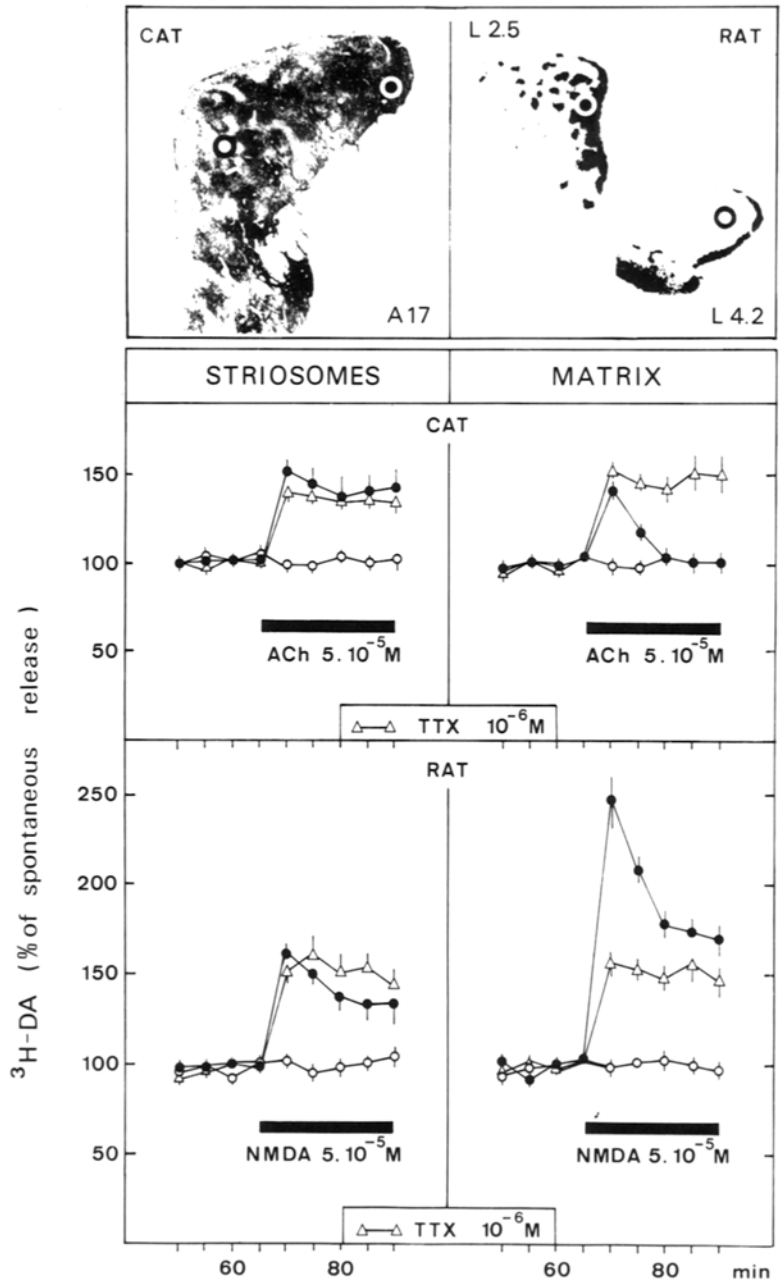

Fig. 4. Tetrodotoxin-sensitive and insensitive effects of ACH and NMDA on ^{3}H-DA release in striosomal- and matrix-enriched area. Frontal or sagittal brain slices (1 mm thick) from the rat striatum or the cat caudate nucleus were kept in physiological conditions in a specially designed superfusion chamber. Selected areas corresponding to striosomal- and matrix-enriched zones were superfused using micro-superfusion devices and the release of ^{3}H-DA continuously synthesized from ^{3}H-tyrosine was estimated in successive 5 min fractions. ACh or NMDA (5×10^{-5} M) were applied 65 min after the onset of superfusion with ^{3}H-tyrosine. When applied, TTX (10^{-6} M) was added into the superfusion medium from the beginning of the experiment. Results correspond to the mean $\pm$ SEM ($N = 7$ to 11) of individual values expressed as a percentage of the mean spontaneous release of ^{3}H-DA determined in the four fractions preceding the application of either NMDA or ACh. In all cases, NMDA- and

and NMDA receptors involved in the presynaptic control of DA release. However, since each compartment is innervated by heterogeneous populations of DA fibers we cannot be sure that all DA fibers in each compartment possess these two types of receptors.

Contrasting with previous results, important differences between the two compartments were seen in the presynaptic regulation of DA when experiments were made in the absence of TTX (Fig. 4). These differences indicate that local circuits play a much more important role in the presynaptic control of DA transmission in the matrix. For instance, in this condition, the ACh-evoked release of DA was of short duration in the matrix but not in the striosomal-enriched areas of the cat caudate nucleus (Fig. 4) (Kemel et al., 1989). In addition, as revealed by experiments made with either atropine or pempidine or both types of cholinergic antagonists, two opposite indirect regulations of DA release triggered by ACh could be selectively demonstrated in the matrix. One is facilitatory and involves nicotinic receptors located on yet unidentified neurons. The other which seems more prominent is inhibitory and mediated by muscarinic receptors (Kemel et al., 1989). Complementary data indicated that the ACh-evoked inhibitory response is mediated by dynorphine-containing neurons at least in the matrix area superfused (Gauchy et al., 1991). As far as NMDA-evoked responses are concerned, the stimulatory effect of NMDA on DA release in the rat striatum was of much larger amplitude in the matrix than in the striosomes (Krebs et al., 1990b), these marked differences being still observed when NMDA-evoked responses were potentiated by added glycine (Fig. 4) (Krebs et al., 1989). In other words, the TTX-sensitive component of the NMDA-evoked response was much more important in the matrix. We have yet no indication on the identity of the neurons responsible for this indirect stimulatory effect of NMDA.

Although caution must be taken in the interpretation of results based on data obtained in different species, the TTX-sensitive component of the NMDA-evoked responses occurring in the matrix seems not to involve the cholinergic neurons. Indeed, as discussed previously ACh exerts a powerful indirect inhibitory effect on DA release. Complementary experiments are in progress using both cat and rat striatal slices in order to verify this hypothesis. In any case, these results which provide for the first time indications about functional processes

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ACh-evoked responses observed in the presence or absence of TTX were significantly different from respective controls (○) $*p < 0.05$, effect of ACh or NMDA (−) when compared to the effect of the agonists in the presence of TTX (⇌). The upper part of the figure illustrates the localizations of the superfused areas (black or white circles) in the cat and the rat. In the cat experiments, the schematic drawing of the superfusion sites was superposed to the histochemical visualization of AChE activity in coronal sections (50 mm thickness) of cat caudate nucleus. The superfusions were performed in a prominent striosomal area (AChE poor zone, in clear) and in the matrix (AChE rich zone, in dark) located in the core and in the lateral corner of the caudate nucleus respectively. In the rat, the striosomes (dark) and the matrix (clear) were identified using ^{3}H-naloxone binding performed on sagittal brain sections (20 μm thickness). The striosomal- and matrix-enriched areas superfused were located respectively in the antero-medial part and in the lateral border of the striatum

operating in striatal compartments reveal the complexity of the local circuits responsible for the control of DA transmission. They also further extend the notion previously discussed that as a result of these presynaptic regulations, and depending on their localization (striosomes or matrix), DA fibers may operate in certain conditions as independent functional units (Glowinski and Chéramy, 1981). This concept should be taken into consideration for understanding further the role of DA neurons in the control of signals delivered and emerging from the striatum, the main input structure of the basal ganglia.

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References

Akaike A, Ohno Y, Sasa M, Takaori S (1987) Brain Res 418: 262–272
Barbeito L, Chéramy A, Godeheu G, Desce JM, Glowinski J (1990) Europ J Neurosci 2: 304–311
Barbeito L, Girault JA, Godeheu G, Pittaluga A, Glowinski J, Chéramy A (1989) Neuroscience 28: 365–374
Baruch P, Artaud F, Godeheu G, Barbeito L, Glowinski J, Chéramy A (1988) Neuroscience 25: 889–898
Besson MJ, Girault JA, Truong NA, Glowinski J, Savaki HE (1984) Clin Neuropharmacol 7: 380–381
Bolam JP (1984) Synapses of identified neurons in the neostriatum. In: Evered D, O'Connor M (eds) Functions of the basal ganglia. Pitman, London, pp 30–47
Carlson JH, Bergstrom DA, Walters JR (1987) Brain Res 400: 205–218
Carter CJ, L'Heureux R, Scatton B (1988) J Neurochem 51: 462–468
Chesselet MF (1984) Neuroscience 12: 347–375
Chéramy A, Romo R, Godeheu G, Baruch P, Glowinski J (1986) Neuroscience 19: 1081–1090
Clow DW, Jhamandas K (1989) J Pharmacol Exp Ther 248: 722–728
Desban M, Gauchy C, Kemel ML, Besson MJ, Glowinski J (1989) Neuroscience 29: 551–566
Desce JM, Godeheu G, Galli T, Artaud F, Chéramy A, Glowinski J (1991) J Pharmacol Exp Ther (in press)
Galli T, Godeheu G, Artaud F, Desce JM, Pittaluga A, Barbeito L, Glowinski J, Chéramy A (1991) Neuroscience 42: 19–28
Gauchy C, Des ban M, Krebs MO, Glowinski J, Kemel ML (1991) Neuroscience (in press)
Gerfen CR (1984) Nature 311: 461–463
Gerfen CR (1989) Science 246: 385–388
Gerfen CR, Engber TM, Mahan LC, Susel Z, Chase TN, Monsma FJ, Sibley DR (1990) Science 250: 1429–1432
Gerfen CR, Herkenham M, Thibault J (1987) J Neuroscience 7: 3915–3934
Gerfen CR, Young S (1988) Brain Res 460: 161–167
Giorguieff MF, Kemel ML, Glowinski J (1977a) Neurosci Lett 6: 73–77
Giorguieff MF, Le Floch ML, Glowinski J, Besson MJ (1977b) J Pharmacol Exp Ther 200: 535–544
Giorguieff MF, Le Floch ML, Westfall TC, Glowinski J, Besson MJ (1976) Brain Res 106: 117–131
Girault JA, Spampinato U, Desban M, Glowinski J, Besson MJ (1986) Brain Res 374: 362–366

Glowinski J, Chéramy A (1981) Dendritic release of dopamine: its role in the substantia nigra. In: Stjarne L, Hedqvist P, Lagercrantz H, Wennmalm A (eds) Chemical neurotransmission, 75 years. Academic Press, London, pp 284–299
Godukhin OV, Zharikova AD, Budantsev AY (1984) Neuroscience 12: 377–383
Graybiel AM (1990) TINS 13: 244–254
Graybiel AM, Baugham RW, Eckenstein F (1986) Nature 323: 625–627
Guyenet PG, Agid Y, Javoy F, Beaujouan JC, Rossier J, Glowinski J (1975) Brain Res 84: 227–244
Hu XT, Wang RY (1988) J Neurosci 8: 4340–4348
Jimenez-Castellanos J, Graybiel AM (1987) Neuroscience 23: 223–242
Kemel ML, Desban M, Glowinski J, Gauchy C (1989) Proc Nat Acad Sci (USA) 86: 9006–9010
Krebs MO, Desce JM, Kemel ML, Gauchy C, Godeheu G, Chéramy A, Glowinski J (1991a) J Neurochem 56: 81–85
Krebs MO, Kemel ML, Gauchy C, Desban M, Glowinski J (1989) Europ J Pharmacol 166: 567–570
Krebs MO, Trovero F, Desban M, Gauchy C, Glowinski J, Kemel ML (1991b) J Neurochem (in press)
Lehmann J, Langer SZ (1983) Neuroscience 10: 1105–1120
Mitchell PR, Doggett NS (1980) Life Sci 26: 2073–2081
Nastuk MA, Graybiel AM (1988) J Neurosci 8: 1052–1062
Nieoullon A, Chéramy A, Glowinski J (1978) Brain Res 145: 69–83
Nieoullon A, Kerkerian L, Dusticier N (1982) Life 30: 1165–1172
Nieoullon A, Kerkerian L, Dusticier N (1983) Neurosci Lett 43: 191–196
Pin JP, Van Vliet BJ, Bockaert J (1989) Europ J Pharmacol 172: 81–91
Reid MS, Herrera-Marschitz M, Kehr J, Ungerstedt U (1991a) Acta Physiol Scand (in press)
Reid MS, Herrera-Marschitz M, Ungerstedt U (1991b) Neuroscience (in press)
Roberts PJ, Anderson SD (1979) J Neurochem 32: 1539–1545
Roberts PJ, Sharif NA (1978) Brain Res 157: 391–395
Romo R, Chéramy A, Godeheu G, Glowinski J (1984) Brain Res 308: 43–52
Romo R, Chéramy A, Godeheu G, Glowinski J (1986a) Neuroscience 19: 1067–1079
Romo R, Chéramy A, Godeheu G, Glowinski J (1986b) Neuroscience 19: 1091–1099
Rowlands GJ, Roberts PJ (1980) Europ J Pharmacol 62: 241–242
Salin P, Kerkerian L, Nieoullon A (1990) Exp Brain Res 81: 363–371
Salin P, Kerkerian-Le Goff L, Heidet V, Epelbaum J, Nieoullon A (1990) Brain Res 521: 23–32
Scatton B, Lehmann J (1982) Nature 297: 422–424
Smith AD, Bolam JP (1990) TINS 13: 259–265
Snell LD, Johnson KM (1986) J Pharmacol Exp Ther 238: 938–946
Stadler H, Lloyd KG, Gadea-Ciria M, Bartholini G (1973) Brain Res 55: 476–480
Williams GV, Millar J (1990) Europ J Neurosci 2: 658–661
Young WS, Bonner TI, Brann MR (1986) Proc Nat Acad Sci (USA) 83: 9827–9831

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