Naunyn-Schmiedeberg's Arch Pharmacol (1993) 347:415–420

Naunyn-Schmiedeberg's
Archives of
Pharmacology

Zona incerta-lateral hypothalamus as an output structure for impulses involved in neuroleptic drug-induced catalepsy

Krystyna Ossowska, Marzena Karcz-Kubicha, Jadwiga Wardas, Agata Krężołek, and Stanisław Wolfarth

Department of Neuropharmacology, Institute of Pharmacology, Polish Academy of Sciences, 12, Smetna Street, PL-31-343 Krakow, Poland

Received August 13, 1992/Accepted December 4, 1992

Summary. Our previous studies showed that the neuronal impulses connected with catalepsy, which have their origin at dopamine D_2 receptors in the ventro-rostral part of the nucleus caudatus-putamen in rats, are conveyed to the zona incerta-lateral hypothalamic region. The aim of the present study was to investigate the route of the neuronal impulses between these structures. The experiments were carried out on rats with cannulae chronically implanted in the brain structures. We showed that (1) bilateral injection of bicuculline methiodide (5–50 ng) into the ventro-medial part of the globus pallidus (GPv) and (2) bilateral injection of muscimol (2.5–25 ng) into the substantia nigra pars reticulata (SNR) inhibit, in a dose dependent manner, the catalepsy induced by sulpiride (1 μg) administered bilaterally into the ventro-rostral part of the nucleus caudatus-putamen. It was also demonstrated that muscimol (25 ng), injected bilaterally into the ventro-medial part of the globus pallidus, induces catalepsy which, in turn, is dose-dependently inhibited by either (1) muscimol (5–25 ng) injected into the substantia nigra pars reticulata, or (2) bicuculline (1.0–2.5 ng) injected into the zona incerta-lateral hypothalamus (ZI-LH). Moreover, even a dose as high as 50 ng of bicuculline, injected into the ventro-medial part of the globus pallidus, had no significant effect on the locomotor activity of rats. On the basis of these results together with anatomical considerations it is concluded that GABA-A receptors in the ventro-medial part of the globus pallidus and substantia nigra pars reticulata successively convey neuronal impulses, pertinent to the neuroleptic drug-induced catalepsy, from the nucleus caudatus-putamen to the zona incerta-lateral hypothalamus.

Key words: Catalepsy – Zona incerta-lateral hypothalamus – Striatum – Globus pallidus – Substantia nigra pars reticulata – Dopamine D_2 receptor – GABA-A receptor

Correspondence to S. Wolfarth at the above address

Introduction

The catalepsy observed in animals after administration of neuroleptic drugs is generally accepted as a laboratory model of the neuroleptic drug-induced parkinsonism in humans. Our previous studies showed that the catalepsy evoked by neuroleptic drugs, injected into the nucleus caudatus-putamen (CP) or peripherally, was dose-dependently inhibited by injections of bicuculline into the zona incerta-lateral hypothalamus (ZI-LH) (Ossowska et al. 1990a, b; Wardas et al. 1988). Moreover, it was shown that muscimol, injected into the zona incerta-lateral hypothalamus, evoked catalepsy in a dose-dependent manner (Wardas et al. 1988). Hence we conclude that the impulses connected with catalepsy, which have their origin at the dopamine D_2 receptors in the ventro-rostral part of the nucleus caudatus-putamen of rats, are conveyed to the zona incerta-lateral hypothalamus. However, it was not known how impulses generated in the striatum reached the zona incerta-lateral hypothalamus. Hence our next task was to investigate the route of the neuronal impulses connected with the appearance of neuroleptic catalepsy from the ventro-rostral part of the nucleus caudatus-putamen to the zona incerta-lateral hypothalamus.

In rats, the nucleus caudatus-putamen has three main GABAergic efferent projections. One projects to the globus pallidus (GP) (Nagy et al. 1978; Staines et al. 1980), one to the nucleus entopeduncularis (EP) (Nagy et al. 1978; Staines et al. 1980) and one to the substantia nigra pars reticulata (SNR) (Araki et al. 1985; Jessel et al. 1978; Nagy et al. 1978; Staines et al. 1980).

All the above mentioned nucleus caudatus-putamen output structures have been suggested to be involved in the catalepsy induced by neuroleptic drugs (Kolasiewicz et al. 1988; Morelli et al. 1981; Ossowska et al. 1984; Scheel-Krüger 1986). These structures have direct and/or indirect projections to the zona incerta-lateral hypothalamus (Parent 1990; Ricardo 1981; Scheel-Krüger 1986; Shammah-Lagnado et al. 1985; Barone et al. 1981).

However, results of in situ hybridization experiments have shown that D_2 dopamine receptors are expressed

predominantly by striatal neurons which utilize GABA as a neurotransmitter and which project to the globus pallidus (Beckstead 1988; Beckstead and Cruz 1986; Beckstead and Kersey 1985; Gerfen et al. 1990; Le Moine et al. 1990). Therefore it is assumed that injections of a substance which specifically inhibits dopamine D_2 receptors in the nucleus caudatus-putamen may predominantly affect those axons which form a striopallidal projection. Moreover, anatomical data suggest that the GABAergic, striopallidal projection originates in rostral parts of the nucleus caudatus-putamen (Nagy et al. 1978; Staines et al. 1980) and we have previously observed catalepsy after injections into the rostral nucleus caudatus-putamen of very low doses of sulpiride (Ossowska et al. 1990a, b), a neuroleptic drug which specifically blocks dopamine D_2 receptors. In contrast, it has been postulated that the neurons of the GABAergic strionigral pathway (on which D_1 receptors are located) originate mainly in the intermediate parts of the nucleus caudatus-putamen (Araki et al. 1985; Jessel et al. 1978; Nagy et al. 1978; Staines et al. 1980).

It is noteworthy that axons of the striopallidal pathway, which start from the ventro-rostral part of the nucleus caudatus-putamen adjacent to the nucleus accumbens, reach the ventro-medial part of the globus pallidus (GPv) (Swanson and Cowan 1975).

The aim of the present study was to find out whether GABAergic receptors of the ventral part of the globus pallidus and substantia nigra pars reticulata successively convey impulses, pertinent to the catalepsy induced by

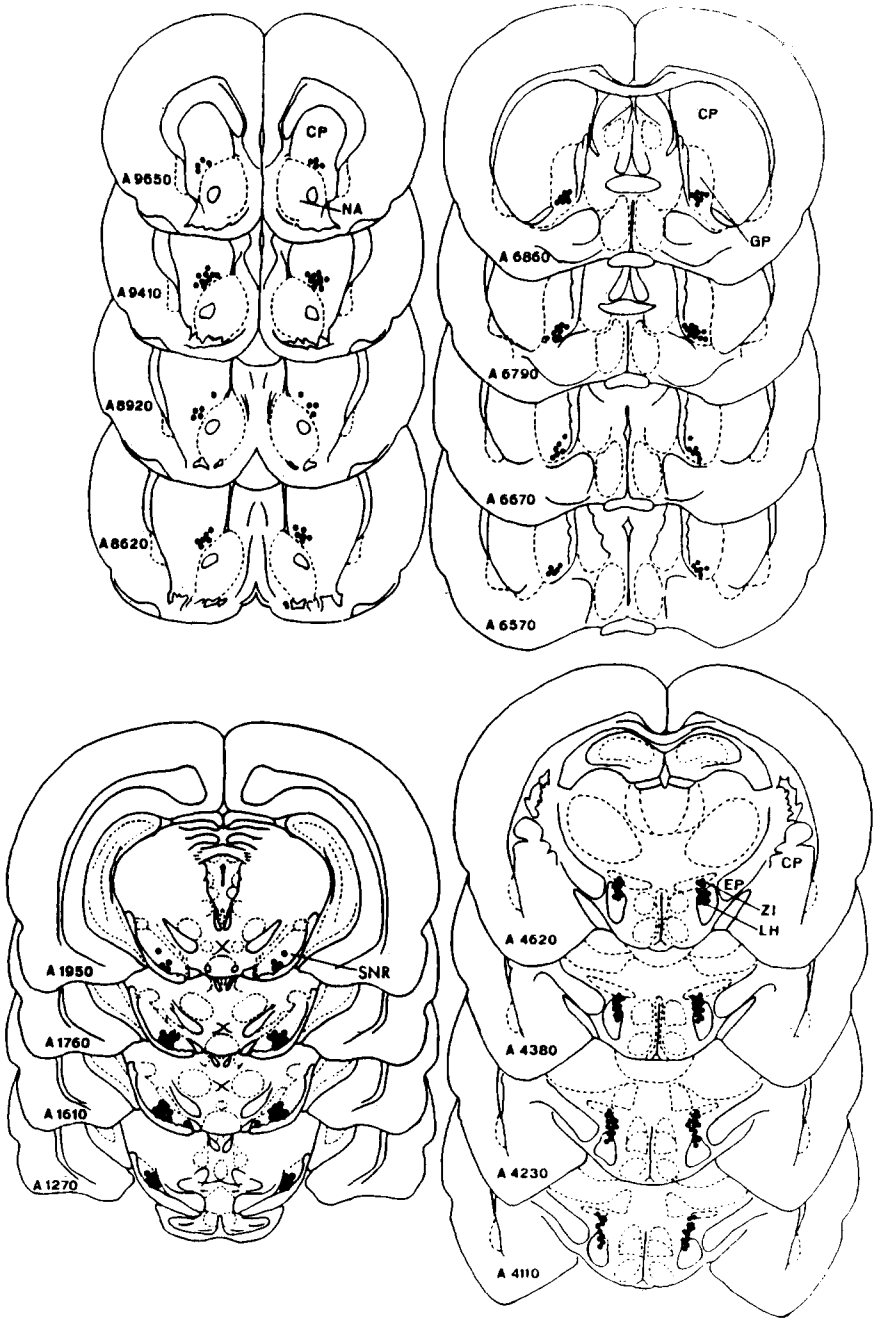

Fig. 1. Localization of cannula tips (*black dots*) on frontal sections of the rat brain numbered according to König and Klippel (1963). *Left upper section*, localization within the nucleus caudatus-putamen (*CP*): note that the cannula tips were located only in the ventro-rostral part of the nucleus caudatus-putamen (*CPvr*). *Right upper section*, localization within the globus pallidus (*GP*): note that the cannula tips were located only in the ventro-medial part of the globus pallidus (*GPv*). *Left lower section*, localization within the substantia nigra pars reticulata (*SNR*). *Right lower section*, localization within the zona incerta-lateral hypothalamus (*ZI-LH*). *A*, Anterior plane; *NA*, nucleus accumbens; *EP*, nucleus entopeduncularis

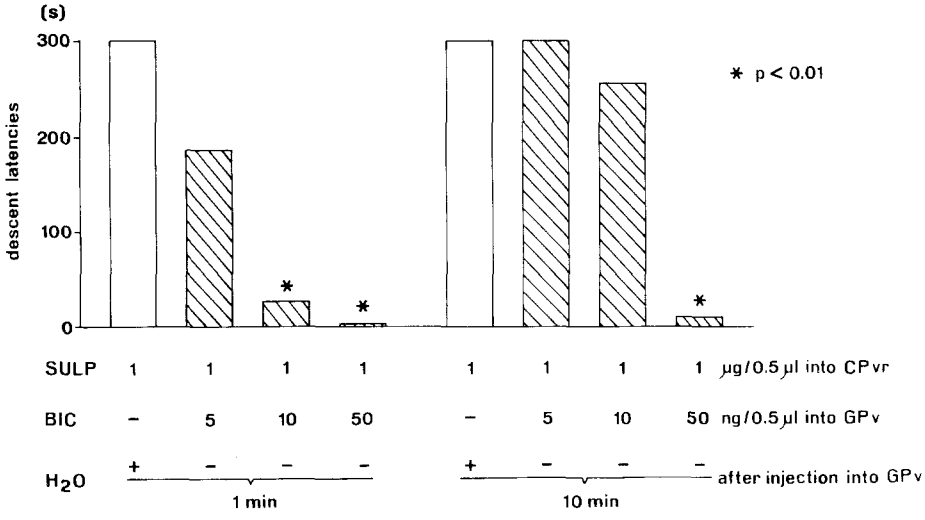

Fig. 2. Inhibition of the catalepsy induced by sulpiride (*SULP;* 1 µg) injected into the ventro-rostral part of the nucleus caudatus-putamen (*CPvr*), by bicuculline methiodide (*BIC*; 5, 10 or 50 ng) administered to the ventral part of the globus pallidus (*GPv*). The catalepsy was measured 1 and 10 min after the injections of bicuculline were completed. SULP was injected 1 h before bicuculline. Numbers of rats used: SULP alone, $n = 10$; BIC 5, $n = 7$; BIC 10, $n = 10$; BIC 50, $n = 10$. *Column heights* show median values. Significance of difference from SULP alone: $^*P < 0.01$ by Kruskal-Wallis and Mann-Whitney U tests

sulpiride, from the ventro-rostral part of the nucleus caudatus-putamen to the zona incerta-lateral hypothalamus.

Methods

The experiments were carried out on male Wistar rats, weighing 250–300 g, which were stereotaxically implanted with stainless steel guide cannulae (0.4 mm o.d.) under pentobarbital (Vetbutal, Poland, 30 mg/kg i.p.) anaesthesia. One week later, bilateral injections were made using inner cannulae (0.3 mm o.d.), which protruded from the end of the guide cannulae by 0.6 mm. The injections were directed, in accordance with König and Klippel (1963), to: (1) the ventro-rostral part of the nucleus caudatus-putamen: A 9410 µ, L 2.5 mm, H −5.5 mm; (2) the ventral part of the globus pallidus: A 6790 µ, L 2.5 mm, H −6.5 mm; (3) the substantia nigra pars reticulata: A 1610 µ, L 2.1 mm, H −2.5 mm; (4) the zona incerta-lateral hypothalamus: A 4620 µ, L 1.3 mm, H −2.3 mm. The following drugs were used for intracerebral injections: (±)sulpiride (base, Sigma, St. Lous, Mo., USA) dissolved in 0.5 µl of 1% lactic acid, muscimol (base, Sigma, St. Louis, Mo., USA) and (−)bicuculline methiodide (Sigma, St. Louis, Mo., USA), dissolved in 0.5 µl of redistilled water. The doses of sulpiride and muscimol used in the study refer to bases, whereas the doses of bicuculline refer to the salt of the drug. Injections, which lasted 2 min, were made simultaneously on both sides, and the injection cannulae were left in place for 1 min afterwards. Each rat was used only once for estimation of either catalepsy or locomotor activity. The catalepsy was assessed by a '9-cm cork test'. The time, up to 300 s, of keeping both forepaws on the cork (descent latency) was measured and median values were calculated. Catalepsy determinations were carried out at different times after the drug injections (see Results). The locomotor activity was measured by two methods: (1) using photoresistor square actometers with two light beams (for a period of 30 min), and (2) by an open field test as described by Janssen et al. (1960). In the Janssen open field test, the rat, after intracerebral injection, was gently placed in the centre of a black circular platform (1 m in diameter) which was divided into 6 symmetrical sectors. During a 5-minute experimental session, the following parameters were estimated: the time spent walking, the number of sectors crossed (ambulation), and the number of episodes of rearing and looking under the edge of the platform (peeping). Results quantifying the locomotor activity are presented as mean values ± SEM. After the experiment, all rats were killed by an overdose of pentobarbital, their brains were removed, and the localization of all of the injection cannula tips was checked histologically (Fig. 1). The statistical evaluation was carried out by the Kruskal-Wallis test, the Mann-Whitney U-test and Student's *t*-test.

Results

The specific antagonist of dopamine D_2 receptors sulpiride, when injected bilaterally, in a dose of 1 µg, into the ventro-rostral part of the nucleus caudatus-putamen, evoked catalepsy. Bicuculline methiodide, a GABA-A antagonist (5–50 ng), administered into the ventro-medial part of the globus pallidus (GPv) 1 h after such an injection of sulpiride, dose-dependently counteracted the catalepsy 1 min after injection (Fig. 2). When the catalepsy was measured 10 min after bicuculline, only the highest dose of this drug was effective (Fig. 2). The GABA-A agonist muscimol (2.5–25 ng), when injected into the substantia nigra pars reticulata 1 h after sulpiride treatment, antagonized the catalepsy in a dose-dependent manner 1, 10 and 20 min after injection (Fig. 3).

Muscimol (25 ng), injected into the ventro-medial part of the globus pallidus, induced catalepsy which was

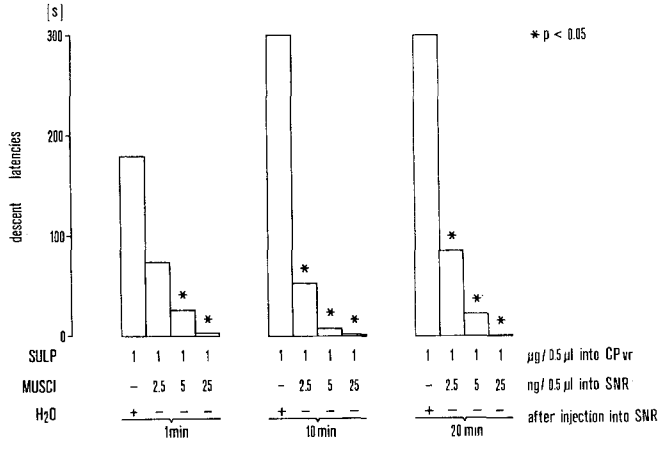

Fig. 3. Inhibition of the catalepsy induced by sulpiride (*SULP;* 1 µg) injected into the ventro-rostral part of the nucleus caudatus-putamen (*CPvr*), by muscimol (*MUSCI*) administered to the substantia nigra pars reticulata (*SNR*). SULP was injected 1 h before MUSCI. Numbers of rats used: SULP alone ($n = 7$), MUSCI 2.5 ($n = 5$), MUSCI 5 ($n = 7$), MUSCI 25 ($n = 3$). *Column heights* show median values. Significance of difference from SULP alone: $^*P < 0.05$ by Kruskal-Wallis and Mann-Whitney U tests

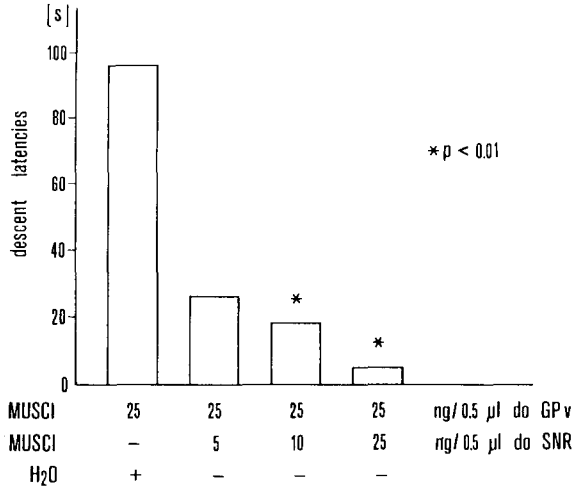

Fig. 4. Inhibition of the catalepsy induced by muscimol (*MUSCI;* 25 ng) injected into the ventral part of the globus pallidus (*GPv*), by muscimol (5, 10 or 25 ng) injected to the substantia nigra pars reticulata (*SNR*). MUSCI was injected simultaneously into both structures. The catalepsy was measured 1 min after the injections were completed. Numbers of rats used: MUSCI into the GPv alone, $n = 6$; MUSCI into the GPv + MUSCI 5 ng into the SNR, $n = 7$; MUSCI into the GPv + MUSCI 10 ng into the SNR, $n = 5$; MUSCI into the GPv + MUSCI 25 ng into the SNR, $n = 4$. *Column heights* show median values. Significance of difference from MUSCI into the GPv alone: $*P < 0.01$ by Kruskal-Wallis and Mann-Whitney U tests

inhibited in a dose-dependent manner either by simultaneous injections of muscimol (5, 10 and 25 ng) into the substantia nigra pars reticulata (Fig. 4), or by prior (3 min earlier) administration of bicuculline (1.0 and 2.5 ng) into the zona incerta-lateral hypothalamus (Fig. 5). Catalepsy was measured 1 min after the injections to both these structures were completed (Fig. 4 and 5).

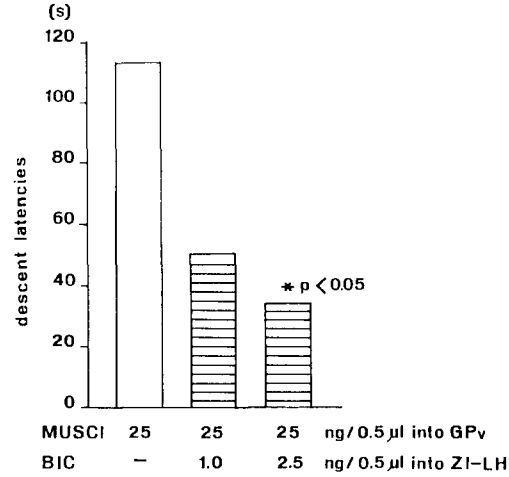

Fig. 5. Inhibition of the catalepsy induced by muscimol (*MUSCI;* 25 ng) injected into the ventral part of the globus pallidus (*GPv*), by bicuculline methiodide (*BIC*; 1.0 or 2.5 ng) injected into the zona incerta-lateral hypothalamus (*ZI-LH*). BIC was injected 3 min before muscimol. Catalepsy was measured 1 min after the injections of muscimol were completed. Numbers of rats used: MUSCI alone ($n = 10$), BIC 1.0 ($n = 6$), BIC 2.5 ($n = 6$). *Column heights* show median values. Significance of difference from MUSCI into the GPv alone: $*P < 0.05$ by Kruskal-Wallis and Mann-Whitney U tests

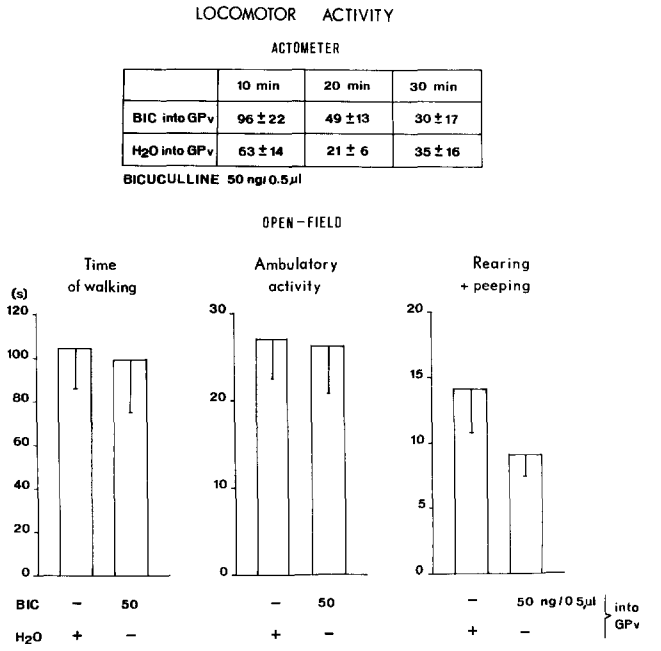

Fig. 6. The effects of bicuculline methiodide (*BIC*; 50 ng) injected into the ventro-medial part of the globus pallidus (*GPv*) on locomotor activity estimated by two light-beam actometers 10, 20 and 30 min after drug injections and in the open field test. The time spent walking is given in seconds (s); the ambulatory activity (assessed as the number of sectors crossed, and rearing and peeping) is given as the sum of the numbers in the respective episodes. Numbers of rats used: $n = 6-7$ for the open field test and 9–12 for the actometer test: note that none of the differences between groups was statistically significant (Student's *t*-test). Results are presented as mean values ± SEM

The locomotor activity, measured in either actometers or the open field test after bicuculline (50 ng) had been injected into the ventro-medial part of the globus pallidus, was not significantly changed (Fig. 6).

Discussion

The results obtained show that impulses pertinent to neuroleptic drug-induced catalepsy, the initiation of which has its origin at the dopamine D_2 receptors of the ventro-rostral part of the caudatus-putamen, are transmitted to the zona incerta-lateral hypothalamus via the ventro-medial part of the globus pallidus and substantia nigra pars reticulata (Fig. 7). It has been shown that (1) inhibition of GABA-A receptors of the ventro-medial part of the globus pallidus, (2) stimulation of GABA-A receptors of the substantia nigra pars reticulata, and (3) inhibition of GABA-A receptors of the zona incerta-lateral hypothalamus (Ossowska et al. 1990b) prevent the downstream flow of impulses which are responsible for the catalepsy induced by sulpiride administered to the ventro-rostral part of the nucleus caudatus-putamen (Fig. 7). It has also been shown that stimulation of GABA-A receptors of the ventro-medial part of the globus pallidus by muscimol opens a pathway for impulses inducing catalepsy which, in turn, is dose-dependently inhibited by (1) muscimol, when used to stimulate GABA-A receptors of the substantia nigra pars reticulata,

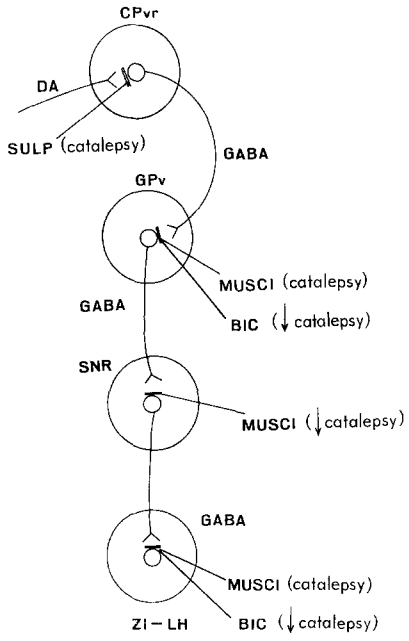

Fig. 7. Neuronal pathways conveying impulses pertinent to catalepsy, from the ventro-rostral part of the caudatus-putamen (*CPvr*) to the zona incerta-lateral hypothalamus (*ZI-LH*) via the ventro-medial part of the globus pallidus (*GPv*) and substantia nigra pars reticulata (*SNR*). Administration of sulpiride (*SULP*) into the CPvr induces catalepsy which is counteracted by injection of bicuculline (*BIC*) into the GPv (present results) or into the ZI-LH (Ossowska et al. 1990b), and by injection of muscimol (*MUSCI*) into the SNR (↓ catalepsy) (present results). Injection of MUSCI into the GPv induces catalepsy which is inhibited by administration of MUSCI into the SNR, or by injection of BIC into the ZI-LH (↓ catalepsy) (present results) MUSCI injected into the ZI-LH induces a dose-dependent catalepsy (Wardas et al. 1988). *DA*, Dopaminergic nigrostriatal pathway; *GABA*, GABAergic pathways or synapses

and (2) bicuculline, when used to inhibit GABA-A receptors within the zona incerta-lateral hypothalamus (Fig. 7). The sulpiride catalepsy was antagonized by doses of bicuculline that do not stimulate locomotor activity (present results, Wardas et al. 1988). This finding proves that the neuronal impulses connected with catalepsy can be specifically inhibited in the globus pallidus and zona incerta-lateral hypothalamus.

The role of GABAergic connections between the nucleus caudatus-putamen and globus pallidus in neuroleptic drug-induced catalepsy has been well documented. Muscimol, when injected into the globus pallidus, induces catalepsy (Matsui and Kamioka 1978; Moroni et al. 1978; Ossowska et al. 1984; Scheel-Krüger 1986; and the present results). Picrotoxin, when injected into the globus pallidus, counteracts catalepsy previously evoked by systemic injections of neuroleptic drugs (Ossowska et al. 1984; Scheel-Krüger 1986). These behavioural data suggest that neuroleptic drugs disinhibit the GABAergic pathway that conveys impulses to the globus pallidus. A similar opinion was expressed by Amalric and Koob (1989), who found that disinhibition of the GABAergic, striopallidal pathway by haloperidol is responsible for the impairment of motor performance, i.e. response initiation in an operant reaction task in rats. This conclusion is further supported by biochemical results which show that a single, systemic injection of haloperidol increases the GABA turnover rate in the globus pallidus (Mao et al. 1977; Marco et al. 1976). Therefore it is not surprising that bicuculline, when injected into the ventro-medial part of the globus pallidus, inhibits catalepsy previously evoked by direct injection of sulpiride into the ventro-rostral part of the nucleus caudatus-putamen.

It is likely that the substantia nigra pars reticulata transmits impulses coming from the globus pallidus to the zona incerta-lateral hypothalamus, since it has been demonstrated that the globus pallidus sends a massive GABAergic projection to the substantia nigra pars reticulata (Araki et al. 1985; Jessel et al. 1978), and that there is a direct projection from the substantia nigra pars reticulata to the zona incerta-lateral hypothalamus (Barone et al. 1981; Shammah-Lagnado et al. 1985).

The above anatomical data are in line with our results. However, there are also other possibilities which cannot be excluded at present. It could be speculated that there are also other GABA receptors within the above-mentioned structures which could be connected with interneurons and/or presently unknown afferent projections. Moreover, it cannot be excluded that, besides the substantia nigra pars reticulata, other structures such as e.g., the subthalamic nucleus or nucleus entopeduncularis (Scheel-Krüger 1986), are, although less likely, involved in mediating the impulses from the ventro-rostral part of the nucleus caudatus-putamen to the zona incerta-lateral hypothalamus.

For example, it has already been suggested that the nucleus entopeduncularis may play some role in the mediation of catalepsy (Klockgether et al. 1987; Scheel-Krüger 1986). However, our recent unpublished results do not seem to be conclusive in this respect. Bilateral injections of 50 ng of bicuculline methiodide into the nucleus entopeduncularis evoked catalepsy which lasted longer than 30 s only in 9 of the 20 rats examined (none of the 9 rats was cataleptic after 25 ng of bicuculline, and only 2 of the 6 rats injected with 100 ng of the drug were cataleptic). After 40 ng of picrotoxin, only 5 of the 14 rats tested were cataleptic. So far, there has been no explanation for the appearance of catalepsy only in some of these correctly-injected animals, or for the lack of relation between the doses of the drugs used and the effect obtained. Therefore, it seems that it is only the role of the globus pallidus, and of the substantia nigra pars reticulata, in relaying neuronal impulses, pertinent to catalepsy, from the nucleus caudatus-putamen to the zona incerta-lateral hypothalamus that has been well documented up to now.

Summing up, our results show that the zona incerta-lateral hypothalamus should be included in the sequence of brain structures whose dysfunction is likely to play an important role in neuroleptic drug-induced catalepsy, which, in animals is a model for Parkinsonism in humans.

References

Amalric M, Koob GF (1989) Dorsal pallidum as a functional motor output of the corpus striatum. Brain Res 483:389–394

Araki M, McGeer PL, McGeer EG (1985) Striatonigral and pallidonigral pathways studied by combination of retrograde horseradish peroxidase tracing and a pharmacohistochemical method for gamma-aminobutyric acid transaminase. Brain Res 331:17–24

Barone FC, Wayner MJ, Scharoun SL, Guevara-Aguilar R, Aguilar-Baturoni HU (1981) Afferent connections to the lateral hypothalamus: a horseradish peroxidase study in the rat. Brain Res Bull 7:75–88

Beckstead RM (1988) Association of dopamine D1 and D2 receptors with specific cellular elements in the basal ganglia of the cat: the uneven topography of dopamine receptors in the striatum is determined by intrinsic striatal cells, not nigrostriatal axons. Neuroscience 27:851–863

Beckstead RM, Cruz CJ (1986) Striatal axons to the globus pallidus, entopeduncular nucleus and substantia nigra come mainly from separate cell populations in the cat. Neuroscience 19:147–158

Beckstead RM, Kersey KS (1985) Immunohistochemical demonstration of different subtance P-, met-enkephalin- and glutamic-acid-decarboxylase-containing cell body and axon distribution in the corpus striatum of the cat. J Comp Neurol 232:481–498

Gerfen CR, Engber TM, Mahan LC, Susel Z, Chase TN, Monsma FJ Jr, Sibley SR (1990) D1 and D2 dopamine receptor-regulated gene expression of striatonigral and striatopallidal neurons. Science 250:1429–1432

Janssen PAJ, Jagenau AHM, Schellekens KHC (1960) Chemistry and pharmacology of compounds related to 4-14-hydroxy-4-4-phenylpiperidinebutyrophenone. IV. Influence of haloperidol (R-1625) and chlorpromazine on the behaviour of rats in an unfamiliar open field situation. Psychopharmacology (Berl) 1:389–392

Jessel TM, Emson PC, Paxinos G, Cuello AC (1978) Topographic projection of substance P and GABA pathway in the striato- and pallido-nigral system: a biochemical and immunohistochemical study. Brain Res 152:487–498

Klockgether T, Schwarz M, Turski L, Ikonomidou-Turski C, Ossowska K, Heim C, Turski W, Wuellner U, Sontag K-H (1987) Neurotransmitters in the basal ganglia and motor thalamus: their role for the regulation of muscle tone. In: Carpenter MB, Jayaraman A (eds) The basal ganglia, II. Plenum Press, New York, pp 185–202

Kolasiewicz W, Wolfarth S, Ossowska K (1988) The role of the ventromedial thalamic nucleus in the catalepsy evoked from the substantia nigra pars reticulata. Neurosci Lett 90:219–223

König JFR, Klippel RA (1963) The rat brain. A stereotaxic atlas of the forebrain and lower parts of the brain stem. Willams & Wilkins, Baltimore, Md

Le Moine C, Normand E, Guitten AF, Fouque B, Teoule R, Bloch B (1990) Dopamine receptor gene expression by enkephalin neurons in rat forebrain. Proc Natl Acad Sci USA 87:230–234

Mao CC, Cheney DL, Marco E, Revuelta A, Costa E (1977) Turnover times of gamma-aminobutyric acid and acetylcholine in nucleus caudatus, nucleus accumbens, globus pallidus and substantia nigra: effects of repeated administration of haloperidol. Brain Res 132:375–379

Marco E, Mao CC, Cheney CL, Revuelta A, Costa E (1976) The effects of antipsychotics on the turnover rate of GABA and acetylcholine in rat brain nuclei. Nature 264:263–266

Matsui Y, Kamioka T (1978) Cataleptic and anticataleptic effects of muscimol and gabaculine injected into the globus pallidus and substantia nigra, and interactions with haloperidol or benzodiazepines. Naunyn Schmiedeberg's Arch Pharmacol 305:219–225

Morelli M, Porceddu ML, Imperato A, Di Chiara G (1981) Role of substantia nigra pars reticulata in the expression of neuroleptic-induced catalepsy. Brain Res 217:375–379

Moroni F, Cheney DL, Peralta E, Costa E (1978) Opiate receptor agonists as modulators of gamma-aminobutyric acid turnover in the nucleus caudatus, globus pallidus and substantia nigra of the rat. J Pharmacol Exp Ther 207:870–877

Nagy JI, Carter DA, Fibiger HC (1978) Anterior striatal projections to the globus pallidus, entopeduncular nucleus and substantia nigra in the rat: the GABA connection. Brain Res 158:15–29

Ossowska K, Wedzony K, Wolfarth S (1984) The role of the GABA mechanisms of the globus pallidus in mediating catalepsy, stereotypy and locomotor activity. Pharmacol Biochem Behav 21:825–831

Ossowska K, Karcz M, Wardas J, Wolfarth S (1990a) Striatal and nucleus accumbens D_1/D_2 dopamine receptors in neuroleptic catalepsy. Eur J Pharmacol 182:327–334

Ossowska K, Wardas J, Golembiowska K, Wolfarth S (1990b) Lateral hypothalamus-zona incerta region as an output station for the catalepsy induced by the blockade of striatal D_1 and D_2 dopamine receptors. Brain Res 506:311–315

Parent A (1990) Extrinsic connection of the basal ganglia. Trends Neurosci 13:254–258

Ricardo JA (1981) Efferent connections of the subthalamic region in the rat. II. The zona incerta. Brain Res 214:43–60

Scheel-Krüger J (1986) Dopamine-GABA interactions: evidence that GABA transmits, modulates and mediates dopaminergic functions in the basal ganglia and the limbic system. Acta Neurol Scand 107, Suppl.: 9–54

Shammah-Lagnado JJ, Negrao N, Ricardo JA (1985) Afferent connections of the zona incerta: a horseradish peroxidase study in the rat. Neuroscience 15:109–134

Staines WA, Nagy JI, Vincent SR, Fibiger HC (1980) Neurotransmitters contained in the efferents of the striatum. Brain Res 194:391–402

Swanson LW, Cowan WN (1975) A note on the connections and development of the nucleus accumbens. Brain Res 92:324–330

Wardas J, Ossowska K, Wolfarth S (1988) Evidence for the independent role of GABA synapses of the zona incerta-lateral hypothalamic region in haloperidol catalepsy. Brain Res 462:378–382