J. Pharm. Pharmacol. 1990, 42: 79–84
Received March 15, 1989

Effects of Intra-accumbens Administration of Dopamine Agonists on Stress-induced Behavioural Deficit

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Abstract—The effect of post-footshock injections of (+)-amphetamine, the selective D_2-receptor agonist quinpirole (LY 171555), and the D_2-receptor antagonist metoclopramide, into the nucleus accumbens, on the formation of the open field deficit, has been studied in rats. Microinjections of (+)-amphetamine (10 μg) stimulated rat locomotor activity tested 5 min later, while quinpirole (10 μg) significantly inhibited animal motility in the test. The open field behaviour was not changed 24 h after injection of either drug. Amphetamine applied immediately after inescapable footshock did not modify stress-induced locomotor depression, when the rats' behaviour was examined 24 h later. On the other hand, post-shock injections of quinpirole significantly attenuated the long-term effects of the stressor, in the open field. Metoclopramide (10 μg) inhibited rat locomotor activity 5 min, but not 24 h, after local injection. Administration of a solution containing both quinpirole (10 μg) and metoclopramide (1 μg) decreased motor activity of unstressed rats to a smaller degree than did quinpirole (10 μg) alone. Post-footshock injection of metoclopramide did not affect stress-induced hypomotility. It is concluded that the present data support the hypothesis that local depletion of brain dopaminergic stores causes some behavioural effects of stressors.

Brain dopaminergic systems have been thought to be involved in the vegetative, hormonal and behavioural effects of various stressors (Anisman & Zacharko 1982; Pare & Glavin 1986; Robinson et al 1987; Płaźnik et al 1988; Ray et al 1988). It is believed that dopaminergic innervation of the telencephalic limbic structures including the nucleus accumbens septi (NAS), amygdala and medial prefrontal cortex, plays a pivotal role in the central processes evoked by stress (Bannon & Roth 1983; Deutsch et al 1985; Kamata et al 1986; Bowers et al 1987; Robinson et al 1987; Ray et al 1988). For example, it has been shown that inescapable footshock stimulates dopamine turnover rate in the nucleus accumbens (Robinson et al 1987), and that it suppresses the rate of response for intracranial self-stimulation from this brain area (Bowers et al 1987). Moreover, intra-accumbens injections of a D_2-receptor antagonist attenuated the disinhibitory effect of desipramine in the forced swim test (Cervo & Samanin 1987). The effects comparable to that of inescapable shock (a deficit of escape performance) were produced by α-methyl-p-tyrasine (αMPT), reserpine and haloperidol, while (−)-dopa antagonized the escape deficit after dopamine and noradrenaline depletion (Anisman et al 1979).

From these and other data it has been hypothesized that 'when amine utilization is appreciably increased by stressors and exceeds synthesis, it may result in a net reduction of amine stores, thus promoting an appearance of central nervous dysfunctions' (Anisman & Zacharko 1982). On the other hand chronic stress was found to stimulate some adaptatory processes in the brain catecholaminergic systems, e.g. an enhancement of tyrosine hydroxylase activity (Stone & McCarty 1983). It is also noteworthy that though depletion of whole brain dopamine is not evident after an inescapable stressor, dopamine decrease can be found in some more discrete brain areas (Kvetnansky et al 1976; Blanc et al 1980). (+)-Amphetamine, a dopamine releaser, administered both before and after the footshock session, significantly attenuated depression of rat motor activity, while the effect of the stressor was strongest in the chlorpromazine-pretreated group (Płaźnik et al 1988). All these data point to a role of local dopamine depletion in the development of stress-induced behavioural deficits.

In the present experiment we have studied the contribution of accumbens dopaminergic innervation to the footshock-induced locomotor deficit in the open field test, examined 24 h after a single exposure of animals to stress. Such a treatment is known to decrease rat activity in the open field and forced swim tests, studied 24 h after a shock session (Weiss et al 1981; Prince & Anisman 1984; Płaźnik et al 1988). To test the hypothesis advanced by Anisman & Zacharko (1982), we have injected locally (nucleus accumbens septi) (+)-amphetamine as well as a selective D_2-receptor agonist, quinpirole, and a D_2-receptor antagonist, metoclopramide, immediately after exposure of animals to the stressor, i.e. in the period of time believed to be important for formation of behavioural deficits (Kamata et al 1986; Płaźnik et al 1988).

Materials and Methods

Male Wistar rats, 200 ± 20 g, were bought from a licensed breeder. After implantation the animals were kept in wire-mesh cages (30 × 30 × 20 cm) to avoid damage to the socket, with free access to food and water.

The rats were operated upon under light ethyl ether anaesthesia. The socket with two guide cannulae (0·7 mm ext. dia.) was placed stereotaxically according to the atlas of rat brain (Pellegrino et al 1967) (A 9·5 mm; L 1·5 mm; V 5·5 mm; incisor bar 5·5 mm above the i.a.l.) 1 mm above the nucleus accumbens septi (NAS), and fixed to the skull with

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metal screws and dental acrylic cement. Seven days later the rats were subjected to behavioural testing.

Microinjections were given bilaterally to the NAS with two Hamilton microsyringes connected via polyethylene tubing to two metal injection needles (0·3 mm ext. dia.) inserted 1·0 mm below the tip of the guide cannula, i.e. at the level of the commisura anterior (Fig. 1). (+)-Amphetamine sulphate (Astra), quinpirole hydrochloride (LY 171555, Eli Lilly), and metoclopramide hydrochloride (Polfa) were dissolved in distilled water immediately before their administration and were given bilaterally (10 μg in 0·5 μL per side) over 30 s. The control rats received injections of distilled water. The injection needles remained in place for an additional 30 s before they were removed and the stylets replaced. Behavioural tests were started 5 min or 24 h after intracerebral drug injection, and/or 24 h after the inescapable shock session. Each rat was injected twice, at the most. Injections (first distilled water, second drug solution, or vice versa) were separated by an interval of 7 days.

Electric footshock stressor was administered in Plexiglas cages (20 × 25 × 25 cm) with a stainless steel grid floor connected to the programmable electric stimulator (COTM, Białystok). Rats were placed separately in cages and shocks were delivered for 60 min, every 10–50 s (30 s on average) (2·0 mA, 10 s long trains of impulses). Special attention was paid to avoid short circuits, due to cage dirtiness or animals' adaptive posture (clinging to the walls), terminating the shock delivery. Control rats were subjected to a similar procedure, except that no electric footshock was given. In this part of the experiment microinjections were given immediately after footshock session, and behavioural testing was started 24 h later. Each animal was tested only once.

The open field test was performed 24 h after inescapable shock treatment in the same room where the rats were previously subjected to the stressor. The open field performance was examined in a rectangular box (80 × 80 × 20 cm) with the floor divided into 16 smaller squares. The number of squares crossed during 5 min was taken as a measure of locomotor activity. Animal testing was performed in a sound proof chamber under dim light and white noise conditions, by a person who did not know the schedule of drug- and treatment-administration.

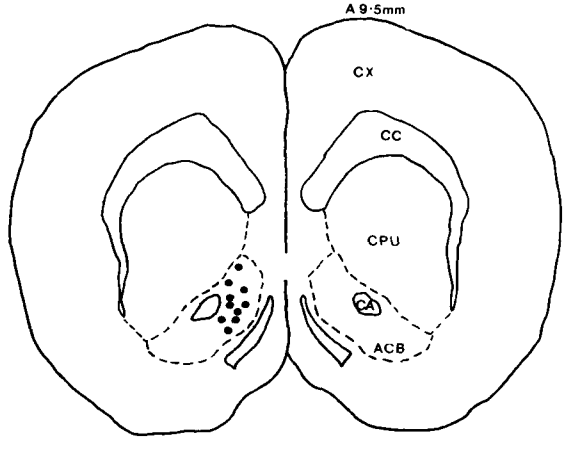

FIG. 1. A schematic drawing showing the typical and accepted dispersion of the sites of microinjections in the NAS. These data refer to both accumbens nuclei. The data have been taken from 10, not preselected, successive rats (closed circles) from the part of the experiments using (+)-amphetamine. CX—cortex; CA—commisura anterior; ACB—nucleus accumbens; CPU—nucleus caudatus, CC—corpus callosum.

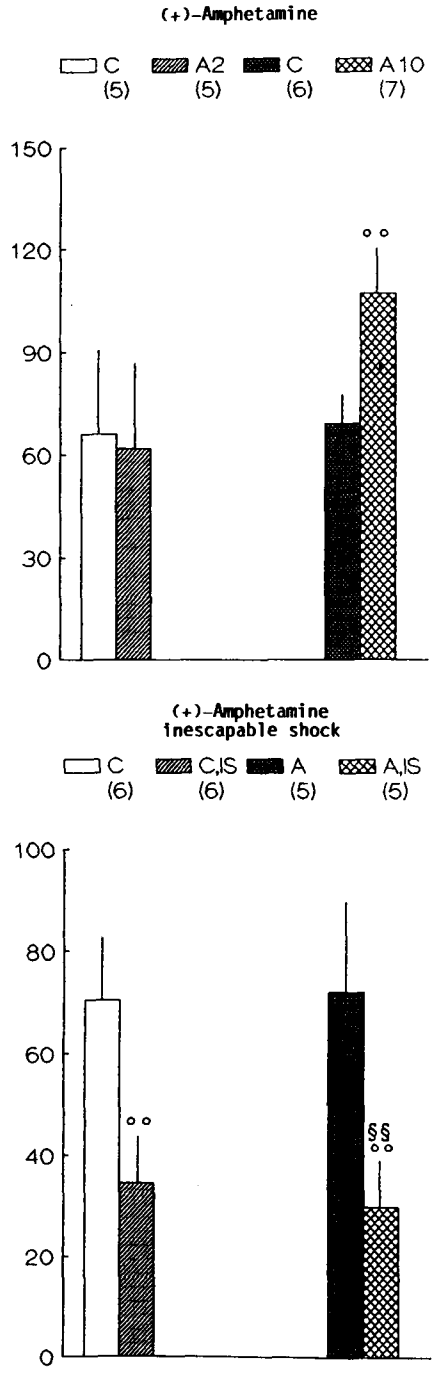

FIG. 2. The effect of intra-accumbens injections of (+)-amphetamine upon rat motility in the open field test. Top part of the figure—behavioural testing 5 min after drug microinjection; bottom part of the figure—behavioural testing 24 h after footshock and microinjections; ordinate—number of squares crossed; C—control; A2—(+)-amphetamine is 2 μg otherwise 10μg; IS—inescapable footshock; number of rats is shown in parenthesis; o—differs from control group; §—differs from amphetamine group. oo, §§ = $P < 0{\cdot}01$.

At the end of the experiment, the animals were killed, their forebrains stored in 5% formalin and then dissected into 40 μm slices and inspected with the aid of Meoflex (40x) to establish the site of injection. The apparatus comprised a magnifying glass and a slide projector.

All data are expressed as mean $\pm$ s.e. The statistical analysis of the results was performed with one-way ANOVA followed by Duncan's Multiple Range Test for independent measurements, or Student's t-test (two-tailed).

Results

Histological analysis showed that the sites of injection were in the central region of NAS, confirming our previous

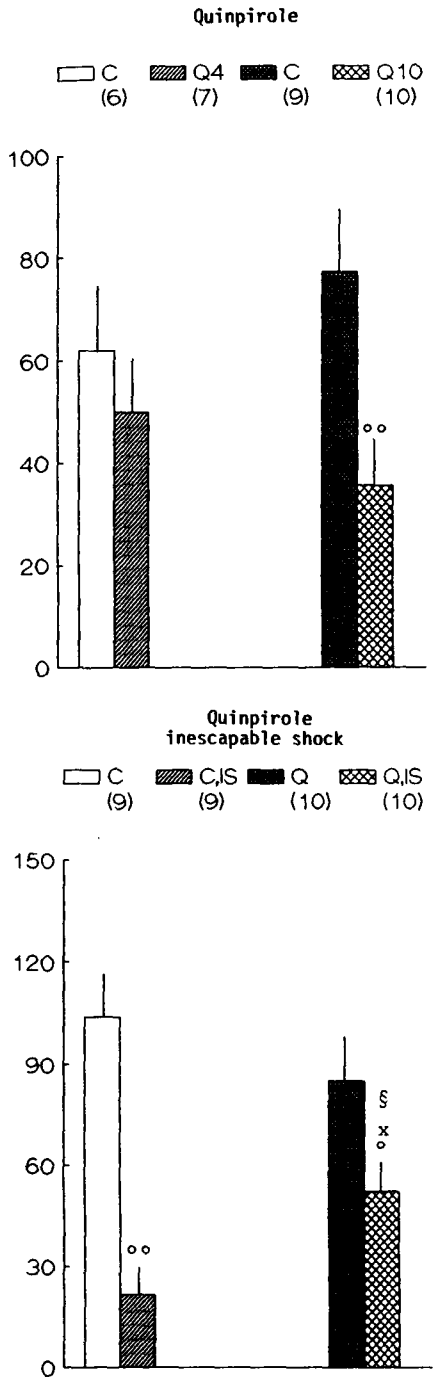

FIG. 3. The effect of intra-accumbens injections of quinpirole upon rat motility in the open field test. Q—quinpirole Q4 is 4 μg, otherwise 10 μg; §—differs from inescapable shock-treated group; x—differs from quinpirole treated group. o, x, § = $P < 0{\cdot}05$; oo = $P < 0{\cdot}01$. All other explanations as in Fig. 2.

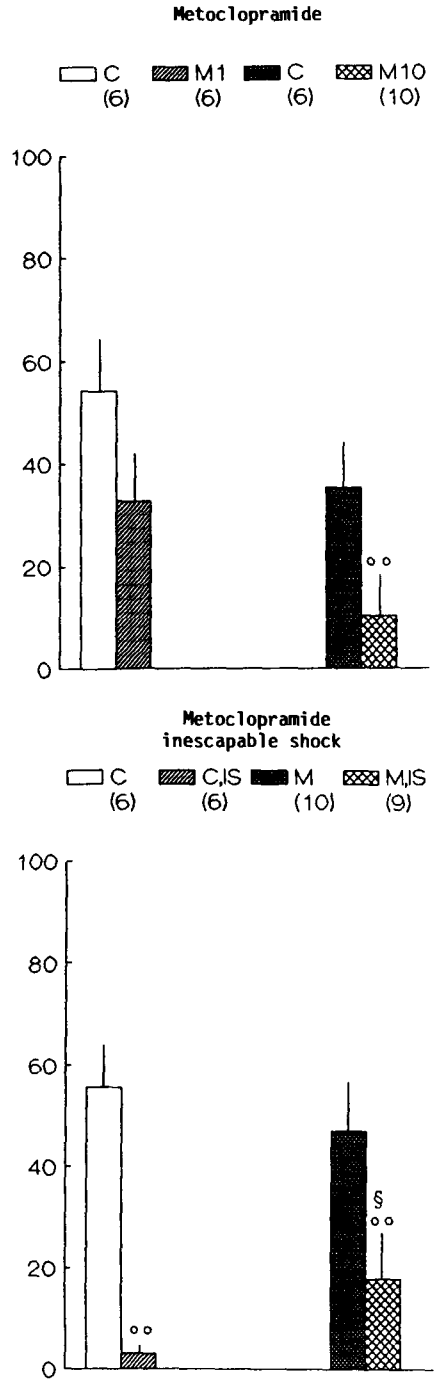

FIG. 4. The effect of intra-accumbens injections of metoclopramide upon rat motility in the open field test. M—metoclopramide M1 is 1 μg otherwise 10 μg; o—differs from control; §—differs from metoclopramide treated group. § = $P < 0{\cdot}05$; oo = $P < 0{\cdot}01$. All other explanations as in Fig. 2.

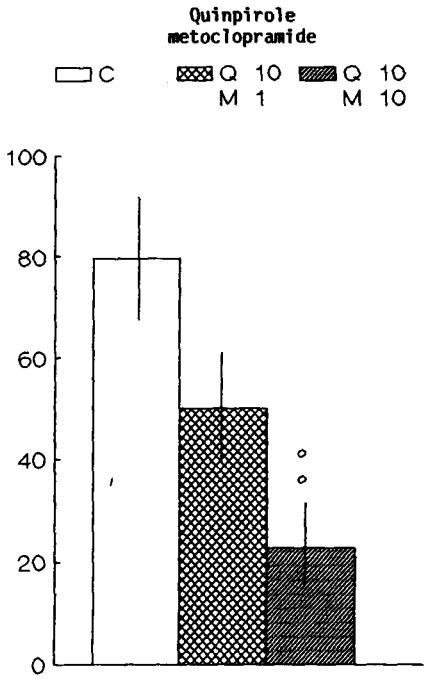

FIG. 5. The effect of intra-accumbens injections of both quinpirole and metoclopramide upon rat motility in the open field test. Q 10, M 1—solution containing 10 μg of quinpirole and 1 μg of metoclopramide. Number of rats: C—8; Q 10+M 1—8; Q 10+M 10—9.

findings (Płaźnik et al 1985). About 10% of rats were rejected due to incorrect placement of injections. Fig. 1 presents schematically the typical and maximal accepted dispersion of the sites of microinjections in the nucleus accumbens region.

Intra-accumbens injections of (+)-amphetamine dose-dependently stimulated rat locomotor behaviour in the open field, tested 5 min later (Fig. 2). The local injection of the drug (10 μg) did not affect the behaviour of naive animals, examined 24 h later. Moreover, post-shock administration of (+)-amphetamine did not interfere with the depressive influence of footshock on rat locomotion in the open field (Fig. 2). Microinjections of quinpirole inhibited rat motility examined 5 min, but not 24 h, after drug administration (Fig. 3). In the stressed rats quinpirole applied immediately after footshock partially, but significantly, attenuated the depressive influence of the stress procedure on rat activity (Fig. 3). Metoclopramide inhibited rats' locomotor activity 5 min, but not 24 h, after local injection (Fig. 4). Post-footshock administration of metoclopramide did not affect stress-induced hypomotility (Fig. 4). Intra-accumbens injections of a solution containing both quinpirole (10 μg) and a sub-active dose of metoclopramide (1 μg) produced less potent motor effects in naive rats than did quinpirole alone (Fig. 5).

Discussion

All drugs produced clear-cut behavioural effects when they were administered in an appropriate dose range to the NAS of naive rats. Amphetamine-induced stimulation of rat locomotion in the open field test can be explained by drug-induced enhancement of local dopamine release. Such an effect has been repeatedly shown after intra-accumbens microinjections of higher doses of the monoamine or (+)-amphetamine (Pijnenburg et al 1976; Płaźnik et al 1985; Carr & White 1987).

The depressant results obtained with quinpirole are much more difficult to interpret. Similar inhibition of locomotor activity has been observed after intracerebral injections of quinpirole to the habenula nuclei of the rat (Thornton et al 1987), and after peripheral administration of the drug to mice (Vasse et al 1988). The mechanism of this phenomenon may involve an enhancement by this direct agonist of D_2-receptors of control feedback mechanisms, regulating, in an inhibitory way, dopamine release (Zetterström et al 1986; Boyar & Altar 1987). Indeed, a strong correlation has been found between the potency of D_2-receptor stimulation, and the extent of dopamine release inhibition in-vivo (Boyar & Altar 1987). Consequently, it may be hypothesized that the inhibitory effect of D_2-receptor agonists on behaviour is due to the decreased stimulation of D_2-receptors by endogenous dopamine. It is now well recognized that the activation of both receptor types is necessary for full expression of postsynaptic effects of dopaminergic agonists (Arnt et al 1987; Carlson et al 1987; Jackson & Hashizume 1987; Vasse et al 1988). Theoretically, one could expect that in the studied model the effect of the D_2-receptor agonist quinpirole should be blocked or attenuated by the D_2-receptor antagonist metoclopramide, even though both drugs were found to similarly affect rat behaviour (although most probably due to different mechanisms). However, we failed to observe in the open field a strong interaction between quinpirole (10 μg) and metoclopramide (10 and 1 μg), examined 5 min after injection. Nevertheless, the effect of a solution containing 10 μg of quinpirole and 1 μg of metoclopramide appeared to be less potent behaviourally (in proportion to control rats' motility, $t = 1{\cdot}96$, $df = 14$, $P < 0{\cdot}068$) and in comparison with the strong influence of quinpirole administered alone. These findings do not necessarily negate the specificity of quinpirole's effect in control and stressed rats. Practically, it is difficult to find an appropriate dose-range for both compounds (quinpirole and metoclopramide), when one takes into account their different D_2-receptor affinities, solubility in lipids, and the balance of pre- versus post-synaptic activity. The above reasoning seems a logical, but unproven, interpretation of some of the phenomena described by us and others. It should be stressed that other selective D_2-receptor agonists such as bromocriptine and pergolide, were also reported to decrease rat locomotor activity, at least at the outset of their action (Arnt 1985; Jackson & Hashizume 1987). This is of special interest in the case of microinjection studies, when only short-term effects of drugs and treatments may be considered as structure specific.

Post-shock microinjections of (+)-amphetamine did not affect stress-induced locomotor suppression, examined 24 h later. This may be due to depletion after stressor of neurochemical substrate for this drug (presynaptic monoamine stores), in a critical period of formation of behavioural deficits. It is noteworthy, that contrary to the present data, peripherally injected (+)-amphetamine, applied immediately after footshock, was recently shown to significantly attenuate the effect of a stressor on rat motor activity (Płaźnik et al 1988). However, the behavioural recovery,

though significant, was only partial. Moreover, it is now well known that accumbens dopamine constitutes only a part of neuronal systems affected by stress. Thus, it is possible that peripherally applied (+)-amphetamine produced more general effects on differently located dopaminergic neurons contributing to the central changes evoked by inescapable footshock. Additionally, amphetamine's effect might also involve the releasing influence on noradrenaline stores. For instance, 6-OHDA-induced lesion of the noradrenergic ventral bundle or locus coeruleus neurons was shown to depress the hyperlocomotor response to peripheral amphetamine (Mohammed et al 1986). Interestingly enough, peripherally administered (+)-amphetamine profoundly suppresses the bioelectrical activity of the locus coeruleus (Bunney et al 1975), whereas stimulation of the structure results in the inhibition of activity in the NAS (Unemoto et al 1985). It appears that local microinjection of (+)-amphetamine into the NAS might produce different results from its peripheral administration where the inhibitory effect on the locus coeruleus (and A_9 and A_{10} dopaminergic cells) activity plays a role, and acute stress-mediated depletion of central dopamine and noradrenaline stores is equally likely.

Microinjections of quinpirole partially, but significantly attenuated behavioural deficit produced by the stressor. This may be tentatively explained as resulting from the direct stimulation by the drug of post-synaptic D_2-receptor-related processes, in a situation when the hypothetical inhibitory presynaptic mechanisms are absent or otherwise disturbed by stress (see above). The intrinsic mechanism of this phenomenon may involve several elements. Firstly, dopaminomimetics are known to antagonize the behavioural effects of stressors (see introduction). Secondly, the temporary hypofunction of mesolimbic dopaminergic neurons after stress can be considered as a functional lesion of the system under study. Accordingly, it is now well recognized that in rats with chemical or functional lesion of dopaminergic neurons (after 6-OHDA) or after chronic treatment with reserpine or α-MPT, the behavioural effects of direct D_2-agonists are enhanced (Arnt & Hyttel 1985; Jackson & Hashizume 1987). It is noteworthy, that even a single central intervention affecting the brain dopaminergic system (e.g. (+)-amphetamine injection or a stress session) may produce long-lasting changes in local dopamine utilization and in behavioural effects of dopaminomimetics (Anisman & Zacharko 1982; Nishikawa et al 1983; Robinson et al 1987). Both acute stress and single (+)-amphetamine injection produce an enhancement of local dopamine utilization and sensitization to subsequent stressors or (+)-amphetamine (cf. Anisman & Zacharko 1982). There are also some indications that the modification of behavioural effects of dopaminergic agents might not directly depend on changes in dopaminergic receptors (Bevan 1983; Ellison & Eison 1983; Marona-Lewicka & Vetulani 1988). On the whole, it may be concluded that some of the mechanisms discussed might contribute to the quinpirole-induced attenuation of stress-related behavioural suppression. However, the problem of the mechanisms of the quinpirole effect apparently needs more research.

The lack of effect of metoclopramide in stressed animals can be explained by a strong depression of rat locomotion after footshock, masking the eventual inhibitory influence of the D_2-antagonist. The mechanism of this phenomenon may involve the local depletion of endogenous dopamine after stress, thus mimicking the effect of D_2-receptor blockers, observed in naive animals.

To summarize, the present data can be viewed as supporting the aforementioned concept of Anisman & Zacharko (1982) on the role of stress- induced changes in the functioning of the brain mesolimbic dopaminergic system. However, since the effect of the D_2-agonist was only partial, the role of changes in other neurotransmitter mechanisms (e.g. noradrenergic) are also very likely.

Acknowledgements

The authors wish to acknowledge the gifts of (+)-amphetamine (Astra Alab), quinpirole (Eli Lilly Co.) and metoclopramide (Polfa). The authors are also indebted to Mrs E. Zawadzka for her technical assistance. The research was supported by a grant from Ministry of Health RPBR MZ. V.

References

Anisman, H., Zacharko, R. M. (1982) Depression: the predisposing influence of stress. Behav. Brain Sci. 5: 89–137.

Anisman, H., Remington, G., Sklar, L. S. (1979) Deficit of escape performance following catecholamine depletion: implication for behavioural deficit induced by uncontrollable stress. Psychopharmacol. 61: 107–124

Arnt, J. (1985) Behavioural stimulation is induced by separate dopamine D1 and D2 receptor sites in reserpine pretreated but not in normal rats. Eur. J. Pharmacol. 113: 79–88

Arnt, J., Hyttel, J. (1985) Differential involvement of dopamine D1 and D2 receptors in the circling behaviour induced by apomorphine, SKF 39393, pergolide and LY 171555 in 6-OHDA lesioned rats. Psychopharmacol. 85: 346–352

Arnt, J., Hyttel, J., Perrgaard, J. (1987) Dopamine D1 agonist combined with the selective D2 agonist quinpirole facilitate the expression of oral stereotyped behaviour in rats. Eur. J. Pharmacol. 133: 137–145

Bannon, M. J., Roth, R. H. (1983) Pharmacology of mesocortical dopamine neurons. Pharmacol. Rev. 35: 53–68

Bevan, P. (1983) Repeated apomorphine treatment causes behavioural supersensitivity and dopamine D2 receptor hyposensitivity. Neurosci. Lett. 35: 185–189

Blanc, G., Herve, D., Simon, H., Lisoprawski, A., Glowinski, J., Tassin, J.P. (1980) Response to stress of mesocortical-frontal dopaminergic neurons in rats after long term isolation. Nature 284: 265–276

Bowers, W. J., Zacharko, R. M., Anisman, H. (1987) Evaluation of stressor effect on intracranial self stimulation from the nucleus accumbens and the substantia nigra in a current intensity paradigm. Behav. Brain Res. 23: 85–93

Boyar, W. C., Altar, C. A. (1987) Modulation of in vivo dopamine release by D2 but not D1 receptor agonist and antagonists. J. Neurochem. 48: 824–830

Bunney, B. S., Walters, J. R., Kuhar, M. J., Roth, R. H., Aghajanian, G. K. (1975) d- and l-Amphetamine stereoisomers: comparative potencies in affecting the firing of central dopaminergic and noradrenergic neurons. Psychopharmacol. Commun. 1: 177–190

Carlson, J. H., Bergstrom, D. A., Walters, J. R. (1987) Stimulation of both D1 and D2 dopamine receptors appears necessary for full expression of postsynaptic effects of dopamine agonists: a neurophysiological study. Brain Res. 400: 205–218

Carr, G. D., White, N. M. (1987) Effects of systemic and intracranial amphetamine injections on behaviour in the open field: a detailed analysis. Pharmacol. Biochem. Behav. 27: 113–122

Cervo, L., Samanin, R. (1987) Evidence that dopamine mechanisms in the nucleus accumbens are selectively involved in the effect of desipramine in the forced swimming test. Neuropharmacol. 26: 1469–1472

Deutsch, A. Y., Tam, S. -Y., Roth, R. H. (1985) Footshock and conditioned stress increase 3,4 dihydroxyphenylacetic acid (DOPAC) in the ventral tegmental area but not substantia nigra. Brain Res. 333: 143–146

Ellison, G. D., Eison, M. S. (1983) Continuous amphetamine intoxication: an animal model of the acute psychotic episodes. Psychol. Med. 13: 751–761

Jackson, D. M., Hashizume, M. (1987) Bromocriptine-induced locomotor stimulation in mice is modulated by dopamine D1 receptors. J. Neural Transm. 69: 131–145

Kamata, K., Yoshida, S., Kameyama, T. (1986) Antagonism of footshock stress-induced inhibition of intracranial self-stimulation by naloxone or methamphetamine. Brain Res. 371: 197–200

Kvetnansky, R., Mitro, A., Palkovits, M., Brownstein, M., Torda, T., Vigas, M., Mikulaj, L. (1976) Catecholamines in individual hypothalamic nuclei in stressed rats. In: Usdin, E., Kventnansky, R., Kopin, I. J. (eds) Catecholamines and Stress, Pergamon Press, Oxford, pp 39–50

Marona-Lewicka, D., Vetulani, J. (1988) Stability and variability of locomotor responses of laboratory rodents. IV. The responses of rats and mice to apomorphine and amphetamine. Pol. J. Pharmacol. Pharm. 40: 281–294

Mohammed, A. K., Danysz, W., Ögren, S. O., Archer, T. (1986) Central noradrenaline depletion attenuates amphetamine-induced locomotor behavior. Neurosci. Lett. 64: 139–144

Nishikawa, T., Mataga, N., Takashima, M., Toru, M. (1983) Behavioural sensitization and relative hyperresponsiveness of striatal and limbic dopaminergic neurons after repeated methamphetamine. Eur. J. Pharmacol. 88: 195–203

Pare, W. P., Glavin, G. B. (1986) Restraint stress in biomedical research: a review. Neurosci. Biobehav. Rev. 10: 339–370

Pellegrino, L. J., Pellegrino, A. S., Cushman, A. J. (1967) A Stereotaxic Atlas of the Rat Brain, Plenum Press, New York

Pijnenburg A., Honig, W. M., van der Heyden, J., van Rossum, J. M. (1976) Effects of chemical stimulation of the mesolimbic DA system upon locomotor activity. Eur. J. Pharmacol. 35: 45–55

Płaźnik, A., Danysz, W., Kostowski, W. (1985) A stimulatory effect of intraaccumbens injections of noradrenaline on the behaviour of rats in the forced swim test. Psychopharmacol. 87: 119–123

Płaźnik, A., Tamborska, E., Hauptmann, M., Bidzinski, A., Kostowski, W. (1988) Brain neurotransmitter systems mediating behavioural deficits produced by inescapable shock treatment in rats. Brain Res. 447: 122–132

Prince, Ch. R., Anisman, H. (1984) Acute and chronic stress effects on performance in a forced swimming task. Behav. Neural Biol. 42: 99–119

Ray, A., Henke, P. G., Sullivan, R. M. (1988) Central dopamine systems and gastric stress pathology in rats. Physiol. Behav. 42: 359–364

Robinson, T. E., Becker, J. B., Young, E. A., Akil, H., Castaneda, E. (1987) The effects of footshock stress on regional brain dopamine metabolism and on pituitary β-endorphin release. Neuropharmacol. 26: 679–691

Stone, E. A., McCarty, R. (1983) Adaptation to stress and brain noradrenergic receptors. Neurosci. Biobehav. Rev. 7: 503–509

Thornton, E. W., Evans, J. A., Wickers, A. (1987) Changes in motor activity induced by microinjections of the selective dopamine agonist LY 171555, quinpirole hydrochloride, and SKF 38393 into the habenula nucleus. Pharmacol. Biochem. Behav. 26: 643–646

Unemoto, H., Sasa, M., Takaori, S. (1985) A noradrenaline-induced inhibition from locus coeruleus of nucleus accumbens neuron receiving input from hippocampus. Japan J. Pharmacol. 39: 233–239

Vasse, M., Chagraoui, A., Protais, Ph. (1988) Climbing and stereotyped behaviours in mice require the stimulation of D1 dopamine receptors. Eur. J. Pharmacol. 148: 221–229

Weiss, J. M., Goodman, P. A., Losito, B. G., Corrigan, S., Charry, J. M., Bailey, W. H. (1981) Behavioural depression produced by an uncontrollable stressor: relationship to noradrenaline, dopamine and serotonin levels in various regions of rat brain. Brain Res. Rev. 3: 167–205

Zetterström, T., Sharp, T., Ungerstedt, U. (1986) Effect of dopamine D1 and D2 receptor selective drugs on dopamine release and metabolism in rat striatum in vivo. Naunyn Schmiedebergs Arch. Pharmacol. 334: 117–124