inhibitor of 5-lipoxygenase. The potency and selectivity of lipoxygenase inhibitors may be altered in accordance with animal species or types of tissues and cells, or experimental conditions.

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Effect of dopaminergic drugs on striatal acetylcholine concentration

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Striatal acetylcholine concentration was determined after administration of varying doses of apomorphine, (+)-PPP and (−)-PPP to rats. (+)-PPP at 3 and 10 mg kg^{-1} is a dopamine agonist, whereas (−)-PPP at 0·3 and 3 mg kg^{-1} is a dopamine antagonist in the striatum.

Dopamine (DA) is an inhibitory neurotransmitter in the striatum (McLennan & York 1967). Treatment with dopamine agonists like (−)-dopa, apomorphine, trivastal, bromocriptine, and lergotrile increases the concentration of acetylcholine (ACh) in the striatum of rats by their inhibitory effect on the intrastriatal cholinergic neurons (Consolo et al 1974; Sethy & VanWoert 1974a, b; Sethy 1979). On the other hand, DA antagonists such as chlopromazine, haloperidol, pimozide, metoclopramide, and molindone decrease striatal ACh concentration by blocking the inhibitory action of DA on the cholinergic neurons (McGeer et al 1974; Sethy & VanWoert 1974a, b, c; Sethy 1976, 1979).

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Recently, the existence of dopamine autoreceptors on the presynaptic terminals of nigrostriatal dopaminergic neurons has been demonstrated and they may serve to regulate the influence of DA neurons on post-synaptic follower cells (Roth 1979). Thus, autoreceptors located on nigrostriatal dopaminergic neurons may affect the activity of follower intrastriatal cholinergic neurons. If presynaptic DA receptors are different from their post-synaptic counterparts, then a specific agonist of autoreceptors may reduce dopamine transmission, leading to an increase in release of ACh and subsequently a decrease in ACh concentration, just like the DA antagonist. Apomorphine, at small doses (DiChiara et al 1978), and (+)- and (−)-PPP (Hjorth et al 1983) have been shown to be autoreceptor agonists of the nigrostriatal dopaminergic system in the rat. Administration of these drugs may *decrease* dopamine transmission, which in turn may reduce ACh concentration in the striatum. The results of such investigations are now described.

Methods

Male Sprague-Dawley rats, 180–240 g were used. Apomorphine hydrochloride, (+)- and (−)-PPP were dissolved in distilled water. Sodium carboxymethylcellulose solution (0·25%) was used to suspend haloperidol. All drugs were administered by the intraperitoneal (i.p.) route. Control rats received an equal volume of the vehicle. Rats were killed by a beam of microwave radiation focused on the skull for 2·6 s (Metabostat, Model 4094, Gerling-Moore). The brains were quickly removed and the bilateral striata dissected out. Acetylcholine was extracted and assayed by the gas chromatographic method (Sethy 1978). Statistical analysis was done using the paired *t*-test.

Results and discussion

Apomorphine, 0·01, 0·03 and 1·0 mg kg^{-1} had no significant effect on striatal ACh concentration but 3·0 and 10·0 mg kg^{-1} significantly ($P < 0·005$) increased it. (+)-PPP, 0·1 and 0·3 mg kg^{-1} had no significant effect, but after 3·0 and 10·0 mg kg^{-1}, a significant ($P < 0·001$ and $<0·03$, respectively) increase in the striatal ACh was observed. (−)-PPP (0·3 and 3·0 mg kg^{-1}) significantly ($P < 0·01$) decreased ACh content in the striatum as did haloperidol ($P < 0·001$) (Table 1).

Apomorphine, 0·025 and 0·2 mg kg^{-1} has been shown to be an autoreceptor stimulant in rodents (DiChiara et al 1978; Roth 1979). Waldmeier (1983) has demonstrated that subcutaneous administration of apomorphine in the doses of 0·01–0·03 mg kg^{-1} significantly reduces striatal ACh concentration in Tif: RAIF (SPF) rats. Treatment with similar doses of apomorphine failed to reduce the ACh concentration in our study. The inconsistency in the results may be due to differences in the strain of animals, route of administration of drug, and method of estimation of ACh. Apomorphine, 3·0 and 10·0 mg kg^{-1}, significantly increased ACh concentration which is consistent with previous observations of Sethy & VanWoert (1974a) and Waldmeier (1983). Like small doses of apomorphine, 0·1 and 0·3 mg kg^{-1} of (+)-PPP had no significant fact on striatal ACh concentration while the higher doses, 3·0 and 10·0 mg kg^{-1}, increased ACh concentration, suggesting that at these doses (+)-PPP may be a postsynaptic dopamine agonist in the striatum. A similar postsynaptic dopamine agonist activity with (+)- and/or (±)-PPP has been observed in biochemical (Waldmeier 1983) and behavioural (Hjorth et al 1983) investigations. Like haloperidol, administration of (−)-PPP in the doses of 0·3 and 3·0 mg kg^{-1} significantly reduced ACh concentration, suggesting that at these doses (−)-PPP may be a postsynaptic antagonist of the dopamine receptor in the striatum. (−)-PPP has recently been reported to be a postsynaptic dopamine antagonist in the mesolimbic area of the rat brain (Hjorth et al 1983).

In conclusion, determination of striatal ACh concentration after administration of apomorphine in small doses and (+)- or (−)-PPP may not be the ideal method for defining autoreceptor activity of the nigrostriatal pathway. (+)-PPP at 3·0 and 10·0 mg kg^{-1} is a dopamine agonist, whereas (−)-PPP at 0·3 and 3·0 mg kg^{-1} is a dopamine antagonist in the striatum.

Table 1. Effect of dopaminergic drugs on ACh concentration in the striatum of rats.

Treatment[1]	mg kg^{-1}	ACh % of control[2,3] (mean ± s.e.)	*P*
Control	—	100 ± 3·3 (9)	
Apomorphine	0·01	97 ± 7·1 (5)	NS
Apomorphine	0·03	94 ± 4·0 (4)	NS
Apomorphine	1·00	96 ± 2·2 (5)	NS
Apomorphine	3·00	120 ± 6·4 (5)	<0·005
Apomorphine	10·00	127 ± 3·6 (5)	<0·002
Control	—	100 ± 1·0 (9)	
(+)-PPP	0·10	97 ± 1·0 (4)	NS
(+)-PPP	0·30	93 ± 4·0 (5)	NS
(+)-PPP	3·00	119 ± 3·3 (5)	<0·001
(+)-PPP	10·00	122 ± 6·7 (4)	<0·030
(−)-PPP	0·10	104 ± 5·6 (4)	NS
(−)-PPP	0·30	91 ± 1·7 (6)	<0·017
(−)-PPP	3·00	83 ± 3·5 (5)	<0·001
Control	—	100 ± 2·9 (4)	
Haloperidol	3·00	52 ± 1·6 (4)	<0·001

[1] Rats were killed 30 min after administration of drug.
[2] ACh concentration in control rats was 79·1 ± 2·4 nmol g^{-1} of tissue.
[3] Figures in parentheses indicate number of experiments.

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