Bupropion, in contrast to DMI and nomifensine, significantly prevented 6-OHDA-induced depletion of brain DA but was ineffective against NA depletion. Dexamphetamine was effective against both DA and NA depletion (Table 1). In the rat striatal dopamine-sensitive adenylate cyclase preparation (Kebabian, Petzhold & Greengard, 1972) bupropion at 100 μM had no effect on the production of either basal or DA-stimulated (100 μM) C-AMP.

The results indicate that dopamine is involved in at least some of the central actions of bupropion. Although not a DA agonist on the adenylate cyclase preparation, the 6-OHDA model suggests that bupropion may inhibit DA uptake *in vivo* in the rat.

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Changes in mesolimbic homovanillic acid content following discrete modulation of striatal dopamine systems

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Many authors have investigated the possibility of regional differences in the interaction of different neuroleptic agents (and many other drugs) with dopamine metabolism in the corpus striatum and mesolimbic structures (see Waldmeier & Maître, 1976; Westerink, Lejeune, Korf & van Praag, 1977). It is fundamental to these studies that the peripheral administration of neuroleptic agent to modify striatal or mesolimbic dopamine metabolism involves a discrete effect of the drug within the appropriate region. The present studies assess the validity of this assumption by directly stimulating and blocking striatal dopamine systems and determining the specificity of changes induced to the striatum by measuring alterations in dopamine metabolism both within the striatum and the mesolimbic structures.

Chronically indwelling cannulae were implanted in the brains of male Sprague-Dawley rats to allow drug or vehicle injection into the caudate-putamen (Ant. 9.0, Vert. +1.5, Lat. ±3.0, De Groot, 1959) (see Costall & Naylor, 1976, for details of the stereotaxic techniques). Fourteen days after surgery drug solutions (administered into the right hemisphere) and vehicle (administered into the left hemisphere) were injected simultaneously in volumes of 1 μl. Behavioural effects of circling and asymmetry were assessed for a 3 h period. Rats were then sacrificed, the brains rapidly removed and the striatum and tuberculum olfactorium dissected out over ice. Tissue from 6 animals was used for each extraction procedure. Homovanillic acid (HVA) concentrations were determined fluorometrically.

In 'control' non-cannulated rats HVA concentrations were 823 ± 97 ng/g (striatum) and 403 ± 73 ng/g (tuberculum olfactorium). In cannulated rats receiving intrastriatal vehicle the HVA concentrations were the same as those recorded for non-cannulated rats. The unilateral injection of dopamine into the striatum (1–100 μg) increased HVA levels in both the ipsilateral striatum *and* tuberculum olfactorium. Significant changes were not recorded for the other hemisphere. Whilst contralateral asymmetry and circling movements were apparently associated with the effects of dopamine (100 μg), lower doses of dopamine, although increasing HVA levels by 2× to 2× control values, failed to induce any obvious behavioural changes. The unilateral injection of fluphenazine (1–25 μg) also caused an increase (up to 7× control values) in HVA levels in the striatum *and* tuberculum olfactorium in *both* the ipsilateral and contralateral hemispheres. Ipsilateral asymmetry and circling were observed using the larger doses of fluphenazine but, although the lower doses of fluphenazine caused significant elevation in HVA levels, again these were not associated with any behavioural change.

The results indicate, firstly, that manipulation of

dopamine mechanisms in the extrapyramidal system can influence dopamine metabolism in an anatomically distinct area of the mesolimbic system. Secondly, that appreciable changes in HVA levels are not necessarily accompanied by functional changes characteristic of dopamine receptor stimulation or blockade. These two factors should be considered in interpreting the significance of changes in mesolimbic and extrapyramidal HVA levels after peripheral neuroleptic treatment.

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A comparison of the effects of GABA and glycine on the release of [^{3}H]-dopamine from rat striatal slices

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Both γ-aminobutyric acid (GABA) (Giourgueff, Kemel, Glowinski & Besson, 1978) and glycine (Anderson & Roberts, 1978) can stimulate the efflux of [^{3}H]-dopamine ([^{3}H]-DA) from rat striatal slices. We have therefore decided to compare the effects of these two amino acids on the efflux of [^{3}H]-DA, [^{3}H]-5-hydroxytryptamine ([^{3}H]-5HT) and [^{3}H]-GABA from rat striatal slices in an attempt to determine whether or not GABA and glycine act at the same receptor site in the striatum. The methods used to study the release of preloaded radio-labelled transmitter from superfused brain slices *in vitro* have been described in detail elsewhere (Kerwin & Pycock, 1978). Aminooxyacetic acid (10 μM) or pargyline (50 μM) were present to inhibit labelled transmitter metabolism where appropriate.

A depolarizing stimulus (50 mM KCl) stimulated the rate of efflux of [^{3}H]-5HT, [^{3}H]-DA and [^{3}H]-GABA from striatal slices. In all cases the effect of K^+ was markedly reduced in a low calcium, magnesium-substituted medium. Glycine (200–400 μM) and Gaba (50–200 μM) caused an increase in the rate of basal efflux of [^{3}H]-DA. Neither GABA nor glycine at 1mM had any effect on the efflux of [^{3}H]-5HT or [^{3}H]-GABA. At 200 μM both GABA and glycine potentiated the ability of 20 mM K^+ to stimulate [^{3}H]-DA efflux. Picrotoxin (50 μM) prevented GABA (400 μM) from stimulating the efflux of [^{3}H]-DA, whereas glycine's ability to stimulate [^{3}H]-DA release was unaffected. On the other hand strychnine hydrochloride (0.5 μM) prevented the effects of both GABA and glycine.

The ability of a low dose of strychnine to block the effects of GABA may suggest that GABA evoked [^{3}H]-DA release, may, in part, be mediated through receptors for glycine or other neutral amino acids. In addition this may rationalize the observation that the specific GABA agonist 3-aminopropane sulphonic acid is ineffective at stimulating [^{3}H]-DA release from striatal slices (Starr, 1978), although in our study we have shown that muscimol (100 μM) can stimulate [^{3}H]-DA efflux in a manner which is partially sensitive to picrotoxin (50 μM).

In additional studies using [^{3}H]-glycine, 50 mM K^+ effectively stimulated the efflux of radioactivity from neonatal rat spinal cord and striatal slices. In both cases this effect was calcium dependent, suggesting a possible neurotransmitter status for glycine.

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