Relative potency of some neuroleptics as antagonists at dopamine-receptors *in vivo* compared with their reported ability to displace haloperidol binding *in vitro*

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It is uncertain whether the ability of a compound to displace tritiated haloperidol from its specific central binding sites actually reflects the potency of the compound to block central dopamine receptors *in vivo*. We have used measurements of the ability of some neuroleptics to antagonise apomorphine-induced stereotyped climbing (Farrant, Thompson & Schnieden, 1977), and hypothermia (Cox & Lee, 1978) and obtained relative orders of antagonist potency for comparison with those published from binding studies (Leysen, Gommeren & Laduron, 1978).

Measurement of the rightward shift of full dose response curves to apomorphine produced by the neuroleptics allowed the determination of pA_2 equivalents *in vivo* (Cox & Weinstock, 1964). In all cases the slope of the log (DR-1) v-log (M/kg) was not significantly different from unity. Domperidone, a dopamine antagonist which does not penetrate the brain, did not antagonise apomorphine indicating that apomorphine was acting centrally. The relative order of antagonist potency of the compounds was the same in climbing and binding studies (Table 1). This suggests that binding to striatal homogenates does reflect the ability of the compound to combine with the striatal dopamine receptors involved in the climbing response (Protais, Costentin & Schwartz, 1976). When the antagonism of hypothermia was compared with haloperidol displacement there was not such a close correlation since sulpiride was ineffective and thioridazine not only failed to antagonise apomorphine, but actually caused potentiation. The receptors mediating hypothermia are not found in the striatum but in the hypothalamus. The inability of sulpiride and thioridazine to antagonise apomorphine is unlikely to be due to dispositional factors since the block of striatal receptors proves it penetrates the brain. An alternative possibility is that there are two populations of dopamine receptors and that sulpiride and thioridazine differentiated between them.

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Table 1 'pA_2 equivalents' for the antagonism of apomorphine induced stereotyped climbing and hypothermia in mice compared with pIC_{50} values* for displacement of [^{3}H]-haloperidol binding in striatal homogenates

Antagonist	*pIC_{50} values* [^3H]*-haloperidol displacement*	*pA_2 equivalents* *Stereotyped climbing*	*Hypothermia*
Domperidone	8.8	No antagonism	No antagonism
Spiroperidol	9.4	9.2	8.4
Pimozide	8.5	6.4	6.8
Haloperidol	8.5	7.3	6.2
Thioridazine	7.4	5.8	No antagonism
Sulpiride	7.1	4.2	No antagonism

* From Leysen, Gommeren & Laduron (1978).