Effect of a reduction in brain 5-hydroxytryptamine on the concentration of homovanillic acid in the rat caudate nucleus

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A reduction of brain 5-hydroxytryptamine (5-HT) has been found to decrease the catalepsy induced by neuroleptics (Kostowski, Gumulka & Czlonkowski, 1972). We were able to show that animals treated with tryptophan or 5-hydroxytryptophan (5-HTP) show an increased cataleptic response to neuroleptics, while methysergide and *p*-chlorophenylalanine (PCPA) reduce it (Fuenmayor & Vogt, 1977). These observations suggest that the tryptaminergic system might regulate the activity of the nigrostriatal dopaminergic neurons. This possibility was explored by studying the effect of a reduction in brain 5-HT content on the concentration of homovanillic acid (HVA) in rats, some of which had also been treated with neuroleptics.

HVA and dopamine (DA) were measured in the caudate nucleus whilst 5-HT was estimated in the forebrain. PCPA (300 mg/kg) was given 48 h before killing; 5-HTP (10 mg/kg) was administered 75 min before killing.

The administration of PCPA reduced by 84% the concentration of 5-HT and by 26.3% that of HVA with no modification in the concentration of DA. The reduction of HVA was only partially antagonized by the administration of 5-HTP. These results suggested that the release of DA is reduced by the lack of 5-HT.

Other experiments explored the effect of PCPA on the HVA increase produced by tetrabenazine or by 4'fluoro-4-((4-(*p*-fluorophenyl)-3-cyclohexen-1-yl) amino) butyrophenone, a butyrophenone with monoamine depleting properties (Lahti & Lednicer, 1974). The HVA increase produced by these drugs was antagonized by PCPA but this effect of PCPA was not modified by the low dose of 5-HTP used. A reduction by PCPA of the HVA increase produced by haloperidol has been reported to occur not only in the striatum but also in mesolimbic regions (Westerink & Korf, 1975).

Finally, experiments were carried out on the effect of PCPA on the accumulation of HVA by probenecid. This drug blocks the transport system which removes HVA from the brain. After PCPA the accumulation of HVA normally seen 3 h after probenecid was almost abolished; the vehicle-treated animals showed, in contrast, a 111% increase in the HVA concentration.

The results suggest that the lack of brain 5-HT reduces the turnover of DA in the caudate nucleus. However, the lack in brain 5-HT also decreases neuroleptic catalepsy, supposed to be caused by a blockade of the striatal DA receptors, which in turn increases HVA production. The effect of the tryptaminergic system on the DA turnover is, therefore, probably the consequence of an action at some site other than primarily on the cell bodies or terminals of the nigro-striatal DA pathway. It might be at some site at which dopaminergic cells can be activated or inhibited. This explanation is not unlikely in view of the fact that tryptaminergic projections from the raphe nuclei to the substantia nigra have been described (Fuxe, 1965).

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