Rotational behaviour and striatal dopamine metabolism following unilateral activation of nigral GABA mechanisms: GABA-like modulation of dopaminergic and non-dopaminergic neurons in rat substantia nigra

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It is well established that unilateral activation of nigral GABA mechanisms by putative GABA-like agents induces a contralateral rotational response in rats (Waddington, 1977a, b; Oberlander, Dumont & Boissier, 1977; Olpe, Schellenberg & Koella, 1977). The direction of rotation is opposite to that expected if the only effect of striatonigral GABA neurons is to inhibit activity in nigrostriatal dopamine (DA) neurons (Dray & Straughan, 1976). Concentrations of DA and the DA metabolites dihydroxyphenylacetic acid (DOPAC) and homovanillic acid (HVA) in the striatum, as well as rotational behaviour measures, have been assessed following unilateral activation of nigral GABA mechanisms to clarify the nature of GABA/DA interactions in the substantia nigra (SN).

Male Sprague–Dawley rats, 150–200 g, were anaesthetized with ether and unilateral stereotaxic injections in 1 μl saline were made into histologically confirmed sites in SN. Immediately following injection animals were placed in automated rotameter bowls for continuous recording of rotations prior to decapitation, dissection and freezing of striata and subsequent assay of DA by fluorimetry and HVA and DOPAC by GLC.

Unilateral injections of the GABA-agonist muscimol (5–30 ng) and the GABA derivative baclofen (100–500 ng) into SN induced a strong dose-related contralateral rotational response. Saline and β-phenylethylamine (100 ng) induced negligible rotation, suggesting that the phenylethylamine moiety of baclofen is not responsible for the observed response (Curtis, Game, Johnston & McCulloch, 1974).

Muscimol (100 ng) induced a vigorous contralateral rotation. Assays carried out on striata dissected and frozen 45 min after injection revealed increases in levels of striatal DA (+98%, $P < 0.02$) and DOPAC (+71%, $P < 0.01$) in the hemisphere receiving SN injection of muscimol. HVA levels were unchanged. This rotational response to 100 ng muscimol was only weakly attenuated (−33%, $P < 0.05$) by pretreatment with the DA-antagonist haloperidol (0.4 mg/kg i.p.). This dose of haloperidol completely abolished the contralateral rotational response to the DA-agonist apomorphine in rats with unilateral 6-hydroxydopamine lesions of the median forebrain bundle.

Neurochemical measures revealed muscimol-induced increases in DA and DOPAC levels that are consistent with reduced impulse flow in nigrostriatal DA neurons (Walters, Roth & Aghajanian, 1973) and therefore with a striatonigral inhibition of activity in the nigrostriatal DA system mediated via GABA (Dray & Straughan, 1976). The insensitivity of the resulting rotational responses to antagonism by the neuroleptic haloperidol suggests that this behaviour is independent of DA mechanisms (Di Chiara, Olianas, Del Fiacco, Spano & Tagliamonte, 1977). As rotational responses are dissociable from neurochemical changes in terms of the roles of GABA and DA, these results may reflect a GABA-like inhibition of both dopaminergic and non-dopaminergic neurons in SN.

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