Comparison of circling behaviour following unilateral inhibition of GABA-transaminase or discrete electrolytic lesioning in the rat substantia nigra

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The concentration of GABA can be elevated unilaterally in the rat substantia nigra by local injection of ethanolamine-*O*-sulphate (EOS) (Dray, Oakley & Simmonds, 1975) an irreversible active-site-directed inhibitor of GABA-transaminase (GABA-T) (Fowler & John, 1972; Fowler, 1973). In such animals both apomorphine and amphetamine have been shown to produce *ipsilateral* turning behaviour (Dray *et al.*, 1975). We wish to report further correlates of motor activity changes following discrete unilateral electrolytic lesions or unilateral elevation of endogenous GABA concentration in one substantia nigra.

Male albino rats (200-250 g) were anaesthetized with halothane and unilateral injections of EOS (200 μg kg^{-1} in 1.5 μl) were made stereotaxically into the substantia nigra:zona reticulata (SNR). Discrete unilateral electrolytic lesions (1 mA for 20 s) were made either in the substantia nigra : zona compacta (SNC) or in the SNR. Both injection and lesion sites were confirmed histologically.

Animals with EOS injected into the SNR showed tight ipsilateral circling behaviour after an i.p. injection of apomorphine (4 mg kg^{-1}) or amphetamine (4 mg kg^{-1}). This was observed at 4-6 h after the EOS injection in some animals and by 24 h in all animals. The intensity of circling decreased after 3-5 days and was absent after 10 days.

The circling behaviour was associated with a significant reduction in GABA-T activity and an elevated GABA concentration in the injected SNR compared with the contralateral side. There was a significant decrease in ipsilateral striatal dopamine content but no consistent differences in striatal noradrenaline. By contrast, animals injected with EOS above the substantia nigra showed no circling behaviour after apomorphine or amphetamine and SNR GABA-T activity and GABA concentration was normal.

Unilateral electrolytic lesioning in the SNC produced the expected contralateral turning after apomorphine and ipsilateral turning after amphetamine (Ungerstedt, 1971a,b). However, after discrete lesions in the SNR, animals exhibited *ipsilateral* circling when challenged with either apomorphine or amphetamine. These responses could still be consistently produced 7 weeks after lesioning.

In both EOS injected and electrolytically lesioned animals, circling behaviour in the same direction as that produced by apomorphine could also be produced by i.p. injections (10-50 mg kg^{-1}) of the dopamine-receptor stimulant bromocriptine (Corrodi, Fuxe, Hökfelt, Lidbrink & Ungerstedt, 1973). However, this compound had a more prolonged onset and duration of action than apomorphine and circling behaviour was generally less intense.

These results suggest that similar changes in induced locomotor activity may be produced by two different experimental procedures, i.e. the elevation of GABA concentration or discrete electrolytic lesions in one SNR. These changes may be tentatively accounted for by postulating an ipsilateral increase in ascending nigro-striatal dopaminergic neurotransmission. This could result from the reduced activity of non-GABA inhibitory interneurones within the SNR either by their GABA-mediated inhibition following EOS, or by their electrolytic destruction.

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