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Lack of serotonergic involvement in turning behaviour induced by a unilateral lesion of the locus coeruleus in rats

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Unilateral lesions of the rat locus coeruleus produce circling behaviour apparently due to an asymmetry of striatal dopamine receptor activity (Donaldson, Dolphin, Jenner, Marsden & Pycock, 1976). Such circling may be mediated indirectly via the raphe nuclei since there is biochemical and histological evidence for a projection from locus coeruleus to the raphe system (Kostowski, Samanin, Bareggi, Marc, Garattini & Valzelli, 1974; Dahlstrom & Fuxe, 1964). We have investigated this possibility.

Ten days after a unilateral electrolytic lesion of locus coeruleus animals circled contraversively in response to apomorphine HCl (0.5 mg/kg, s.c.). At this time after surgery there was fall in ipsilateral forebrain noradrenaline (NA) levels ($P < 0.05$), but ipsilateral dopamine (DA), 5-hydroxytryptamine (5-HT), and 5-hydroxyindoleacetic acid (5-HIAA) levels were unchanged ($P > 0.05$).

Bilateral electrolytic lesions of locus coeruleus produced no obvious behavioural changes. Three and ten days following surgery, cortical NA levels were decreased bilaterally ($P < 0.05$), forebrain DA and 5-HT levels were unchanged ($P > 0.05$) but cortical and midbrain 5-HIAA levels were elevated ($P < 0.05$). Pretreatment of animals at three days with *p*-chlorophenylalanine methyl ester HCl (200 mg/kg 36 h and 12 h prior to death) decreased striatal and mesolimbic 5-HT levels bilaterally in comparison to identically treated sham operated animals ($P < 0.02$).

This data provides evidence for increased 5-HT turnover following bilateral locus coeruleus lesions.

Pretreatment of animals with a unilateral locus coeruleus lesion at three days with α -methyl-*p*-tyrosine methyl ester HCl (200 mg/kg 18 h and 1.5 h prior to death) decreased cortical, mesolimbic and midbrain NA on the unlesioned side in comparison to identically treated sham operated animals ($P < 0.05$). This data provides evidence for an increase in NA turnover in the contralateral forebrain, following a unilateral locus coeruleus lesion.

Electrolytic bilateral lesioning of the dorsal and median raphe nuclei and a unilateral lesion of locus coeruleus (on the same or a subsequent occasion) produced a bilateral fall in cortical, striatal, mesolimbic, hypothalamic and mid-brain 5-HT ($P < 0.05$) and a unilateral fall in cortical and mesolimbic NA ($P < 0.05$) ten days following surgery. These animals were hyperactive and showed spontaneous contralateral rotation.

This data indicates a bilateral input from locus coeruleus to the raphe nuclei that regulates 5-HT activity. However, a unilateral locus coeruleus lesion did not affect 5-HT turnover, and the resulting circling behaviour was not prevented by bilateral raphe nuclei lesions.

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