Lesions of the frontal cortex of the rat: changes in neurotransmitter systems in sub-cortical regions

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The frontal cortex is known to contain dopamine (DA) and noradrenaline (NA) terminals arising from projections of mesencephalic and brain stem located cell bodies respectively (Lindvall, Björklund & Divac, 1978). Ablation of this region of the cortex stimulates motor behaviour in the rat (Iversen, 1971) although the exact functional roles of the catecholamine neurotransmitters have yet to be established. Initial observations suggest a behaviourally inhibitory role for DA in the frontal cortex as opposed to its excitant properties in the classical sub-cortical regions (Carter & Pycock, 1978; Tassin, Stinus, Simon, Blanc, Thierry, Le Moal, Cardo & Glowinski, 1978). We now report the effects of lesions aimed at the frontal cortical DA system on monoamine concentrations in extrapyramidal and limbic areas.

Bilateral electrolytic (2 mA for 10 s), 6-hydroxydopamine (6-OHDA) (8 μg/2 μl) alone, 6-OHDA plus desipramine (DMI, 20 mg/kg i.p.) or sham lesions were placed stereotaxically in frontal cortex of male Porton rats (A 10.3, L ± 0.8, V + 1.5; König & Klippel, 1963). Monoamine concentrations were assayed by radiometric and fluorimetric techniques 8 days after surgery and GABA concentrations by the method of dansylation. Catecholamine turnover was assessed at 5 days both by measuring the concentration of amine metabolites and by observing the decline in parent amine levels after inhibition of tyrosine hydroxylase with α-methyl-*p*-tyrosine (250 mg/kg, i.p.).

All types of lesions caused a significant fall in cortical NA (24% of sham, $P < 0.001$), although this was reduced by DMI pretreatment (39% of sham, $P < 0.001$). Only the electrolytic and 6-OHDA/DMI lesions decreased frontal cortical DA concentrations (40 and 56% of shams respectively, $P < 0.001$), the 6-OHDA alone lesion paradoxically increased DA levels (158% of sham, $P < 0.001$). Both 6-OHDA lesions elevated striatal DA concentrations (+16%, $P < 0.05$) and the 6-OHDA/DMI combination also increased accumbens DA levels (+23%, $P < 0.05$).

The 6-OHDA/DMI lesion enhanced extrapyramidal and limbic DA turnover as suggested by elevated DA metabolite concentrations and an increase in the rate of disappearance of DA from striatal and accumbens areas after α-methyl-*p*-tyrosine. This type of lesion also decreased 5-HT and its metabolite concentrations in some sub-cortical areas, and resulted in significant loss of GABA from substantia nigra and globus pallidus ($P < 0.01$).

In the previous study (Carter & Pycock, 1978) the most pronounced effects in terms of increased motor behaviour were seen following 6-OHDA/DMI lesions. Biochemically this lesion produces the most selective destruction of DA systems within the frontal cortex as well as enhanced DA utilisation within sub-cortical regions, suggesting that these biochemical changes, at least in part, explain certain behavioural observations. Although the importance of other neurotransmitter systems in this cortical region cannot be ignored, these studies suggest that catecholamine activity within the frontal cortex is able to modify neurotransmitter turnover in sub-cortical structures, with important implications in the aetiology of various psychotic and neurological disorders.

References

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