Blockade of the electrocortical changes induced by perfusion of amphetamine in the brain stem reticular formation

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In sleeping cats perfusion of (−)-noradrenaline (NA) or (−)-α-methyl-noradrenaline (MNA) bilaterally into the pontine and mesencephalic reticular formation (MRF) using push-pull cannulae produces short periods of electrocortical desynchronization followed by tonic desynchronization and behavioural arousal. A secondary sedative effect is observed if concentrations in excess of 10^{-3} M are used (Key, 1975).

In the present experiments bilateral perfusion for 5 min of (+)-amphetamine into the MRF of 30 cat *encéphale isolé* preparations mimicked the phasic and tonic electrocortical desynchronization responses induced by NA, but did not produce the secondary sedative effects even when concentrations as high as 10^{-2} M were used. Perfusion of dopamine (10^{-6} to 10^{-3} M) had little or no effect. Concentrations of NA, α-MNA or amphetamine which consistently produced tonic electrocortical desynchronization, were used to study the effects of 6-hydroxydopamine (6-OHDA). Perfusion of 6-OHDA (10^{-4} M) initially produced electrocortical desynchronization which lasted for approximately 30 minutes. After a 1-1.5 h perfusion the electrocortical changes induced by NA or α-MNA (10^{-4} M) were unaltered, but that produced by amphetamine (10^{-3} M) was reduced or abolished, providing the perfusion of amphetamine preceded that of NA or α-MNA. If NA or α-MNA was the first drug tested after 6-OHDA, subsequent perfusion of amphetamine induced electrocortical changes.

These results suggest that amphetamine has a presynaptic action on NA terminals within the MRF and that the NA terminals, although depleted, are still capable of taking up exogenously applied NA or α-MNA after a 1 h perfusion of 6-OHDA. These findings have been further investigated using histochemical methods.

Catecholamine terminals in the MRF of the adult cat are extremely difficult to visualize with the conventional formaldehyde-induced fluorescence method. However, α-MNA is equipotent with NA in its electrocortical effects and since this compound is resistant to monoamine oxidase and also produces a strong fluorophore, it has been used in an attempt to visualize the catecholamine terminals involved in the electrocortical effects produced by amphetamine using the fluorescence method of Falck & Owman (1965). After perfusion of α-MNA (10^{-4} M) for 5 min, catecholamine terminals were observed in the MRF in the vicinity of the cannula tips. The cannula tips were close to the dorsal noradrenergic pathway and uptake of α-MNA was also observed in the axons of this pathway. After perfusion of 6-OHDA (10^{-4} M) for 1 h with prior perfusion of α-MNA, no catecholamine terminals could be observed in the vicinity of the cannula tips. The lack of terminal fluorescence would appear to be due to depletion, since perfusion of artificial CSF for 1 h after a 5 min perfusion of α-MNA did not lead to the disappearance of catecholamine fluorescence. However, after perfusion of 6-OHDA for 1 h followed by perfusion of α-MNA, catecholamine fluorescence, although weak, was still observed in the terminals, indicating that 6-OHDA had not caused complete degeneration in the time interval used. The histochemical data thus support the pharmacological results.

References

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