Iontophoretic studies with 'false transmitters' on cerebellar Purkinje cells

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The concepts of 'false transmitter' accumulation and release from aminergic neurones are of increasing interest in attempts to understand both the physiology and pharmacology of aminergic neuronal systems (cf. Kopin, 1972). With few exceptions, however, false transmitter candidates have not been tested for their ability to alter central neuronal activity, using single unit recording and iontophoretic techniques. Therefore, we have compared the effects of octopamine (OCT) and para-hydroxynorephedrine (PHN) with those of noradrenaline (NA) on Purkinje (P) and unidentified cells in the cerebellar vermis of rats. P cell responses were judged to be of particular interest because of their postulated noradrenergic input (see Hoffer, Siggins, Oliver & Bloom, 1973) and both octopamine (Kopin, Fisher, Musacchio, Horst & Weise, 1965) and PHN (Brodie, Cho & Gessa, 1969) may, under certain conditions, be false transmitters in noradrenergic neurones. In addition, the effects of iontophoretically applied amphetamine were compared with those of NA, OCT and PHN. Comparisons were also made between NA and amphetamine effects on P cells in naïve and α-methyl-p-tyrosine (α-MpT) pretreated animals.

Standard single-cell techniques were employed on Sprague-Dawley rats anaesthetized with either a mixture of O_2, N_2O and methoxyflurane or chloral hydrate (300 mg/kg initially, with supplements as required), whose body temperature was maintained at 37° C. all drugs were in 0.2 M solutions at pH 4.0-4.5. P cells were 'identified' by their irregular, high rate of spontaneous discharge and by the presence of 'inactivation potentials' (Woodward, Hoffer & Lapham, 1969).

NA (20-100 nA, 30-60 s) depressed the activity of a high proportion of both P (21/22 : 95%) and unidentified (17/23 : 74%) cells. On cells inhibited by NA, the effects of amphetamine, OCT, and PHN were also assessed. Equal application of amphetamine generally mimicked the potency and time-course of NA effects on both types of cells. Interestingly, however, α-MpT pretreatment (200 mg/kg, i.p. .2-5 h prior to recording) did not attenuate the effects of iontophoretically applied amphetamine on P cells, although tyrosine hydroxylase was inhibited by this pretreatment as evidenced by a 52% reduction in the CNS content of NA.

Compared to NA and amphetamine both OCT and PHN were weak agonists in their abilities to inhibit cerebellar cell firing and did not affect cells not inhibited by NA. Using equal (to NA) ejection times and currents, OCT inhibited 10 out of 21 P cells depressed by NA and 9 out of 17 unidentified cells. Similarly, PHN inhibited 7 out of 21 P cells and 8 of 17 unidentified cells. On P cells the effects of OCT and PHN were generally weaker than that of NA; whereas when they inhibited unidentified cells, the effects were often as potent as NA. An additive effect on P cell firing between OCT or PHN and NA was frequently observed.

Thus if OCT and PHN are false transmitters in the CNS, then these studies suggest they should reduce noradrenergic inhibition of cerebellar P cells.

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