Interactions of putative neurotransmitters in the region of the raphé nuclei of the rat

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There is increasing evidence to suggest that neurotransmitter release in the brain is subject to control by other locally released transmitters (e.g., Reubi, Iversen & Jessell, 1977). We have examined the possibility that synaptic transmission in the 5-hydroxytryptamine (5-HT)-containing cell bodies of the raphé nuclei may be subject to similar influences. We have studied the effect of putative neurotransmitters on the release of 5-HT and γ-aminobutyric acid (GABA) from this region. After removal of the brain, horizontal cuts were made, one just below the cerebral aqueduct and the other above the medial lemniscus, at the level of A350 (König & Klippel, 1963). The central 1 mm portion of brain was taken and chopped in two directions at 0.2 mm intervals; this region containing dorsal and median raphé cell groups. The subsequent methods used to study the release of preloaded radiolabelled transmitter from superfused tissue slices *in vitro* have been described in detail elsewhere (Kerwin & Pycock 1979). Amino-oxyacetic acid (10 μM) or pargyline (50 μM) were present to inhibit labelled transmitter metabolism where appropriate.

A depolarizing stimulus (20 and 50 mM KCl) stimulated the rate of efflux of [^{3}H]-5-HT and [^{3}H]-GABA from raphé slices. The effect of KCl was markedly reduced in a low calcium, magnesium-substituted medium. In addition, tissue slices accumulated these labelled transmitters with apparent high affinity kinetics (Km = 1.50 μM for [^{3}H]-5-HT and 9.58 μM for [^{3}H]-GABA; substrate concentrations of 0.2–2 μM for 5 min). These results suggest the tissue slices contain functionally intact nerve terminals for these transmitters. GABA (100 and 500 μM) stimulated the spontaneous efflux of [^{3}H]-5HT from raphé slices. The effect was blocked by picrotoxin (50 μM) but not by strychnine hydrochloride (1 μM). Other inhibitory amino acids, β-alanine, glycine and taurine (all at 1 mM) were without effect on [^{3}H]-5-HT efflux. The efflux of [^{3}H]-5-HT was also stimulated by substance P (SP) at 50 and 100 μM. L-Noradrenaline (NA) (0.2–1 mM) stimulated the efflux of [^{3}H]-GABA but not that of [^{3}H]-5-HT. Neither dopamine nor 5-HT influenced the efflux of [^{3}H]-GABA.

This data may provide insight into the neuronal interactions within the raphé nuclei. The demonstration of NA-stimulated GABA release complements the hypothesis of Gallagher & Aghajanian (1976) that adrenergic influence on the raphé is mediated indirectly via GABA interneurones. Secondly the effect of GABA on raphé cell firing (Gallagher & Aghajanian 1976) may be associated with a concomitant modulatory release of 5-HT from dendrites or terminals, within this region. Although the raphé possesses SP-containing terminals (Cuello & Kanazawa 1978), the possible functional relevance of SP-stimulated 5-HT release is not yet clear.

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Behavioural and neurochemical studies on the striatonigral GABA pathway

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We have recently shown that denervation of nigral γ-aminobutyric acid (GABA) receptors by destruction of the striatonigral GABA pathway results in an enhanced dopamine (DA)—independent contralateral rotational response to unilateral intranigral injections of the GABA agonist, muscimol and elevated nigral [^{3}H]-GABA binding; this apparent denervation supersensitivity is characterised by an increase in the number of high affinity [^{3}H]-GABA binding sites (Waddington & Cross, 1978a). In this study we describe interrelationships between various behavioural and neurochemical indices of the integrity of the striatonigral GABA pathway.