The effects of noradrenaline and 5-hydroxytryptamine on the responses of dorsal horn neurones to noxious and innocuous skin stimuli

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There are numerous reports relating noradrenergic (NA) and tryptaminergic (5-HT) systems to the analgesia induced both by morphine and by stimulation in the midbrain (see Oliveras, Hosobuchi, Redjemi, Guilbaud & Besson, 1977, for references). Such an interaction could occur at the termination of descending NA or 5-HT fibres in the substantia gelatinosa of the spinal cord, a region in which morphine and methionine enkephalin amide have been shown to be active in reducing the nociceptive responses of neurones in laminae IV and V (Duggan, Hall & Headley, 1976, 1977). We have now tested NA and 5-HT administered electrophoretically in the dorsal horn.

Experiments were performed on 12 spinal cats anaesthetized with α-chloralose, paralysed with gallamine and artificially ventilated. The noxious stimulus to a hindlimb footpad was radiant heat (skin temperature $>45°C$). Such a stimulus was alternated with an innocuous stimulus produced by deflection of nearby hairs by a moving airjet. Extracellular recordings were obtained with a multibarrel pipette positioned in spinal lamina IV or V, and drugs were ejected either from this pipette or from a second electrode positioned in the substantia gelatinosa, 50–760 μm dorsal and up to 100 μm lateral to the recording electrode. Results were obtained from 26 cells.

Administered in the substantia gelatinosa, NA (20–100 nA) and 5-HT (30–250 nA) reduced the nociceptive responses of 20/20 and 13/19 cells respectively. Selectivity (i.e. no reduction of responses to innocuous stimuli) occurred with 9 cells using NA and 6 cells using 5-HT; with most other neurones non-nociceptive responses were also reduced but to a lesser extent than were nociceptive responses. The time course of these effects was prolonged. Recovery from NA took 2–15 min and with 5-HT recovery took more than 20 min on 7 of 13 occasions. These actions contrast with the lack of effect of acetylcholine (150–200 nA, 7 cells), GABA (100–200 nA, 11 cells) and excitant amino acids (Duggan *et al.*, 1977).

Ejected near cell bodies 5-HT (22–100 nA) reduced both nociceptive and non-nociceptive responses of 4 of 6 cells tested and GABA (12–100 nA) was similarly non-selective on 7 of 10 cells. NA (10–40 nA) was slightly selective on 9 of 10 cells, but the degree of this selectivity was much less than with administration into the substantia gelatinosa.

Thus the monoamines, but not amino acids, were similar to morphine and enkephalin in being more selective for nociceptive responses when administered in the substantia gelatinosa. The opiate antagonist naloxone reduces the analgesia produced by stimulation in a nucleus of origin of descending 5-HT fibres (Oliveras *et al.*, 1977); we are currently testing naloxone for interaction with the monoamines administered in the substantia gelatinosa.

Reference

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Correlation between effects of brain-stem stimulation and effects of 5-hydroxytryptamine and noradrenaline on non-nociceptive and nociceptive spinal interneurones

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Electrical stimulation in the area of the brain stem raphé nuclei produces analgesia in the cat (Mayer & Liebeskind, 1974) which is thought to be produced by activation of a descending influence to cause inhibition of nociceptive impulses at the spinal level (Liebeskind, Guilbaud, Besson & Oliveras, 1973). It has been suggested that this descending pathway is tryptaminergic (Guilbaud, Besson, Oliveras & Liebeskind, 1973; Vogt, 1974). In order to investigate this possibility further, 5-hydroxytryptamine (5-HT) and noradrenaline (NA) were applied locally to identified dorsal horn interneurones and an attempt to correlate their effects on spontaneous and stimulus-evoked firing with effects of brain stem stimulation on their activity was made.

Cells were identified as having a nociceptive input if their activity was altered by injection of small amounts