Responses of dorsal horn units in cat spinal cord to some putative transmitters and to cutaneous stimulation

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Although attempts have been made to study the pharmacology of sensory transmission in the spinal cord (Game & Lodge, 1975; Henry, Krnjević & Morris, 1975; Randić & Yu, 1975) our knowledge remains limited.

In decerebrated or chloralose-anaesthetized cats, single units in the dorsal horn of the lumbar cord were studied to determine whether a correlation exists between responses to microiontophoretic application of some putative transmitters and those to peripheral stimulation. Stimuli used were: noxious thermal (radiant heat from a 250 W infrared bulb) and non-noxious (air stream, camel hair brush, gentle manual pressure).

One hundred and fifteen units were tested. Most units, regardless of the response to natural stimulation, were excited by glutamate and depressed by GABA. Substance P and bradykinin caused slow prolonged excitation of nociceptive units but failed to affect non-nociceptive units. Noradrenaline most commonly caused depression, although no correlation was found with a specific peripheral stimulus. 5-Hydroxytryptamine caused excitation and depression of approximately equal numbers of units; neither effect was clearly associated with a specific stimulus. In general, units located more dorsally tended to be depressed by 5-hydroxytryptamine, while those located more ventrally tended to be excited. Acetylcholine was usually without effect.

Although the pharmacology of pathways involved with specific sensory modalities is still far from clear these results suggest that Substance P and bradykinin may be associated with chemical transmission in spinal pathways subserving nociception and that glutamate and GABA might also be involved in transmission, although their effects are not associated with a specific sensory modality.

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GABA antagonism as a possible basis for the convulsant action of a series of bicyclic phosphorus esters

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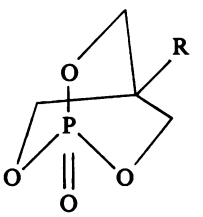

Figure 1

Compounds with the general formula 4(R)-1-Phospha 2,6,7-trioxabicyclo (2,2,2) octane-1-oxide ((R)PTBO where R = alkyl group, Figure 1) are potent convulsants (Bellet & Casida, 1973).

Intravenous or topical application of the isopropyl (IPTBO), ethyl (EPTBO) or pentyl (PPTBO) derivatives antagonizes the depressant action of microiontophoretically applied GABA in the rat medulla (Bowery, Collins & Hill, 1976). A quantitative comparison of the PTBO series as GABA antagonists was accordingly made *in vitro* on the isolated superior cervical ganglion of the rat (Bowery & Brown, 1974) and on the isolated hemisected spinal cord of the frog (Tebecis & Phillis, 1969).

Ganglia were excised from rats under urethane anaesthesia (1.5 g/kg) and suspended between two

non-polarizable $Ag^+/AgCl$ electrodes placed in contact with the post-ganglionic trunk and the ganglion body. The tissue was superfused at 1 ml/min with Krebs solution (containing hyoscine 2.6 μm) at 25°C and the potential difference across the electrodes monitored on a Servoscribe 1 s chart recorder. Addition of GABA or carbachol to the superfusate produced a dose dependent depolarization of the ganglion (Bowery & Brown, 1974). Concurrent application of PTBO derivatives antagonized the depolarizing action of GABA but not that of carbachol.

Spinal cords were dissected from decerebrated frogs and hemisected. Half-cords were transferred to a cooled perfusion apparatus (10°C) and dorsal roots mounted on $Ag^+/AgCl$ electrodes for DC recordings. The trans-synaptic actions of drugs were eliminated by the addition of procaine to the superfusing solutions as described by Evans & Watkins (1975) and Tris buffer was used to maintain pH neutrality. Application of GABA, glycine or glutamate (0.5 to 4 mM) produced dose-dependent depolarization of dorsal roots. Concurrent exposure to the PTBO compounds produced antagonism of the GABA-induced depolarization but did not reduce the glutamate or glycine responses.

In both ganglion and dorsal root the potency ranking of the compounds as GABA antagonists was IPTBO > EPTBO > PPTBO which is in the same order as the convulsant potency. The potency of IPTBO as a GABA antagonist was comparable with that of bicuculline methochloride and picrotoxin. It was, therefore, concluded that the PTBO compounds are effective and specific GABA antagonists when tested on either preparation. The potency ranking suggests that the convulsant properties of the PTBO series may be due to antagonism of the actions of synaptically-released GABA.

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Evidence for a specific somatosensory receptor in the cat skin that responds to irritant chemicals

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The irritant chemical dibenzoxazepine (CR) produces a sensation of burning pain when applied to the human skin (Ballentyne, Beswick & Price-Thomas, 1973) and acts on somatosensory receptors in the cat related to unmyelinated nerve fibres (Foster & Ramage, 1975). Further investigations have sought to classify the type of sensory receptor acted upon by CR and by *w*-chloroacetophenone (CN), *o*-chlorobenzylidene malononitrile (CS), *n*-nonyl vanillylamide (VAN) and capsaicin (CAP).

Cats were anaesthetized with α-chloralose (70–90 mg/kg). Multifibre or single unit activity was recorded (Iggo, 1960) from the saphenous nerve.

Irritants (5×10^{-4} M in saline to 10^{-1} M in alcohol) were tested by topical application to the receptor area. Analysis of results employed a computer method (Foster & Ramage, 1976).

In 18 low threshold alpha mechanoreceptor units activity was only induced indirectly when local oedema was caused by the irritant.

Twenty moderate to high threshold alpha delta mechanoreceptor units which are believed to be responsible for a sensation of sharp pain (Landau & Bishop, 1958), were not activated by the irritants; nor were 10 low threshold C-mechanoreceptor units.

Very high threshold C-mechanoreceptor units, which adapt rapidly, and a cold thermoreceptor unit were not activated by the irritants. A warm thermoreceptor unit did show an increase in activity to CR 10^{-4} M (Foster & Ramage, 1975) but