

The effects of 2-2'-pyridylisatogen tosylate on the electrical activity of smooth muscle of the isolated taenia caeci of the guinea-pig

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2-Substituted isatogen derivatives cause a slowly developing relaxation of the guinea-pig taenia caeci

which is not correlated with the ability of some of these derivatives to antagonize the inhibitory effects of ATP (Foster, Hooper, Spedding, Sweetman & Weetman, 1978).

2-2'-Pyridylisatogen tosylate (PIT) both relaxes the taenia and antagonizes ATP (Spedding, Sweetman & Weetman, 1975). In the present experiments we have examined the effects of PIT on the electrical activity of the taenia.

Intracellular recordings of electrical activity with simultaneous measurement of tension were made by the method of Small & Weston (1977). Tissues were mounted under a resting tension of 1 g in Krebs' solution (37.5°C) containing hyoscine (0.3 μ M).

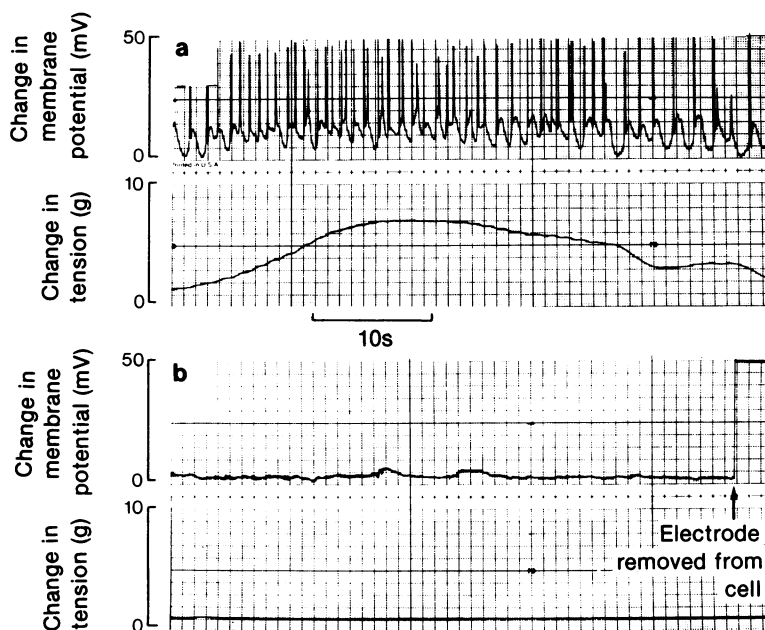


Figure 1 The effects of 2-2'-pyridylisatogen tosylate on the electrical and mechanical activity of the isolated taenia caeci of the guinea-pig.

The upper record in each case represents membrane potential changes, whilst the lower record represents tension changes (increase in tension upwards).

a: spontaneous activity recorded prior to PIT.

b: activity recorded from another cell after 20 min exposure to PIT (50 μ M).

The effects of PIT on the electrical activity were examined by impalement of five cells prior to drug exposure. Resting membrane potential was equated with the potential change on withdrawal of the electrode from the cell. Twenty min after first exposure to PIT, the electrical activity of a further five cells in the same region of tissue was recorded.

Prior to exposure to PIT, all cells exhibited spike activity whose frequency increased during a spontaneous tension wave (Figure 1a). After exposure to PIT (50–100 μ M), spontaneous tension waves were abolished and most cells failed to exhibit spike activity. However, these cells had similar transmembrane potentials to those tested prior to PIT exposure (Figure 1b).

Since the relaxant effects of ATP are associated with hyperpolarization of the taenia (Tomita & Watanabe, 1973; Jager, 1974) whereas PIT causes relaxation without change of membrane potential, we conclude that the spasmolytic effect of PIT is not mediated by the activation of receptors for ATP.

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Nitrous oxide in practical classes

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Practical classes on effects of mixtures of nitrous oxide and oxygen have long been given by one of us (Wilson, Crockett, Exton-Smith & Steinberg, 1950) and have recently been introduced in Manchester.

They illustrate for students ideas such as: 1, a drug which is most commonly classified 'anaesthetic' has various other effects at low doses; 2, these effects can be measured selectively and quantitatively by brief and simple test methods, and dose-response relations can be demonstrated.

Changes in the following have been assessed: 1, the efficiency of carrying out intellectual, perceptual and motor tasks (Steinberg, 1954; Legge, Steinberg & Summerfield, 1964); 2, pain thresholds; 3, subjective effects (Steinberg, 1964), mainly by means of adjective check lists and questionnaires.

Two kinds of 'control' were used: first, each student carried out a set of tests before (baseline) and then, again, while breathing a gas mixture from a Douglas bag; secondly, in addition to the gas mixtures (20%, 30% and 40% nitrous oxide in oxygen), there was an oxygen (or, in some experiments, air) control group of students.

Observed changes were usually in the direction of impairment of performance, raised pain thresholds

and exaggeration of 'normal' subjective reactions, both pleasant and unpleasant.

The students' attention was especially drawn to the consistency of the average effects, even with small numbers of students and despite variations in test procedures over the years; and to the wide range of individual differences in response. Handwriting size was found to be one of the most successful indices of the action of the drug, and subjective reactions yielded particularly interesting 'profiles', which have obvious implications for clinical practice. With students, the classes appear to be popular and effective.

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