

9

EXPERIMENT NINE

Rabbit Jejunum

The isolated innervated rabbit jejunum (Finkelman preparation) provides a way of studying drug effects on sympathetic nerve function.

Sympathetic adrenergic nerve fibres reach the intestine by way of perivascular nerves in the mesentery. Repetitive stimulation of these nerves inhibits rhythmic activity in the enteric autonomic plexuses, and leads to relaxation of the intestine or reduction of activity.

The adrenergic neurone-blocking drug guanethidine prevents the release of transmitter from the adrenergic terminals. In this way it blocks the effects of perivascular nerve stimulation with little effect on the sensitivity of the intestine to noradrenaline.

Dissection

Remove the jejunum from the rabbit and cut out a suitable length to transfer to a dish of physiological saline. Cut portions of 20–30 mm in length, with the mesentery remaining intact. The mesenteric attachment is threaded through close-fitting ring electrodes and the jejunum mounted in an organ bath at 37 °C. Allow the preparation to equilibrate for 30 minutes at a resting tension of 1–2 g wt.

Plate 14 shows the rabbit small intestine (jejunum), with appropriate cutting sites marked. Plate 15 shows the ring electrodes with mesentery pulled through. One end of the jejunum is tied to a post, the other attached by a thread to the force transducer.

Experiment

Chart Settings

This is a single-channel arrangement with a PowerLab, Bridge Amp, and force transducer. In Chart, the range should be chosen to suit the maximum force to be exerted on the transducer. The final scale after units conversion and so on should be –1 to 8 g wt. The sampling rate should be at least 100 samples per minute. The view compression should be 1:1. A high-pass filter of 2 Hz should be chosen in the Bridge Amplifier dialog box. Data Pad miniwindows can be set up to show the comment number and text, and the twitch amplitude (using the Max–Min function).

Stimulation

Ensure that the cathode is the electrode closest to the muscle. If necessary, reverse the electrode connections. Typical stimulus parameters are 0.3 ms pulses at 20 Hz for 10 to 15 seconds every 4 minutes.

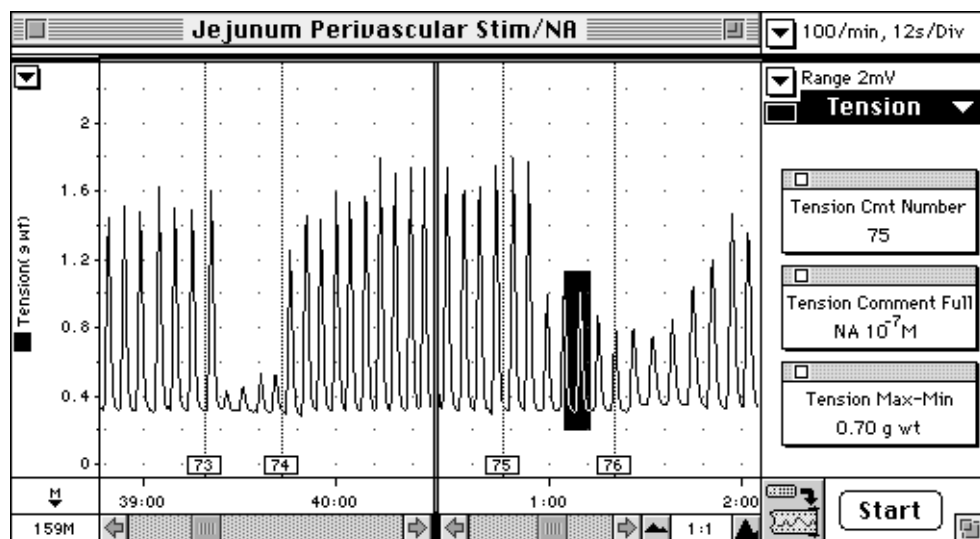
Protocol

Apply trains of stimuli as described above, and find the voltage that produces maximal inhibition of the pendular movement. Start at 5 volts and increase by 5 volts each time you stimulate. When maximal inhibition has been determined, switch the stimulus off. Spontaneous pendular movements should be observed. Do not over-wash the preparation, as continual washing will disrupt these movements.

Determine a half-log concentration–response curve to noradrenaline, starting at 10^{-8} M. Wash out each dose of noradrenaline before trying the next. Figure 9–1 shows spontaneous pendular movements of rabbit jejunum. The Chart window has been split to show two responses: pendular movements inhibited by perivascular nerve stimulation in the left pane, and by noradrenaline in the right pane. The Data Pad function Max–Min is used to measure the strength of contractions in a data selection, as shown in the miniwindows.

Figure 9–1

Spontaneous pendular movements of rabbit jejunum, inhibited by perivascular nerve stimulation (20 Hz) at comment #73 and by noradrenaline 10^{-7} M at comment #75.



Add guanethidine (5×10^{-6} M) and leave in contact for 15 minutes before repeating the nerve stimulus. Using the standard stimulation train, stimulate until the inhibitory response is blocked. If there is no block after 10 minutes, add a further dose of guanethidine. When a clear blocking effect of guanethidine is observed, repeat the dose–response curve for noradrenaline. The sensitivity to noradrenaline should be maintained during neuronal block by guanethidine.

The effects of guanethidine are very slow to wash out, presumably owing to active uptake into the adrenergic nerve terminals.

Plate 14. Section of rabbit gut showing mesentery and arcades of blood vessels, and where to cut the preparation.



Plate 15. Isolated rabbit jejunum (Finkelman preparation) on holder. (This is a segment such as that cut in Plate 14.)

