

FINCH, L. & HAEUSLER, G. (1973b). The cardiovascular effects of apomorphine in the anaesthetized rat. *Eur. J. Pharmac.*, **21**, 264-270.

SCHMITT, H., SCHMITT, H. & FENARD, S. (1973). Action of α -adrenergic drugs on sympathetic centres and their interactions with the central sympatho-inhibitory effect of clonidine. *Arzneim.-Forsch.*, **23**, 40-45.

VAN ZWIETEN, P.A. (1975). Interactions between centrally acting hypotensive drugs and tricyclic antidepressants. *Arch. int. Pharmacodyn. Ther.*, **214**, 12-30.

WELLENS, D., VAN NEUTEN, J.M. & JANSSEN, P.A.J. (1975). Centrally induced hypotension unrelated to α -adrenergic stimulation. *Arch. int. Pharmacodyn. Ther.*, **213**, 334-337.

Evaluation of narcotic and narcotic antagonist analgesic drugs in the dog dental pulp stimulation test

A.S. MARRIOTT, M. SKINGLE & M.B. TYERS

Pharmacology Department, Allen & Hanburys Research Ltd., Ware, Hertfordshire SG12 0DJ

In antinociceptive tests based on electrical stimulation of the dental pulp it is difficult to identify the response to electrical stimulation and to quantify the degree to which this response is changed by drugs. In the present work a procedure in the conscious dog is described in which the effects of drugs and placebo were measured in terms of changes in the stimulus threshold for eliciting a minimal response to dental pulp stimulation. Using this procedure reproducible, dose-dependent increases in stimulation threshold can be obtained with narcotic and narcotic antagonist analgesic drugs.

Adult, male beagle dogs were trained to sit in well ventilated individual boxes (32 x 23 x 28 in high). The boxes were illuminated inside and were fitted with a clear plate glass door for observation of the dogs. Following a training period, which ranged from 1-4 weeks, stainless steel stimulation electrodes were implanted in an upper canine tooth under pentobarbitone anaesthesia, using an operative technique similar to that described by Neat & Peacock (1971). Leads from the electrodes were passed subcutaneously to an external connector located on the back of the neck. The dogs were ready for testing 7-10 days post-operatively.

All tests were carried out such that the operator did not know whether a dog had received a drug or placebo. Each dog received one placebo and one drug trial each week. Drugs were administered either orally in gelatin capsules or subcutaneously. Groups of at least five dogs were used for each dose-level. Electrical stimulation thresholds

(0.5-1.5 V) to cause a characteristic, minimal response (i.e. licking, chewing, head movement, etc.) were determined for each dog prior to, and then at 30 min intervals up to 3 h after drug administration. Stimulus trains were delivered from a Devices isolated stimulator using square wave pulses of 5 ms pulse width, 10 Hz frequency and 10 s train duration; at least 30 s was allowed between trains of impulses during threshold determinations. The resistances of the tooth pulp electrodes (4-30 k) were monitored continuously on an oscilloscope as a check for open circuits.

The mean change (\pm s.e.) in stimulation threshold during placebo trials was $-0.14 \pm 0.41\%$ ($n=20$). Maximum drug-induced changes in stimulation thresholds ranged from +35 to +40%. Statistically significant ($P=0.05$), dose-dependent increases in stimulation thresholds were obtained with subcutaneous doses (mg/kg) of pentazocine (0.25-2) and nalorphine (0.1-1) and with oral doses (mg/kg) of morphine (0.25-3) and codeine (2-5). The potencies of these analgesic drugs were therefore similar to those found clinically. Results obtained with aspirin (100 mg/kg orally) were inconsistent. The following non-analgesic drugs (mg/kg orally) were inactive: atropine (1.0), mepyramine (0.5), phenolamine (1.0) and propranolol (1.0).

In our experience, dental pulp stimulation in the beagle dog provides an accurate and reproducible model for the evaluation of the antinociceptive activities of narcotic and narcotic antagonist analgesic drugs.

We are grateful to Mr R. Peacock for carrying out the electrode implantation operations and to Mr D. Harrison for constructing the electrode connectors.

Reference

NEAT, M.L. & PEACOCK, R. (1971). Implantation of electrodes in the dentine of an upper canine tooth in the dog. *Br. J. Pharmac.*, **43**, 476P.