DEMONSTRATIONS

A digital computer system for the on-line analysis of cardiovascular data

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The quantitative assessment of cardiac and haemodynamics by conventional recording techniques is time consuming and limits the nature and quality of data obtainable. We have attempted to overcome some of the associated problems by using a programmable on-line data acquisition and reduction system. Although designed primarily for the analysis of cardiovascular data from e.g. anaesthetised dogs, it may be readily adapted for a wide range of on- and off-line purposes.

Specialised analysis of cardiac dynamics requires left ventricular and aortic pressure signals for cardiac cycle recognition. The absolute and derived parameters from pressure, flow and other signals, are used as defined by Hawthorne, Walker, Hinds & Kraft-Hunter (1973).

The system may be used in a variety of modes during the course of an experiment and will sample and print data on command, at selected times, or measure peak changes in response to interventions such as drug administration. In some modes inspection of the visual display allows the editing or removal of unrepresentative beats or signals from the sample.

The computer equipment consists of a suite or programs, which runs on a standard CED real time computer system. The computer system comprises: a (Computer Automation) 16 bit minicomputer with 16 K words of memory, an analogue interface system, a dual floppy disc system, an XY cathode ray tube display, a visual display unit (VDU) control terminal and a printer/plotter.

The computer program makes extensive use of overlaying techniques to enable a large and powerful range of program options to be run in the relatively small memory. The control, display and plotting sections are written in FORTRAN, with the data acquisition and pattern recognition work—such as beat identification—done by modular interrupt driven assembler code routines.

The analogue interface digitises a selected range of analogue voltages that represent experimental signals, resolved to an accuracy of better than 1 part in 4000. It also provides sampling signals and allows accurate measurement of elapsed time during the operation.

Immediate visual feedback of a number of selected signals, and derived parameters is available by inspection of traces on the cathode ray tube and of the numerical display on the VDU. Data is stored throughout the experiment on low cost magnetic floppy discs, from which most of the important results may be retrieved at a later date. The printer/plotter is used during the experiment to tabulate the individual parameters of each test and to record certain immediate numerical results, such as responses to drug interventions on operator request. After the experiment, it is used to present the results of more extended analysis in numerical or graphical form.

Throughout the operations, the user has immediate control of the system by typing commands at the VDU keyboard, though the system is intended to allow automatic operation with the minimum of attention by the operator.

Reference

HAWTHORN, E.W., WALKER, M.L., HINDS, J.E. & KRAFT-HUNTER, F. (1973). A user-interactive data acquisition and reduction system for the study of cardiac dynamics. In: Chronically implanted cardiovascular instrumentation ed. McCutcheon, E.P. pp. 455–478. Academic Press.

The measurement of gastric motor function by real-time ultrasound

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Current techniques for measuring the effects of drugs on gastric motor function *in vivo* are invasive and unsuitable for repeated use in patients (Sheiner, 1975; Bateman, Leeman, Metreweli & Willson, 1977). Both the rate of emptying of gastric contents, and the activity of gastric peristaltic waves reflect motor activity in the stomach but none of the techniques currently available can assess these functions concurrently.

A Toshiba SAL 20 linear array real-time ultrasound scanner, with frame freeze facility, has been used to measure gastric volumes. Gastric volume is estimated from a series of parallel, cross-sectional images spaced at regular (1 cm) intervals along the longitudinal axis of the stomach. By recording gastric volumes at various times after a liquid meal the rate of gastric emptying is calculated.

Studies were performed on five healthy subjects after an overnight fast. Each consumed 500 ml warm (37°) orange cordial over 30 s, and gastric volumes were measured at 5, 10, 20, 30 and 40 minutes. In all subjects gastric volume declined monoexponentially (Half life 22.6 min $\pm$ 2.7 min).

In addition to measuring gastric volume, gastric peristaltic activity can be directly visualised on the scanner, and the nature and frequency of the contractions recorded.

Real time ultrasound is safe, and non-invasive. It is ideally suited to the measurement of drug effects on gastric motor function in man.

This work is supported by a grant from the Wellcome Trust.

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Nociceptive responses of neurones in trigeminal nucleus caudalis of the rat

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The trigeminal nucleus caudalis is the primary relay for pain sensation from the face and although this area has received extensive study in the cat and monkey it has been little studied in the rat (Anderson & Matthews, 1977). We have developed techniques for studying excitatory and inhibitory inputs to trigeminal caudalis neurones in the anaesthetized rat and are now examining the pharmacology of the neurotransmitter systems within this nucleus.

Experiments are performed on rats anaesthetized with urethane and prepared for recording as previously described (Ayliffe & Hill, 1979). Recordings are made with conventional extracellular micropipettes, and drugs are applied to single neurones by microiontophoresis.

Activation of low threshold neurones is readily achieved by low intensity cutaneous electrical, tactile or air jet stimuli and conduction velocity measurements suggest this input is via Aβ fibres (Ayliffe & Hill, 1979). Toothpulp electrical stimulation excites high threshold neurones principally via Aδ fibres but with some C fibres activated by very intense stimuli and electrical stimulation of cornea produces an excitation exclusively via C fibres (Ayliffe & Hill, 1979). Long latency neuronal excitation of high threshold neurones is also produced by noxious pressure or application of thermal stimuli in excess of 45°C.

Supported by the Wellcome Trust, Royal Society and M.R.C.

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A comparison of the analgesic activity of ketamine using two different methods of assessment

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The assessment of analgesic activity of anaesthetic agents using the rat tail-flick test (immersion of the tip of the tail in water at 60°C and measuring the response time) has previously been reported to the Society (Lawrence & Livingston, 1979). The results of those experiments have been compared with the analgesic potency measured using the rat foot pressure response with an apparatus which gives an increasing pressure that can be measured in terms of a digital readout (Figure 1). The comparison of the two groups of experiments indicated that the analgesic responses under the effects of ketamine showed a strong degree of agreement and that the two methods of testing both had advantages and disadvantages. The major difficulty with the tail-flick test was the rapid responses in the control situation. In the system used a control (unanaesthetized) time of about 2 s was obtained, and it was possible that observer response time could play a major part in the errors of these values. With the pad pressure test the control response time was adjustable and this problem could be avoided. The foot pad pressure test, however, had a less precise end point, in terms of the animal's desire to remove its foot from the pressure point, particularly when under anaesthesia as compared to the unanaesthetised control. The degree of agreement in the results obtained from the two methods would indicate that the response measured was valid in terms of the analgesic potency of ketamine.

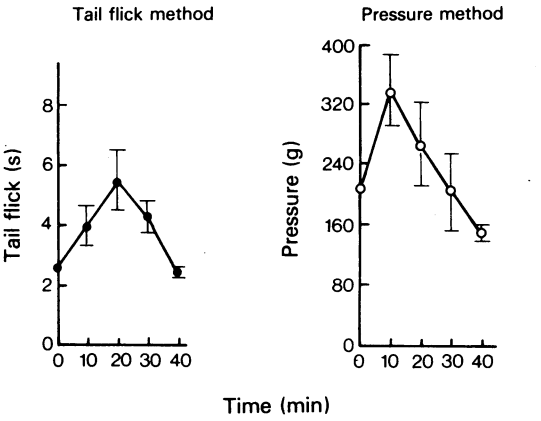

Figure 1 Comparison of the response to analgesic testing by the tail-flick reaction time and the foot pad pressure response during ketamine (100 mg/kg, i.p.) anaesthesia in the rat.

Reference

LAWRENCE, D. & LIVINGSTON, A. (1979). The effect of physostigmine and neostigmine on ketamine anaesthesia and analgesia. *Br. J. Pharmac.*, **67**, 426P.

A cheap and simple ultrasonic device for quantifying animal activity

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The Heathkit ultrasonic intrusion alarm (Model GD-39, The Informer®) has been adapted for use as an animal activity detector by applying the 50–150 Hz output signal from the LF amplifier and detector through a reed relay which switches a −24 V bias to operate a pulse former (Campden Instruments model 321) to produce −24 V pulses of 40 msec duration. These pulses can be used to trigger a printer-counter or cumulative counter so that a quantitative estimate of the amount of movement occurring in the field covered by the ultrasound transducers can be obtained.

The sensitivity range of the apparatus is sufficient to encompass the movements of a single mouse in a cage at 1 metre to large animal movements at 10 metres. The addition of further Campden Instrument modules enables the periods of detection to be programmed in advance. This device is considerably cheaper and more versatile than commercially available activity monitors and when not in use for experimental purposes it can be employed as a conventional burglar alarm to protect the laboratory from intruders.

The release of met-enkephalin from the intact brain

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Detection of the spontaneous and evoked release of met-enkephalin can now be reliably reproduced using brain slice preparations and radioimmunoassay. The detection methods used for *in vitro* studies have now been used to investigate the release of met-enkephalin from the intact brain. The methods and experimental conditions for studying met-enkephalin release from deep nuclei in the anaesthetized rabbit will be demonstrated.

Some uses of PET computers in pharmacology

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Microcomputers, such as the Commodore PET series, are inexpensive and extremely convenient. They occupy little space, need only a domestic power supply, use little current, and are very simple to operate. Although they do away with most of the jargon and mystique associated with large computers, they are nevertheless powerful and rapid and can be used to meet a wide range of laboratory needs. This will be demonstrated by showing some applications of PET computers, printers and twin floppy disc systems:

1. To the handling of experimental results in pharmacology and chemical pharmacology, including statistics, bioassay and radioimmunoassay calculations, least-squares line-fitting (linear and non-linear), fitting results to the Hansch equation, the calculation of pK_a and of apparent molal volumes, and in the preparation of HPLC histograms;
2. As teaching aids for illustrating adsorption processes and the relation between drug blood-levels and time after administration;
3. As word processors in the handling of letters;
4. As aids to psychorefreshment.

Maximizing the positive: techniques for the presentation and publication of pharmacological data

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