A COMPUTER-SIMULATED TIBIALIS ANTERIOR - SCIATIC NERVE PREPARATION (IN VIVO) FOR TEACHING NEUROMUSCULAR PHARMACOLOGY

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Computer simulated pharmacological preparations can be utilised in teaching in a variety of different ways. Using a simulation before the actual practical class helps the student to be better prepared to take advantage of the limited practical experience, especially involving in vivo preparations, provided in many courses. In addition, designs for experiments can be tested in a situation where mistakes & misconceptions do not lead to a real animal being wasted. Furthermore, experiments done only as formal demonstrations can be replaced by simulations; students then have to think for themselves what drugs to use, in what sequence and at what dose and may gain more from the use of a simulation than from a preset demonstration using a real animal or a videotape recording.
A computer simulated tibialis anterior - sciatic nerve preparation will be demonstrated. The programs (BASIC; BBC, IBM) produce a record (Figure 1), on a printer, of muscle contraction either in response to single shocks (0.5 or 0.05 Hz) or to a brief tetanus. Various drugs can be administered i.v. as required in any sequence & at any dose. Tubocurarine, gallamine, pancuronium, C10, fazadinium, atracurium, dantroline, neostigmine, physostigmine, edrophonium, triethylcholine, choline, 4-aminopyridine, atropine, succinylcholine and C6 can be used. In addition, succinylcholine, acetylcholine, carbachol or K^+ may be administered by close intra-arterial injection. Once a blocker has been administered it will wear off slowly according to its t-half or time can be 'advanced' to allow a faster reversal of effect. The program can provide 'unknown blockers' the pharmacological nature of which (along with relative potency and t-half) can be discovered by experiment.

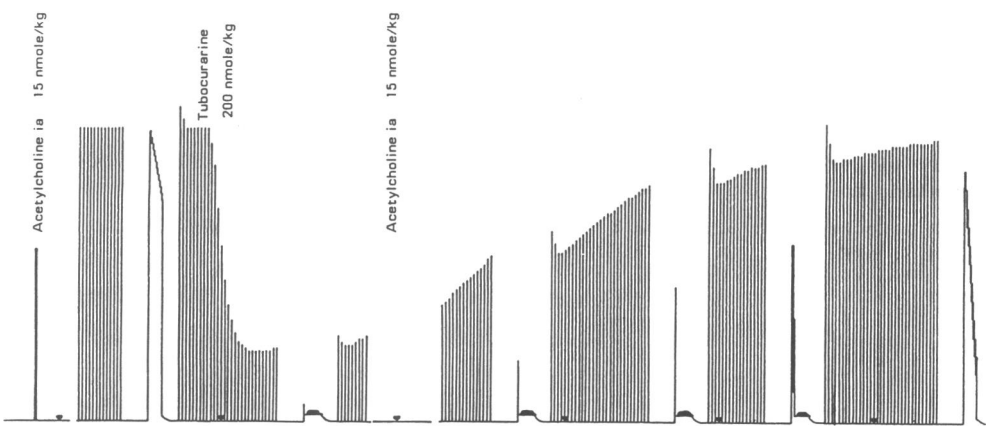

Figure 1 Simulated tibialis anterior - sciatic nerve preparation

STANDARDISATION OF RESTING DIMENSIONS IN LARGE ARTERIAL RING PREPARATIONS

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Standard resting dimensions of isolated arterial ring preparations are essential in order to make meaningful comparisons of responses. Two methods to standardise resting dimensions in resistance vessels and canine large arteries have been described. In each case the observed relationship between internal circumference and effective circumferential wall tension/unit length in the passively stretched vessel is compared with the theoretical linear relationship between these parameters were the vessel distended by 100mmHg transmural pressure. The intercept of the theoretical isobar and an exponential curve fitting the observed data is determined and L_{100}, the vessel's internal circumference at this tension, is defined. In these vessels maximum active contractions are subsequently generated when the vessel is set to 0.8-0.9L_{100}. (Mulvany and Halpern, 1977; Angus et al, 1986).

We report the development of a simple program for hand-held programmable calculator, which determines L_{100}, prompts for the desired fraction of this and displays the micrometer setting needed to achieve it. The program is written for a Hewlett Packard HP 41CV programmable calculator with card reader. The program is versatile but the version in use in our laboratory differs essentially from that of Mulvany and Halpern in that the observed data are not fitted by an exponential curve: instead, observed and theoretical wall tensions are simultaneously determined and the difference between them displayed. We have found the programs used by Mulvany and by Angus inapplicable to our own studies in human large arteries, the first having been specifically designed for the study of resistance vessels under magnification and the second requiring an immediately adjacent mainframe terminal.

Ring segments of vessel of known length are mounted in tissue baths on hooks of known diameter and isometric tension measured in standard fashion. Hook diameters, vessel length and baseline micrometer setting (hooks touching) are entered into the program as constants. The vessel segment is then stretched incrementally by controlled separation of the hooks. At each stage, until L_{100} has been achieved, the new micrometer setting and force developed at 1 min are prompted for and entered. Internal circumference, observed and theoretical wall tensions are then calculated and the percentage difference between these tensions displayed as a guide to the next micrometer setting.

Using this program in preliminary experiments in human arteries we have found the length / tension relationships to be superimposable on those of comparable canine vessels (Angus et al., 1986). Maximum active tension in basilar arteries is generated when the internal circumference is set initially to 0.9L_{100} (corresponding to 1-4g initial tension).

Angus, J.A., Cocks, T.M. & Satoh, K. (1986) Br. J. Pharmac. 88, 767-777.
Mulvany, M.J. & Halpern, W. (1977) Circulation Res. 41, 19-26.

A MICROCOMPUTER SYSTEM TO MONITOR AND ANALYSE LOCOMOTION AND FEEDING AND DRINKING BEHAVIOURS

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We have developed an inexpensive system based on the BBC microcomputer to collect and analyse data on small animal locomotion, feeding and drinking. Locomotor activity is usually detected by a single infrared beam which bisects the cage although two beams can be used when greater sensitivity is required. Activity is recorded as the number of beam breakages over a preset accumulation interval. To assess feeding and drinking detachable hoppers are mounted on the outside of the cages such that the animals must break the infrared beam to gain access to food or drink. These behaviours are recorded as the number of attendances at the hopper and the total duration of attendance over a preset accumulation period. The system can acquire data from up to 16 fully instrumented cages. Detection of the beam breakages is carried out by custom designed printed circuit boards each supporting inputs from 8 sensors. Up to 8 of these boards can be mounted in a eurorack which also contains the circuitry to interface the data into the computer via the 1 Mhz bus.

The software is divided into three modules 1) experiment design, 2) data collection and 3) data analysis. The experiment design module allows the user to select the number of animals in use, the duration of the experiment, the accumulation interval for data and the behaviour(s) to be monitored. The user is then prompted to enter the drug treatment, in terms of dose and soe units, for each animal. The experimental cage, drug treatment and animal (in order taken from the stock cage) can be randomised and an injection schedule printed. To ensure that an experiment cannot fail by running out of disk space the system checks the floppy disk to ensure that space is available for the proposed experiment and then reserves it by creating a pre-extended file. The data collection module is entered by activating a prepared experiment. During data collection the operator can follow the progress of the experiment on the VDU. One the experiment is completed the file is flagged to prevent accidental re-activation. The analysis module allows the operator to select groups of animals on the criteria of drug treatment, drug dose and experiment duration. Once the criteria have been input the system searches the current data disk for experiments containing animals meeting these criteria. The filenames of these experiments are displayed and the user allowed to select those he wishes included in the analysis. The data for individual animals meeting the search criteria is then extracted. Multiple data disks can be searched for data. Data from up to 6 groups of animals can be accumulated. The data from each animal over the time course of the experiment can then be presented as a histogram to allow exclusion of clearly aberrant animals from further analysis. The groups of data can then be analysed to extract means, SEM's and medians at each time point and total activities over the whole experiment. Kruskal-Wallis nonparametric one way ANOVA is used to compare groups at each time point. The results of the analysis can be plotted on the VDU or on a HP-GL compatible pen plotter.

This system provides a comprehensive range of facilities for the collection and analysis of behavioural data but is easy to use because it requires little knowledge of computers. A version of the system to run with IBM compatible computers is under preparation.