MULTICHANNEL ANALYSIS OF GASTROINTESTINAL ELECTRICAL SPIKING ACTIVITY

G.R. Francis, A.E. Glen and C.M. McClelland (introduced by D.H. Turner) Beecham Pharmaceuticals Research Division, The Pinnacles, Harlow, Essex. CM19 5AD

The recording of myoelectric activity is a well-established technique to assess the effect of drugs on gastrointestinal function. The visual inspection of accumulated data, although valuable, is both laborious and time consuming. We have developed a device to electronically analyse (after accelerated replay) spiking activity which not only provides an accurate, condensed, record of myoelectric activity patterns but additionally is versatile, inexpensive and compact.

The analyser output allows a rapid visual scan of collated data for drug induced changes in myoelectric activity to be undertaken. Further analysis, if required, could be carried out using a more elaborate, computerised, system.

The equipment demonstrated comprises of 4 independent channels. It is designed to be used in conjunction with a Racal Store 14D or similar instrumentation tape recorder and a chart recorder.

The general arrangement for one channel is illustrated (Figure 1). Gastric signals are amplified, Bessel bandpass-filtered to remove slow-wave activity and high frequency noise, and then rectified. The resulting unipolar spikes provide the input to a comparator with a variable threshold that allows baseline noise to be rejected. Spikes whose amplitude exceed the threshold operate the output gate of the comparator and cause clock pulses to be stored in a 12-bit binary counter. The outputs from this counter are fed, in parallel, to a 12-bit digital-to-analogue converter (DAC). The output from the DAC is buffered and filtered to provide either an incrementing or a histogram style display whose amplitude in the range 0 to +1V corresponds to spike activity. The display is reset to zero at intervals of one minute. An audio amplifier is included in the instrument so that an audible indication of spiking activity can be obtained.

The analyser has provided a useful, low-cost, method for the reduction and interpretation of gastrointestinal myoelectric data (McClelland, 1987). Both the hardware and software costs associated with any subsequent microcomputer-based analyser (Latour and Ferré, 1985) would be reduced by employing this equipment as a 'front-end' data logger.

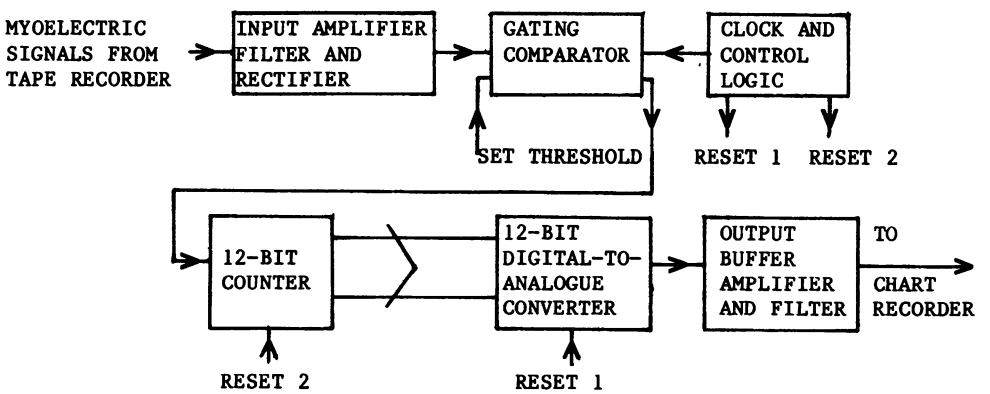

FIGURE 1: One channel of the gastrointestinal activity monitor

Latoure, A. and Ferré J.P. (1985). J.Biomed.Eng. 7, 127-131
McClelland, C.M. (1987). This meeting.

MEASUREMENT AND ANALYSIS OF ANALOGUE SIGNALS FROM LINSEIS CHART RECORDER USING A BBC MICROCOMPUTER

I.A. Dainty, C.J. Daly, J.C. McGrath, J. Sinclair & M. Spedding[1], Autonomic Physiology Unit, Institute of Physiology, University of Glasgow, Glasgow and [1]Department of Pharmacology, Syntex Research Centre, Edinburgh EH14 4AS

The analysis of experimental data recorded on chart recorders by measuring traces is time consuming if a number of different parameters are to be measured from one trace e.g. tension at set times, tension at plateau of response, and time between events. The use of an inexpensive, widely available microcomputer to retrieve 'raw' data directly from the chart recorder would be of some benefit since this raw data could then be stored and analysed in several different ways.

We have designed a system for the BBC microcomputer which has the ability to retrieve data from a Linseis chart recorder. As with the majority of serious software applications for the BBC microcomputer, the system is 'soft key driven' i.e. it utilises the programmable 'soft keys' of the computer, and is therefore simple to use. The Linseis chart recorder can be supplied with an analogue to digital converter and an RS232 serial interface which allows bidirectional data-transmission. Digitised data is sent via the interface, to the computer, which then stores it on disc. This data can then be retrieved and analysed at leisure.

The data retrieval system allows each channel of the recorder to be sampled individually or, more usefully, continuously at set time intervals. Due to a minimum time interval of 2 seconds between sampling, the system, at present, is not suitable for recording rapid events such as twitch responses and blood pressure waveforms. One of the main advantages for the user is that the recorded data can be expanded in various ways for more detailed inspection. Data items selected from the sampled data can be simply printed, or directly entered into the data storage and retrieval system, DATAFILE (Dainty et al., 1985), thus allowing it to be rapidly retrieved for analysis, further manipulation, print-out or plotting.

In addition to this data-retrieval function, the system provides the user with complete, remote control of all of the 'chart' functions of the chart recorder (sensitivity cannot be changed via the computer). This facility allows the user to 'program' a series of instructions for the recorder to follow. For example, the recorder can be switched on and off at set periods of time and the speed can be altered at set times for various lengths of time.

The system was designed using a Master series BBC microcomputer but may be used with the BBC model B+ microcomputer. The minimum requirements for the system are a single sided, double disc drive, a BBC B+ microcomputer and a Linseis chart recorder with a serial interface.

In summary, the system removes the need for 'manual' measurement of traces from the recorder, provides full control of the recorder facilities, and gives the user the ability to program the recorder to carry out a series of actions.

Dainty, I.A. et al. (1985). Br. J. Pharmac. 89, 884P.

A MICROCOMPUTER CONTROLLED SYSTEM FOR FULLY AUTOMATED TESTING OF DRUGS ON IN VITRO TISSUE PREPARATIONS

J.R. Brown, S. Dhuna[1], C.C. Jordan and I.K. Wright, Department of Neuropharmacology, Glaxo Group Research Ltd., Ware, Herts., SG12 0DJ, and [1]Computer Science Department, Glaxo Group Research Ltd., Greenford, Middlesex.

An automated assay system will be demonstrated which utilises a Z 80 based microcomputer to control the administration of drugs to, and analyse responses from, isolated smooth muscle preparations in vitro. Four tissue baths are operated independently and a high degree of flexibility in the control software permits a wide variety of dosing schedules to be performed. Experimental parameters are set using interactive software at the beginning of each experiment.

Agonists and antagonists are administered by a modified Gilson, Model 212, liquid handler coupled to a Hamilton Microlab M syringe pump. This combination allows up to 24 compounds to be tested per tissue and obviates the need for multiple infusion syringes and associated piping.

Tissue responses are monitored electronically and written to both disc storage and directly to a chart recorder.

DYSKINESIA IN MPTP-TREATED PRIMATES ON LONG-TERM LEVODOPA THERAPY: A VALUABLE EXPERIMENTAL MODEL

C.E. Clarke, S. Boyce, M.A. Sambrook and A.R. Crossman.
Experimental Neurology Group, Department of Cell and Structural Biology, The Medical School, University of Manchester, Manchester, M13 9PT.

The management of Parkinson's disease is complicated by the occurrence of drug-induced involuntary movements and response fluctuations. It has been suggested that this form of dyskinesia is precipitated by chronic levodopa therapy itself. We have therefore maintained a colony of 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)-treated primates on levodopa for 3 months to investigate the relationship between chronic levodopa and the development of dyskinesia.

Six Macaca fascicularis received 2.6-27.0 mg/kg MPTP i.v. at 1-2 week intervals until parkinsonian features reached Hoehn and Yahr stage IV (1967). Levodopa was commenced in 3 animals 1.5-7.0 months after the termination of MPTP at a dose of 75 mg of Sinemet-110 thrice daily. The response to Apomorphine (APO., 0.025-0.2 mg/kg i.m.) of 2 treated and 2 non-treated monkeys was assessed pre- and 3 months post-levodopa treatment in an observation cage fitted with 3 activity counters. Using videotape recordings, dyskinesia was quantified in the upper and lower limbs and the face at 5 minute intervals over 90 minutes according to the scale: 0-none, 1-intermittent, 2-continuous, 3-severe (interfering with normal activity). Trials were performed in duplicate.

MPTP produced marked hypo- and bradykinesia, rigidity and both resting and postural tremor which progressed in a predictable step-wise manner with each injection. On cessation of MPTP, animals showed a mild impovement for 3-4 weeks after which their condition remained stable. Levodopa reversed this parkinsonian syndrome in all primates, but did not initially cause dyskinesia at the dose used. Following 4-8 weeks therapy, all 3 primates showed mild choreiform movements of the lower limbs. These gradually worsened and after 3 months affected the upper limbs and face. The severity of dyskinesia was dose-dependent, although the onset of moderate chorea was associated with a suppression of general motor activity (Table 1). Involuntary movements were not seen over the 3 month period in non-levodopa treated animals when challenged with APO. at doses which induced dyskinesia in levodopa-treated subjects.

Table 1 Cumulative dyskinesia and activity counts over 90 minutes following apomorphine in 2 primates after levodopa therapy for 3 months

APO Dose(mg/kg)	0	0.025	0.05	0.10	0.15	0.20
CYN 114						
Dyskinesia	0	3	3	5	6	12
Activity	96	323	879	689	629	664
CYN 133						
Dyskinesia	0	1	5	5	5	11
Activity	300	532	816	714	725	519

Since parkinsonian features remained constant in the non-treated animals, the onset and progression of dyskinesia in the treated animals must relate to levodopa treatment rather than disease progression. This confirms the results of clinical trials and suggests that the introduction of levodopa therapy in the treatment of Parkinson's disease should be delayed and that it should be used at the lowest therapeutic dose.

Hoehn, M.M. et al., (1967) Neurology 17, 427.