A novel and inexpensive method for detecting and quantitating the occurrence of cardiac arrhythmias

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The most time-consuming part of work aimed at finding anti-arrhythmic drugs is identification and quantification of normal and ectopic ECG complexes. Commercial equipment is expensive and, being clinically orientated, does not present data in a form ideally suited to experimental work.

This demonstration illustrates some variations of a novel method of recognizing normal (sinus) ECG complexes in the presence of multifocal ventricular dysrhythmias. The method entails the successive triggering (within a prescribed interval) of two (or more) phototransistors placed over the face of a display oscilloscope. A simple voltage *versus* time display of an ECG may be employed, but some ectopic QRS complexes can take the form of sinus complexes. Therefore, the preferred method uses triggering of the phototransistors by vectorcardiogram loops formed from ECG leads I and II, after suitable band-pass filtering to eliminate slow and fast ECG artefacts. Oscilloscope beam brightness modulation of suitable duration is also employed, and enables the display of complete normal vectorcardiograms, whilst limiting display of ectopics (wide QRS complexes) to shorter sections of loop. This helps reduce false recognition of ectopics as normals. A modification of this method may be employed when only one ECG lead is available. For equal amplitudes, normal ECG complexes have greater high frequency content, by virtue of their short duration, than do ectopic complexes, which are generally of long QRS duration. By filtering the single ECG signal through suitably adjusted high and low frequency band-pass filters, two signals may be derived. These signals will form X:Y display loops with sufficient difference between normal and ectopic loops to permit satisfactory normal complex recognition.

Using these methods of normal ECG identification, a computer has been developed which, whilst counting all ECG complexes, derives from the absence of normal complexes a count of ectopic beats. These data permit computation of mean ventricular rate, mean ectopic rate and percentage occurrence of ectopics, each over one minute intervals. Each result is inscribed in turn for 20 s of the succeeding minute on a single channel oscillograph.

These methods of analysis have been developed and used satisfactorily over the past three years to investigate the actions of known and novel chemical compounds.

Electron microscopic autoradiographic localization of [^{3}H]-dopamine in the dendrites of the dopaminergic neurones of the rat substantia nigra *in vivo*

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Previous studies from this laboratory suggested that the dendrites of the dopaminergic neurones in the substantia nigra of rat brain were capable of accumulating and releasing dopamine in a manner indistinguishable from that of dopaminergic nerve terminals in the corpus striatum (Geffen, Jessell, Cuello & Iversen, 1976). This evidence was, however, indirect and depended on the assumption that the sites of accumulation of exogenous [^{3}H]-dopamine in freshly microdissected slices of substantia nigra were predominantly in the cell bodies and dendrites of the dopaminergic neurones. Although this assumption is in agreement with the known morphology of the substantia nigra (Hajdu, Hassler & Bak, 1973) and is supported by fluorescence microscopy results (Björklund & Lindvall, 1975), it was possible that [^{3}H]-dopamine could be accumulated by an unsuspected population of dopaminergic or non-dopaminergic nerve terminals in the substantia nigra. This possibility has now been examined *in vivo* by the microinjection of 9.25 nmol of [^{3}H]-dopamine (specific activity 2.7 Ci/mmol) dissolved in 2 µl of

artificial CSF, directly into the substantia nigra of rat brain from a stereotactically placed fine glass micropipette with a tip diameter of 25 μm. Fifteen minutes later the animal was killed by perfusion fixation with 5% buffered glutaraldehyde, and the substantia nigra prepared for autoradiographic examination as described previously (Kelly & Dick, 1976). Light and electron microscopic autoradiographs showed the autoradiographic activity to be predominantly localized over the dopaminergic cell bodies in the pars compacta and over their dendrites in the pars reticulata. Silver grains were only rarely seen over nerve terminals. Control experiments showed [^{3}H]-GABA to be accumulated solely by nerve terminals in the substantia nigra (Kelly & Dick, 1976).

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A variable programme controller for sequential drug administration

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A solid state controller, using complimentary metal oxide semiconductor (CMOS) logic, has been developed for automating procedures in which drugs are administered at various times in one or two separate sequences, for example, with and without antagonist present. The unit can be programmed from potentiometers and switches on its front panel.

A schematic diagram is shown in Figure 1. The multiplexed clock controls the time between drug additions (1 min to 1 h) by altering the frequency of an oscillator which feeds into a binary counter. The counter output is fed into the appropriate sequencer which initiates the drug addition and selects the next drug's timing interval. At full capacity, 8 drugs can be administered sequentially in each of two independent channels (A and B). Up to 10 such channel cycles can be selected within a non-repeating programme and channels can be changed at the end of any preselected cycle. There is provision for introducing a delay of either 30 or 60 min when changing from channel A to B and this facility is useful, for instance, to enable antagonists to reach equilibrium with the tissue before any further agonists are added.

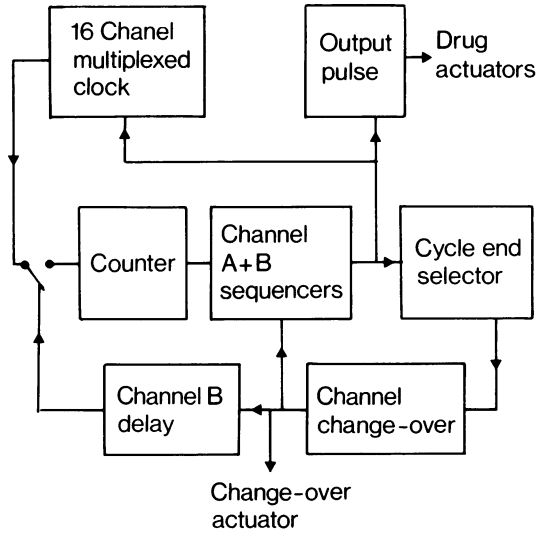

Figure 1