

DEMONSTRATIONS

Intravenous self-administration of heroin in the rat: experimental technique and computer analysis

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Heroin-seeking behaviour has been studied in the rat using an operant conditioning technique by which the animal responds (lever-presses) for a reinforcement of an intravenous infusion of an additive drug such as cocaine or morphine (reviewed by Schuster & Thompson, 1969).

In the experiment to be performed a rat with an indwelling intravenous cannula is placed in a modified Skinner box. The cannula is connected by polythene tubing which passes through a stainless steel and teflon saddle on the animal's back through a light spring leash to a swivel-joint. From this, tubing passes via a peristaltic pump to a reservoir. This enables infusions to be given to a fairly free-moving animal. When the rat presses a lever-switch a set number of times the animal receives an infusion. The schedule of reinforcement is programmed by solid state logic circuits. Responses and reinforcements are marked on cumulative event chart recorders.

Chart records are digitized onto paper tape using a Pencil Follower (Christianson, Dinneen, James & Perkins, 1967). A special technique developed for the acquisition and annotation of the data points keeps the Pencil Follower work to a minimum. The standard variables input to the computer are time, lever-presses and infusions. Non-standard variables, such as animal body temperature and weight can be defined and updated at any time, and are input together with normal data and analysed in the same way as the standard variables. Paper tape encoded data are converted by computer programmes into a series of individually timed events which are stored on magnetic tape or disc files. During this stage some types of data errors are corrected automatically. The files are then processed to give output in the form of graphs and histograms on a conventional high speed line-printer. The time element of the data may be retrieved on either an absolute (data and time of day) or a relative basis (with reference to the start or any point during the experiment).

Parameters fed to the computer at run time allow great flexibility in choice of analyses and general format of results. For example, any variable may be analysed by histogram or plotted against another variable, and the results can be presented in any convenient scale or units. There is a comprehensive choice in the section(s) of the data file that may be analysed. The programmes are written in ASA Fortran and run on an ICL 1904A computer.

With these procedures we have shown that the intensity of dependence on heroin is related to the total amount of drug infused and the frequency and total duration of exposure. With high concentrations of heroin, lever-pressing increased still further on withdrawal, indicating negative reinforcement that was not seen with low concentrations of drug, where reinforcement was positive.

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REFERENCES

- CHRISTIANSON, A. H., DINNEEN, L. C., JAMES, G. W. L. & PERKINS, A. C. (1967). A method for measurement and statistical analysis of large numbers of experimental tracings. *J. Pharm. Pharmac.*, **19**, 837-840.
- SCHUSTER, C. R. & THOMPSON, T. (1969). Self administration of and behavioural dependence on drugs. *Ann. Rev. Pharmac.*, **9**, 483-502.

An improved technique for the continuous measurement of arterial blood pressure in the conscious unrestrained cat

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Hall, Gomersall & Heneage (1967) described a one-way valve made from perspex and screwed into the skull which, after connection to a carotid artery, could be used for repeated periods of blood pressure measurement in the conscious, unrestrained cat. These workers used an identical valve for connection to a vein to enable drugs to be injected.

We found this method had several disadvantages which suggested that further development of the system was desirable. The main problems we encountered using the method of Hall *et al.* (1967) were: (1) Drilling of the skull for insertion of the valve bodies lengthened the operative procedure and was a potential source of failure.

(2) Some cats were bothered by the position of the valves and attempted to remove them.

(3) The valves tended to leak after several weeks in use and this led to blood clotting in the catheters.

(4) Skin surrounding the valve base frequently became necrotic and this led to unsightly weeping wounds which often became infected.

We have modified the arterial valve in several ways. Our valve is mounted on a base which is inserted beneath the skin at the back of the neck thus allowing some sideways movement. The valve and base are now made from a single piece of tetrafluoroethylene (P.T.F.E.) which has virtually abolished the skin necrosis. The height of the valve body has been increased and flat grooves added to each side so that it may be firmly held whilst making or breaking the connection to the recording device. The tendency for the valve to seep has been prevented by increasing the length of the internal stainless steel spring and by replacing the steel ball and rubber washer by a nylon ball and a neoprene washer.

The valve for the venous side has been dispensed with and replaced by a length of fine polyethylene tubing (pp 30) closed with a pin.

The valve arrangement has been used for periods up to 6 months without trouble and thus allows long-term changes in cardiovascular responses to be measured. The valve, together with connector and dust cap, all of which are now commercially available, will be demonstrated in use.

REFERENCE

- HALL, G. H., GOMERSALL, J. C. R. & HENEAGE, E. (1967). A simple device for recording blood pressure or for intravenous injection of drugs in the conscious unrestrained cat. *Physiol. Behav.* **3**, 205-206.