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Telemetry-Controlled System for Chronic Drug Self-Administration in Unrestrained Monkeys

by

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Growing interest in the self-administration of drugs has led to the development of a variety of procedures that permit automatically controlled infusion of drugs in restrained or partially restrained animals. Coppock and Chambers (1954) and Headlee, Coppock and Nichols (1955) described an apparatus permitting intravenous or intraperitoneal infusion of solutions in restrained rats. Weeks (1961, 1962)[2] reduced the amount of restraint required by equipping rats with a leather and metal saddle attached to a lightweight sprocket chain. Intravenous cathete: tubing was brought from a small incision on the animal's back and fed through the links of the sprocket chain and through a liquid-tight swivel (permitting 360 degree rotation without twisting the tubing). Davis and Miller (1963) have used Weeks' procedure to study barbiturate self-administration in a conflict situation in rats.

Several investigators have described procedures permitting intravenous drug infusion in monkeys. Based on a procedure originally developed by Dr. John Mason of Walter Reed Army Institute of Research (Werdegar et al, in press), Neimann, Schuster and Thompson (1962) developed a method for chronic infusion of drugs

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[2] Weeks 1964, p. 48) reports that the first self-administration experiments were conducted with rats in his laboratory in 1960, although as indicated above, Headlee, Coppock and Nichols (1955) had been working along very similar lines for several years. The first report of intravenous morphine self-administration was in Weeks' Federation Proceeding abstract (1961). The following year, Weeks (1962) and Schuster and Thompson (1962) provided more complete descriptions of intravenous self-administration preparations.

in monkeys restrained in standard primate chairs. Their method has proved viable permitting investigation of basic processes in drug dependence in monkeys (Schuster and Thompson, 1962; Thompson and Schuster, 1964). In a continuing effort to reduce the amount of restraint required in such animal experiments, Weeks (1964) and Yanagita, Deneau and Seevers (1963) developed a partial restraint system for monkeys designed specifically for jugular self-infusion. This system has been used for the past two years in the Pharmacology Department at the University of Michigan, and it appears to represent an improvement over the restraining-chair method that is more widely used. In this system, the monkey wears a light-weight, tubular stainless steel harness, connected by an elbow-arm arrangement to one corner of a rather large cubicle. The monkey can move about relatively freely, being limited only by the flexibility of the joints.

Experimental requirements in this laboratory have made necessary the development of a system permitting self-administration of drugs in completely unrestrained animals. We have spent the past year and a half synthesizing the technology of the harness arrangement used in the Michigan Pharmacology Department with a telemetry control system described by Delgado (1963). The purpose of this report is to describe the resulting telemetry-controlled system that permits drug self-administration in completely unrestrained monkeys.

METHOD

Subjects: Male Rhesus monkeys weighing from 14 to 18 pounds are the most desirable subjects for use with our method. Fitting the existing harness to smaller sized animals gives rise to several problems, including the necessity of adjusting the size of the catheter tubing to fit the veins of the small animal.

Apparatus: The apparatus is composed of the following four basic parts: (1) The catheter tubing which is inserted into the internal jugular vein (B-D vivosil No. 7002-03 [I.D. = .030, O.D. - .065]). The end that is inserted into the vein is cut at a 45 degree angle with a razor blade, the other end is fitted with a female Leur-Lok attachment that matches the output connector of the infusion pump. (2) A Nebraska Medical Instrument infusion pump. The catheter tubing is connected with a matching Luer-Lok male fitting to the infusion pump. The Nebraska Medical Instrument pump must be operated from rechargeable Nicad six-volt batteries at a flow rate of 1 cc/minute. Flow rate varies directly with D.C. voltage applied to the pump. A resistor and Zener diode are used to provide a constant six volts to the pump independent of charge state. (3) Kraft custom superhetrodyne model-airplane receiver. The power from the battery to the pump is switched by a relay in the receiver, and the antenna from the receiver is fixed to the back of the backpack with epoxy cement as an insulator. (4) Backpack. The infusion pump, battery, and receiver are situated inside a 2 x 4 x 6 inch aluminum chassis which is bolted to a harness. A 1/8-inch thick aluminum top-hinged door is screwed to the chassis to permit ready access to the componenets. The backpack and harness weight 525 gm., and the harness, which supports the backpack, is constructed of 1/4-inch diameter stainless steel tubing (see Figure 1). The harness design has been modified to accommodate the backpack and to permit slightly greater freedom of movement.

The arrangement of the internal components is illustrated in Figure 2. Notice that the pump and dacron and silastic reservoir (with a 30 ml capacity) take up approximately half the space inside the pack. The Nicad battery and receiver combined require approximately the same amount of space. All these components are held in place by foam rubber cushions between the components and the botton of the aluminum chassis, by silastic adhesive and a cable clamp. Thus far, no component has been damaged by the movement of the monkey in the cage, suggesting that less cushioning may be feasible.

The Kraft custom transistorized transmitter is situated outside the animal's cage. A 24-inch length of #22 wire, which is imbedded in a 1/2-inch diameter bakelite rod, is inserted in the animal's cage as an antenna. The transmitter is battery operated, with the power switched by relays in an adjacent control room. The transmitter battery (nine-volt Nicad) is changed once weekly; the receiver battery and the solution in the infusion pump are changed once every 24 hours. Changing batteries requires that the subject back up to an opening in the cage and allow the door to the backpack to be opened while the components are being changed. Therefore, preliminary hand shaping must be done so that the animal will stand quietly while these procedures are being carried out. We have used a conditioning method very similar to that described by Levison, et al (1964), however, the response topography is quite different.

References

Coppock, H. W. and Chambers, R. M. Reinforcement of position preference by automatic intravenous injections of glucose. J. Comp. Physiol. Psychol. 1954, 47, 355.

Davis, J. D. and Miller, N. E. Fear and pain: their effects on self-injection of amobarbital sodium by rats. Science, 1963, 141, 1286.

Delgado, J. M. R. Cerebral heterostimulation in a monkey colony. Science, 1963, 141, 161.

Epstein, A. N. and Teitlebaum, P. A watertight swivel joint permitting chronic injection into moving animals. J. Appl. Physiol. 1962, 17, 171.

Headlee, C. P., Coppock, H. W. and Nichols, J. R. Apparatus and technique involved in a laboratory method of detecting the addictiveness of drugs. J. Amer. Pharm. Assn. (Sci. ed.), 1955, 44, 229.

Levison, P. K., Ferster, C. B., Niemann, W. H. and Findley, J. D. A method for training unrestrained primates to receive drug injections. J. Exp. Anal. Behav. 1964, 7, 253.

Neiman, W. H., Schuster, C. R. and Thompson, T. A surgical preparation for chronic intravenous infusion in Rhesus monkeys. Lab. of Psychopharm. Technical Report, Univ. of Md., No. 30-62, Sept. 1962.

Schuster, C. R. and Thompson, T. Self-administration of morphine in physically dependent Rhesus monkeys. Lab. of Psychopharm. Technical Report, Univ. of Md., No. 29-62, July 1962.

Thompson, T. and Schuster, C. R. Morphine self-administration, food-reinforced, and avoidance behaviors in Rhesus monkeys. Psychopharmacologia, 1964, 5, 87.

Weeks, J. R. Self-maintained morphine "addiction"--a method for chronic programmed intravenous injections in unrestrained rats. Fed. Proc. 1961, 20, 397 (Abst.).

Weeks, J. R. Experimental morphine addiction: method for automatic intravenous injections in unrestrained rats. Science, 1962, 138, 143.

Weeks, J. R. Experimental narcotic addiction. Scientific American, 1964, 210, 46.

Werdegar, D., Johnson, D. G. and Mason, J. W. A technique for continuous measurement of arterial blood pressure in unanesthetized monkeys. J. Appl. Physiol. (in press).

Yanagita, T., Deneau, G. and Seevers, M. H. Physical dependence to opiates in the monkey, with demonstration. (personal communication, 1963).

Figure Legends

Figure 1. Rhesus monkey with harness and backpack in place. The antenna (1) can be seen cemented to the hinged lid (2) of the backpack (3). These components are bolted to the stainless steel tubular harness (4).

Figure 2. The interior arrangement of the backpack components. The Kraft superhetrodyne receiver, Nebraska Medical Instrument Co. pump (1) and Nicad battery (5) are attached to the underside of the lid. The drug solution is pumped from the reservoir (2) (made of dacron-reinforced vivosil sheeting) through a vivosil tubing (3) running through the pump by five rollers. The tubing exiting from the pump is connected with the vivosil catheter (4) which is brought through a hole in the underside of the backpack. All of these components are cushioned by a one-inch thick sheet of foam rubber cemented to the underside of the backpack (6).


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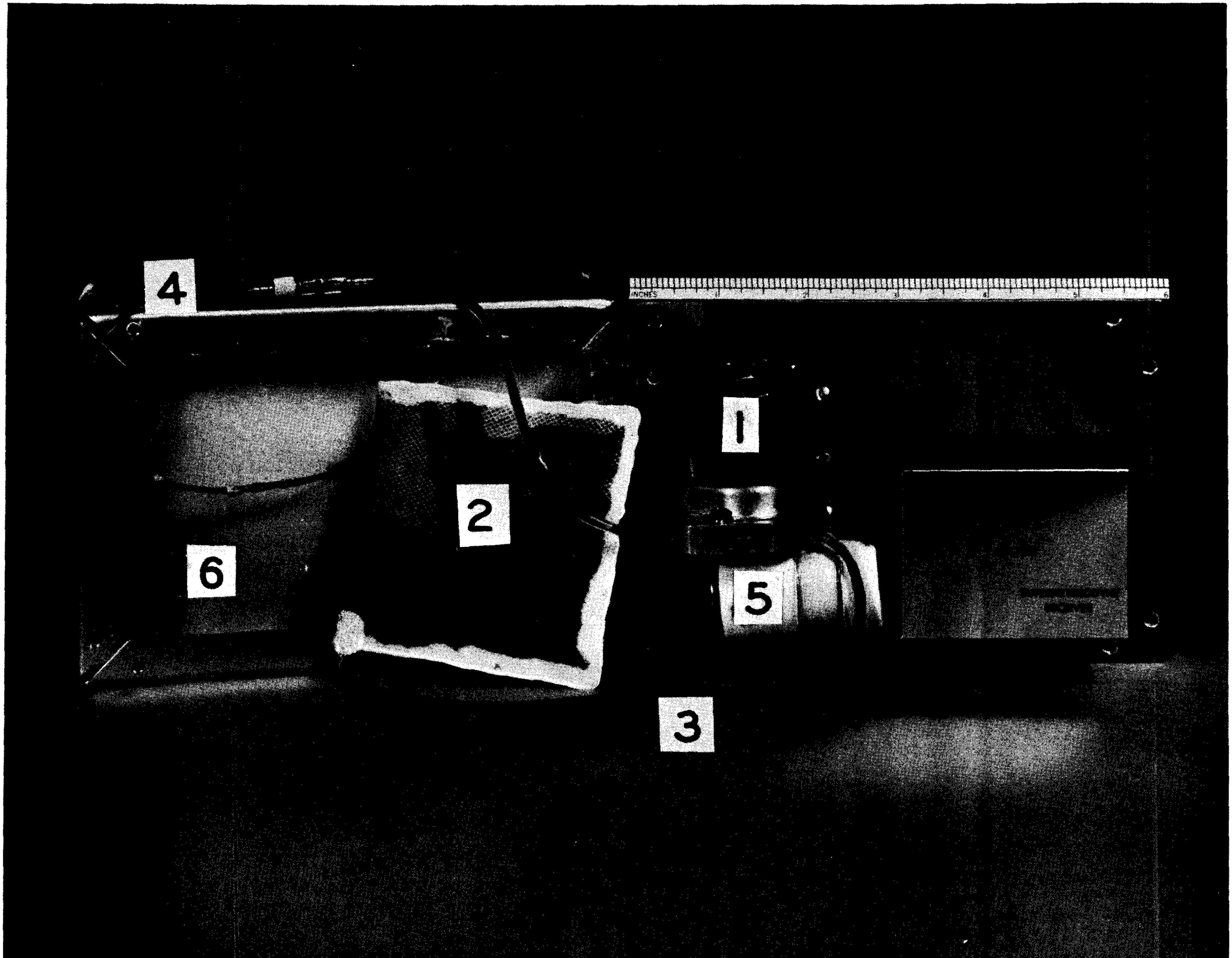
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