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The "pill popper": A device for drug capsule self-administration by primates

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An apparatus for establishing self-administration of drugs in capsule preparation form by nonhuman primates is described. The system includes a capsule loading unit combined with a pressurized liquid dispenser and mouth-operated drinking tube lever. Operation of the mouth lever results in forced ingestion of a capsule or other solid substance and a measured quantity of liquid. The components of the system are separately programmable and adjustable to permit shaping of pressurized liquid and capsule ingestion through successive approximations. Examination of absorption factors and temporal variables associated with delay of drug reinforcement onset, as well as precision in oral dosage, are thus possible in a model which approximates the most common method and features of drug self-administration in humans.

Self-sdministration via the intravenous route has been the principle mode for investigating the reinforcing properties of behaviorally active drugs in nonhuman subjects. Despite technical difficulties involved in surgical procedures and instrumentation, administration of drugs through indwelling venous catheters has been a reliable method, while investigation of oral drug self-administration has been problematic due to taste and absorption factors (Schuster & Thompson, 1969). Two procedural developments have facilitated analysis of drug self-administration via the oral route. Siegel, Johnson, Brewster, and Jarvik (1976) have developed cocaine self-administration in nonhuman primates using gum laced with the drug. Due to absorption factors, this technique is particularly useful for cocaine but may have only limited value for many other substances. The development of oral self-administration of other drugs in solution, particularly ethanol, has been achieved through the procedure of schedule-induced polydipsia (Anderson & Thompson, 1974; Falk, 1961; Falk, Samson, & Winger, 1972). Ingestion of drugs in solution induced through manipulation of environmental contingencies provides a behavioral analogue to the most common route of administration in humans. However, presentation of drugs in solution does have limitations due to pharmacological and other factors.

Various specialized liquid-dispensing units have been described in the literature (e.g., Green, 1964; Thompson, Schuster, Dockens, & Lee, 1964). The device described below includes an alternative unit for primates. Additionally, the apparatus permits self-administration of measured amounts of a drug in capsule or other solid forms by primates.

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SYSTEM DESCRIPTION

The "pill popper" system consists of three units including: (1) mouth-operated lever/drinking tube and liquid solenoid, (2) capsule storage magazine and solenoid-operated loading mechanism, and (3) presurized liquid reservoir. The liquid and capsule dispenser are mounted on a single piece of Lucite (20 x 15 x 1.3 cm) attached to a standard BRS/LVE large primate test cage (No. 143-45) by an aluminum bracket.

Liquid Dispenser (Figures 1a and 1b)

The stainless steel mouth-operated drinking tube (OD, 1.8 cm; ID, 1.0 cm) extends 4 cm into the cage and is centrally positioned in the front panel. The lever extends 1.5 cm into the cage. When depressed, the lever is recessed into a slot in the bottom of the drinking tube. This enables the animal to firmly grasp the tube with its mouth. (An extension to the short operandum can be attached to facilitate shaping but is removed to insure greatest insertion into the animal's mouth once the behavior is acquired.) Mouth manipulation of the lever operates a microswitch (ISXI-T, MS24547-1) which activates a BRS/LVE solid state programming unit (CX-207). The stainless steel drinking tube is threaded and connected to a Lucite cylinder (1, 1.2 cm; OD, 2.5 cm; ID, 1.0 cm). Liquid enters the cylinder through a connector just anterior to the capsule magazine via Tygon tubing from a water solenoid (Allied Control Company 20393). The solenoid is programmed for operation through a BRS/LVE solid state unit (OS-204).

Capsule Dispenser (Figures 1a and 1b)

The dispensing component includes a magazine for storage, with each capsule dropping into position for loading following operation of a 24-V solenoid

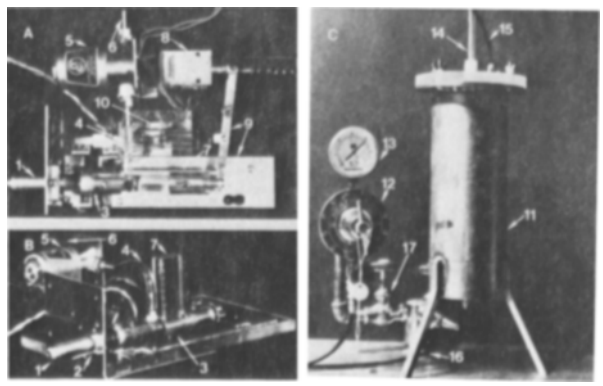

Figure 1. (a) Top view of liquid and capsule loading-dispensing units; (b) front/side view of units indicating capsule magazine position and size of drinking tube and mouth lever; (c) liquid pressure system. Components identified in a, b, and c are (1) water/capsule dispensing tube, (2) mouth-operated lever, (3) water/capsule loading cylinder, (4) water input, (5) water solenoid, (6) tubing to liquid reservoir, (7) capsule magazine, (8) capsule loading solenoid, (9) loading mechanism, (10) loading mechanism damper, (11) liquid reservoir, (12) pressure adjustment valve, (13) regulating gauge, (14) tubing from pressure, (15) tubing to liquid solenoid, (16) laboratory air supply.

(Dormeyer). A piston in the Lucite dispensing tube, connected by a stainless steel arm, retracts when the solenoid is activated; this permits capsule loading. The force of the piston return propels the capsule into the liquid-dispensing section of the cylinder forward of the liquid entry tube. The return action is increased by a spring attached to the solenoid arm, and mechanical jarring is reduced through an air piston attached to the arm between the solenoid arm fulcrum point and the capsule loading piston. Rubber gaskets in combination with the solenoid and spring force prevent leakage of liquid under pressure into the capsule loading and magazine units. Interchangeable magazines of differing inside diameter may be used to permit accommodation of standard No. 2 through No. 10 capsules or spherical pellets to .7 cm in diam.

Pressurized Liquid Reservoir (Figure 1c)

The pressurized liquid-dispensing system which provides the propellant force for capsule dispensing consists of a 2-liter-capacity stainless steel cylinder (height, 30.5 cm; ID, 10.0 cm; OD, 11.0 cm) with an integral ring extending 2.0 cm from the top of the cylinder. A 1.4-cm Lucite plate is fastened to the ring with bolts and wing nuts, and a rubber gasket serves as a seal between the surfaces. An aluminum rod with a float extends into a calibrated, sealed glass tube extending from the center of the Plexiglas and provides a convenient visual indication of the reservoir fluid level. Sealed fittings at the bottom of the cylinder and through the Lucite top serve for liquid output and air input, respectively. Imperial Eastman Polyflo tubing (rated to 100/in.^{2}) connects the liquid output fitting with the liquid-dispensing solenoid. Polyflo tubing also connects the reservoir with a regulating pressure gauge (Matheson 40-L) with fittings adapted for connection to a standard laboratory air system or air tank. Air source shut off prior to opening the reservoir or disconnecting liquid tubing is advisable.

The liquid pressure and dispensing system can be used to provide water or drug solution. A magnetic stirring unit can maintain drug in solution in the pressure cylinder. When the liquid reservoir, filled with water, is used as the propellant force for capsules loaded by the capsule dispenser, ingestion is determined by observation through closed circuit television or by inspection of the wastepan for the remains of capsules that were not ingested. Successful capsule ingestion is in part dependent on the relative length of the dispensing tube and the mouth operandum, as well as pressure. The dispensing tube described here has been used with rhesus monkeys. Nonhuman primates of different species or sizes may require larger or smaller dispensing tubes.

Programming of the unit for capsule dispensing through electronic or electromechanical equipment must include provisions for temporal separation of capsule loading and mouth lever activation of the units controlling the liquid solenoid to prevent backflow of water into the capsule magazine. A protective coating (Puffer & Crowell, 1967) must be used if drugs are prepared in gelatin capsules. The coating permits up to 12 h resistance to dissolution in water but dissolves in less than 20 min at normal stomach pH.

Effective use of the apparatus requires that a subject place his mouth firmly over the dispenser tube. Animals are hand shaped to facilitate acquisition of the necessary response topography. A 24-h water deprivation period precedes shaping sessions. Subjects are observed and the terminal behavior reinforced through successive approximations using a hand-held remote control switch connected with the water solenoid circuit of the dispensing unit.

Two specific aspects of the shaping procedure requir-

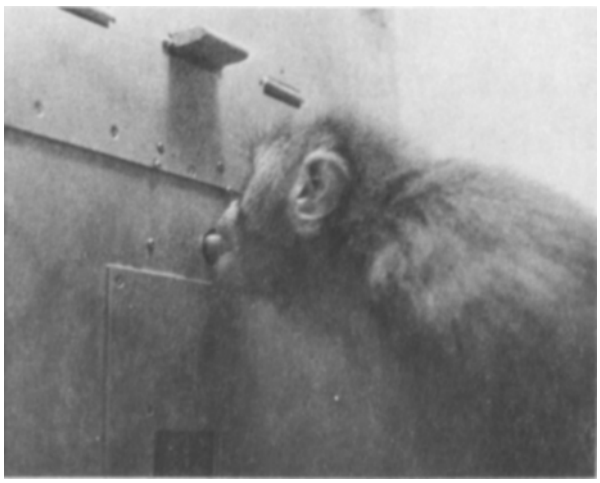

Figure 2. Terminal topography of operant response on lip lever/dispensing tube.

ing special attention are that a subject's mouth firmly grasp the maximum length of the dispensing unit tube and that a pressurized water flow be tolerated. Increasing the length of the dispensing tube grasped is accomplished by attaching an extension to the mouth-operated lever. The length of the lever is gradually decreased thereby requiring increasing insertion of the tube into the animal's mouth. Tolerance of pressure is established after the terminal response topography has been developed. Initially, pressure is confined to gravity flow. Subsequently, pressure is established. (See Figure 2.)

Advantages and disadvantages exist in administering drugs to nonhuman primates in capsule or pill form. Capsule ingestion has not always been consistent. Approximately 60% of capsules containing thiopental sodium were ingested during early trials. Initially, capsules not swallowed were chewed before they were spit out. The behavior of chewing capsules subsided rapidly, presumably due to the unpleasant taste of the barbiturates. Small-diameter (.2-cm) capsules were ingested with greater consistency than larger diameter (.7-cm) capsules, perhaps because subjects had been less able to obstruct passage or "catch" them with the tongue. Currently, coated .3-cm spherical secobarbital pills are being presented and the effects compared to thiopental sodium. Effects of thiopental sodium capsule ingestion (30 mg, approximately 3 mg/kg) have been observed as pronounced but transient disruption of performance on an FR 100 food component of the maintenance multiple schedule following liquid/drug ingestion.

Drugs have not been established as reinforcers using the apparatus. To the extent that rapidity of onset of drug effects contribues to establishing a drug as a reinforcer, the delay between ingestion and onset may be viewed as a disadvantage. Administration of drugs in capsule or pill preparation form permits analysis of drug effects, as well as consideration of absorption and other factors, with a procedure equivalent to the most common human case.

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