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Schedule-induced water and saccharin polydipsia under haloperidol

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Two white rats exhibited water and .4% saccharin polydipsia under a fixed-time 1-min feeding schedule. Oral administration of haloperidol in doses of .25, .50, and .75 mg reduced consumption of both fluids in direct proportion to dose, but saccharin intakes always exceeded those of water. Thus, the suppression of water polydipsia by haloperidol (Keehn, Coulson, & Klieb, 1976) is not merely the result of sedation. We argue that polydipsia occurs because food plus fluid is a greater reinforcer than food alone and that excessive drinking is a side effect of a normal reinforcement process that overpowers homeostatic mechanisms; the effect of haloperidol is to redress this imbalance.

Rats reinforced intermittently with dry food pellets drink excessively by consistently consuming water after reinforcement (Falk, 1961, 1972). Such drinking is attenuated by atropine (Burks & Fisher, 1970), trihexyphenidyl (Keehn & Matsunaga, 1971), and haloperidol (Keehn, Coulson, & Klieb, 1976). Although haloperidol is a powerful antidipsogen (Fisher, 1973), it is also a sedative that depresses motor activity and eating by rats (Janssen, 1967; Keehn et al., 1976). As schedule-induced drinking occurs after eating and requires movement between food cup and water spout, haloperidol could depress such drinking through sedation alone. We tested this possibility by comparing effects of haloperidol on water and saccharin polydipsia. If haloperidol sedates rats so that they are unable to drink, then saccharin and water intakes should be equally low under the drug. But if the drug reduces motivation to drink, it should suppress water consumption more than saccharin consumption owing to the greater palatability of saccharin.

METHOD

Two male Wistar rats were maintained at approximately 80% of their free-feeding adult body weights. They were 115 days old when the experiment began and weighed 243 g (R6) and 285 g (R14). Experimental sessions were conducted in two Grason-Stadler two-bar rat chambers (Type E 3125 B) fitted with calibrated drinking tubes on the outside of each door. The tube outlets were 5 cm above floor level and 9 cm from the wall containing the food cup. The response bars were inoperative. Drinking-tube contacts were registered on electromagnetic counters and Gerbrands cumulative recorders via Grason-Stadler drinkometers, Model E4690A-1. The chambers were in standard Grason-Stadler enclosures that included fans which masked extraneous noises, but the enclosures were open to permit vidoetape recording. Electromagnetic programming and recording equipment was in a separate room.

Subjects were given three 50-min experimental periods daily, at 9:30 a.m., 12:30 p.m., and 3:30 p.m., in which a 45-mg Noyes food pellet was delivered at the end of every minute (FT 1 min). The animals were placed in the experimental chambers with 100 food pellets to consume before the first experimental period, and remained in the chambers until the end of the third period. Then they were fed as necessary to maintain body weight in individual home cages with ad lib water. On weekdays for 3 weeks, tap water and .4% saccharin in tap water were available for all experimental periods on alternate days, except that saccharin was occasionally presented in alcohol. No drug was given in these weeks. For the next 10 weekdays, 0, 25, 50, or 75 of the 100 prefed pellets were replaced by an identical number of identical pellets, each of which contained .01 mg haloperidol. Water (W) or saccharin (S) availability and drug doses on these days was in the order W(25), S(0), S(25), W(0), S(50), W(50), S(0), S(75), W(0), W(75). Water was available between all experimental periods, but food was unobtainable.

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RESULTS

During prefeeding both rats ate all 100 pellets within 30 min regardless of the proportion containing haloperidol. They also consumed all 50 pellets delivered in each experimental period. On drug-free days nearly every pellet was eaten and followed by a drink as soon as it was delivered; on drug days R14 stayed at the feeder for several minutes before moving away to drink, and then remained at the drinking tube while two or three pellets accumulated in the feeder. R6 moved between feeder and drinking tube normally but less often and more slowly on drug days.

Figure 1 shows dose-response curves of saccharin and water intakes in experimental periods. The zero-dose points are means of the five daily intakes of each fluid directly preceding drug treatment; other points are single-day measures. The water intake curves are like those of Keehn et al. (1976, Figure 5) over the same dose range. Saccharin intakes averaged about 2 ml/min above water intakes at all dose levels, and the dose-response curves are almost parallel in the case of R14. With R6, the .25-mg haloperidol dose did not reduce saccharin intake below the mean zero-dose level for this animal, but otherwise the saccharin intake curve is like the water intake curve displaced upward.

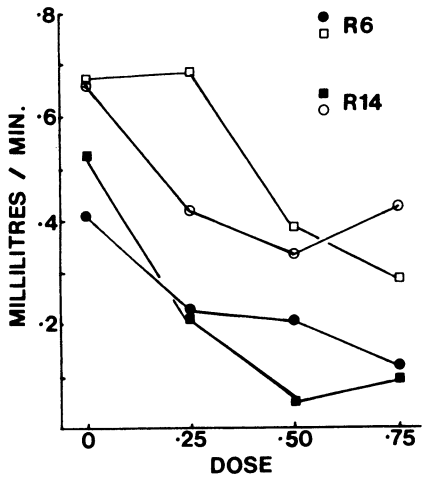

Figure 1. Haloperidol dose effects on water (solid symbols) and .4% saccharin intakes induced by a fixed-time 1-min feeding schedule.

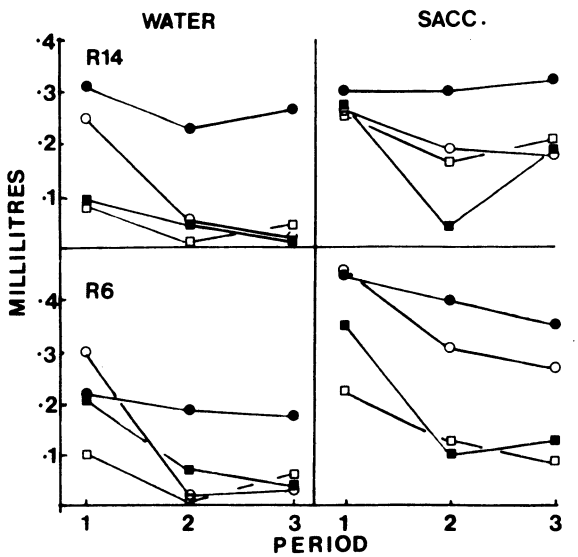

Figure 2. Water and .4% saccharin intakes per minute induced by a FT 1-min feeding schedule immediately (Period 1), 3 h (Period 2), and 6 h (Period 3) after haloperidol consumption. Zero-, .25-, .50-, and .75-mg doses are represented by solid circles, open circles, solid squares, and open squares, respectively.

Figure 2 shows the time course of the drug effect on fluid intake. The drug-free data are from the day before drug treatment. The effect on drinking in the first 50-min period after drug treatment was directly dose-related, although saccharin intake by R14 was hardly affected by any dose at this time. In every case drug effects increased in the second period, 3 h later, but fluid intakes were no longer dose related. With water, the greatest fall in intake between Period 1 and Period 2 occurred with the .25-mg drug dose; with saccharin it occurred with the .50-mg dose. Some recovery occurred in Period 3, with water at the .75-mg dose level and with saccharin at the .50-mg dose level. In general, haloperidol affected water and saccharin intakes similarly over time, with saccharin intake exceeding water consumption at all times with all doses.

Figures 3 and 4 contain typical cumulative records of licks for water and saccharin, respectively, at 0- and .75-mg haloperidol doses. Figure 3 shows how the drug effect on water intake developed through Period 1 (A), continued through Period 2 (B), and diminished in the course of Period 3(C). Drinking was sporadic rather than regular, and while drug-free licks usually promptly followed reinforcement (Record D), licks under the drug more often occurred in the middle of interpellet intervals. Figure 4 shows a much smaller effect of the drug on saccharin drinking than Figure 3 shows on water drinking, but the general course of events is similar in both cases.

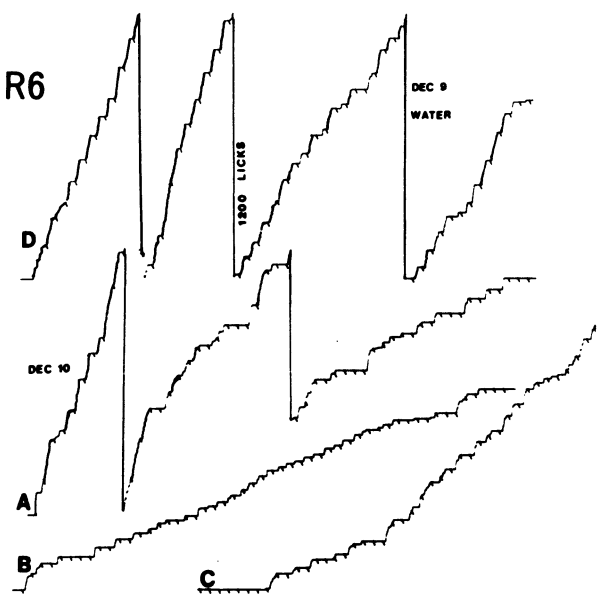

Figure 3. Cumulative lick records of R6 for water immediately (A), 3 h (B), and 6 h (C) after .75-mg haloperidol consumption. D is a typical drug-free record. Spurs on the records indicate pellet deliveries at 1-min intervals. Partly retouched for reproduction.

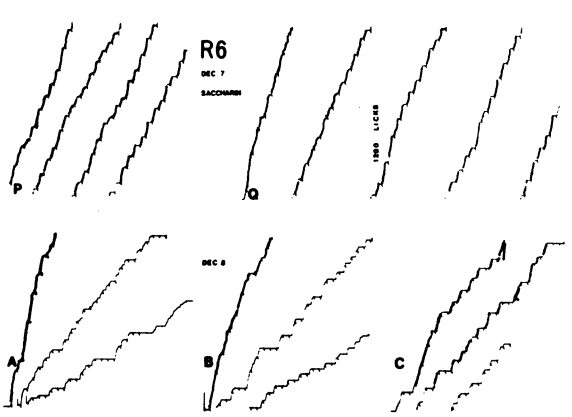

Figure 4. Cumulative lick records of R6 for .4% saccharin immediately (A), 3 h (B), and 6 h (C) after .75-mg haloperidol consumption. P and Q are typical drug-free records. All records except Q are collapsed along the time base but are in order from left to right. Spurs on the records indicate pellet deliveries at 1-min intervals. Partly retouched for reproduction.

DISCUSSION

Although some drug-induced lethargy was evident in each animal, plainly haloperidol in the doses used in this and an earlier experiment (Keehn et al., 1976) does not attenuate schedule-induced polydipsia merely by making animals incapable of drinking. Provision of a fluid more palatable than water elevated fluid consumption above water intake levels. And, as the dose-response curves are similar with saccharin and water, the drug's mechanism of action is likely to be the same with both fluids. This mechanism may be that described by Fisher (1973), wherein haloperidol blocks drinking elicited by angiotensin, but a fuller account requires also an explanation of schedule-induced polydipsia.

A theory of schedule-induced polydipsia must explain two events: (1) the eat-drink sequence that develops with intermittent feeding, and (2) the exceptional fluid consumption occasioned by this sequence. The first of these events develops from a normal rat behavior of drinking during meals (Kissileff, 1969). With free food and water, rats switch unpredictably between eating and drinking (Keehn & Colotla, 1970; Premack, 1965), but when their meals are regularly interrupted (e.g., by intermittent reinforcement) they learn to drink during interruptions unless the interruptions are unpredictable (Millenson, Allen, & Pinker, in press). And once an animal begins interpellet drinking it encounters a reinforcer (food plus water) of greater magnitude than food alone. Thus, by drinking, an animal chooses a greater over a lesser reinforcer just as it chooses a sweetened over a regular pellet of food. The second event, excessive fluid intake, follows from this choice because consumption is continued until hunger, not thirst, is satisfied.

By this account, excessive drinking with periodic reinforcement resembles excessive sugar consumption occasioned by sweetened foods. It exemplifies a normal reinforcement process accompanied by an unfortunate physiological side effect in which the mechanism of reinforcement overpowers the mechanism of homeostasis. Haloperidol, it appears, redresses this imbalance by its physiological blocking effect on drinking.

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