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BRIEF COMMUNICATION

Effects of Quipazine on Behavior Under a Multiple Schedule of Reinforcement[1]

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POLING, A. AND J. B. APPEL. *Effects of quipazine on behavior under a multiple schedule of reinforcment.* PHARMAC. BIOCHEM. BEHAV. 8(4) 491–492, 1978. – The effects of three doses of quipazine (1.0, 5.0 and 10.0 mg/kg) on the performance of rats under a multiple fixed-ratio 15 fixed-interval 60-sec schedule of food reinforcement were examined. In the absence of drug, response rates under the fixed-ratio component were much higher than response rates under the fixed-interval component. Rates under the fixed-ratio component were decreased by quipazine in dose-dependent fashion, while response rates under the fixed-interval component were increased by the lowest dose and decreased by the two higher doses of the drug.

Quipazine Multiple-schedule Rate-dependency

QUIPAZINE (2-piperazinyl quinoline), a putative serotonin (5–HT) agonist [2, 4, 6], has recently engendered considerable research interest. In rats, the discriminative stimulus properties of this compound are similar to those of LSD and are blocked by 5–HT antagonists such as methiothepin, cyproheptadine, and cinanserin [8]. Moreover, the disruptive (rate-decreasing) effects of quipazine, LSD, psilocybin, and mescaline on fixed-ratio performance are potentiated by pretreatment with compounds such as p-chlorphenylalanine and 5,7-dihydroxytryptamine, which lower the concentration of 5–HT in brain [2].

The effects of quipazine on performance under schedules of reinforcement other than fixed-ratio have not yet been evaluated and consequently cannot be compared with those of other drugs. Many behaviorally active agents decrease the high rates of responding typically obtained under fixed-ratio schedules, while increasing lower response rates, such as those engendered by fixed-interval schedules [5,7]. The present study therefore examined the effects of three doses of quipazine on performance under a multiple fixed-ratio 15 fixed-interval 60-sec food reinforcement schedule.

METHOD

Animals

Three adult male Sprague-Dawley rats, maintained at 85% of free-feeding weights, were used. They had previously served in a signal detection experiment and had received acute, intraperitoneal (IP) administration of morphine sulfate.

Apparatus

A Lehigh Valley Electronics (Model 1316) operant conditioning chamber was equipped with two levers and a 0.10 ml liquid dipper. The chamber was enclosed in a sound-attenuating cubicle; electromechanical control and recording equipment were located in an adjoining room.

Procedure

During the first session, each animal was exposed to 100 response-independent presentations of the dipper, filled with sweetened condensed milk. Dipper presentations occurred at 45-sec intervals. At the end of this session, all animals were observed to drink from the raised dipper. During the second session, a fixed-ratio (FR 1) schedule was imposed for left-lever presses. Under this schedule, the dipper was presented following each response. The second session terminated after 30 dipper presentations had been earned. During the third session, a tone of 2-min duration was scheduled to occur at 2-min intervals. During the absence of the tone, responses were reinforced under an FR 1 schedule. When the tone was present, lever presses were reinforced under a fixed-interval 5-sec (FI 5-sec) schedule, where dipper presentation followed the first response emitted at least 5 sec after the preceding dipper presentation. The third and all subsequent daily sessions

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TABLE 1

MEAN RESPONSES PER MINUTE BY EACH ANIMAL UNDER ALL EXPERIMENTAL CONDITIONS

	Quipazine Dose (mg/kg)							
	FI 60-sec Component				FR 15 Component			
	Baseline	1	5	10	Baseline	1	5	10
S-1	13.1 (12.0–14.4)	16.1	7.9	0	68.4 (62.1–79.3)	58.9	34.2	0
S-2	18.4 (16.7–21.2)	23.4	6.2	0	90.7 (84.9–99.4)	65.5	11.3	0
S-3	15.4 (13.2–17.9)	19.2	3.1	0	77.4 (70.2–81.1)	59.0	9.7	0

Conditions are labelled according to the dose of quipazine given. The first number under Baseline represents mean control response rate during the sessions which immediately preceded drug injections; the numbers in parentheses represent the range of response rates across these three control sessions.

were one hr in length. Over a number of sessions following initiation of the tone, response requirements were gradually raised to FI 60-sec in the presence of the tone, and FR 15 in the absence of the tone (i.e., a multiple FR 15 FI 60-sec schedule was in effect).

When all animals consistently responded under the multiple FR 15 FI 60-sec schedule, an injection regimen was begun in which subjects received saline or 1.0, 5.0 or 10 mg/kg of quipazine (IP) 30 min prior to each session. Doses are expressed in terms of the total salt. Quipazine was dissolved in isotonic saline, prepared so that the volume injected was always 1 ml/kg of body weight. Each animal received each dose a single time, in an irregular order. Drug was given only when the mean response rates during both the FR and FI components had evidenced no obvious trend across three consecutive sessions: saline injections (1 ml/kg) preceded all other sessions.

RESULTS

Table 1 shows mean responses per minute by each animal under all experimental condition. During baseline (saline control) sessions, each animal responded at a relatively low overall rate (13–19 responses/minute) under the FI 60-sec component, and at a much higher overall rate (68–91 responses/minute) under the FR 15 component. Quipazine produced dose-dependent decreases in the rates maintained under the FR 15 component, with no responding occurring when the 10 mg/kg dose was given. The lowest dose of quipazine (1 mg/kg) increased response rates under the FI 60-sec component, while the higher doses decreased response rates under this component. No animal responded under the FI 60-sec component when the 10 mg/kg dose was given.

DISCUSSION

The effects of quipazine in the present study depended conjointly on the dose administered and the baseline response rate maintained in the absence of the drug: the lowest dose increased a low rate operant (FI responding) and decreased a high rate operant (FR responding), while higher doses reduced responding regardless of baseline rates. Similar effects, which have been termed rate-dependent, have been reported for a variety of behaviorally active compounds [5,7]. The ability of quipazine to decrease response rates under a fixed-ratio schedule has also been noted elsewhere [2].

Rate-dependent effects have been previously described for LSD [1,3]. Thus, the effects of LSD and quipazine on schedule-controlled behavior seem to be similar, as are their discriminative stimulus properties [8]. However, a variety of different pharmacological agents (e.g., amphetamine, barbiturates) produce rate-dependent effects, and the finding that LSD and quipazine similarly effect schedule-controlled behavior does not necessarily indicate that these compounds act through similar pharmacological mechanisms (e.g., central serotonin agonism) although other evidence suggests that they do [2, 4, 6].

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