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Behavioral processes mediating phencyclidine-induced decreases in voluntary sucrose consumption

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Abstract

Prior exposure to phencyclidine (PCP) has been shown to decrease voluntary sucrose consumption in rats, which may indicate reduced reward function. To further characterize the effects of PCP on sucrose consumption, we examined the dose–response relationship between PCP and sucrose consumption, the longevity of the effect, the effects of repeated injections of PCP, variation of the PCP effect across sucrose concentrations, and the effects of PCP on gustatory hedonic responses. A single injection of PCP (2.5–20 mg/kg) dose-dependently suppressed sucrose consumption 20 h post-injection, with significant decreases after 15 and 20 mg/kg PCP. These decreases were sustained three days following withdrawal from PCP. Repeated injections of PCP (7.5 mg/kg bid for 7 days) decreased sucrose consumption 20 h after withdrawal, which returned to baseline on the second day. A single injection of PCP (15 mg/kg) suppressed 0.15 M sucrose more than 1 M sucrose consumption, with no effect on 0.3 M sucrose, suggesting that PCP suppressed intake of moderately rewarding taste stimuli. Finally, a single injection of PCP (15 mg/kg) suppressed brief access (20 s) licking for the majority of concentrations of sucrose solutions offered (0.031 M, 0.062 M, 0.125 M, 0.25 M, 0.5 M, and 1.0 M), while it had no effect on licking for 0.016 M sucrose, water, or for bitter quinine hydrochloride solutions (range: 0.94 mM–30 mM), suggesting that the PCP effect is specific to palatable taste stimuli without disruption of sensitivity to taste quality or intensity. We conclude that PCP produces moderate anhedonia as reflected through a specific decrease in the sustained consumption of moderately palatable sucrose solutions.

Keywords: Phencyclidine; Taste; Anhedonia; Schizophrenia; Sucrose; Intake

1. Introduction

Phencyclidine (PCP) is a dissociative anesthetic that produces psychotomimetic symptoms in humans (Allen and Young, 1978; Bakker and Amini, 1961) and has been investigated for its usefulness in modeling the schizophrenic condition in animals (Javitt and Zukin, 1991; Jentsch and Roth, 1999). Recent data suggest that PCP decreases reward functions in rats, effects which have been argued to model the negative schizophrenic symptom of anhedonia. Withdrawal from acute (5 or 10 mg/kg) or chronic (10, 15, or 20 mg/kg/day for 14 days via osmotic minipump) PCP increases the threshold for intracranial self-stimulation (ICSS) of the lateral hypothalamus (Spielewoy and Markou, 2003), and withdrawal from acute (15 mg/kg) PCP decreases voluntary sucrose consumption (Turgeon and Hoge, 2003). A number of authors have relied upon decreases in sucrose consumption as an indicator of the presence of anhedonia (Papp et al., 1991; Papp and Moryl, 1994; Przegalinski et al., 1995; Willner et al., 1994; Zurita et al., 1996, 2000; Zurita and Molina, 1999; Sammut et al., 2001). However, volume intake measurements used as the sole measure of anhedonia are problematic because of alternative explanations for changes in intake as a function of treatment. The goal of the current study, therefore, was to provide a broader characterization of the effects of PCP on the suppression of sucrose consumption. We examined different doses of PCP, the longevity of the effect, the dependence of this effect on sucrose concentration, and how gustatory responses were modified under PCP treatment, in order to better pinpoint the psychophysical processes contributing to the observed post-PCP sucrose intake suppression.

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2. Materials and methods

2.1. Animals

Animals for all experiments were male Sprague–Dawley rats (Charles River, Wilmington, MA) weighing 300–500 g at experiment onset. Animals arrived in the facility at least five days before experiments began, were housed individually, and were maintained on a 12-hour light–dark cycle. Rats were allowed *ad libitum* access to food (Purina rat chow 5001; Lab Diets, St. Louis, MO) and water throughout the experiments. All procedures were approved by the Amherst College Institutional Animal Use and Care Committee.

2.2. Experiment 1: dose effects of PCP on 0.15 M sucrose consumption

To train the rats to drink sucrose, water bottles were replaced with 0.15 M sucrose solution for 30 min on three of the seven days preceding the experiment, during the dark phase. If the rats ingested less than 5 ml on the first day of sucrose exposure then a fourth day of habituation was added. Thereafter, on day 1 of the experiment, animals were given access to a 0.15 M sucrose solution for 30 min 4.5 h after dark onset, which was then replaced by water 5 h after dark onset. Volume intake during the 30 min test was recorded. On Day 2, rats were weighed and water consumption for the prior 23.5 h was recorded 4.5 h after dark onset. The rats were then given another 30 min sucrose test as on the previous day. 4 h after the end of this sucrose test, rats were injected with either PCP (2.5 ($n=8$), 5 ($n=6$), 10 ($n=6$), 15 ($n=6$), or 20 mg/kg ($n=6$) in 2 ml/kg saline, i.p.) or isotonic saline (2 ml/kg, i.p.; $n=6$). On Days 3–5, 23.5 h water consumption and 30 min sucrose consumption were recorded as for Days 1 and 2. Consumption as a function of body weight (ml/kg) is reported as %-Day 2 consumption (prior to drug exposure). Due to bottle error, sucrose data for 1 animal in the 15 mg/kg group were lost after Day 3. In addition, sucrose and water data on Day 5 were inadvertently only collected from 4 animals in the 10, 15, and 20 mg/kg groups and 5 animals in the saline group.

Sucrose, water, and total fluid consumption (sucrose + water) were compared using separate repeated-measures ANOVAs with DRUG (PCP vs. SAL) as the between-subjects variable and DAY as the within-subjects variable. Student–Newman–Keuls *post-hoc* tests were used to assess the effects of individual doses of PCP on consumption.

2.3. Experiment 2: effects of subchronic PCP on voluntary sucrose intake

The methods were identical to those described for Experiment 1 except that rats were trained to ingest 0.15 M sucrose on each of 7 days prior to the first administration of PCP. PCP (7.5 mg/kg in 2 ml/kg saline, i.p.) or saline ($n=6$ per group) was then administered twice a day at 12 h intervals for 7 days, during which time sucrose consumption tests were not performed. Beginning 24 h after the final PCP injection, the rats received daily 30-min sucrose tests during the dark phase. Both 0.5 h sucrose and 23.5 h water consumption were monitored for 5 days. One animal from the saline group was eliminated prior to injections due to his failure to drink sucrose during the first 7 days (<3 ml/day). Consumption on each test day was calculated as % of the consumption on the day that immediately preceded the initial drug exposure. The data were analyzed using a repeated-measures ANOVA with DRUG as the between-subjects factor and DAY as the within-subjects factor.

2.4. Experiment 3: effects of PCP on a sucrose concentration–intake function

The methods used were identical to those described in Experiment 1, except that the concentration of sucrose was varied across groups such that after PCP or vehicle injection rats were offered either 0.15 M, 0.3 M, or 1.0 M sucrose, and only a single dose of PCP (15 mg/kg) was administered. Rats received habituation training with the concentration of sucrose to be tested, as in Experiment 1. Also as in Experiment 1, rats were then treated with PCP or isotonic saline (veh) on Day 2 (4 h following sucrose exposure) and sucrose and water consumption were evaluated on Day 3. Six groups were tested: veh-0.15 M ($n=6$), PCP-0.15 M ($n=6$), veh-0.3 M ($n=6$), PCP-0.3 M ($n=6$), veh-1 M ($n=6$), and PCP-1 M ($n=6$).

Because sucrose consumption was expected to vary as a function of concentration, the amount of sucrose consumed on Day 3 was compared using a 2×3 ANOVA with between-subjects variables of DRUG (saline, PCP) and sucrose concentration (0.15 M, 0.3 M, 1 M). Water consumption and total fluid consumption were also examined on both Day 2 and Day 3, as Day 2 water consumption was measured prior to drug injection, so any Day 2–Day 3 difference may reflect drug-induced changes in water consumption.

2.5. Experiment 4: effects of PCP on brief access licking for sucrose or quinine

Experimentally naive rats were tested daily in an automated lickometer referred to as the "Davis Rig" (Davis MS-160, DiLog Instruments, Tallahassee, FL). Unlike single-bottle tests, the Davis Rig allows the presentation of up to 16 different taste stimuli (one at a time) within a single behavioral session, with a minimum inter-presentation interval of 5 s (Rhinehart-Doty et al., 1994; Smith, 2001). Rats were placed in a plastic rectangular cage (30×14.5×18 cm) with a wire mesh floor and had access to a single sipper tube (when a computer-operated shutter was lifted) via an oval opening centered in the front wall of the test chamber. Spout licks were recorded by microcomputer using a circuit that recorded the time of tongue contact with the spout (in milliseconds). The data were collected and stored in individual files for each trial, with licking behavior for each taste trial presentation recorded separately.

Rats were assigned to either a sucrose ($n=4$) or a quinine hydrochloride (QHCl; $n=7$) group and tested individually during the first 3 h of the dark phase of the light cycle. The rats were habituated to the Davis Rig over daily sessions under

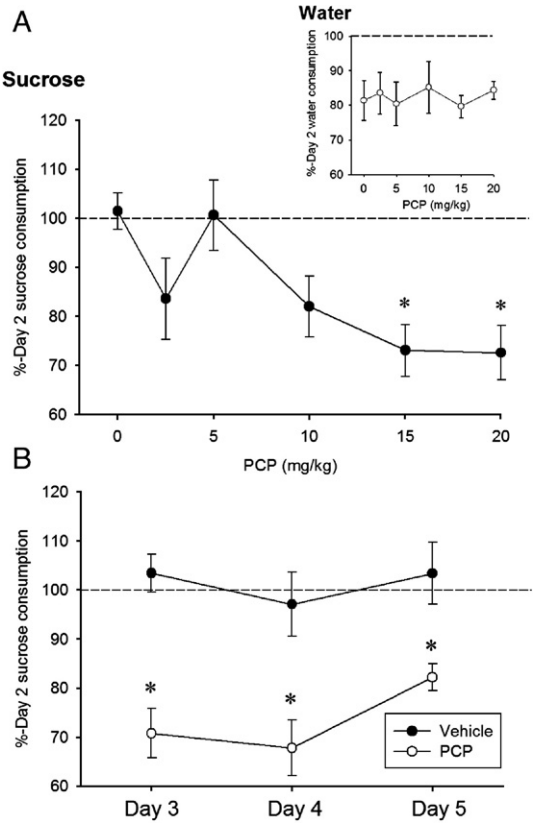

Fig. 1. (A) Twenty hours following injection (Day 3), PCP produced a dose-dependent decrease in voluntary sucrose consumption (expressed as a %-Day 2 consumption) with no effect on water consumption (inset). *$p<0.05$ SNK *post-hoc* test (B) Decreases in voluntary sucrose consumption seen following a single injection of 15 or 20 mg/kg PCP lasted for 3 days.

23.75 h water deprivation conditions as follows. On training day 1, rats were offered a single 15-min trial of distilled water (clock beginning with the first lick). On training day 2, rats were given a series of 32 presentations of dH_2O using 8 bottles housed on a motorized track outside the test chamber, with 4 presentations per bottle. Each bottle was presented for 20 s after licking onset, with up to 60 s wait time for the first lick. The inter-presentation interval was 40 s, during which time a metal plate covered the access hole and the solution bottles were moved on their track to position the next bottle. On session 3, rats in the sucrose group received twenty presentations (using 4 bottles) of 0.5 M sucrose using the same parameters as for water training, while the QHCl group continued to receive water as in session 2.

After training, rats were presented with daily tests in which licking for water and several concentrations of either sucrose (15, 31, 62, 125, 250, 500, and 1000 mM) or QHCl (0.94, 1.88, 3.75, 7.5, 15, and 30 mM) was assessed. Rats remained on complete water restriction for the QHCl tests but were only water-deprived for 4 h before the sucrose tests. On each test day, rats sampled tastants in 2 descending and 2 ascending concentration series (Rhinehart-Doty et al., 1994), in fully counterbalanced order. After three days of stable baseline responding, rats were given i.p. injections of either PCP (15 mg/kg) or sterile isotonic saline (2 ml/kg), 4 h after tastant exposure. Rats were then tested under identical conditions for an additional three days. Stimulus bottles were weighed to the nearest 0.01 g before and after the session to monitor intake for each bottle.

The mean number of licks for each concentration trial of each taste solution was determined. Licking for sucrose and for QHCl was also standardized to water consumption using a tastant/water lick ratio in which each rat's mean lick count for a taste stimulus was divided by its mean lick count for water (see also Baird et al., 2006; Eylam et al., 2005). Data were analyzed using a 3-way repeated-measures ANOVA for each tastant group (drug × tastant concentration × trial). Drug × tastant concentration interactions were explored using simple–simple effects comparisons, which hold constant the risk of type I errors (Keppel and Wickens, 2004).

3. Results

3.1. Dose effects of PCP on 0.15 M sucrose consumption

Because sucrose and water intake were measured over different time periods in the same animals, separate repeated-measures ANOVAs were run for the two data sets. PCP significantly decreased sucrose consumption ($F(5,24)=3.6$, $p<0.05$); however, there was no effect of DAY and no significant interaction effect. For water consumption, there was a significant effect of DAY ($F(2,50)=6.7$, $p=0.01$) but no

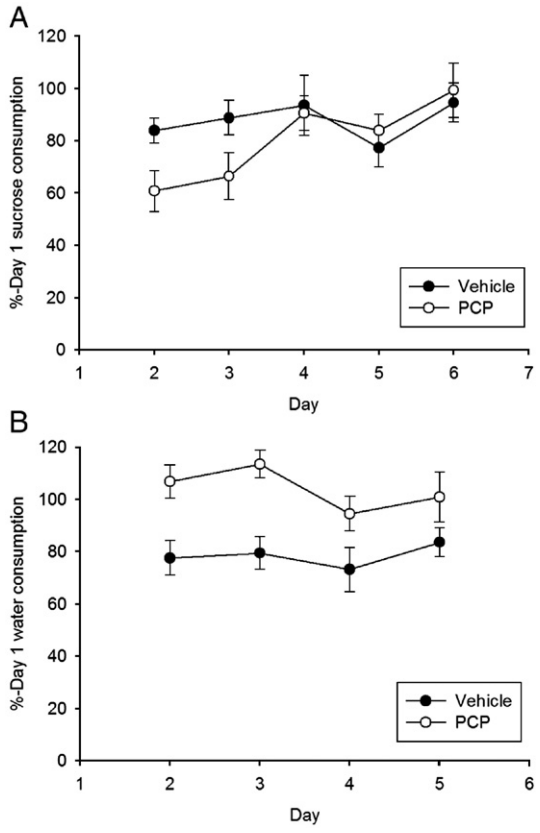

Fig. 2. (A) Subchronic PCP decreased voluntary sucrose consumption 20 h after the cessation of treatment; however, the effect was only significant on the first day following withdrawal. (B) Sucrose-induced water intake suppression was reversed for 2 days following cessation of subchronic PCP treatment.

effect of DRUG and no significant interaction, with water intake on Day 4 significantly less than that on Day 5 ($p=0.003$). Total fluid consumption was affected by DAY ($F(3,72)=34.5$, $p<0.001$), but not DRUG, with peak consumption on Day 4, then declining total volume thereafter. The dose–response curves for sucrose and water consumption on Day 3 are shown in Fig. 1A.

Student–Newman–Keuls *post-hoc* tests following this initial ANOVA did not reveal significant differences in sucrose consumption between any PCP dose and control. However, the limited number of animals in the 15 and 20 mg/kg groups tested through to Day 5 meant that animals in these groups inadvertently not tested on Day 5 were excluded from the analysis on Days 3 and 4. Therefore, another repeated-measures ANOVA using all animals was run for Days 3 and 4 only. This analysis revealed a significant effect of DRUG ($F(1,31)=4.6$, $p<0.005$) and the SNK *post-hoc* tests revealed that both the 15 and 20 mg/kg groups drank significantly less sucrose. In order to determine if the effect of PCP was also significant on Day 5, the 15 and 20 mg/kg groups were combined and compared with saline-treated rats using a repeated-measures ANOVA across the three days. Only data from animals for whom data was available for Days 3 through 5 were included (saline: $n=5$, PCP: $n=7$). This analysis revealed that PCP significantly suppressed sucrose consumption ($F(1,10)=35.5$, $p<0.001$; Fig. 1B). There was no significant effect of DAY and no significant interaction effect. There were no significant effects of either PCP or DAY on water consumption.

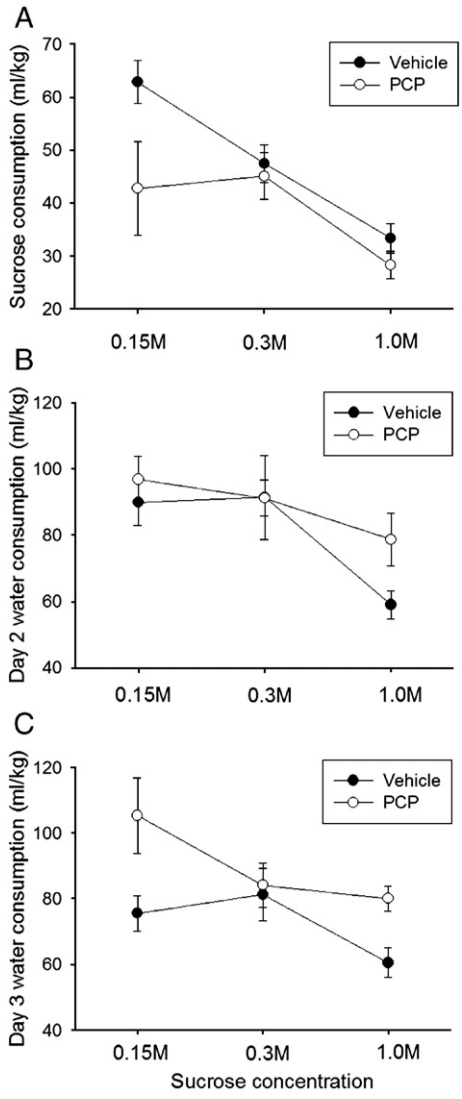

Fig. 3. (A) PCP produced an overall decrease in voluntary sucrose consumption across all sucrose concentrations 24 h after injection. (B) PCP did not alter water consumption on Day 2 of the experiment (during which time PCP was administered). (C) Water consumption on Day 3 (immediately following the sucrose test) was increased by PCP.

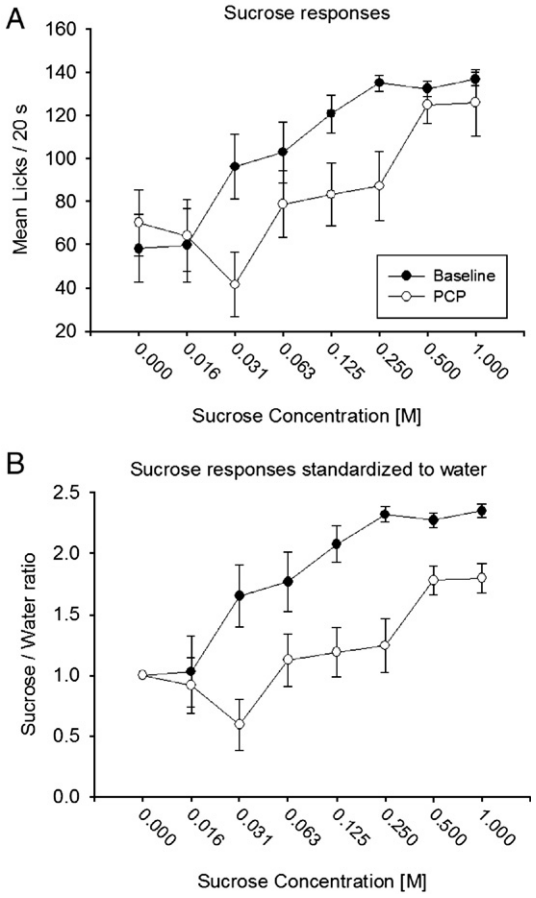

Fig. 4. (A) Concentration–response curve for sucrose (mean ± standard error) 4 h before (filled circles) and 20 h after (open circles) 15 mg/kg PCP treatment ($n=4$). (B) Same data standardized to the water response for each rat.

Animals treated with 15 mg/kg and 20 mg/kg drank 16.5 + 8.0 ml and 16.8 + 1.3 ml of sucrose on Day 3 respectively, indicating that the absence of a further decrease in the 20 mg/kg groups was not due to a floor effect. Finally, paired *t*-tests revealed that sucrose intake on the two days prior to PCP administration (Day 1 vs Day 2) did not differ.

3.2. Effects of subchronic PCP on voluntary sucrose intake

The repeated-measures ANOVA examining the effects of subchronic PCP on sucrose consumption revealed a significant DAY × DRUG interaction ($F(4,36)=3.1$, $p<0.05$), with sucrose

consumption dropping initially in the PCP group and then returning to the same levels as saline by Day 4 (Fig. 2A). A repeated-measures ANOVA also revealed that subchronic PCP increased water consumption ($F(1,9)=10.1$, $p<0.05$) but there were no effects of DAY or DAY × DRUG (Fig. 2B). Total fluid consumption varied by DAY ($F(4,36)=8.6$, $p<0.001$) but not by DRUG.

Paired *t*-tests comparing sucrose consumption on the two days prior to the onset of subchronic PCP administration (Day 0 vs. Day 1) revealed that consumption was higher on Day 1 than Day 0 ($t(10)=3.2$, $p<0.05$). However, when the analyses were rerun using the average of Day 0 and Day 1 as the baseline level, the DAY ($F(4,36)=5.7$, $p<0.005$) and DAY × DRUG ($F(4,36)=2.8$, $p<0.05$) effects remained significant.

3.3. Effects of PCP on a sucrose concentration–intake function

A 2×3 ANOVA revealed a significant decrease in sucrose consumption with increasing sucrose concentration ($F(2,30)=11.0$, $p<0.001$) and a PCP-induced decrease in sucrose consumption ($F(1,30)=5.5$, $p<0.05$ but no significant DRUG × CONCENTRATION interaction (Fig. 3A). Rats given higher concentrations of sucrose also drank less water on Day 2 ($F(2,30)=5.7$, $p<0.01$; Fig. 3B) and Day 3 ($F(2,30)=4.1$, $p<0.01$; Fig. 3C) and PCP-treated rats drank more water on Day 3 ($F(1,30)=8.9$, $p<0.005$). Total daily fluid intake was lower in animals given higher concentrations of sucrose on both Day 2 ($F(2,30)=22.4$, $p<0.001$) and Day 3 ($F(2,30)=11.6$, $p<0.001$), but there was no effect of PCP on either day. SNK *post-hoc* tests revealed that for all measures except Day 3 water consumption, animals offered 1 M sucrose consumed less than animals in the other two groups. For Day 3 water consumption, 1 M was only different from 0.15 M.

Finally, paired *t*-tests revealed that sucrose intake on the two days prior to PCP administration (Day 1 vs Day 2) did not differ.

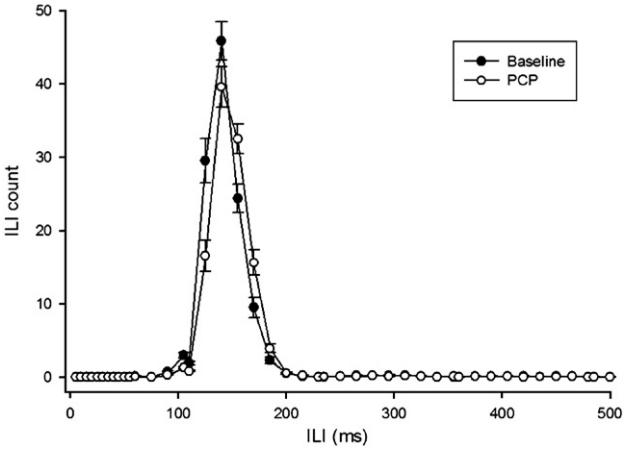

Fig. 5. Interlick interval (ILI) frequency distribution (for ILIs<500 ms) for sucrose data depicted in Fig. 4. While PCP reduced the number of licks (hence ILIs) expressed for sucrose, there was no significant shift in the mean of the ILI distribution, indicating no disruption of oromotor coordination after PCP treatment.

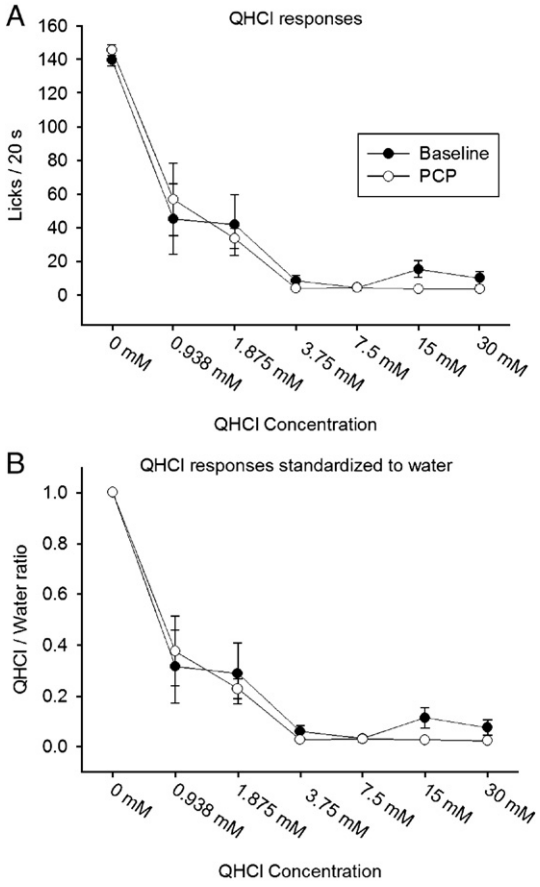

Fig. 6. (A) Concentration–response curve for quinine hydrochloride (QHCl; mean±standard error) 4 h before (filled circles) and 20 h after (open circles) 15 mg/kg PCP treatment ($n=7$). (B) Same data standardized to the water response for each rat.

3.4. Effects of PCP on brief access licking for sucrose or quinine

3.4.1. Sucrose

Lick counts during the brief 20 s sampling trials increased monotonically as sucrose solutions were more concentrated (CONCENTRATION: $F(7,21)=7.98$, $p<0.001$; see Fig. 4A). Overall, PCP appeared to significantly reduce licking for sucrose at several concentrations, as supported by a statistically significant DRUG × CONCENTRATION interaction term ($F(7,21)=7.92$, $p<0.04$) and a marginally significant main effect of DRUG ($F(1,3)=7.47$, $p<0.07$). When sucrose responses were standardized to the water response, concentration differences remained similar (CONCENTRATION: $F(6,18)=10.16$, $p<0.001$) with a reversal of the statistical significance of the DRUG × CONCENTRATION interaction term ($F(6,18)=2.36$, $p<0.07$) and the main DRUG term (DRUG: $F(1,3)=23.10$, $p<0.02$), indicating that the marginal main drug effect in the raw data was due in part to the lack of a difference across water licking conditions (Fig. 4B), and that the lack of water difference also influenced the interaction term. A separate ANOVA confirmed the former conclusion, as there was no significant drug effect across water conditions ($F(1,3)=1.04$, $p=0.38$). Simple–simple effects comparisons of baseline-PCP

differences at each sucrose concentration (collapsed across trials) indicated that PCP significantly suppressed licking at all sucrose concentrations ($ps < 0.01$) except the 0.016 M concentration ($p = 0.20$). Analysis of inter-lick intervals (ILIs) indicated that there was no significant effect of PCP on the mean rate of licking among ILIs less than 250 ms ($t(3) = -1.3$, $p = 0.26$; see Fig. 5), or on the proportion of ILIs 250 ms–999 ms in duration ($t(3) = -0.75$, $p = 0.51$). Finally, PCP produced no significant change in the number of taste trials (out of 32) in which rats failed to sample from the spout (baseline mean = 5.25 ± 1.25; PCP mean = 7.50 ± 2.10; $t(3) = -0.90$, $p = 0.43$).

3.4.2. Quinine

Most concentrations of QHCl (3.75 mM–30 mM) strongly suppressed licking relative to water (Fig. 6A), as supported by a robust main effect of the CONCENTRATION term ($F(6,36) = 34.37$, $p < 0.001$), with middling responses at the two weakest QHCl concentrations (0.9 mM and 1.8 mM). PCP treatment had no effect on any of these responses as indicated by a non-significant main effect of DRUG ($F(1,6) = 0.42$, $p = 0.54$) and no significant interaction terms ($ps > 0.12$). Standardizing QHCl responses to water (Fig. 6B) similarly indicated no significant effects for any terms, except for the main effect of CONCENTRATION ($F(5,30) = 4.69$, $p < 0.003$).

4. Discussion

In this study a variety of tests were conducted in order to further characterize the behavioral properties of PCP-induced sucrose intake suppression, and to begin to gain insight into some of the psychophysical processes that underlie this effect. The effects of acute or subchronic PCP injections were therefore characterized across a range of PCP doses, sucrose and QHCl concentrations, and test days. To better characterize whether the suppressive effects of PCP on sucrose consumption reflected a sensory "anhedonia," gustatory concentration–response functions for palatable sucrose and aversive QHCl taste stimuli were also determined using brief access licking testing, an established paradigm for the evaluation of gustation in rodents (Rhinehart-Doty et al., 1994; Mueller et al., 2005; Smith, 2001; Spector et al., 1996, 2002). In this paradigm, several concentrations of a taste stimulus are presented for very brief (5–30 s) trials, allowing a concentration–licking function to be determined. The brief nature of the taste trials ensures that post-ingestive feedback influences are minimized, allowing the effects of PCP on orosensory processing to be revealed through curve shifts in the concentration–response function (e.g., Eylam et al., 2005; Mueller et al., 2005; Rhinehart-Doty, 1994; Spector et al., 1996; Spector and Kopka, 2002). Comparisons with water responses also provide a means to control for any non-gustatory effects of the drug treatment. In addition, a detailed analysis of the temporal pattern of licking (millisecond resolution) during these brief trials, commonly known as licking microstructure analysis (Davis and Levine, 1977), can reveal oromotor deficits, signs of conditioned taste aversion, and other temporal features typical of palatable and aversive taste evaluation (Baird et al., 2005).

The first experiment examined the dose–response relationship between PCP and suppression of sucrose intake as well as the longevity of this effect. Twenty hours after a single injection of PCP, a dose–response relationship between PCP and suppression of sucrose intake was observed with significant suppression below baseline seen at 15 and 20 mg/kg PCP. However, suppression appeared to level off after 15 mg/kg, as 20 mg/kg did not produce significantly more suppression than 15 mg/kg. Sucrose consumption remained suppressed in the 15 and 20 mg/kg groups for three days after injection.

Previous experiments examining the effect of different doses of PCP on reward threshold for ICSS of the lateral hypothalamus found that a single injection of either 5 or 10 mg/kg PCP elevated the electrical current threshold required to sustain reinforcing behavior 24 h following injection, but that threshold had returned to baseline by 48 h post-injection (Spielewoy and Markou, 2003). These results differ from ours in that we did not see any effect of 5 mg/kg PCP on sucrose consumption and only a trend at 10 mg/kg PCP. In addition, the effect of 15 or 20 mg/kg PCP in our study was longer-lasting than that seen in the prior study (Spielewoy and Markou, 2003), which used lower PCP doses. As in the present study, Spielewoy and Markou (2003) found that PCP produced modest changes that were not further enhanced by escalating doses: 10 mg/kg PCP did not increase ICSS threshold above the level seen at 5 mg/kg.

The second set of experiments examined the effect of subchronic PCP injection on sucrose consumption. There was a significant DAY × DRUG interaction which appeared to be driven by less sucrose consumption on the first day following cessation of PCP treatment (Day 2), followed by a return to saline condition levels by Day 4. The observation that a single injection of PCP produces a longer-lasting decrease in sucrose consumption than repeated injections is surprising and suggests that the differences between the neurochemical effects of a single injection and repeated injections is qualitative and not merely quantitative. These results contrast with those of Spielewoy and Markou (2003), who found longer-lasting effects on ICSS threshold after long-term PCP exposure. Spielewoy and Markou (2003) suggested that the increases in ICSS threshold seen in the first day or two following withdrawal from either single injections or continuous infusion of PCP resulted from compensatory changes in the primary system affected by the drug (presumably NMDA-mediated), whereas the long-lasting changes seen only following continuous infusion of higher doses of PCP result from compensatory changes in secondary systems, perhaps involving dopamine-serotonin balance (see Spielewoy and Markou, 2003 for discussion). However, their long-term PCP studies used continuous infusion of PCP whereas we used subchronic injection, a difference that may have prevented compensatory changes in secondary systems, due either to injection stress or non-continuous levels of drug. Alternatively, the ICSS threshold and sucrose consumption measures may simply have assayed different aspects of motivation.

The third experiment examined the effect of PCP on sucrose consumption using different concentrations of sucrose to provide a range of solutions varied in taste and caloric reward

value. Higher concentrations of sucrose are more palatable and produce greater levels of learned preference due to higher caloric content (Sclafani and Nissenbaum, 1988). The results of this experiment suggest that the effects of PCP on reward are moderate, as the greatest effects (although not significantly different from other concentrations) were seen with 0.15 M sucrose, which is only mildly palatable and produces only moderate learned preferences. When more reinforcing concentrations of sucrose were tested, the effects of PCP were less marked.

In Experiments 1–3, rats consumed approximately 20% less water after they were introduced to sucrose in baseline testing conditions, probably due to the volume of water also consumed in the sucrose solution. In Experiments 2 and 3, PCP significantly reversed this effect, in most cases returning water consumption to pre-sucrose baseline levels. This likely represents a compensatory rebound due to the PCP-induced suppression of sucrose consumption, as there were no effects of PCP on total daily intake. This result also indicates that water intake regulation was not hindered by PCP, and thus the decreases in sucrose consumption were not related to motor deficits—a result confirmed in Experiment 4 (discussed below). One exception to this general pattern was observed in Experiment 3. Rats offered 1 M sucrose consumed less total fluid than animals offered 0.15 M or 0.3 M sucrose. This may have resulted from decreased water consumption due to enhanced negative contrast (Flaherty and Largen, 1975) such that the water seemed much less palatable when offered after the 1 M solution. However, PCP-treated rats drank more water, suggesting that they possibly experienced reduced negative contrast, which would be an effect consistent with a decrease in the perceived reward value of the sucrose.

Consistent with Experiments 1 through 3, brief access responses to a majority of sucrose concentrations were suppressed after PCP treatment in Experiment 4. Under baseline conditions, rats expressed preferentially more licks for sucrose over water at concentrations greater than 0.031 M sucrose, with asymptotic (maximal) responses for sucrose concentrations of 0.25 M and greater. PCP treatment suppressed licking for all but the weakest (0.016 M) concentration of sucrose tested, producing a noticeably flatter concentration–response function, most clearly seen when corrected for water consumption (Fig. 4B). While PCP withdrawal suppressed licking for sucrose, there was no similar effect on responses to bitter QHCl (Fig. 6), and no effect on responses to water in either group. These results indicate that the PCP effects were specific to palatable taste stimuli.

4.1. PCP intake suppression: incapacity, aversion, apathy, ageusia, or anhedonia?

Previous studies have measured anhedonia by demonstrating reductions of intake in sucrose consumption measured volumetrically in long-term tests, as also shown in Experiments 1 to 3. Long-term volumetric consumption analyses, however, are difficult to use as measures of perceived reward value or taste evaluation per se, even when used in preference tests, because volume intake is influenced by numerous other factors, including inhibitory ingestive feedback derived from the caloric content of the ingestate (enhanced satiety), visceral malaise, conditioned taste aversion (CTA), motoric disruption or dyscoordination, and the evocation of competing behaviors such as locomotion, sleep, or stereotypy.

Several of our findings rule out the hypothesis that PCP produced a motor disruption that constrained either the rats' ability to approach and maintain presence at the spout or their oromotor coordination. There was no decline in water responses after PCP in any experiment, nor did PCP suppress licking for the moderately aversive concentrations of QHCl (0.9 mM and 1.8 mM). Analysis of ILIs also revealed that PCP treatment did not affect the shape of the ILI frequency distribution (Fig. 5), indicating no deficit in the capacity of the oromotor pattern generator in the reticular formation to produce lick cycles of normal frequency and duration (Travers et al., 1997).

It is possible that PCP selectively suppressed sucrose consumption because it produced a CTA due to the association of the sucrose taste with a putative PCP-induced malaise. However, several findings do not support this conclusion. Parker (1993) previously showed that PCP (10 mg/kg) produced no increase in oromotor rejection behaviors (aversive taste reactivity) and no decline in oromotor ingestive responses to a 0.5 M sucrose solution, effects that were obtained after the induction of a CTA using a lithium chloride injection. Recently, we also determined that the formation of a CTA is characterized by a more than twenty-fold increase in the ratio of longer (250–999 ms) to shorter (<250 ms) ILIs (Baird et al., 2005). There was no significant increase in this ratio after PCP treatment (Experiment 4). Finally, as a positive control, there was no deficit in the capacity of the rats to respond to aversive stimuli as indicated by unchanged responses to the 0.9 mM and 1.8 mM QHCl solutions. We conclude, therefore, that PCP-treated rats did not subsequently avoid sucrose because they found it to be aversive.

The failure of PCP to suppress licking for weakly aversive concentrations of QHCl also eliminates the possibility that PCP produced a generalized diminution of perceived taste intensity, or a global flattening of affective taste responses. If PCP reduced the perceived gustatory intensity of weak taste stimuli, PCP would be expected to have left-shifted the QHCl concentration–licking curve in concert with the right shift that was observed for sucrose. However, PCP did not enhance QHCl licking despite significant thirst and several QHCl concentrations tested at which licking increases could have been expressed. It is unlikely that an increased state of thirst in rats in the QHCl tests blocked an effect of PCP because rats exhibited a wide behavioral range of licking responses to QHCl indicating that their state of thirst did not drive licking indiscriminately. Moreover, PCP never suppressed responding for water whether the rats were non-deprived (Experiments 1–3), mildly water-deprived (Experiment 4 sucrose), or thirsty (Experiment 4 QHCl). Conversely, one might expect PCP to enhance sensitivity to QHCl, as clinical depression commonly involves a tendency to focus on the aversive nature or qualities of events. However, PCP did not enhance the suppressive effects of QHCl, as the middling responses to the low

concentrations of QHCl were unchanged. The results suggest, rather, that PCP treatment reduced the hedonic appraisal of only palatable tastants, a result consistent with the report that PCP also increased the threshold for rewarding ICSS (Spielewoy and Markou, 2003). Overall, the prevailing data support the hypothesis that PCP treatment reduces the rewarding experience of sucrose.

In recent years, distinctions within the concept of reward have been proposed. Tastants or other objects of consumption give rise to unlearned sensations that reinforce subsequent acquisition and correspond to reports of pleasurable sensation, an aspect of reward that has been termed "liking" (Berridge and Robinson, 1998). PCP at a dose comparable to this study (10 mg/kg) was reported to produce no deficit in the ingestive oromotor reactions to an intraoral 0.5 M sucrose injection, suggesting that PCP does not suppress rapid orosensory affective responses to sucrose (Parker, 1993). The differential effects of PCP across sucrose and QHCl responses observed in this study also support the conclusion that PCP appears unlikely to change the sensory character or quality of the tastant.

A second distinction of reward relates to the motivation to acquire or to continue to acquire the stimulus/object of intent, termed incentive motivation or "wanting" (Berridge and Robinson, 1998). While the results of this study suggest that PCP did not suppress the motivation to approach the spout because rats continued to sample sucrose with no significant reduction in the number of times they engaged the spout (Experiment 4), PCP did appear to cause a reduction in the capacity of the sucrose solution to sustain prolonged sampling, as indicated by relatively less licking during the 20 s access periods to several concentrations of sucrose. Together, these results suggest a diminution in the hedonic evaluation of the tastant at a phase of processing that occurs after the initial sensory identification of the tastant and after the decision to ingest the stimulus. Overall, the results support the interpretation that PCP treatment produced anhedonia through a specific reduction of the incentive motivation to sustain ingestion of palatable sucrose solutions.

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