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Activation of the immune system in rats with lipopolysaccharide reduces voluntary sucrose intake but not intraoral intake

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Abstract

Traditional intake measures of voluntary consumption of food or fluid from a specific location involve both appetitive and consummatory behaviors. Appetitive behaviors are food finding behaviors displayed by an animal prior to the consumption of the food, whereas consummatory behaviors are the behaviors involved in the actual consumption of the food. Intraoral intake of a fluid can be measured by directly infusing it into the oral cavity of an animal and quantifying the consummatory behaviors. The present study compared the effects of immune activation (lipopolysaccharide, LPS) and toxin (lithium chloride, LiCl)-induced changes on both a traditional intake measure (bottle drinking) and an intraoral intake measure. In Experiment 1, rats were injected intraperitoneally with LPS (200 μg/kg), LiCl (0.15 M, 20 ml/kg) or NaCl vehicle, and voluntary sucrose (0.3 M) intake was monitored for 1 h from a graduated drinking tube. Voluntary intake was again assessed on a second test day, 72 h later under the same conditions. In Experiment 2, a continuous intraoral infusion of sucrose (0.3 M) was given via intraoral cannulae following systemic injections of LPS, LiCl or NaCl vehicle on two different test days, 72 h apart. Rats injected with LiCl displayed reduced sucrose intake on both the voluntary intake measure and the intraoral intake measure relative to controls (P's $< .05$). The reduced intake observed was of greater magnitude on the second test day of both experiments, consistent with conditioning effects. In contrast, LPS reduced sucrose intake only when assessed with the traditional intake measure. Intraoral sucrose intake remained unchanged relative to controls. The present results provide further evidence that activation of the immune system has adverse effects on the appetitive phase of ingestion, whereas the consummatory aspects are unaffected.

Keywords: Appetitive behaviors; Consummatory behaviors; LiCl; Drinking; Taste reactivity; Endotoxin; Sickness behaviors

1. Introduction

Foraging for, and ingesting food, requires an animal to progress through two phases, an appetitive phase and then a consummatory phase as first suggested by Craig (1918). The appetitive phase of ingestion involves those behaviors displayed by the animal prior to the actual consumption of food, such as recognizing that food has been made available, orienting to the food and subsequent approach movements. In contrast, consummatory behaviors (such as licking, chewing and swallowing) are the more stereotyped behaviors involved in the actual consumption of the food. Any pharmacological or neurological manipulation can alter ingestion by acting primarily on the appetitive phase, on the consummatory phase or on both phases. Traditional intake measures, which require the animal to voluntarily ingest food from a specific location (such as a food hopper) or fluid from a bottle, involve both appetitive and consummatory behaviors. As such, any manipulation that produces changes in intake can result from an influence on either the appetitive and/or the consummatory phase.

The taste reactivity method originally developed by Grill and Norgren (1978) allows for examination of the consummatory behaviors alone without the appetitive phase. In this paradigm, liquid foods are infused directly into the mouth of an animal (typically rats) via a surgically implanted intraoral cannula. The animal can then "choose" to consume the fluid by producing positive ingestive behaviors such as tongue protrusions and rhythmical mouth movements, actively reject the fluid by producing active aversive responses such as gaping and chin rubbing or passively reject the fluid by letting it drip out of its mouth without reacting to it. A continuous intraoral infusion of the fluid allows an experimenter to determine a measure of "intraoral intake." Intraoral intake

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tests have been shown to be sensitive to the same factors and manipulations as those that affect traditional intake paradigms. For instance, intraoral intake is dependent on the concentration and hedonics of the infused tastant (Flynn and Grill, 1988a,b), as well as being sensitive to gastric preloads (Seeley et al., 1994) and the administration of cholecystokinin (Grill and Smith, 1988), in a manner similar to traditional intake measures. As such, the results obtained from these two measures often parallel one another.

However, there are several lines of evidence that indicate that intraoral intake and voluntary consumption are in fact independent of one another. When rats are injected with the orexigenic agent neuropeptide Y (NPY), a robust increase in voluntary food intake is observed (e.g., Clark et al., 1984). In contrast, several studies have demonstrated that NPY administration does not alter intraoral intake of a variety of fluids (Ammar et al., 2000; Sederholm et al., 2002; Seeley et al., 1995; Woods et al., 1998). Administration of amphetamine in rats has been shown to produce robust decreases in the amount of sweetened milk voluntarily consumed from a bottle, yet when this same fluid is infused intraorally, intake volume is unaffected (Wolgin et al., 1988). Similarly, gastrin-releasing peptide (GRP) has been shown to produce significant intake reductions of both sucrose and milk from a bottle but has no effect on intraoral intake of either solution (Rushing and Houpt, 1999).

One of the hallmark symptoms following activation of the immune system is a reduction in food intake. Injections of lipopolysaccharide (LPS) or the individual cytokines themselves result in robust decreases in food intake (e.g., Langhans et al., 1990, 1991; Plata-Salamán, 1994; Plata-Salamán and Borkoski, 1993) as well as reduced intake of palatable substances such as sucrose (Cross-Mellor et al., 1999), saccharin (Yirmiya, 1996) and sweetened milk (Swiergiel et al., 1997a,b). Recent evidence suggests that the reduction in feeding seen following immune activation is the result of specific effects on appetitive behaviors. Studies have shown that there is significant reduction in operant responding for food following injections of either LPS or specific cytokines (such as interleukin-1β, IL-1β) (Bret-Dibat et al., 1995, 1997; Kent et al., 1996; Larson et al., 2002). Because an operant response is necessary before the animal will receive any food, this test is often considered a measure of appetitive behavior. More recently, it has been shown that while LPS reduced sucrose intake from a bottle, sucrose palatability as assessed by a taste reactivity analysis remained unchanged (Cross-Mellor et al., 1999). Furthermore, it was found that systemic administration of LPS resulted in significant reductions in voluntary water intake, but the same dose actually increased positive ingestive reactions to brief intraoral infusions of water (Cross-Mellor et al., 2000). These latter studies examined very brief infusions (60 s) of fluids following activation of the immune system and did not assess the actual volume consumed during a continuous intraoral infusion.

The present study compared the effects of immune activation on both intraoral intake and voluntary bottle intake of a sucrose solution. The immune system manipulation was also compared with the effects seen following toxin administration. The toxin lithium chloride (LiCl) produces robust conditioned avoidances of flavors or foods that have been previously paired with its administration (e.g., Garcia et al., 1974). It also has been well documented that LiCl produces changes in taste reactivity responding indicative of a conditioned aversion (e.g., Ossenkopp and Eckel, 1995; Eckel and Ossenkopp, 1996; Spector et al., 1988). Therefore, the present study assessed the effects of exogenous administration of both LPS and LiCl on voluntary sucrose intake from a bottle versus intraoral intake (when sucrose is infused intraorally), which bypasses the appetitive phase of ingestion.

2. Materials and methods

2.1. Subjects

Subjects were naïve, male adult Long–Evans hooded rats (Charles River, Quebec) weighing between 250 and 300 g at the start of the experiments. Rats were housed individually in either polypropylene cages (voluntary intake) or stainless steel wire mesh cages (intraoral intake) and maintained in a temperature-controlled room (21 ± 1 °C) on a 12:12 light/dark cycle (lights on between 07:00 and 19:00 h). Food and water were provided ad libitum unless otherwise specified. All procedures were carried out in compliance with the guidelines set forth by the Canadian Council of Animal Care (CCAC). Different animals were used for each experiment ($n = 21$ for voluntary intake and $n = 21$ for intraoral intake).

2.2. Drug administration schedule

On the first test day of each experiment, rats were randomly assigned to one of three experimental groups, which received an intraperitoneal injection of LPS (200 μg/kg, from *Escherichia coli* 0111:B4, L-2630; Sigma, St. Louis, MO) that was dissolved in 0.9% saline, an intraperitoneal LiCl (0.15 M, 3 mEq) injection or a control intraperitoneal injection of the saline vehicle (NaCl, 1 ml/kg). Two hours after LPS injections or 10 min after LiCl or NaCl injections, sucrose (0.3 M) intake was monitored (bottle intake in Experiment 1 and intraoral intake in Experiment 2). The second test day occurred 72 h after the first test day and involved exactly the same injection and handling procedures.

Studies that examined the effects of LPS on sickness behaviors have utilized doses that range between 50 (e.g., Langhans et al., 1991) and 1000 (Yirmiya, 1996) μg/kg. The present dose (200 μg/kg) was chosen to ensure that the previously shown aversive effects on behavior by systemic injections LPS would be observed. Furthermore, past research in our laboratory demonstrated that LPS at a dose of 200 μg/kg produced differential effects on taste reactivity responses and fluid intake (Cross-Mellor et al., 1999, 2000).

2.3. Experiment 1: voluntary sucrose intake

Rats were food and water deprived for 24 h prior to each test day (Days 1 and 4). Either 2 h (LPS, $n=7$) or 10 min (LiCl, $n=7$; NaCl, $n=7$) after injections, a graduated drinking tube containing 0.3-M sucrose solution was made available in the home cage. Fluid intake (± 0.5 ml) was monitored for 1 h after which food and water were made available. On Day 4, the same injection, handling and testing procedures occurred. Body weights were recorded immediately before injections on each test day and 24 h later to note any changes. All testing was carried out between 10:00 and 12:00 h.

2.4. Experiment 2: intraoral intake

2.4.1. Intraoral cannulation

Rats received surgical implantation of intraoral cannulae according to the procedures described by Parker (1980) 1 week after arriving in the laboratory. Following 24 h of food deprivation, animals were anesthetized by an intraperitoneal injection of sodium pentobarbital (Somnotol, 50 mg/kg). A 15-gauge stainless steel needle was inserted into the dorsal midneck region of the rat and guided subcutaneously along the cheek where it exited the oral cavity just rostral to the first maxillary molar. A 10-cm piece of polyethylene tubing (PE 90) was threaded through the barrel of the needle and was secured in place at the neck by a 20-gauge intramedic adapter cap and in the mouth by heat flaring the end of the tubing with a smooth plastic washer (5 mm in diameter) in place. The puncture sites were swabbed with alcohol and animals were given 4 days to recover from surgery before habituation began (see below). Cannulae were flushed with tap water daily to prevent blockage.

2.4.2. Taste reactivity test chambers

At the start of each testing session, rats were placed individually in a testing chamber made of Plexiglas ($29 \times 25 \times 29$ cm). A mirror was mounted beneath the transparent floor of the chamber at a 45° angle, which facilitated videotaping the ventral view of the rat. Intraoral infusions at a rate of 0.78 ml/min were delivered through an infusion hose (PE 90 tubing, 1 m in length) attached to an infusion pump (model 341-A; Sage Instruments, Cambridge, MA) and to the rat's cannula. The behavioral responses produced by the rat during the intraoral infusions were videotaped with a video camera (Panasonic AG-195; London, Ontario, Canada), located 1 m from the mirror, and a videocassette recorder (Panasonic AG-1970).

2.4.3. Habituation

All rats were habituated to the general testing procedure on 3 consecutive days prior to the first test day. During habituation, rats were placed in the test chamber for a 15-min period followed by a 2-min infusion of water.

2.4.4. Intraoral intake procedure

Rats were food and water deprived for 24 h prior to each test day. Test days were separated by 72 h (Days 1 and 4). On each test day, animals received an intraperitoneal injection as described in Experiment 1: LPS, LiCl or NaCl ($n=7$ per group). Two hours after the LPS injection and 10 min after either LiCl or NaCl injection, rats were placed individually in the testing chamber where they received a 15-min continuous intraoral infusion of 0.3-M sucrose. The orofacial and somatic responses produced by the rats were videotaped. The time at which the animal rejected the fluid and the latency of the first episode of rejection were noted. Rejection was defined as three active aversive responses or five passive drips within a 30-s period. The volume of sucrose ingested was calculated by multiplying the amount of time the animal spent ingesting the fluid by the rate of infusion (0.78 ml/min). Body weight was recorded immediately before the first injection on each test day and 24 h later to note any changes. All testing occurred between 10:00 and 12:00 h.

Behavioral responses were scored according to those developed by Grill and Norgren (1978) and later elaborated on by Ossenkopp and Eckel (1995). Active aversive responses included chin rubs (body of rat projected forward while the mouth or chin is in direct contact with the floor or wall of the chamber), gapes (triangular opening of the mouth), forelimb flails and headshakes with fluid expulsion.

The data from each experiment were analyzed with a mixed-design analysis of variance (ANOVA) procedure with Drug as the between-subjects factor (at three levels: LPS, LiCl and NaCl) and Day as the within-subjects factor (at two levels: Day 1 and Day 4). Post hoc analyses of significant main effects and interactions were analyzed using Tukey's HSD test with α=.05 as the criterion for significance.

3. Results

3.1. Experiment 1: voluntary intake

The 24-h change in body weight (rats had been food and water deprived for 24 h prior to testing) for the three experimental groups is depicted in Fig. 1. Statistical analysis revealed significant main effects of Day [$F(1,18)=41.488$, $P<.001$] and Drug [$F(2,18)=91.415$, $P<.001$] as well as a significant Day × Drug interaction [$F(2,18)=7.049$, P=.005]. Animals injected with LPS showed a significantly (P's $<.05$) lower gain in body weight relative to both LiCl-treated and NaCl-treated rats after the first test day. In addition, LiCl-treated rats gained significantly ($P<.05$) more weight than NaCl-treated controls. After the second conditioning day, LiCl treatment resulted in significantly (P's $<.05$) greater gain in body weight relative to LPS and NaCl treatment. NaCl-treated and LPS-treated rats showed similar increases in body weight after the second conditioning day.

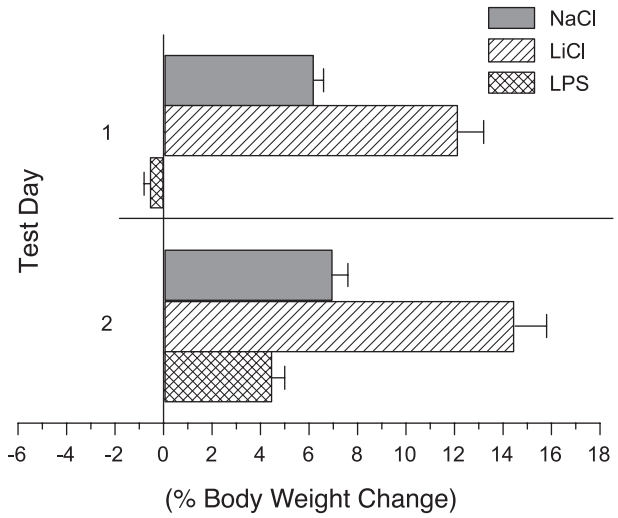

Fig. 1. The 24-h change in body weight following injections of LPS (200 μg/kg, $n=7$), LiCl (0.15 M, 20 ml/kg, $n=7$) or NaCl (1 ml/kg) on each of the two voluntary sucrose intake test days. Test days were separated by 72 h. Animals were food and water deprived 24 h prior to each test day, and after voluntary sucrose intake was monitored for 1 h, food and water were again made available. Values represent means ± S.E.M.

Analysis of the total sucrose intake across the days of testing (see Fig. 2) revealed a significant main effect of Drug [$F(2,18)=10.588$, $P=.001$] and a significant Day × Drug interaction [$F(2,18)=3.935$, $P=.038$]. Animals injected with LPS showed a significantly (P's < .05) reduced level of sucrose intake relative to both NaCl-treated and LiCl-treated animals on the first test day. On the second test day, NaCl-treated controls drank significantly more sucrose than both LPS-treated and LiCl-treated rats (P's < .05). It should be noted that LiCl-treated rats displayed a decrease in sucrose intake relative to the intake observed on the first test day, whereas LPS treatment resulted in increased sucrose intake from the first to the second test day.

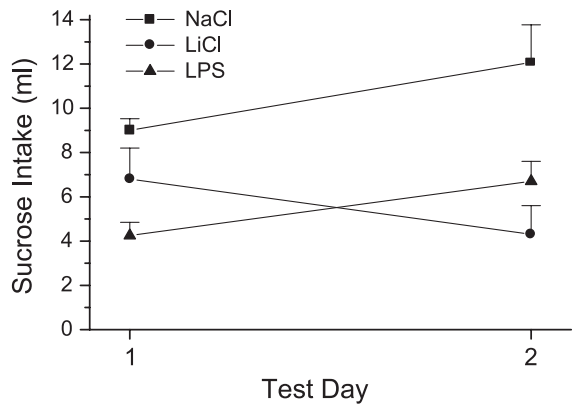

Fig. 2. The daily voluntary sucrose (0.3 M) intake (1 h) from a bottle across 2 test days. Test days were separated by 72 h. Voluntary intake was assessed either 2 h after an LPS (n=7) injection or 10 min after a LiCl (n=7) or NaCl (n=7) injection. Animals were food and water deprived 24 h prior to testing. Values represent means ± S.E.M.

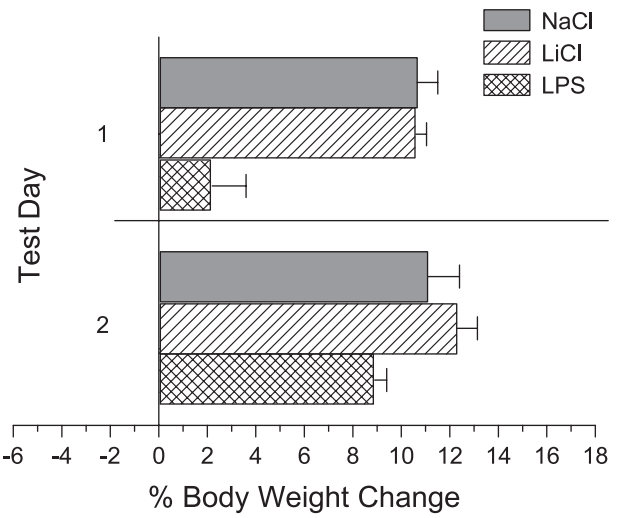

Fig. 3. The 24-h change in body weight following injections of LPS (200 μg/kg, $n=7$), LiCl (0.15 M, 20 ml/kg, $n=7$) or NaCl (1 ml/kg) on each of the two intraoral sucrose intake test days. Test days were separated by 72 h. Animals were food and water deprived 24 h prior to each test day, and after intraoral sucrose intake was assessed, food and water were again made available. Values represent means ± S.E.M.

3.2. Experiment 2: intraoral intake

The percent change in body weight 24 h after injection across the test days (animals were food and water deprived 24 h prior to testing) is depicted in Fig. 3. Analysis revealed significant main effects of Day [$F(1,18)=18.819$, $P<.001$] and Drug [$F(2,18)=53.23$, $P<.001$] as well as a significant Day × Drug interaction [$F(2,18)=8.484$, $P=.003$]. Following the first test day, animals injected with LPS gained significantly (P's < 0.05) less weight than either NaCl-treated or LiCl-treated rats. After the second test day, LPS treatment resulted in significantly ($P<.05$) less weight gain relative to only the LiCl-treated rats.

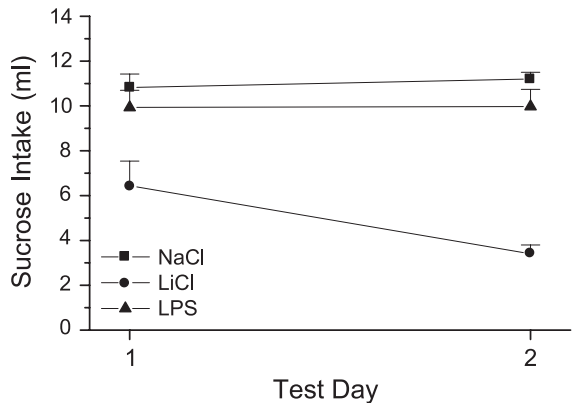

Fig. 4. The volume of sucrose (0.3 M) ingested during the intraoral intake procedure across the 2 test days. Test days were separated by 72 h. Intraoral sucrose intake assessment occurred either 2 h after an LPS ($n=7$) injection or 10 min after a LiCl ($n=7$) or NaCl ($n=7$) injection. Animals were food and water deprived 24 h prior to testing. Sucrose was infused at a rate of 0.78 ml/min. Values represent means ± S.E.M.

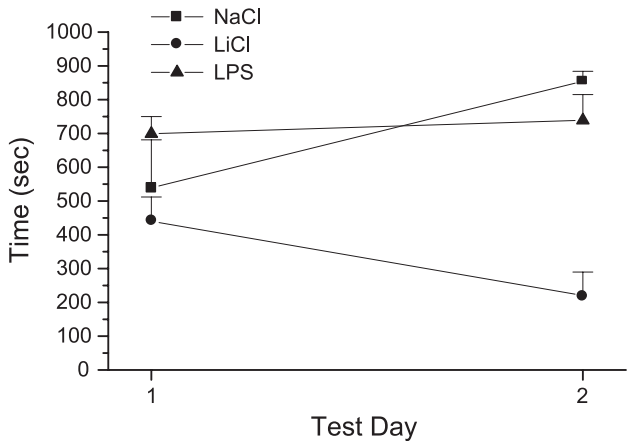

Fig. 5. Mean latency (s) to the first episode of rejection on each of the two intraoral sucrose intake test days. Test days were separated by 72 h. Animals were injected with LPS (2 h prior, $n=7$), LiCl (10 min prior, $n=7$) or NaCl (10 min prior, $n=7$) before intraoral sucrose intake was assessed. Rejection was defined as three active aversive responses or five passive drips within a 30-s period. Values represent means ± S.E.M.

The volume of sucrose ingested during the intraoral infusions across test days for each experimental group is depicted in Fig. 4. Statistical analysis revealed a significant main effect of Drug [$F(2,18)=26.561$, $P<.001$] and a significant Day × Drug interaction [$F(2,18)=3.973$, $P=.037$]. Post hoc comparisons showed that LiCl treatment resulted in significantly (P's <0.05) less sucrose intake relative to both LPS-treated and NaCl-treated rats on both test days (Days 1 and 4). There were no significant differences between LPS and NaCl treatment in the volume of sucrose consumed on either test day.

Analysis of the time of first rejection displayed by each animal across the test days (see Fig. 5) revealed a significant main effect of Drug [$F(2,18)=10.104$, $P=.001$] and a significant Day × Drug interaction [$F(2,18)=9.171$, $P=.002$]. There were no significant differences in the time of first rejection among the groups on the first test day. On the second test day (Day 4), LiCl-treated rats displayed rejection responses significantly (P's $<.05$) sooner than both LPS-treated and NaCl-treated animals.

4. Discussion

The present findings demonstrate that toxin administration (LiCl) results in significant reductions of sucrose intake when voluntarily consumed from a bottle as well as reduced sucrose intake when assessed with an intraoral intake measure. The present study also shows a clear dissociation between the two measures of intake following activation of the immune system. Injections of LPS produced a robust decrease in voluntary intake of the sucrose solution, yet when the same solution was infused directly into the mouth of the rat, these animals did not display any reductions in intake.

In Experiment 1, it was shown that although rats treated with LiCl showed a reduced level of voluntary sucrose intake on the first test day relative to saline-treated controls, this decrease did not reach statistical significance. There was, however, a significant reduction in sucrose intake from the bottle on the second test day. This result is consistent with the notion that systemic application of LiCl has specific conditioning effects that result in decreased intake of food and fluids. Past research has shown that when a novel palatable flavor is paired with the illness caused by administration of LiCl, the animal will avoid that flavor in the future (e.g., Garcia et al., 1974; Nachman and Ashe, 1973). In the present experiment, animals treated with LiCl showed greater decrements in sucrose consumption on the second test day relative to the first day consistent with conditioning effects. In Experiment 2, sucrose intake was assessed using the intraoral infusion procedure and LiCl treatment again resulted in significant decreases in intake relative to saline controls. This result is consistent with past research demonstrating pronounced decreases in positive ingestive responses after LiCl administration (e.g., Breslin et al., 1992; Ossenkopp and Eckel, 1995; Spector et al., 1988). Thus, the similar results from the two intake measures, following treatment with LiCl in the present study, suggest that LiCl affects ingestion by either altering both appetitive and consummatory phases or affecting the consummatory phase alone.

The finding that LiCl-treated animals displayed a greater increase in body weight after the voluntary intake measure than after the intraoral intake assessment is somewhat puzzling. Although LiCl has been shown to reduce intake relative to controls (Curtis et al., 1994; Nachman and Ashe, 1973), it also has been shown that LiCl treatment results in decreased motor activity (Ladowsky and Ossenkopp, 1986), which potentially could contribute to the increase in body weight observed in the present experiment. Furthermore, Baptista et al. (1991) have shown dose-dependent increases in body weight following LiCl treatment in female rats. Taken together, these results suggest that there is much variability with regards to body weight changes following LiCl administration and this variability is most likely dependent on the methodology used during experimentation. However, it is clear that LiCl treatment results in decreased sucrose intake, whether assessed with a voluntary intake measure or with an intraoral infusion procedure.

In contrast, administration of LPS produced selective reductions in intake when assessed with a traditional intake paradigm but not with the intraoral infusion method. That is, LPS-treated rats displayed marked reductions in sucrose intake from a bottle on both test days. The reduction on the first test day was significantly more pronounced than that observed in the LiCl-treated rats. This finding is consistent with past research that has shown robust decreases in food intake (e.g., Langhans et al., 1990, 1991) assessed with traditional intake paradigms. Furthermore, numerous studies have shown that immune system activation induced decreases in intake of palatable substances including sucrose

(Cross-Mellor et al., 1999) as well as sweetened milk (Swiergiel et al., 1997a,b) and saccharin (Yirmiya, 1996). However, the present study showed that when the same sucrose solution that was used in the traditional intake paradigm was continuously infused directly into the oral cavity of rats, LPS treatment did not alter the sucrose intake. Thus, LPS-treated rats consumed the same amount of sucrose as saline controls, which was significantly greater than in the LiCl-treated rats. In addition, LPS treatment did not alter the latency to reject the sucrose solution, whereas LiCl-treated animals showed rejection responses significantly sooner than both NaCl-treated and LPS-treated groups. This study is to the best of our knowledge the first examination of intraoral intake following LPS-induced activation of the immune system. Tolerance has been shown to develop to many of the behavioral effects produced by LPS including decreased locomotion (Engeland et al., 2003) and decreased food intake (Langhans et al., 1991). Although the present data do not support the suggestion that repeated injections of LPS produced tolerance-like effects on either intake measure, further studies that utilize several days of testing would be beneficial to clarify the effects of tolerance on both intraoral and voluntary intake measures.

Other research has provided evidence that suggests that traditional intake measures (e.g., voluntary sucrose intake from a bottle) and intraoral intake measures are independent of one another. For instance, both leptin and NPY have been found to produce decreased and increased sucrose consumption from a bottle, respectively (Ammar et al., 2000). However, when the same sucrose solution is infused intraorally, leptin administration results in increased consumption whereas NPY treatment results in decreased sucrose consumption (Ammar et al., 2000). Various drugs of reward, such as amphetamine, morphine and cocaine, result in decreased intake when assessed using a traditional intake paradigm, but when taste reactivity responses are assessed, these agents do not produce any changes in the pattern of behaviors relative to saline-treated controls (see Parker, 1995 for a review). In addition, Spray et al. (2000) have shown that the pattern of c-*fos* activation within the brain is different when a conditioned taste aversion with LiCl is produced in rats using an intraoral intake method versus that produced by a traditional intake procedure. Moreover, it has been shown that the amygdala plays a crucial role in the establishment of a conditioned taste aversion when the conditioning occurs with intraoral intake infusions of the tastant but not when the same tastant is consumed from a bottle (Schafe et al., 1998). Taken together with the present results from the LPS-treated animals, it seems that voluntary consumption from a bottle and intraoral intake are independent of one another and the neural circuitry underlying the two may be fundamentally different.

The finding that LPS affects sucrose intake only when assessed with a traditional intake procedure provides evidence that immune activation has specific effects on the appetitive component of ingestion. The intraoral intake procedure used in the present study bypasses the appetitive aspects necessary for ingestion by directly infusing the tastant into the mouth of the animal, thus assessing only the consummatory behaviors involved in feeding. Because LPS treatment did not result in any changes in the amount of sucrose consumed relative to saline-treated controls using this procedure, it is unlikely that LPS treatment produced any adverse effects on the consummatory phase of ingestion. By examining operant responses to obtain a food reward, one can obtain a measure of appetitive behavior. Indeed, it has been shown that activation of the immune system with administration of either LPS or IL-1β (Bret-Dibat et al., 1995, 1997; Kent et al., 1992; Larson et al., 2002) produces robust decreases in operant responding for food. Furthermore, it has recently been shown that LPS treatment results in decreased voluntary sucrose (Cross-Mellor et al., 1999) and water intake (Cross-Mellor et al., 2000) relative to controls. However, when palatability was assessed using a detailed taste reactivity analysis, no significant differences between LPS and saline controls were observed. These studies demonstrated that the reduced sucrose and water intake observed in the LPS-treated animals was not a result of alterations in palatability (Cross-Mellor et al., 1999, 2000), suggesting that immune activation selectively affects the appetitive component of ingestion, which is consistent with the present results.

In summary, the present study demonstrated that toxin administration (LiCl) results in reduced sucrose intake when assessed both with a traditional bottle intake and with intraoral infusions, whereas immune activation (LPS) reduces sucrose intake only when assessed with traditional intake measures. Both the current results and the findings from previous research suggest that activation of the immune system produces adverse affects on the appetitive behavioral components of ingestion, which then results in the decreased food consumption observed. Future research should examine the exact manner in which immune activation affects the appetitive aspects involved in feeding and drinking.

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