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Strain-dependent differences in schedule-induced polydipsia: an assessment in Lewis and Fischer rats

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Abstract

Strain-dependent differences have been used to highlight unknown genetic contributions to important behavioral and physiological end points. In this regard, the Fischer (F344) and Lewis (LEW) rat strains have often been studied because they exhibit a myriad of behavioral and physiological differences. Recently, schedule-induced polydipsia (SIP), a potential model of stress and drug abuse, has been reported to differ between the two strains (see [Pharmacol. Biochem. Behav. 67 (2002) 809]) with F344 rats displaying greater levels of consumption than LEW rats. Given the importance of SIP as a behavioral model of stress and of drug abuse, the present study further explored SIP in F344 and LEW strains by assessing the acquisition and steady-state performance of SIP (under a fixed-time 30 schedule of food delivery; FT30), its characteristic postprandial temporal licking pattern and its modulation by variations in the food delivery schedule (FT15, FT30 and FT60). F344 rats acquired SIP at a faster rate and drank at a higher asymptotic level than LEW rats. Both strains displayed the typical inverted U-shaped post-pellet pattern of drinking and changes in levels of consumption (and displacement of the initiation of post-pellet drinking) with changes in the FT value, supporting the position that the increased drinking seen in both groups was schedule induced. These strain differences in SIP are consistent with the fact that the F344 and LEW strains differ on other behavioral and physiological indices of stress and raise the issue of the use of this model in the assessment of differential drug intake between the two strains.

Keywords: Schedule-induced polydipsia; Strain differences; F344; LEW; Stress

1. Introduction

Inbred animal strains are useful tools in the assessment of genetically based physiological and behavioral effects (Ktorza et al., 1997; Morse et al., 1995; Reed et al., 1997). Among these inbred strains are the Fischer (F344) and Lewis (LEW) rats that have been characterized by their differential reactivity to a variety of pro-inflammatory stimuli, including carrageenan (Misiewicz et al., 1996a; Gomez-Serrano et al., 2001), streptococcal cell walls (Sternberg et al., 1989) and endotoxins such as lipopolysaccharide (LPS) (Grota et al., 1997; Gomez-Serrano et al., 2002). In addition to the differences in inflammatory reactivity, the two strains have been reported to differ on a number of biochemical (Beitner-Johnson et al., 1991; Minabe et al., 1995), physiological (Glowa et al., 1992a,b) and behavioral endpoints (Ambrosio et al., 1995; Baumann et al., 2000; Glowa et al., 1994; Gomez-Serrano et al., 2001; Haile and Kosten, 2001; Kosten et al., 1997; Lancellotti et al., 2001; Morgan et al., 1999; Pryce et al., 1999; Stohr et al., 1998; Varty and Geyer, 1998; see Kosten and Ambrosio, 2002 for a recent review).

Recently, the two strains have been reported to differ in schedule-induced polydipsia (SIP) (see Stohr et al., 2000). SIP is a phenomenon whereby animals receiving spaced pellet deliveries drink large volumes of water during the experimental session. Water consumption generally follows an inverted U-shaped function such that drinking begins immediately following pellet delivery, peaks shortly there-

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after and diminishes prior to the delivery of the next pellet (Falk, 1961, 1966a,b, 1971, 1977). Interest in SIP, in general, and with strain differences, more specifically, stems from two issues related to the model. First, the development of SIP appears to be mediated in part by stress (Brett and Levine, 1979, 1981; Cirulli et al., 1994; Dantzer et al., 1988; Levine and Levine, 1989; Tazi et al., 1986, 1988; Wallace et al., 1983; see also Lin et al., 1988). Specifically, intermittent food delivery has been reported to induce arousal and SIP has been considered to be a coping response to the stress produced by the intermittent delivery of food. Interestingly, animals that display SIP under conditions of spaced food delivery have reduced corticosterone levels (relative to animals without access to water during the same spaced food deliveries) (Brett and Levine, 1979, 1981; Dantzer et al., 1988; Tazi et al., 1986; though see Mittleman et al., 1988). Further, manipulations known to decrease corticosterone are reported to block or attenuate SIP (Cirulli et al., 1994; Levine and Levine, 1989; Lin et al., 1988; though see Devenport, 1978; Katovic et al., 1999), whereas manipulations that increase corticosterone levels increase SIP (Levine and Levine, 1989; Lin et al., 1988; Mittleman et al., 1992; though see Cole and Koob, 1994). Interestingly, the LEW and F344 strains have been reported to differ in reactivity to a variety of exogenous stressors (Gomez-Serrano et al., 2001, 2002; Sternberg et al., 1989, 1992) with the F344 strain being hyper-responsive in relation to HPA activity, whereas the LEW strain is hypo-responsive (Dhabhar et al., 1993; Glowa et al., 1992a,b; Griffin and Whitacre, 1991; Misiewicz et al., 1996a,b; Oritz et al., 1995; Simar et al., 1996; Sternberg et al., 1989; Stohr et al., 2000). Given this and the fact that the two strains perform differently on a number of other behavioral tasks thought to be mediated by stress (Glowa et al., 1992a,b; Gomez-Serrano et al., 2001; Varty and Geyer, 1998; Stohr et al., 1998, 2000), they might also be expected to differ in SIP. As such, SIP might be a sensitive behavioral model of differences in stress reactivity between the two strains. Secondly, SIP has been used as an animal model of drug use, in that animals exposed to spaced food delivery during which alcohol is made available drink alcohol to the point of intoxication (McMillan et al., 1976; Meisch, 1975; Meisch and Thompson, 1972; Riley and Wetherington, 1989; see Lau et al., 1992; Tang and Falk, 1987 for similar results with cocaine). Although the F344 and LEW strains have been reported to differ in the relative self-administration of a variety of compounds (see Kosten and Ambrosio, 2002), little has been reported on the differential intake of alcohol (or its subsequent abuse; though see Suzuki et al., 1988). Given that SIP is an animal model useful in inducing alcohol intake in outbred rats, it may be useful as well in assessing the differential sensitivity of the F344 and LEW strains to alcohol.

As noted, Stohr et al. (2000) have recently assessed SIP in F344 and LEW rats. In their assessment, food-deprived F344 and LEW rats were given daily 30-min sessions in which a single 45-mg food pellet was delivered noncontingently once every 60 s for a total of 30 pellet deliveries. Water was freely available under this schedule of spaced pellet delivery. This procedure was repeated daily for 14 days. Under these conditions, female F344 rats drank at greater levels than female LEW rats (no differences were reported between F344 and LEW males). Although SIP appeared to differ between the two strains, there was no independent assessment that the drinking was induced by the schedule. One way to characterize drinking as schedule induced is by its post-pellet temporal distribution. Generally, animals begin drinking immediately after delivery of the pellet, with drinking peaking shortly thereafter and decreasing prior to the delivery of the next pellet. This inverted U-shaped post-pellet pattern of drinking is intrinsic to SIP as well as other schedule-induced behaviors (Falk, 1961; Killeen, 1975; Roper, 1980). A second way to characterize drinking under free-food deliveries as schedule induced is by the changes in drinking (both amount and pattern) with variations in the schedule of food delivery. Under such variations, the levels and temporal characteristics of SIP change. Specifically, as the interpellet interval increases up to several minutes the overall level of consumption increases (with greater interpellet intervals, consumption tends to decrease) and the period of peak post-pellet licking shifts further into the interpellet interval (see Falk, 1961, 1967; Flory, 1971; Killeen, 1975; Roper, 1980; Segal et al., 1965; Wetherington, 1979). In the Stohr et al.'s (2000) report, only consumption is reported, and as such the temporal patterning of drinking is not known. Further, consumption is assessed only under a single schedule condition. Thus, although animals did drink (and differ) under the schedule of food delivery in the Stohr et al.'s (2000) assessment, it is unknown to what extent the consumption of the two strains reflects differences in SIP. To that end, the present experiment assessed the acquisition and steady-state performance of SIP in the F344 and LEW strains. Specifically, all subjects were given noncontingent food delivery with free access to water until asymptotic levels of fluid intake were reached. The temporal distribution of licking, number of food pellets consumed and the percentage of pellets followed by a lick were recorded to characterize the drinking as schedule induced and to determine the basis for any differences that might be evident. Finally, the schedule of food delivery was varied to determine if the levels and patterns of licking displayed were affected by variations in the schedule as generally reported.

2. Methods

2.1. Subjects

The subjects were six experimentally naive female inbred LEW rats (beginning mean weight = 175 g) and six experimentally naïve female inbred F344 rats (beginning mean

weight = 142 g). Each animal was approximately 70 days of age at the start of the experiment. Animals were housed individually in wire-mesh cages and were maintained on a 12-h light/12-h dark cycle and at an ambient temperature of 23 °C, with ad-libitum access to water in the home cages.

2.2. Apparatus

SIP training occurred in six identical chambers (27.7 × 19.8 × 20.0 cm). These chambers were constructed of 0.6-cm clear Plexiglas and a grid floor of 0.4-cm diameter stainless steel rods spaced approximately 2 cm apart. A 1 × 1-cm food hopper was centered on the front wall 2 cm above the grid floor. A graduated Nalgene drinking tube located outside the front wall of the chamber was affixed such that the metal drinking spout was flush with the outer wall 2.5 cm above the grid floor and 7 cm from the side of the hopper. Licking was detected by a drinkometer (Lafayette Model 58008). A continuously illuminated 28-V houselight was centered on the front wall of each chamber 13.5 cm above the grid floor. All schedule events were programmed on a desktop IBM Aptiva (Microsoft Windows 95) and interfaced to the boxes via a Med Associates Interfacer Logic 1 that also recorded all lick responses.

2.3. Procedure

2.3.1. Food adaptation

All subjects were deprived to 85% of their free feeding weight and given ad-libitum access to water in their home cages. Once training began, food was given post session once daily to maintain the animals at 85% body weight. Animals were handled and weighed daily.

2.3.2. Phase I: acquisition

On Days 1–25, each animal was weighed and placed in an experimental chamber at approximately the same time each day for a 30-min experimental session. During these daily sessions, standard formula 45-mg Noyes food pellets were delivered once every 30 s independent of the animal's behavior on an FT30 schedule for a total of 60 pellets per day. Licks were recorded throughout the session in 5-s intervals (for the subsequent analysis of the post-pellet temporal distribution of licking). Water intake was recorded at the termination of each session, and the number of food pellets remaining in the hopper was noted.

2.3.3. Phase II: variations in food delivery schedule

In this phase, animals were treated as above except that the schedule by which food was delivered varied. Specifically, on Days 26–36, 60 45-mg Noyes food pellets were delivered once every 15 s on an FT15 schedule. On Days 37–46, 60 45-mg Noyes food pellets were delivered once every 60 s on an FT60 schedule. Finally, on Days 47–55, 60 45-mg Noyes food pellets were delivered once every 30 s on an FT30 schedule. Total session time was 15, 30 and 60 min for the FT15, FT30 and FT60 schedules, respectively. As in Phase I, the temporal distribution of licks, as well as pellet and water consumption, were recorded.

2.4. Statistical analysis

2.4.1. Phase I: acquisition

Differences in the amount of water consumed during each trial, the number of pellets consumed and the percent of pellets after which at least one lick occurred were analyzed for the two strains using a 2 × 25 repeated measures analysis of variance (ANOVA) with the between-subjects variable of strain (F344 and LEW) and the within-subjects variable of day (1–25). The repeated measures ANOVAs were followed by one-way ANOVAs for each trial and pair-wise comparisons, using Fisher's PLSD post-hoc tests. Differences between strains in the temporal distribution of licking were analyzed using a 2 × 6 repeated measures ANOVA with the between-subjects variable of strain (F344 and LEW) and the within-subjects variable of time interval (1–5, 6–10, 11–15, 16–20, 21–25 and 26–30 s post-pellet). All determinations of statistical significance were made at $P < .05$.

2.4.2. Phase II: variations in food delivery schedule

Differences in the amount of water consumed during each trial, the number of pellets consumed and the percent of pellets after which at least one lick occurred were analyzed for the two strains using a 2 × 3 repeated measures ANOVA. The between-subjects variable was strain (F344 and LEW) and the within-subjects variable was schedule (FT15, FT30 and FT60). As above, the repeated measures ANOVAs were followed by one-way ANOVAs for each trial and pair-wise comparisons using Fisher's PLSD post-hoc tests. Differences between strains in the temporal distribution of licking for each FT value were analyzed using a 2 × 5 (FT15) and 2 × 6 (FT30 and FT60) repeated

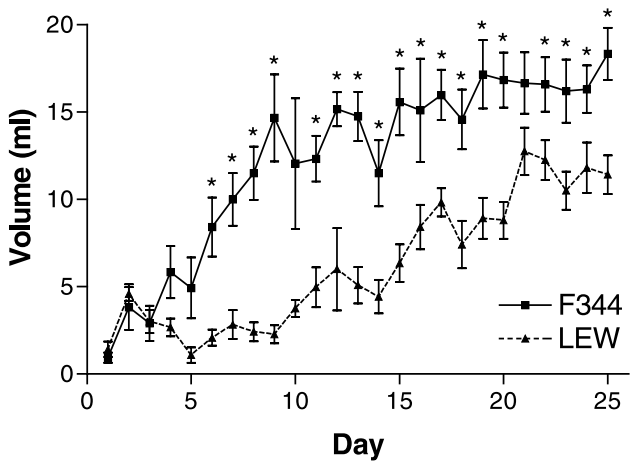

Fig. 1. Mean (± S.E.M.) amount of water consumed (ml) by F344 and LEW strains over the 25 days of exposure to a FT60 schedule of pellet delivery (acquisition). * Significant difference between strains.

measures ANOVA with the between-subjects variable of strain (F344 and LEW) and the within-subjects variable of time interval.

3. Results

3.1. Phase I: acquisition

Fig. 1 illustrates water consumption for F344 and LEW rats on each of the 25 sessions during the acquisition of SIP. There was a significant effect of Strain [$F(1,10) = 15.706$, $P = .0027$] and Day [$F(24,240) = 35.067$, $P < .0001$] as well as a significant Strain × Day interaction [$F(24,240) = 5.394$, $P < .0001$]. In relation to the Strain effect, F344 rats consumed significantly more water than LEW rats. The Day effect reflects the acquisition of SIP, during which rats of both strains consumed little at the outset of training, but high levels as training progressed. The Strain × Day interaction is consistent with a differential acquisition of SIP for the two strains. On Days 6–9, 11–20 and 22–25, F344 rats consumed significantly more water than LEW rats ($P < .05$).

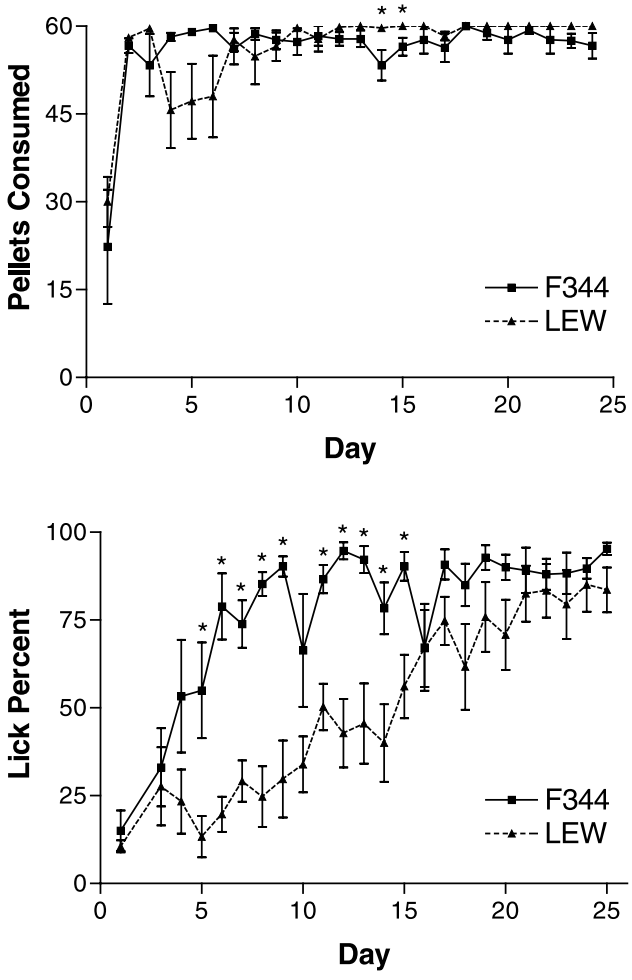

Fig. 2. Top panel: mean (±S.E.M.) number of pellets consumed (out of 60) by F344 and LEW strains over the 25 days of exposure to a FT60 schedule of pellet delivery (acquisition). Bottom panel: mean (±S.E.M.) percent of pellets followed by at least a single lick (lick percent) by F344 and LEW strains over the 25 days of exposure to a FT60 schedule of pellet delivery (acquisition). * Significant difference between strains.

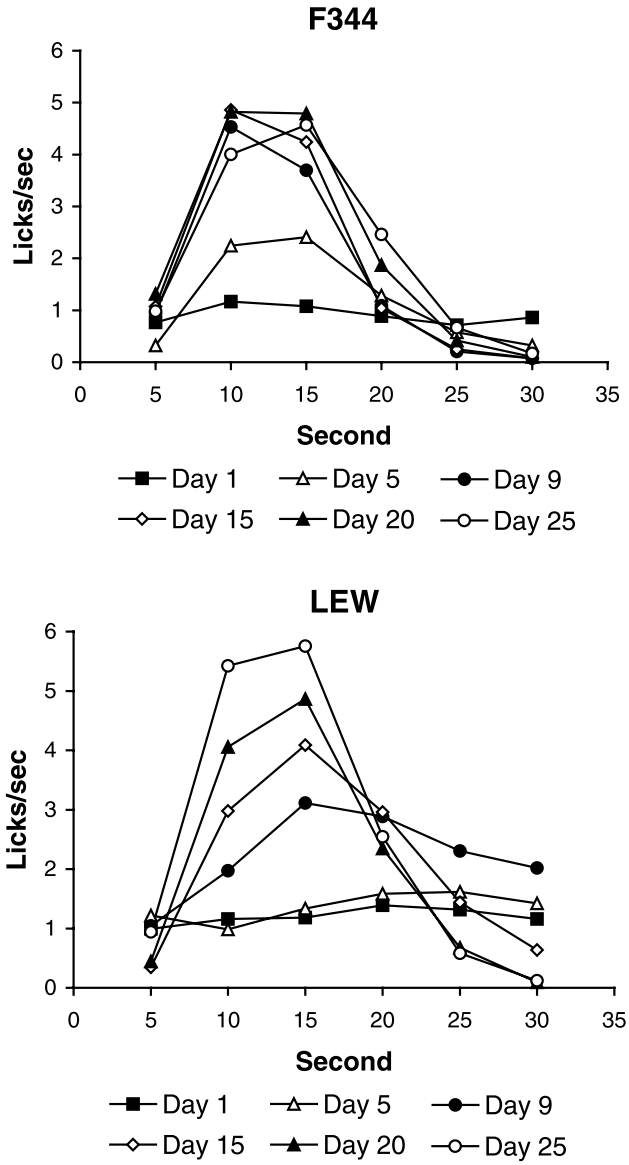

Fig. 3. Post-pellet distribution of licking under the FT60 schedule of pellet delivery for F344 and LEW strains on Days 1, 5, 9, 15, 20 and 25. For each 5-s bin, the number of licks was averaged across the 60 pellets.

The top panel of Fig. 2 illustrates the total number of pellets consumed by the F344 and LEW rats during each of the 25 training sessions. There was no significant effect of Strain [$F(1,10) = 0.072$, $P = .7938$], but there was a significant effect of Day [$F(23,230) = 11.869$, $P < .0001$]. Specifically, rats consumed few pellets during the initial three days, but consumed most (if not all) pellets as training progressed (Days 4–25). There was a significant Strain × Day interaction [$F(23,230) = 1.832$, $P = .0138$] with LEW rats eating significantly more pellets than F344 rats on Days 14 and 15 (P's $< .05$).

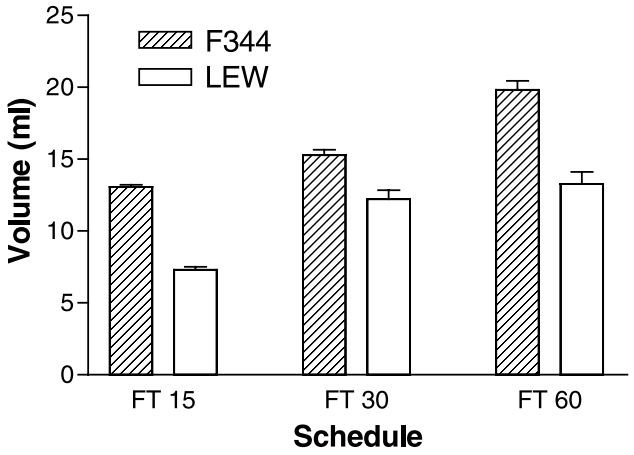

Fig. 4. Mean (±S.E.M.) amount of water consumed (ml) by F344 and LEW strains over the last 4 days of each schedule of food delivery (i.e., FT15, FT30 and FT60).

The bottom panel of Fig. 2 illustrates the percent of pellets after which at least one lick occurred. There was a significant effect of strain [$F(1,10)=10.365$, $P=.0092$] and Day [$F(23,230)=25.752$, $P<.0001$] and a significant Strain × Day interaction [$F(23,230)=5.839$, $P<.0001$]. Overall, the F344 rats displayed a greater likelihood of initiating a post-pellet lick than did the LEW rats. For both strains, the percent of pellets after which a lick occurred increased over repeated experimental sessions, reflecting the acquisition of SIP. The significant Stain × Day interaction is consistent with the position that the F344 rats acquired SIP at a faster rate than the LEW rats (see Days 5–9 and 11–15; Fisher's PLSD, all P's $<.05$).

Fig. 3 illustrates the temporal distribution of licking by F344 (top panel) and LEW (bottom panel) rats on Days 1, 5, 9 (data for Day 10 were not collected due to a computer problem), 15, 20 and 25. Each point represents the mean number of licks for each successive 5-s period within the interpellet interval (averaged over the 60 pellets for each session). On Day 1, there was no significant effect of Strain [$F(1,10)=0.681$, $P=.4284$] or Time Interval [$F(5,50)=0.488$, $P=.7839$] and there was no significant Strain × Time Interval interaction [$F(5,50)=0.568$, $P=.7238$]. Licking was minimal for both strains at every post-pellet interval. On Day 5, there was no significant effect of Strain [$F(1,10)=0.112$, $P=.7445$], but there was a significant effect of Time Interval [$F(5,50)=4.406$, $P=.0021$]. There was also a significant Strain × Time Interval interaction [$F(5,50)=6.732$, $P<.0001$], suggesting that the temporal distribution of licking was being differentially acquired by the two strains; the F344 strain displayed an inverted U-shaped pattern and the LEW strain drank at a low but constant level over the inter-pellet interval. On Day 9, there was no significant Strain effect [$F(1,10)=2.844$, $P=.1226$]. There was a significant effect of Time Interval [$F(5,50)=23.099$, $P<.0001$] and a significant Strain × Time Interval interaction [$F(5,50)=29.474$, $P<.0001$]. F344 subjects licked significantly more than the LEW subjects during the 6–10-s post-pellet period ($P<.0001$), while LEW rats licked significantly more than F344 rats during the 16–20- ($P<.0001$), 21–25- ($P=.0009$) and 26–30-s ($P=.0011$) post-pellet periods. On Day 15, there was again no significant Strain effect [$F(1,10)=0.00024$, $P=.9879$], but there was a significant effect of Time Interval [$F(5,50)=35.491$, $P<.0001$] and a significant Strain × Time Interval interaction [$F(5,50)=4.351$, $P=.0023$]. F344 rats licked significantly more than LEW rats during the 1–5- ($P=.0249$) and 6–10-s ($p=0.0279$) post-pellet periods. By Day 20 (and again on Day 25), there was an overall significant effect of Time Interval [$F(5,50)=44.846$ and 74.679, respectively, both P's $<.0001$] but not of Strain [$F(1,10)=0.078$ and 0.502, respectively, both P's $>.495$] and there was no significant

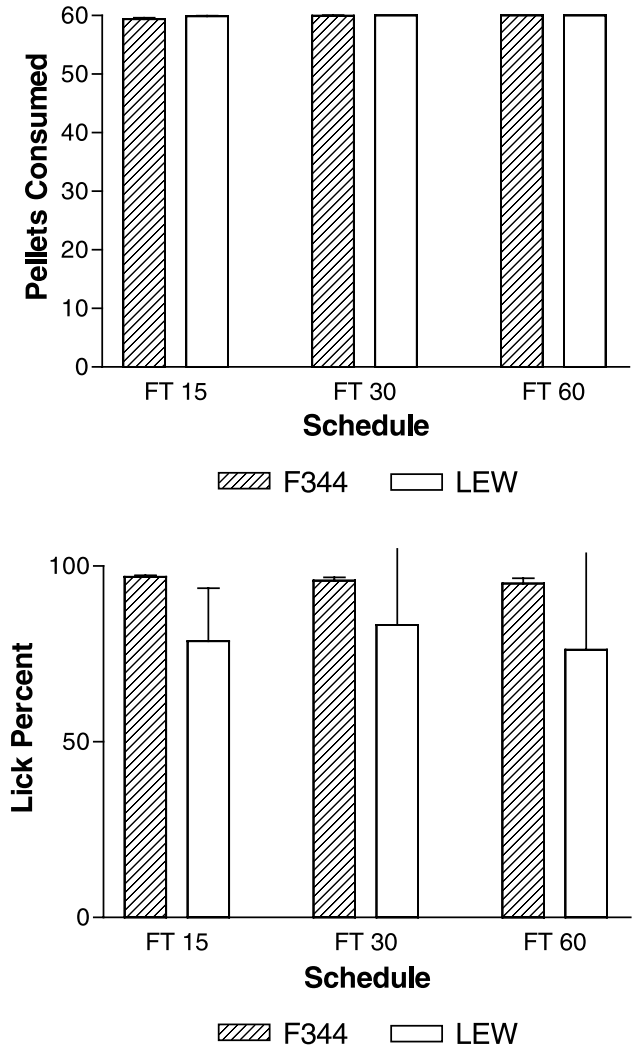

Fig. 5. Top panel: mean (±S.E.M.) number of pellets consumed (out of 60) by F344 and LEW strains over the last 4 days of each schedule of food delivery (i.e., FT15, FT30 and FT60). Bottom panel: mean (±S.E.M.) percent of pellets followed by at least a single lick (lick percent) by F344 and LEW strains over the last 4 days of each schedule of food delivery (i.e., FT15, FT30 and FT60).

Strain × Time Interval interaction [$F(5,50) = 0.822$ and 1.214, respectively, both P's>.316].

3.2. Phase II: variations in food delivery schedule

Fig. 4 illustrates the mean water consumption for each strain averaged over the last four days of each schedule of food delivery. There was an overall Strain effect [$F(1,10) = 8.317$, $P < .0163$] with F344 rats consuming significantly greater amounts than LEW rats and an overall effect of schedule [$F(2,20) = 27.99$, $P < .0001$] with greater amounts consumed as the Schedule value increased. There was no significant Strain × Schedule interaction [$F(2,20) = 2.401$, $P < .1163$].

The top panel of Fig. 5 illustrates the total number of pellets consumed by the F344 and LEW rats averaged over the last four days of each schedule of food delivery. There was no significant effect of Strain [$F(1,10) = 0.088$, P=.7727] or Schedule [$F(2,20) = 1.823$, P=.1875] (nor a significant Strain × Schedule interaction [$F(2,20) = 0.037$, P=.9636]). All animals consistently consumed all 60 pellets delivered during each experimental session and under each of the three schedules. There was also no significant effect of Strain [$F(1,10) = 3.979$, $P < .0740$] or Schedule [$F(2,20) = 0.652$, P=.5317] or a significant Strain × Sched-Schedule interaction [$F(2,20) = 0.481$, P=.6252] in the percentage of pellets after which a lick occurred (see bottom panel of Fig. 5).

Fig. 6 illustrates the temporal distribution of licks for both F344 and LEW rats for each of the three schedule conditions. Under the FT15 schedule (top panel), there was no significant effect of Strain [$F(1,10) = 0.445$, P=.5199]. However, there was a significant effect of Time Interval [$F(4,40) = 63.725$, $P < .0001$] and a significant Strain × Time Interval interaction [$F(4,40) = 2.675$, P=.0456]. F344 rats licked significantly more during the 3–6-s interval (P=.0382), and LEW rats licked significantly more during the 12–15-s interval (P=.0106). Similarly, there was no significant effect of Strain [$F(1,10) = 0.086$, P=.7758] under the FT30 schedule (middle panel), although there was a significant effect of Time Interval [$F(5,50) = 31.042$, $P < .0001$] and a significant Strain × Interval interaction [$F(5,50) = 5.517$, P=.0004]. LEW rats licked significantly more during the 6–10-s interval (P=.0037), and F344 rats licked significantly more during the 21–25-s interval (P=.0191). Under the FT60 schedule (bottom panel), there was a significant Time Interval effect [$F(5,40) = 30.656$, $P < .0001$], but no significant Strain effect [$F(1,8) = 0.045$, P=.8366] nor Strain × Time Interval interaction [$F(5,40) = 1.777$, P=.1398].

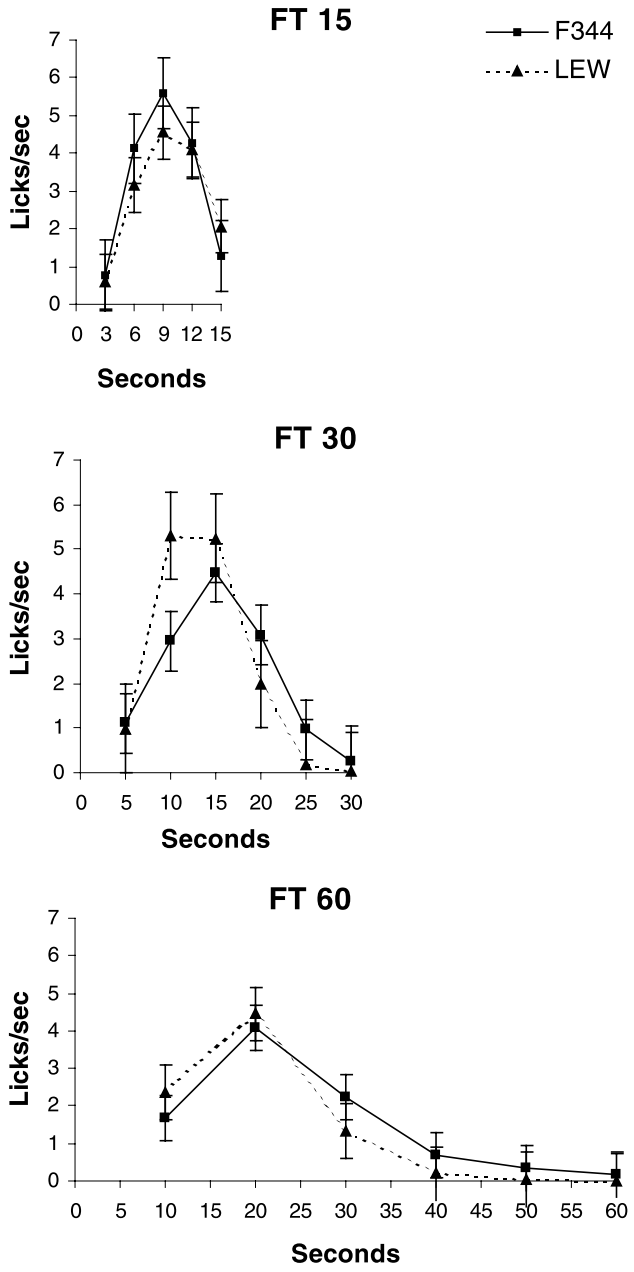

Fig. 6. Post-pellet distribution of licking for F344 and LEW strains during the FT15 (top panel), FT30 (middle panel) and FT60 (bottom panel) schedules of food delivery. For each 5-s bin, the number of licks was averaged across the 60 pellets over the last 4 days of each schedule of food delivery.

4. Discussion

In addition to the myriad of behavioral and physiological endpoints on which the F344 and LEW strains have been reported to differ, F344 female rats have recently been reported to display higher levels of SIP than LEW females (see Stohr et al., 2000). SIP is important as a behavioral preparation in that it appears to be mediated in part by stress and it has been described as an animal model of drug self-administration (see above). Given that the F344 and LEW strains have been reported to differ in stress reactivity and in drug self-administration (see above), this preparation may be a useful model for assessing the effects of stress and the vulnerability to drug use and abuse in the two strains.

Although Stohr et al. (2000) reported differences in SIP between the two strains, as noted above there was no independent assessment that the consumption was induced by the schedule of food delivery. Accordingly, the present experiment examined the acquisition and steady-state performance of drinking under a schedule of spaced food delivery and attempted to characterize this drinking as schedule induced by assessing its temporal distribution (Phase I) and its modification by variations in the interpellet interval (Phase II).

As described, both F344 and LEW rats acquired SIP, drinking levels of water generally reported under similar schedules of spaced food delivery. Further, the inverted U-shaped pattern of post-pellet drinking within each session was characteristic of SIP, suggesting that the drinking was, in fact, schedule-induced (Falk, 1961, 1966a,b). This position is strengthened by the fact that the overall levels of consumption varied with the value of the FT schedule for both strains. At low FT values (similar to those assessed in the present experiment), consumption tends to increase as the FT value increases (with even further increases in the FT value, consumption has been reported to decrease). Although the present study did not assess SIP under these latter schedule values, the fact that consumption increased as the FT value increased from 15 to 60 is consistent with previous reports in outbred rats displaying SIP (Falk, 1961; Flory, 1971; Roper, 1980; Segal et al., 1965; Wetherington, 1979). Further, under all three FT schedules, both strains continued to display the typical inverted U-shaped distribution of licking with the period of peak post-pellet licking displaced further into the interpellet interval as the FT value increased (see Falk, 1967; Killeen, 1975; Segal et al., 1965).

Although both strains displayed SIP, the rate at which SIP was acquired and the steady-state level of consumption differed significantly for the two strains. Specifically, the F344 strain developed schedule-induced drinking at a significantly faster rate than the LEW strain and reached an overall higher asymptotic level. The development of the typical post-pellet drinking pattern was also consistent with a more rapid acquisition by the F344 strain. As described, the F344 strain displayed an inverted U-shaped pattern on Day 5, whereas the LEW rats licked at a low and consistent rate across the interpellet interval on this day. On Day 9, the post-pellet pattern of licking for the F344 rats was stable and characteristic of SIP. This pattern of licking developed more slowly for the LEW strain and did not mimic the pattern of the F344 rats until Day 20. The overall differences in consumption were maintained under the schedule variations in Phase II, although the temporal distribution of licking did not consistently differ between the two strains as the FT schedule was varied (compare FT15 and FT30).

The differences in the rates of acquisition and the asymptotic levels of consumption were not a function of the differential intake of pellets, a factor that has been reported to affect SIP (see Geter et al., 1991). Subjects from both strains readily consumed all pellets and did not differ consistently in pellet consumption. Differences in the overall amount of water consumed appear instead to reflect a difference in the initiation and/or degree of post-pellet consumption. As described, during acquisition the LEW strain had a significantly reduced probability of licking following pellet delivery compared to the F344 strain. Interestingly, when licking did occur it was less efficient, e.g., over the last four days of acquisition, the mean volume (ml) consumed per lick was 0.0037 and 0.0047 for the LEW and F344 strains, respectively. Although these differences in lick efficiency were maintained under the various FT schedules, there was no longer a significant difference in the initiation of licking (percent of pellets followed by a lick), suggesting that any differences in amount consumed between the two strains at this point were not a function of the probability of licking following pellet delivery.

As described above, interest in SIP in the F344 and LEW rat strains stems from several issues. First, SIP has been described as being mediated in part by stress. Accordingly, this baseline might provide a behavioral assessment of differences in stress reactivity between the two strains. Secondly, outbred rats have been reported to self-administer a variety of drugs under schedules that generate SIP. Accordingly, the baseline may provide a model by which differences in drug intake between the F344 and LEW strains can be measured. The present results (along with those of Stohr et al. 2000) demonstrate that F344 and LEW rat strains develop SIP (and do so differently). Although the present results are consistent with the reported mediation of SIP by stress, further work is needed to assess the role of stress in the reported strain differences (e.g., by correlating and/or manipulating corticosterone levels for the two strains during the development and maintenance of SIP). Also, although spaced feeding clearly induces fluid consumption in the two strains, it remains to be demonstrated to what extent drug intake can be induced by spaced food delivery in F344 and LEW rats and if the patterns of drug intake generated under schedule induction parallel those reported under more traditional assays of drug self-administration.

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