Available online at www.sciencedirect.com
SCIENCE DIRECT
Pharmacology, Biochemistry and Behavior 79 (2004) 303–308
PHARMACOLOGY BIOCHEMISTRY AND BEHAVIOR
www.elsevier.com/locate/pharmbiochembeh

Lithium-chloride-induced conditioned taste aversions in the Lewis and Fischer 344 rat strains

Melissa M. Foynes, Anthony L. Riley*

Psychopharmacology Laboratory, Department of Psychology, American University, 4400 Massachusetts Avenue, NW, Washington, DC 20016, United States

Received 24 June 2004; accepted 2 August 2004
Available online 1 September 2004

Abstract

Conditioned taste aversions (CTAs) are differentially induced by cocaine and morphine in the Lewis and Fisher 344 (LEW and F344, respectively) rat strains. Although the acquisition of LiCl-induced aversions has recently been reported to be comparable between the two strains, these aversions were induced by the oral consumption of LiCl, and the possibility exists that, given their different weights, that differential doses were functionally administered. To address the issue of LiCl-induced aversions in LEW and F344 rats (and to control for this possible confound), the present study assessed the ability of intraperitoneally (ip) administered LiCl to induce aversions in the two strains. Specifically, rats from both strains were given 20-min access to saccharin and injected immediately, thereafter, with 0.3, 0.6, 0.9 or 1.2 mEq/kg, 0.15 M LiCl (or its distilled water vehicle). Under these conditions, both strains acquired dose-dependent aversions that increased over repeated trials. Although there was no overall strain difference in LiCl-induced aversions, LEW rats displayed a stronger aversion at the 0.3 mEq/kg dose (on Trial 3) and acquired the aversion at this dose more rapidly than the F344 rats did (by Trial 2 vs. Trial 3). Although evident, this strain difference with LiCl does not parallel that reported with morphine (in which F344 rats are more sensitive than LEW rats) or with cocaine (in which the differences between LEW and F344 rats are larger and occur at more doses and on more trials). These cross-drug comparisons suggest that strain differences in aversion learning are drug dependent. Because drug acceptability has been reported to be a function of the balance between the reinforcing and aversive effects of various compounds, the examination of possible strain differences in aversion learning with a range of such compounds may provide insight into drug acceptability (and use) in these strains.

Keywords: LiCl; Strain differences; Lewis; Fischer 344; Conditioned taste aversion

1. Introduction

The Lewis (LEW) and Fischer 344 (F344) inbred rat strains differ on a myriad behavioral and physiological endpoints (DeCarolis et al., 2003; Gomez-Serrano et al., 2001, 2002; Sternberg et al., 1989, 1992; Stohr et al., 1998b, 2000; for a review, see Kosten and Ambrosio, 2002). One specific area in which they have been reported to differ is in their response to a variety of recreational drugs. Of particular interest in this regard is their affective reactivity to drugs of abuse, in which LEW rats exhibit greater sensitivity to the rewarding properties of drugs compared with F344 rats (Ambrosio et al., 1995; Brower et al., 2002; Horan et al., 1997; Kosten et al., 1994, 1997; Martin et al., 1999; Suzuki et al., 1988a,b, 1992; although see Stohr et al., 1998a).

These strain differences are not limited to the rewarding effects of drugs. Specifically, the examination of their aversive properties has also demonstrated strain differences. For example, Glowa et al. (1994) found that although LEW and F344 rats acquired similar cocaine-induced aversions at a dose of 50 mg/kg, LEW rats acquired greater conditioned taste aversions (CTAs) at 18 and 32 mg/kg (Grigson and Freet, 2000; although see Kosten et al., 1994). Conversely, Lancellotti et al. (2001) found that F344 rats acquired a

* Corresponding author. Fax: +1 202 885 1081.
E-mail address: alriley@american.edu (A.L. Riley).

0091-3057/$ - see front matter © 2004 Elsevier Inc. All rights reserved.
doi:10.1016/j.pbb.2004.08.002

morphine-induced CTA at 10, 32 and 56 mg/kg, whereas LEW rats did not acquire CTAs at any of these doses. Although LEW and F344 rats differ in morphine- and cocaine-induced CTAs, it is unknown to what extent (if any) these strain differences generalize to other drugs of abuse or even to drugs, in general.

The only other drug for which aversions have been compared between the two strains is the emetic LiCl (Grigson and Freet, 2000). In that report, LEW and F344 rats were initially allowed 5-min access to a 0.15% saccharin solution and then injected intraperitoneally (ip) with either 0.15 M NaCl or 0.009 M LiCl. Because all LiCl-injected subjects decreased saccharin consumption after the first pairing, the procedure was modified such that LiCl was administered *orally* rather than injected intraperitoneally. Specifically, subjects that were previously injected with LiCl were given a saline solution, and subjects that were originally injected with NaCl were given a solution of LiCl. Subjects were given 5-min access to these solutions on six different trials, with LiCl-treated subjects receiving 0.009 M LiCl during the first three trials and 0.15 M LiCl during the last three trials. Although both LEW and F344 rats failed to demonstrate an LiCl-induced CTA at the lower dose of 0.009 M, both strains demonstrated strong LiCl-induced CTAs following the consumption of the 0.15 M LiCl solution, with no evidence of any significant differences between the two strains. From these data, Grigson and Freet (2000) concluded that LEW and F344 rats acquired LiCl-induced CTAs of equal magnitude and that there were no significant strain differences.

Although suggestive of no strain differences, several procedural issues may limit this conclusion. For example, the subjects were given a fluid-access period of only 5 min and all subjects consumed comparable amounts of the LiCl solution during this period. At the start of the experiment, however, the subjects differed significantly in body weight (LEW rats weighed approximately 312–384 g and F344 rats weighed approximately 241–271 g). Given their equivalent consumption of LiCl, despite differences in body weights that ranged anywhere from 41–143 g, subjects may have been exposed to differential doses of LiCl (mg/kg). If, in fact, subjects did receive differential doses of LiCl, yet no significant strain differences were found, these data may reflect differential acquisition of LiCl-induced CTAs.

To assess the generality of the reported differences in taste aversion learning between the LEW and F344 rat strains and to circumvent any potential problems associated with the oral administration of LiCl, the present study examined the ability of the two strains to acquire aversions to a novel saccharin solution paired with intraperitoneally administered LiCl. Specifically, different groups of rats from the LEW and F344 rat strains were allowed 20-min access to saccharin, followed by an intraperitoneal (ip) injection of either saline or one of four doses of LiCl (0.3, 0.6, 0.9 and 1.2 mEq/kg, 0.15 M). Following four such conditioning trials, all subjects were given a final test of their aversion to saccharin.

2. General method

2.1. Subjects

Subjects were 39 Lewis (LEW/SsNHsd) and 40 Fischer (F344/NHsd) experimentally naive female rats (purchased from Harlan Sprague Dawley, Indianapolis, IN). At the start of the experiment, LEW rats weighed approximately 176–220 g and F344 rats weighed approximately 147–196 g. The subjects were maintained on a 12L:12D cycle (lights on at 0800 h) and at an ambient temperature of 23 °C for the duration of the experiment. Each rat was given ad libitum food and water prior to habituation. Procedures recommended by the Guide for the Care and Use of Laboratory Animals (1996), the Guidelines for the Care and Use of Mammals in Neuroscience and Behavioral Research (2003) and the Institutional Animal Care and Use Committee at American University were followed at all times.

2.2. Apparatus

Subjects were individually housed in stainless steel, wire-mesh cages. Graduated Nalgene 50-ml centrifuge tubes were attached to the front of the cages to provide 20-min access to water or saccharin.

2.3. Procedure

2.3.1. Phase I: Habituation

Following $23^{2/3}$-h water deprivation, all subjects were given 20-min access to water. Subjects were divided into three groups such that LEW and F344 rats were evenly distributed among each group. The fluid-access period was administered to each group separately. This procedure was repeated daily until water consumption stabilized for both strains. At this point, subjects within each strain did not vary in the amount consumed by more than 1–2 ml over three consecutive days. Furthermore, body weights were increasing and at or above 90% of free feeding immediately prior to the initiation of conditioning (see below).

2.3.2. Phase II: Conditioning

On Day 1 of this phase, all subjects in Group 1 (n=24) were given 20-min access to a novel saccharin solution during the fluid-access period, while animals in Groups 2 (n=24) and 3 (n=31) were given 20-min access to water.

Immediately following saccharin access, the subjects in Group 1 were ranked according to saccharin consumption and then placed into one of five groups such that saccharin consumption was comparable among the five groups. Rankings were conducted separately for each strain. Five min following the removal of saccharin, each subject was given an ip injection of 0.3, 0.6, 0.9 or 1.2 mEq/kg, 0.15 M LiCl or 0.9% saline solution (equivolume to the highest dose of LiCl). After the injection, each animal was returned

to its home cage, and no further manipulations followed. For the next 3 days, subjects in Group 1 were given 20-min access to water. One conditioning day and three water-recovery days comprised one full conditioning cycle, and this sequence was repeated until four full conditioning cycles had been completed. All subjects were given 20-min access to saccharin the day following the final water-recovery day. No injections were administered following this session. Subjects in Groups 2 and 3 followed the same procedure as did the subjects in Group 1, but were first conditioned on different days of the experiment (Days 2 and 3, respectively).

2.4. Data analysis

Strain differences in saccharin consumption were analyzed using a 2×5×5 repeated-measures analysis of variance (ANOVA), with between-subjects variables of Strain (LEW and F344) and Dose (0, 0.3, 0.6., 0.9 and 1.2 mEq/kg, 0.15 M LiCl) and within-subjects variable of Trial (Days 1–5). The repeated-measures ANOVA was followed by separate 2×5 ANOVAs for each trial. Following these ANOVAs, independent samples *t*-tests were used to compare decreases in saccharin consumption between each of the four groups receiving doses of LiCl and their respective control groups across trials. Paired samples *t*-tests were then used to assess decreases in saccharin consumption on each trial compared with each group's own baseline. Alpha was set at .05. All statistical analyses were conducted using the Statistical Package for the Social Sciences, Version 10.0 (SPSS, 1999).

3. Results

The 2×5×5 repeated-measures ANOVA revealed significant main effects of Trial [$F(4,276)=379.12$, $p<.001$] and Dose [$F(4,69)=132.972$, $p<.001$] and significant Trial×Strain [$F(4,276)=3.100$, $p<.05$], Trial×Dose [$F(16,276)=40.051$, $p<.001$] and Trial×Strain×Dose

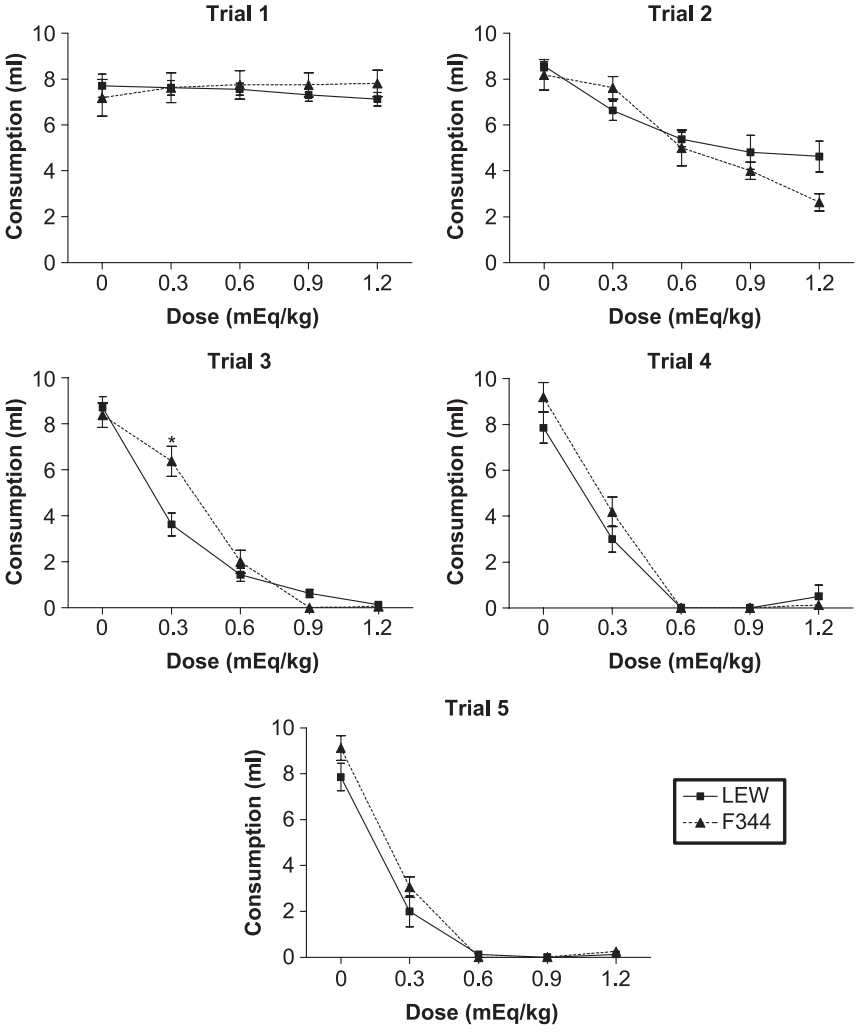

Fig. 1. Mean (±S.E.M.) saccharin consumption of LEW and F344 rats on each of four conditioning trials and on the final aversion test. During conditioning, subjects received access to saccharin, followed by an injection of saline or 0.3, 0.6, 0.9 and 1.2 mEq/kg, 0.15 M LiCl. *$p<.05$.

[$F(16,276)=2.112$, $p<.01$] interactions. There was no significant main effect of Strain [$F(1,69)=3.902$, $p=.308$] and no significant Strain×Dose interaction [$F(4,69)=1.975$, $p=.108$].

Given the significant Trial×Strain×Dose interaction, individual ANOVAs were conducted for each trial to determine where the significant differences occurred (see Fig. 1). On the initial and second conditioning trials, there was no main effect of Strain [Fs(1,69)<2.207, $p<.633$] and no significant Strain×Dose interaction [Fs(4,69)<1.957, ps<.816]. On Trial 3, although there was no main effect of Strain [$F(1,69)=3.355$, $p=.071$], there was a significant Strain×Dose interaction [$F(4,69)=5.945$, $p<.001$] at 0.3 mEq/kg, with LEW rats consuming significantly less saccharin than F344 rats did. On Trial 4, there was neither a significant effect of Strain [$F(1,69)=2.559$, $p=.1143$] nor a significant Strain×Dose interaction [$F(4,69)=1.658$, $p=.1697$]. On the final test day, there was a significant main effect of Strain [$F(1,69)=4.093$, $p=.0469$], with LEW rats generally consuming less saccharin than F344 rats did, but no significant Strain×Dose interaction [$F(4,69)=1.565$, $p=.1933$].

In addition to the aforementioned between-group comparisons, within-group assessments were also conducted to examine strain differences in the rate of CTA acquisition. All subjects, except for the F344 rats injected with 0.3 mEq/kg LiCl (Group F3), acquired LiCl-induced CTAs by the second trial compared with baseline [all ts(7)>2.366, ps<.05] and controls (all ts>3.106, ps<.008) and continued to demonstrate a CTA for the remaining three trials. Group F3, however, demonstrated a delayed acquisition of LiCl-induced CTAs, acquiring the aversion by Trial 3 compared with baseline [$t(7)=2.758$, $p=.028$] and controls ($t=2.374$, $p=.032$). The suppression of saccharin consumption in this group persisted for the remaining two trials.

4. Discussion

Differences between the LEW and F344 inbred rat strains have been found in both cocaine- and morphine-induced CTAs. In terms of cocaine-induced CTAs, LEW rats acquire greater CTAs than do F344 rats at doses of 18 and 32 mg/kg (Glowa et al., 1994). With respect to morphine, however, this trend is reversed, with F344 rats demonstrating CTAs at doses of 10, 32 and 56 mg/kg, whereas LEW rats do not demonstrate CTAs at any of these doses (Lancellotti et al., 2001). Although strain differences in aversion learning have been explored with the aforementioned drugs of abuse, assessments of the generality of these patterns of strain differences have not been conducted. The only other study that has examined differences between LEW and F344 rats in their ability to acquire CTAs utilized the emetic LiCl (Grigson and Freet, 2000). In this report, subjects were allowed 5-min oral access to LiCl (for a total of six exposures). Under these conditions, LEW and F344 rats demonstrated equivalent LiCl-induced CTAs. However, given that the two strains differed in body weight, consumption of the same amount of LiCl may have resulted in the ingestion of differential doses of LiCl, precluding the conclusion that there were no significant strain differences in LiCl-induced CTAs. The present study attempted to control for this potential confound by intraperitoneally injecting LEW and F344 rats with doses of 0.3, 0.6., 0.9 and 1.2 mEq/kg, 0.15 M LiCl following a 20-min saccharin-access period.

As described, both LEW and F344 rats acquired LiCl-induced CTAs. For both strains, the CTAs induced by LiCl were dose dependent and increased over repeated trials. Although there was no overall strain difference, the two strains did differ on Trial 3, in which LEW rats injected with 0.3 mEq/kg LiCl drank significantly less saccharin than did the F344 rats injected with this same dose. Furthermore, the acquisition of the LiCl-induced aversion at 0.3 mEq/kg was delayed for the F344 subjects (relative to that in the LEW strain). Although a strain difference in LiCl-induced aversions was evident, it should be noted that previously reported differences in aversion learning between the two strains have generally been of a greater magnitude (in terms of the degree of difference in the overall amount consumed), as well as in the number of doses and trials at which the differences were reported (see Glowa et al., 1994; Lancellotti et al., 2001).

Although weak, this strain difference is inconsistent with the report by Grigson and Freet (2000), in which the strains were compared under the condition of oral LiCl administration. As noted, in the Grigson and Freet (2000) report, there were no significant differences between the two strains when LiCl was administered orally. The basis for the differences between the two studies is not known, although the fact that the LEW strain was heavier than the F344 strain in their assessment may have functionally resulted in the LEW strain receiving a smaller dose of LiCl. Given that the LEW strain showed a comparable aversion (after receiving a smaller dose) is consistent with this strain being more sensitive to the aversive effects of LiCl. Although possible, it should be noted that the present study and that of Grigson and Freet (2000) differed on a number of parameters, e.g., dose, route of administration, sex, number of trials and spacing of trials, any or all of which may have affected the display of the aversion (see Riley and Freeman, in press). Until assessments of the interaction of such variables with strain are systematically made, their contribution to strain differences remains unknown.

Interestingly, reported differences between the LEW and F344 strains in aversion learning with cocaine and morphine parallel c-Fos activity in areas of the brain thought to mediate such effects, e.g., the parabrachial nucleus, lateral parabrachial nucleus, intermediate nucleus tractus solitarius, caudal nucleus tractus solitarius and area postrema (Bermudez-Rattoni et al., 1998). Specifically, Grabus et al. (2004) demonstrated heightened c-Fos expression in brain regions

associated with aversion learning following morphine administration in F344 rats and following cocaine administration in LEW rats, supporting the previous findings of strain differences in morphine- and cocaine-induced CTAs (Lancellotti et al., 2001; Glowa et al., 1994). These data suggest that the patterns of strain differences in aversion learning may be a function of activity in the brain areas thought to mediate the aversive effects of morphine and cocaine, respectively. Given these findings, it would be interesting to determine if there is a parallel between aversion learning and brain activity following the administration of LiCl. That is, minimal (and dose dependent) strain differences in brain activity following LiCl administration would be consistent with the current findings and would support the role of activity in these specific areas in mediating aversion learning.

According to this position, strain differences in aversion learning are assumed to be mediated by the aversive effects of the injected compounds. However, there are other interpretations of taste aversion learning that do not necessitate this assumption. One such theoretical framework is the reward comparison hypothesis, which posits that CTAs to recreational compounds are mediated by reward rather than aversion (Grigson, 1997). According to this hypothesis, subjects decrease the consumption of a conditioned stimulus (e.g., saccharin) because its perceived reward pales in comparison with that of the unconditioned stimulus (e.g., cocaine). This phenomenon is referred to as anticipatory contrast. Conversely, conditioned taste aversions induced by emetics and toxins (e.g., LiCl) are a function of their aversive effects and, therefore, are mediated in a manner different than those induced by recreational compounds.

Given that LEW rats are more sensitive to the rewarding properties of drugs than are F344 rats (for a review of strain differences found in self-administration, see Brower et al., 2002; Kosten et al., 1997; Martin et al., 1999; Suzuki et al., 1988a, 1992; see Horan et al., 1997, and Kosten et al., 1994, for a review of those found with CPPs), LEW rats would be expected to acquire greater CTAs to drugs of abuse (in accordance with the reward comparison hypothesis). On the other hand, a compound such as LiCl that does not have any reinforcing properties would not be expected to produce strain differences, as the phenomenon of anticipatory contrast would not occur to compounds without such effects. In support of this hypothesis, LEW rats do acquire greater cocaine-induced CTAs than the F344 rats did at 18 and 32 mg/kg. Although the findings with cocaine-induced CTAs are consistent with the reward comparison hypothesis, data from assessments of strain differences with morphine-induced CTAs are not. In fact, F344 rats acquire greater morphine-induced CTAs than do LEW rats at several doses, despite that they are not as sensitive to the rewarding effects of drugs as are LEW rats. The fact that some differences were evident with LiCl in the present experiment also seems inconsistent with the reward comparison hypothesis; that is, compounds without any rewarding properties should have no differential effects in the LEW and F344 strains (see above). Thus, although some data are consistent with the reward comparison hypothesis, the generality of this model remains unknown.

In terms of the ability of LEW and F344 rats to acquire CTAs to LiCl, morphine and cocaine, it is clear that no common pattern of strain differences emerges. Inasmuch as CTAs induced by each of these compounds produce a unique pattern of strain differences, future research should assess differences between LEW and F344 rats with respect to CTAs induced by a variety of drugs of abuse. Interestingly, it has been suggested that the rewarding and aversive motivational properties of drugs of abuse interact in ways that contribute to their overall acceptability (Chester and Cunningham, 1999a,b, 2002; Cunningham et al., 2002; Gauvin et al., 2000; Grakalic and Riley, 2002; Rademacher et al., 2000). If the relative contribution of these two properties plays a role in modulating a drug's overall acceptability, the assessment of these differences in the LEW and F344 rat strains may provide insight into any differential patterns of use by the two strains.

Acknowledgement

This research was supported by a grant from the Mellon Foundation to A.L.R. Request for reprints should be sent to Anthony L. Riley, Psychopharmacology Laboratory, Department of Psychology, American University, Washington, DC 20016.

References

Ambrosio E, Goldberg SR, Elmer GI. Behavior genetic investigation of the relationship between spontaneous locomotor-activity and the acquisition of morphine self-administration behavior. Behav Pharmacol 1995;6:229–37.

Brower VG, Fu Y, Matta SG, Sharp BM. Rat strain differences in nicotine self-administration using an unlimited access paradigm. Brain Res 2002;930:12–20.

Bermudez-Rattoni F, Bures J, Yamamoto T. Paradoxes, projections, and perspectives of CTA research. In: Mackintosh NJ, Schacter D, Shallice T, Treisman A, editors. Conditioned taste aversion: memory of a special kind. Oxford: Oxford University Press; 1998. p. 121–31.

Chester JA, Cunningham CL. Baclofen alters ethanol-stimulated activity but not conditioned place preference or taste aversion in mice. Pharmacol Biochem Behav 1999a;63:325–31.

Chester JA, Cunningham CL. GABA(A) receptors modulate ethanol-induced conditioned place preference and taste aversion in mice. Psychopharmacology (Berlin) 1999b;144:363–72.

Chester JA, Cunningham CL. GABA(A) receptor modulation of the rewarding and aversive effects of ethanol. Alcohol 2002;26:131–43.

Cunningham CL, Tull LE, Rindal KE, Meyer PJ. Distal and proximal pre-exposure to ethanol in the place conditioning task: tolerance to aversive effect, sensitization to activating effect, but no change in rewarding effect. Psychopharmacology (Berlin) 2002;160:414–24.

DeCarolis NA, Myracle A, Erbach J, Glowa J, Flores P, Riley AL. Strain-dependent differences in schedule-induced polydipsia: an assessment in Lewis and Fischer rats. Pharmacol Biochem Behav 2003;74:755–63.

Gauvin DV, Baird TJ, Briscoe RJ. Differential development of behavioral tolerance and the subsequent hedonic effects of alcohol in AA and ANA rats. Psychopharmacology (Berlin) 2000;151:335–43.

Glowa JR, Shaw AE, Riley AL. Cocaine-induced conditioned taste aversions: comparisons between effects in LEW/N and F344/N rat strains. Psychopharmacology (Berlin) 1994;114:229–32.

Gomez-Serrano M, Tonelli L, Listwak S, Sternberg E, Riley AL. Effects of cross fostering on open-field behavior, acoustic startle, lipopolysaccharide-induced corticosterone release, and body weight in Lewis and Fischer rats. Behav Genet 2001;31:427–36.

Gomez-Serrano MA, Sternberg EM, Riley AL. Maternal behavior in F344/N and LEW/N rats Effects on carrageenan-induced inflammatory reactivity and body weight. Physiol Behav 2002;75:493–505.

Grabus SD, Glowa JR, Riley AL. Morphine- and cocaine-induced c-Fos levels in Lewis and Fischer rat strains. Brain Res 2004;998:20–8.

Grakalic I, Riley AL. Asymmetric serial interactions between ethanol and cocaine in taste aversion learning. Pharmacol Biochem Behav 2002;73:787–95.

Grigson PS. Conditioned taste aversions and drugs of abuse: a reinterpretation. Behav Neurosci 1997;111:129–36.

Grigson PS, Freet CS. The suppressive effects of sucrose and cocaine, but not lithium chloride, are greater in Lewis than in Fischer rats: evidence for the reward comparison hypothesis. Behav Neurosci 2000;114:353–63.

Horan B, Smith M, Gardner EL, Lepore M, Ashby Jr CR. (−)-Nicotine produces conditioned place preference in Lewis, but not Fischer 344 rats. Synapse 1997;26:93–4.

Kosten TA, Ambrosio E. HPA axis function and drug addictive behaviors: insights from studies with Lewis and Fischer 344 inbred rats. Psychoneuroendocrinology 2002;27:35–69.

Kosten TA, Miserendino MJ, Chi S, Nestler EJ. Fischer and Lewis rat strains show differential cocaine effects in conditioned place preference and behavioral sensitization but not in locomotor activity or conditioned taste aversion. J Pharmacol Exp Ther 1994;269:137–44.

Kosten TA, Miserendino MJ, Haile CN, DeCaprio JL, Jatlow PI, Nestler EJ. Acquisition and maintenance of intravenous cocaine self-administration in Lewis and Fischer inbred rat strains. Brain Res 1997;778:418–29.

Lancellotti D, Bayer BM, Glowa JR, Houghtling RA, Riley AL. Morphine-induced conditioned taste aversions in the LEW/N and F344/N rat strains. Pharmacol Biochem Behav 2001;68:603–10.

Martin S, Manzanares J, Corchero J, Garcia-Lecumberri C, Crespo JA, Fuentes JA, et al. Differential basal proenkephalin gene expression in dorsal striatum and nucleus accumbens, and vulnerability to morphine self-administration in Fischer 344 and Lewis rats. Brain Res 1999;821:350–355.

National Research Council. Guide for the care and use of laboratory animals. Washington (DC): National Academy Press; 1996.

National Research Council. Guidelines for the care and use of mammals in neuroscience and behavioral research. Washington (DC): National Academy Press; 2003.

Rademacher DJ, Anders KA, Thompson KJ, Steinpreis RE. The failure of some rats to acquire intravenous cocaine self-administration is attributable to conditioned place aversion. Behav Brain Res 2000;117:13–9.

Riley A, Freeman K. Conditioned flavor aversions: assessment of drug-induced suppression of food intake. In: Crawley J, Gerfen C, McKay R, Rogawaki M, Sibley D, Skolnick P, editors. Current protocols in neuroscience. New York: John Wiley and Sons. In press.

Sternberg EM, Hill JM, Chrousos GP, Kamilaris T, Listwak SJ, Gold PW, et al. Inflammatory mediator-induced hypothalamic–pituitary–adrenal axis activation is defective in streptococcal cell wall arthritis-susceptible Lewis rats. Proc Natl Acad Sci U S A 1989;86:2374–8.

Sternberg EM, Glowa JR, Smith MA, Calogero AE, Listwak SJ, Aksentijevich S, et al. Corticotropin releasing hormone related behavioral and neuroendocrine responses to stress in Lewis and Fischer rats. Brain Res 1992;570:54–60.

Stohr T, Schulte WD, Weiner I, Feldon J. Rat strain differences in open-field behavior and the locomotor stimulating and rewarding effects of amphetamine. Pharmacol Biochem Behav 1998a;59:813–8.

Stohr T, Schulte WD, Szuran T, Pliska V, Domeney A, Welzl H, et al. Differential effects of prenatal stress in two inbred strains of rats. Pharmacol Biochem Behav 1998b;59:799–805.

Stohr T, Szuran T, Welzl H, Pliska V, Feldon J, Pryce CR. Lewis/Fischer rat strain differences in endocrine and behavioural responses to environmental challenge. Pharmacol Biochem Behav 2000;67:809–19.

Suzuki T, George FR, Meisch RA. Differential establishment and maintenance of oral ethanol reinforced behavior in Lewis and Fischer 344 inbred rat strains. J Pharmacol Exp Ther 1988;245:164–70.

Suzuki T, Otani K, Koike Y, Misawa M. Genetic differences in preferences for morphine and codeine in Lewis and Fischer 344 inbred rat strains. Jpn J Pharmacol 1988;47:425–31.

Suzuki T, George FR, Meisch RA. Etonitazene delivered orally serves as a reinforcer for Lewis but not Fischer 344 rats. Pharmacol Biochem Behav 1992;42:579–86.