Pharmacology Biochemistry and Behavior, Vol. 45, pp. 905–912, 1993
Printed in the U.S.A.

0091-3057/93 $6.00 + .00

Strain and Housing Affect Cocaine Self-selection and Open-field Locomotor Activity in Mice

ANDREW C. MORSE, V. GENE ERWIN [1] AND BYRON C. JONES[2]

Program in Biobehavioral Health, 210 East Henderson Building
College of Health and Human Development, The Pennsylvania State University, University Park, PA 16802

MORSE, A. C., V. G. ERWIN AND B. C. JONES. *Strain and housing affect cocaine self-selection and open-field locomotor activity in mice.* PHARMACOL BIOCHEM BEHAV. 45(4) 905–912, 1993.—We recently conducted an experiment to investigate the possible cooperation between genetic makeup and differential housing on cocaine self-administration in male and female C57BL/6J and DBA/2J mice. Cocaine self-selection was measured in a two-choice test with one choice being cocaine-HCl solution of 40 mg% in tap water and the other choice being plain tap water. Housing conditions began at weaning (21–23 days of age) and consisted of group housed (GH) with 2–3 mice per cage, and isolated housed (IH) with 1 mouse per cage. The results of this study revealed overall strain, sex and housing differences, with C57BL/6Js consuming more cocaine solution than DBA/2J subjects, females consuming more cocaine solution than males, and group housed consuming more than isolate housed subjects. In a second study, the effect of differential housing on open-field locomotor activity was investigated. Testing was conducted on two consecutive days, with subjects receiving an IP injection of saline on day 1, and 15 mg/kg cocaine HCl on day 2. Four behaviors were recorded, including: total distance, nosepokes, stereotypy, and margin time. Overall, the results revealed significant strain differences for stereotypy and nosepokes, and males were found to be more activated by cocaine than females. Additionally, DBA males tended to be differentially affected by housing condition, with IH showing suppressed locomotor activity as compared to GH subjects. Last, significant strain by housing interactions occurred in nosepokes and stereotypy time.

Differential housing Cocaine Locomotor activity Oral administration Mice

THERE has been an increasing interest in the study of individual differences among animals in cocaine self-administration (3,9,21) and locomotor response to cocaine (4,8,15,25). Previous studies have suggested that the variability in these behaviors may be influenced by factors such as genetic makeup, sex, experiential history, and early housing environment.

Many studies have reported behavioral and neurochemical differences between different rat and mouse strains in response to cocaine (9,16). For instance, it has been shown that short-sleep mice are more sensitive to high doses of cocaine than long-sleep mice (5), and BALB/cBy mice show less liver damage from high doses of cocaine than B6AF1 mice (23). Similarly, it has been shown that DBA/2IbG mice are more sensitive to the hepatotoxic effects of cocaine than C57BL/6IbG mice (2). In addition to the strain differences, significant sex differences in response to cocaine have been reported as well. Studies have described females consuming more cocaine (22) and being more susceptible to cocaine-induced liver damage than males (23).

Experiential history may also play a role in this individual variability. It has been reported that mice exposed to a novel environment show greater initial activation produced by cocaine than subjects with prior experience in the same environment (13). Moreover, it has been shown that a rat's locomotor response to a novel environment can predict its behavioral and neurochemical response to cocaine (12). Lastly, manipulation of the early housing environment has been shown to modify behavioral and neurochemical activity. Specifically, isolate housed mice and rats have been shown to consume less orally delivered cocaine than their group housed counterparts (8,11), are less sensitive to the effects of cocaine (20), and are reported to have altered noradrenaline, dopamine and serotonin functioning (14).

The present study examines the effects of housing condition and experiential history on behavior in genetically defined male and female mice. The first component of the study involved investigation of the effect of group and isolate housing on two-choice self-selection of cocaine in C57BL/6J and DBA/2J mice. In the second component, we examined the effect of differential housing on open field locomotor activity in C57BL/6J and DBA/2J strains of mice. By addressing these factors in one study, our goal was to more completely

[1] Present address: Alcohol Research Center, School of Pharmacy, University of Colorado Health Sciences Center, 4200 E. 9th Ave., Denver, CO 80262-0238.
[2] To whom requests for reprints should be addressed.

TABLE 1

MEANS AND ± SEM'S FOR TOTAL DISTANCE, NOSEPOKES, STEREOTYPY TIME, AND MARGIN TIME FOR GROUP AND ISOLATE HOUSED MICE

Housing and Strain	Sex	Time	Total Distance (cm) Mean (± SEM)		Nosepokes Mean (± SEM)		Stereotypy Time Mean (± SEM)		Margin Time Mean (± SEM)	
Group			Saline	Cocaine	Saline	Cocaine	Saline	Cocaine	Saline	Cocaine
C57BL/6J	Male	0–5	1228 (262)	3160 (160)	5.2 (2.1)	7.4 (4.8)	42.4 (8.2)	52.2 (7.1)	267.2 (6.8)	289.2 (2.2)
		5–10	1236 (88)	3778 (223)	3.2 (2.1)	4.8 (3.5)	41.8 (1.9)	56.6 (9.6)	272.8 (3.8)	288.6 (2.2)
		10–15	951 (72)	3407 (196)	3 (1.4)	8 (5.5)	27 (4.5)	51.4 (11.9)	270.2 (7.5)	284.0 (4.7)
		15–20	908 (160)		6.8 (3.9)		20.8 (5.1)		275.0 (6.8)	
		20–25	726 (153)		5 (2.1)		13.8 (3.7)		278.8 (9.9)	
		25–30	714 (145)		9.8 (5.6)		13.2 (5.3)		274.8 (10.7)	
	Female	0–5	1627 (166)	3394 (109)	8.4 (2.7)	12 (4.1)	54.6 (9.8)	61.2 (12.0)	268.0 (8.5)	285.8 (3.6)
		5–10	1434 (127)	3387 (306)	12.2 (2.4)	11.4 (6.4)	46.8 (9.4)	66.8 (18.2)	268.4 (4.5)	283.6 (6.1)
		10–15	1268 (172)	2643 (244)	11 (2.0)	7 (3.5)	35.8 (9.2)	65.2 (14.7)	270.2 (5.7)	274.4 (5.1)
		15–20	1084 (111)		8.2 (1.9)		37 (10.3)		245.4 (16.5)	
		20–25	1144 (127)		14.6 (2.2)		35 (6.9)		270.2 (5.2)	
		25–30	1216 (158)		16.8 (2.7)		36.2 (4.3)		267.4 (4.6)	
DBA/2J	Male	0–5	1357 (177)	3698 (225)	2.2 (1)	0.4 (0.2)	11 (3.6)	29.6 (8.4)	239.6 (16.5)	268.8 (3.2)
		5–10	1201 (197)	4566 (292)	5.6 (2.6)	2.6 (1.6)	8.2 (1.9)	38.0 (11.4)	270.0 (6.5)	268.0 (6.8)
		10–15	1190 (217)	3667 (193)	6.6 (3.3)	1.4 (0.5)	5.8 (1.6)	26.4 (10.4)	270.2 (8.3)	264.8 (6.5)
		15–20	1152 (175)		5.4 (2.6)		4.4 (1.4)		263.4 (19.0)	
		20–25	1125 (231)		7.4 (3.4)		4.8 (0.3)		263.4 (3.5)	
		25–30	977 (213)		5.2 (2.7)		2.0 (0.8)		273.2 (5.5)	
	Female	0–5	1403 (86)	2912 (222)	4.8 (0.7)	1.6 (0.3)	12.1 (2.8)	27.0 (5.3)	263.1 (4.7)	273.6 (3.3)
		5–10	1291 (59)	3203 (248)	4.8 (0.9)	1.5 (0.4)	9.5 (2.2)	26.5 (6.3)	273.4 (3.2)	276.9 (3.3)
		10–15	1253 (58)	2666 (240)	4.4 (0.8)	1.6 (0.5)	5.2 (1.2)	14.4 (2.9)	275.5 (2.9)	283.0 (3.3)
		15–20	1165 (51)		5.5 (0.9)		4.5 (0.7)		272.5 (3.8)	
		20–25	1099 (58)		10 (2.1)		2.2 (0.6)		274.0 (2.6)	
		25–30	974 (58)		9.2 (1.9)		2.0 (0.5)		275.4 (2.8)	

Isolate										
C57BL/6J	Male	0–5	1423 (214)	3295 (165)	3.2 (0.8)	9.6 (6.5)	46 (9.2)	50.0 (6.8)	271.4 (10.6)	290.6 (3.6)
		5–10	1284 (90)	3450 (520)	6.4 (2.2)	2 (0.7)	36.6 (4.1)	44.4 (10.6)	282.4 (4.1)	281.4 (6.8)
		10–15	935 (108)	3160 (664)	5.8 (4.8)	1 (0.3)	29.6 (4.3)	50.4 (18.7)	280.6 (5.8)	286.0 (7.0)
		15–20	999 (163)		10.2 (4.7)		30.4 (7.3)		276.4 (5.3)	
		20–25	907 (50)		7.8 (3.0)		27.6 (3.0)		271.6 (6.8)	
		25–30	791 (96)		5.2 (2.1)		24 (5.2)		281.2 (6.7)	
	Female	0–5	1676 (94)	2960 (108)	9 (2.8)	8.7 (3.1)	40.5 (8.6)	36.2 (13.0)	270.8 (5.5)	281.0 (5.6)
		5–10	1453 (129)	3099 (202)	13.4 (5.1)	4.4 (1.4)	24.2 (7.8)	24.8 (9.2)	279.0 (2.6)	283.1 (4.1)
		10–15	1227 (52)	2552 (183)	12 (4.4)	4.1 (2.4)	22.2 (6.2)	23.5 (9.6)	271.5 (5.7)	276.1 (5.4)
		15–20	1066 (103)		10.3 (3.6)		13.7 (3.6)		276.7 (2.6)	
		20–25	1050 (91)		15.5 (4.4)		23.5 (5.5)		262.0 (5.8)	
		25–30	957 (77)		8.4 (2.9)		16.5 (5.4)		272.0 (4.9)	
DBA/2J	Male	0–5	1781 (195)	3156 (367)	2.7 (0.6)	2 (0.6)	14.7 (3.0)	49.1 (5.2)	265.9 (4.7)	266.4 (5.5)
		5–10	1406 (185)	3400 (421)	7.7 (1.8)	0.9 (0.3)	9.6 (3.1)	37.0 (6.6)	267.4 (5.4)	285.3 (4.5)
		10–15	1366 (172)	2806 (356)	5.4 (1.9)	0.9 (0.4)	7.3 (2.1)	29.3 (3.8)	272.4 (4.7)	279.9 (4.5)
		15–20	1298 (158)		2.6 (0.9)		8.4 (2.1)		278.5 (4.2)	
		20–25	1168 (121)		5.5 (1.7)		6.2 (1.7)		264.7 (5.4)	
		25–30	1137 (146)		6.4 (1.3)		6.1 (2.0)		271.0 (5.3)	
	Female	0–5	1587 (86)	3652 (126)	2.7 (1.3)	3.1 (1.5)	30.8 (7.6)	36.4 (4.5)	255.0 (7.5)	273.0 (3.7)
		5–10	1616 (167)	3799 (248)	2.7 (1.4)	2.4 (1.1)	25.5 (5.9)	33.0 (6.5)	263.5 (4.9)	281.7 (6.6)
		10–15	1283 (141)	2743 (259)	9.2 (3.9)	2 (1.2)	24.4 (7.2)	32.8 (6.4)	268.7 (6.9)	274.8 (5.1)
		15–20	1534 (122)		5.1 (1.9)		22.2 (6.3)		268.0 (5.0)	
		20–25	1273 (95)		8.7 (3.6)		22.4 (7.6)		269.1 (6.1)	
		25–30	1388 (100)		6.5 (2.3)		14.5 (4.0)		268.1 (4.1)	

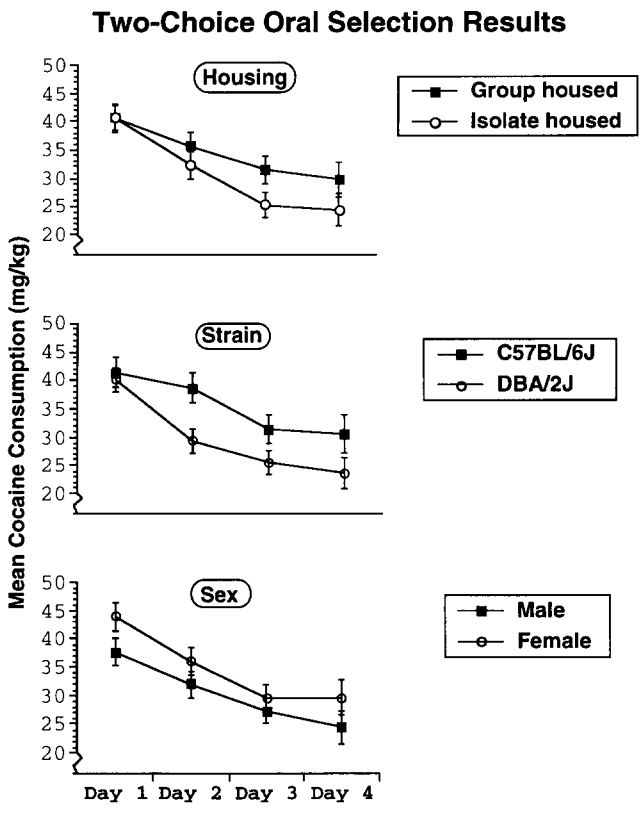

FIG. 1. Effects of housing condition, strain, and sex on mean (±SEM) cocaine consumption (mg/kg) in two-choice oral selection study. Male and female C57BL/6J and DBA/2J mice were tested over 5 days. Subjects had choice between plain tap water and tap water with cocaine HCl (40 mg %).

characterize individual and environment-interactive effects on cocaine related behaviors.

METHOD

Animals

Male and female C57BL/6J and DBA/2J mice derived from our own colony served as subjects in this study. Subjects were weaned into group (2–3 mice/cage) or isolate (1 mouse/cage) conditions between 21 and 22 days of age. Siblings were assigned to different treatment conditions. Temperature and humidity were maintained at 22°C and 20%, respectively, with light cycle, 0700 L : 1900 D. Food and water were available continuously.

Cocaine Self-selection

At weaning (21–23 days of age) subjects were separated into GH or IH conditions. At 63–113 days of age, all subjects were placed into individual cages (30 × 26 × 23 cm Plexiglas chambers) equipped with two drinking-fluid reservoirs. Reservoirs consisted of 15-ml plastic graduated cylinders fitted with stainless-steel ball-stop sipper tubes. Cylinders were placed in the stainless-steel cage top approximately 5 cm apart, extending 1 cm into the cage. Animals were weighed on day 1, and fluid levels were recorded and refilled at the same time for the following 4 days. On the final day, subjects were weighed again. Averaged weights were used to calculate mg/kg cocaine consumed per day.

Activity Monitor Testing

At 63–113 days of age, group and isolate housed animals received an isovolumetric IP injection of sterile saline on day 1, and a 15-mg/kg dose of cocaine HCl dissolved in sterile saline on day 2 (1.2-mg cocaine/ ml saline). Immediately following injections, animals were placed into an automated activity monitor (Omnitech, Inc., Columbus, OH) for 30 min on day 1, and 15 min on day 2. The Digiscan activity monitor is a 40 × 40 × 30.5 cm acrylic cage with vertical and horizontal infrared sensors. The flooring is an elevated acrylic platform with 16 equally spaced holes (4 × 4, approximately 1.5 cm diameter). Total distance, stereotypy time, nosepokes, and margin times (thigmotaxis, a putative measure of anxiety) were recorded during successive 5-min intervals. Stereotypy time was defined as a composite score for all behaviors that caused repeated breaks of the same beam pattern (6,19).

Data Analysis

Statistical analysis of the self-selection and behavioral data was performed using analysis of variance as appropriate for between-subjects and mixed between- and within-subjects experiments. For the oral self-selection data, we used a three between-subjects (housing, strain, sex) and one within-subjects factor (day) design. For the open field behavior data, we used a three between-subjects factors (strain, sex, treatment) and two within-subjects factors (day, time) design. Difference scores for open-field behaviors were calculated by subtracting saline scores from cocaine scores.

RESULTS

Oral Self-selection

Figure 1 illustrates mean cocaine consumption (mg/kg) scores across the 4-day test period for housing (top panel), strain (center panel), and sex (bottom panel). Analysis of variance revealed significant effects for day, $F(3, 252) = 11.66$, $p < 0.0001$; housing (grouped > isolate), $F(1, 84) = 4.29$, $p < 0.05$; strain (C57BL/6J > DBA/2J), $F(1, 84) = 10.91$, $p < 0.001$; and sex (female > male), $F(1, 84) = 6.49$, $p < 0.01$.

Open Field Behavior

Total distance difference scores (Fig. 2) revealed significant differences between males and females at the 10- and 15-min time intervals; $F(1, 54) = 5.015$, $p < .03$; $F(1, 54) = 9.411$, $p < 0.003$, respectively, with males having greater locomotion difference scores than females in both cases. At the 5-min interval there was a significant strain by sex by housing interaction. GH DBA/2J males had higher scores than GH DBA/2J females, but IH DBA/2J males had lower scores than IH DBA/2J females; $F(1, 54) = 5.177$, $p < 0.03$.

Stereotypy difference scores (Fig. 3) showed a significant effect for strain (DBA/2J > C57BL/6J), $F(1, 54) = 7.745$, $p < 0.007$; and sex (males > females), $F(1, 54) = 4.565$, $p < 0.04$ at the 5-min time interval. At the 15-min time interval, sex effect approached, but failed to reach statistical significance, $F(1, 54) = 3.718$, $p < 0.059$.

Nosepoke difference scores (Fig. 4) were significantly different for strain (C57BL/6J > DBA/2J) at 5 min; $F(1, 54) = 7.066$, $p < 0.01$. We also observed a significant difference

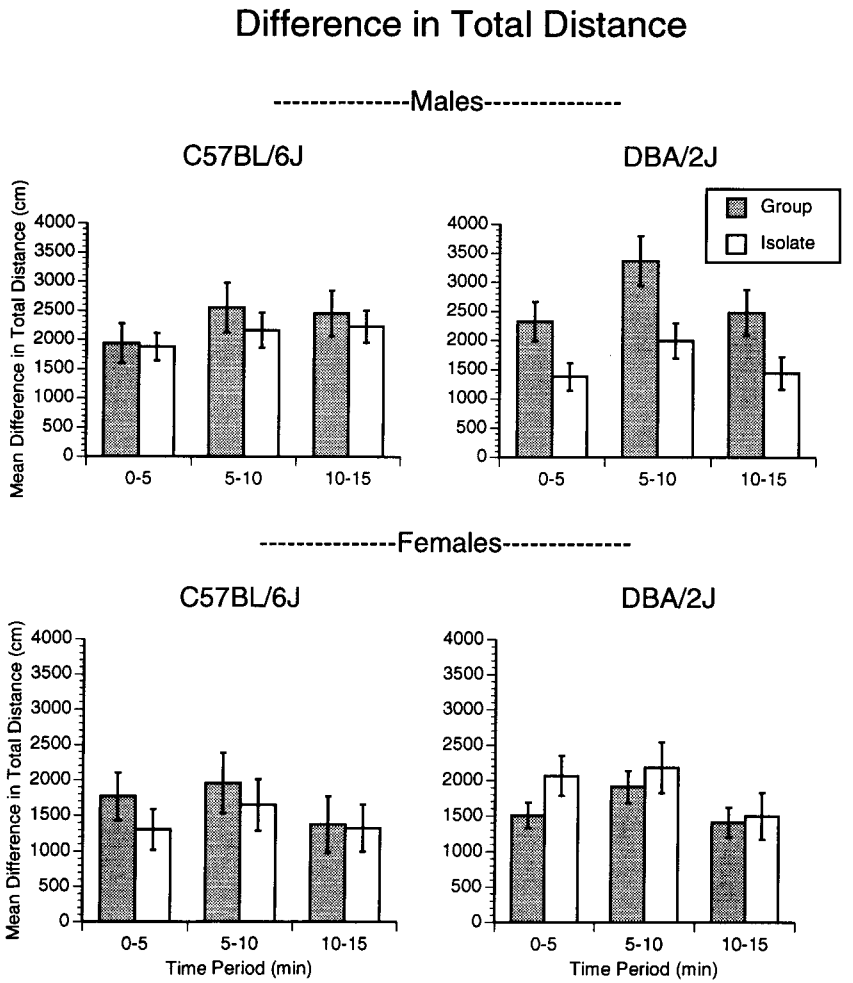

FIG. 2. Effect of housing condition, strain, and sex on total distance traveled (cm) over three 5-min time intervals, 0–15 min. Male and female C57BL/6J and DBA/2J mice were tested on two consecutive days in an automated activity monitor. Saline and cocaine (15 mg/kg) were administered IP on days 1 and 2, respectively. Data are mean (±SEM) difference in total distance (cm) traveled, cocaine minus saline.

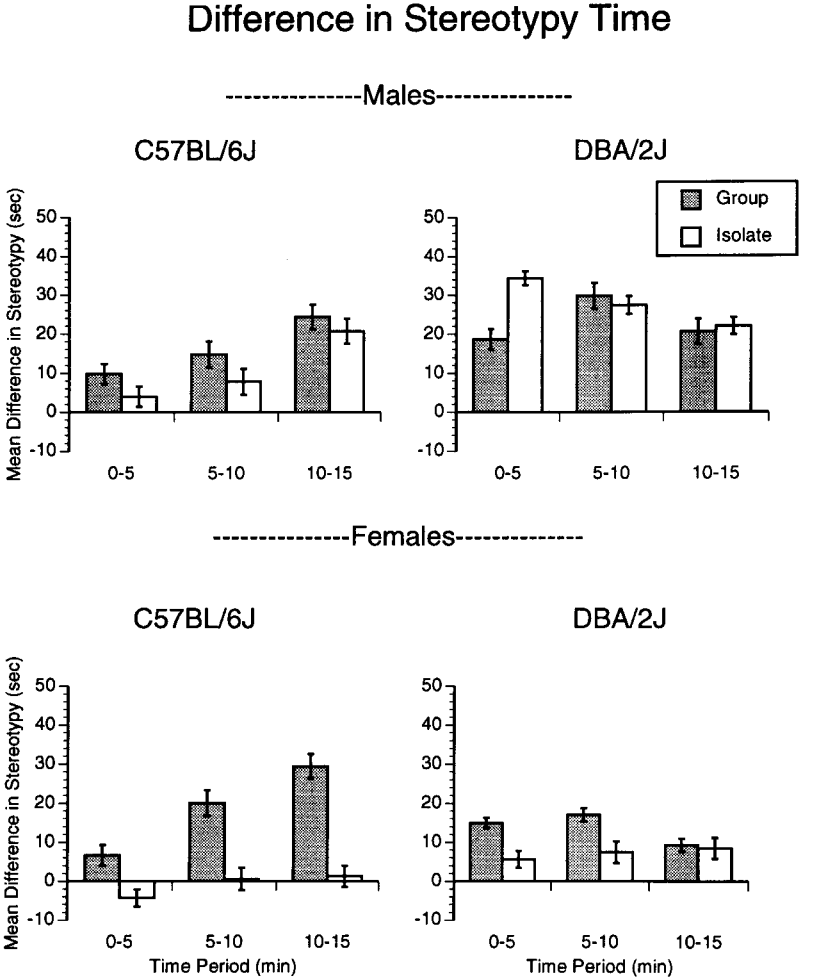

FIG. 3. Effect of housing condition, strain and sex on stereotypy (sec) over three 5-min time intervals, 0–15 min. Male and female C57BL/6J and DBA/2J mice were tested on two consecutive days in an automated activity monitor. Saline and cocaine (15 mg/kg) were administered IP on days 1 and 2 respectively. Data are mean (±SEM) difference in stereotypy, cocaine minus saline.

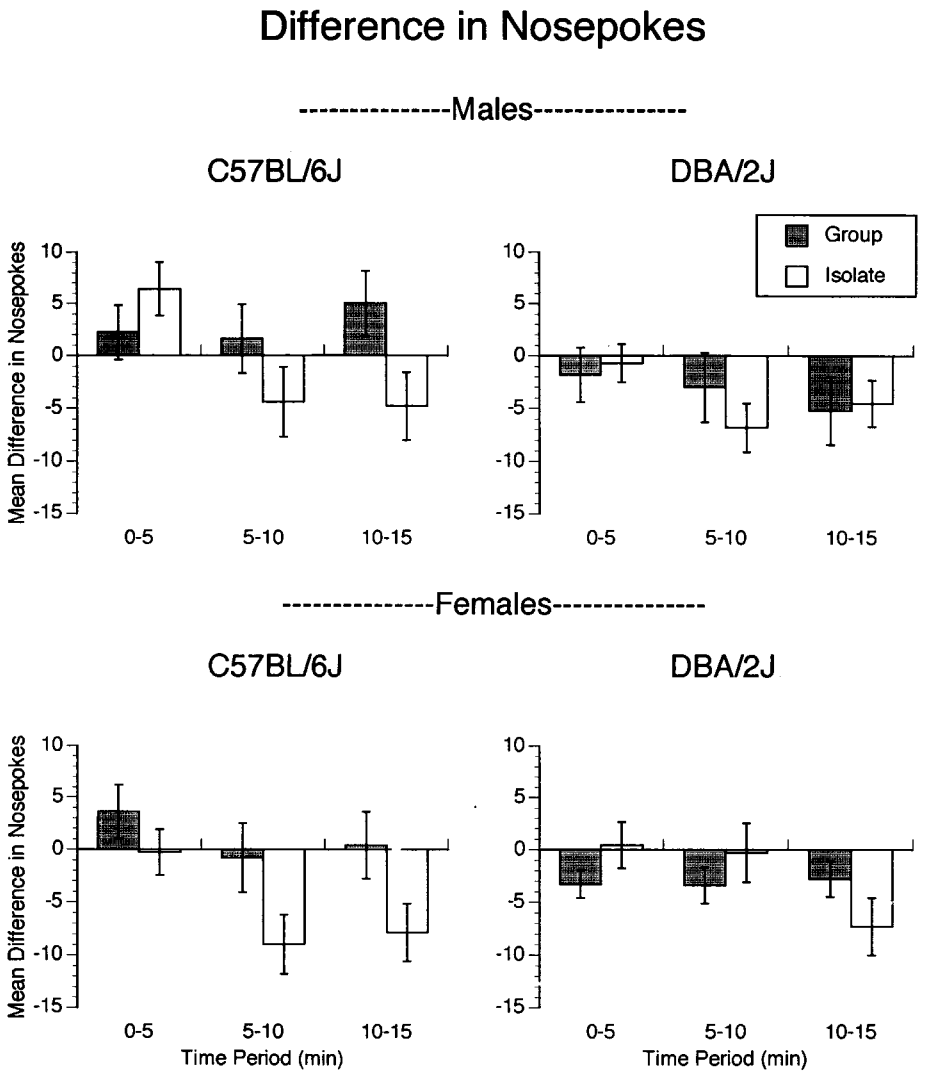

FIG. 4. Effect of housing condition, strain and sex on nosepokes over three 5-min time intervals, 0–15 min. Male and female C57BL/6J and DBA/2J mice were tested on 2 consecutive days in an automated activity monitor. Saline and cocaine (15 mg/kg) were administered IP on days 1 and 2 respectively. Data are mean (±SEM) difference in nosepokes, cocaine minus saline.

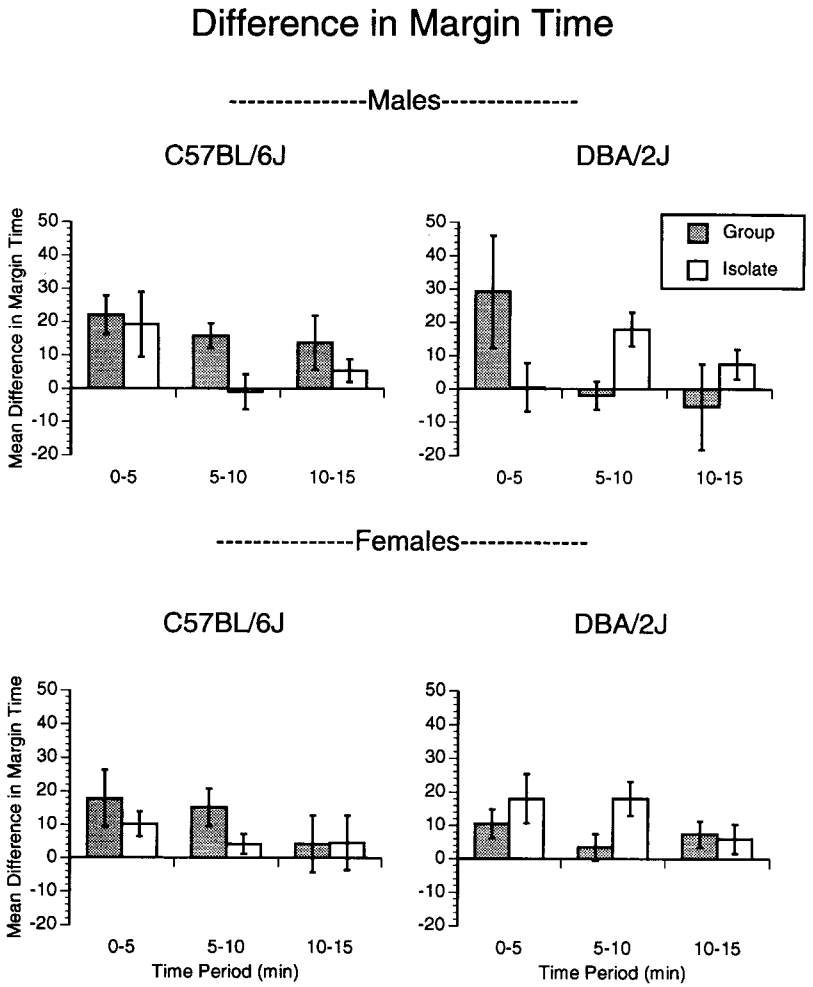

FIG. 5. Effect of housing condition, strain and sex on margin time over three 5-min time intervals, 0–15 min. Male and female C57BL/6J and DBA/2J mice were tested on two consecutive days in an automated activity monitor. Saline and cocaine (15 mg/kg) were administered IP on days 1 and 2, respectively. Data are mean (±SEM) difference in margin time scores, cocaine minus saline.

between housing conditions (group housed > isolate housed) at 15 min; $F(1, 54) = 4.673$, $p < 0.03$. Margin time difference scores (Fig. 5) revealed a significant strain by treatment interaction for males and females at 10 min. C57BL/6J GH had higher scores than IH, and DBA/2J IH had higher scores than GH; $F(1, 54) = 15.568$, $p < 0.0002$. All activity measures recorded for saline and cocaine are presented in Table 1.

DISCUSSION

The results of this study lend further support to the growing body of evidence that genetic makeup, sex, and early housing environment can influence cocaine related behaviors. In the self-selection study, C57BL/6J mice consumed more cocaine solution than DBA/2J's on all days of testing with the exception of the first day. In the open-field locomotor study, the strains differed significantly on measures of stereotypy, and nosepokes. The results of our selection and locomotor studies suggest genetically based variance in preference for cocaine and reactivity to its activating effects.

Our finding of a sex difference in oral cocaine consumption was in agreement with previous research (11), yet it was interesting to note that females also had significantly lower activity scores than males. These results suggest that while females consume more cocaine than males, they show less locomotor activation. Sex differences in cocaine induced hyperlocomotion and avidity for cocaine indicate an area that needs to be more thoroughly addressed in the literature. An overwhelming majority of studies in this area have included only male subjects, and as a consequence do not provide a complete account of the effects of cocaine on a given species. Other animal studies have shown these sex differences to be of significance (22,23), and they may prove to be important in human drug use research. Not all measures showed differences resulting from treatment or sex conditions. For example, stereotypy was refractory to changes in housing condition, and also showed no sex differences. This may indicate that neurobiological systems differ with respect to environmental conditions or gender.

Lastly, our differential housing results were in agreement with previous research, with GH subjects consuming more cocaine solution (8,11), being more sensitive to the activating effects of cocaine (20), and displaying more nosepokes than their isolate housed counterparts. These differential housing results are not surprising when one considers the large body of evidence linking social isolation with alterations in biogenic amine dynamics. Previous research has shown cocaine to inhibit uptake of dopamine (DA), norepinephrine (NE) (18), and serotonin (5-HT) (10,17). Studies with individually housed mice have shown reductions in adrenal catecholamine synthesizing enzymes (1), brain turnover rate of NE (26), and higher dihydroxyphenylalanine (DOPA) and tyrosine levels (27). Additionally, when exposed to a novel environment or aggressive situation, there is a significant increase in the turnover of DA, NE, and 5-HT in IH as compared to GH mice (7,14,24). These environmentally induced changes in combination with the cocaine related alterations of catecholamines may account for the observed behavioral differences between group and isolate housed subjects. The continuous decrease in daily cocaine consumption in both group and isolate housed subjects may be a result of sensitization to the stimulatory effects of cocaine.

In summary, our findings support and extend the observations and conclusions of other researchers demonstrating that genetic makeup, sex, and housing conditions can influence cocaine related behaviors in mice. Future studies in this area should address the influence of factors such as genetics, sex, housing, experiential history, and their interactions. A better understanding of the complex relationships between these factors in animals may lead to the development of more effective treatment strategies in humans.

ACKNOWLEDGEMENTS

This research was supported by USPH grants DA07171 and DA07277.

REFERENCES

1. Axelrod, J.; Mueller, R. A.; Henri, J. P.; Stephens, P. M. Changes in enzymes involved in the biosynthesis and metabolism of noradrenaline and adrenaline after psychosocial stimulation. Nature 225:1059–1060; 1970.
2. Boyer, C. S.; Peterson, D. R. Hepatic biochemical changes as a result of acute cocaine administration in the mouse. Hepatology 14:1209–1216; 1991.
3. Boyle, A. E.; Gill, K.; Smith, B. R.; Amit, Z. Differential effects of an early housing manipulation on cocaine-induced activity and self-administration in laboratory rats. Pharmacol. Biochem. Behav. 39:269–274; 1991.
4. Brain, P. F.; Benton, D. The interpretation of physiological correlates of differential housing in laboratory rats. Life Sci. 24:99–116; 1979.
5. DE Fiebre, C. M.; Ruth, J. A.; Collins, A. C. Differential Sensitivity of long-sleep and short-sleep mice to high doses of cocaine. Pharmacol. Biochem. Behav. 34:887–893;1989.
6. Fitzgerald, R. E.; Berres, M; Schaeppi, U. Validation of a photobeam system for assessment of motor activity in rats. Toxicology 49:433–439; 1988.
7. Garattini, S.; Giacolone, E.; Valzelli, L. Biochemical changes during isolation-induced aggressiveness in mice. In: Garattini, S.; Sigg, E. B., eds. Aggressive behavior. New York: John Wiley & Sons; 1969:179–187.
8. Gentsch, C.; Lichtsteiner, M.; Kraeuchi, K.; Feer, H. Different reaction patterns in individually and socially reared rats during exposures to novel environments. Behav. Brain Res. 4:45–54; 1982.
9. George, F. R.; Elmer, G. I.; Meisch, R. A.; Goldberg, S. R. Orally delivered cocaine functions as a positive reinforcer in C57BL/6J mice. Pharmacol. Biochem. Behav. 38:897–903; 1991.
10. Hanson, G. R.; Matsuda, L. A.; Gibb, J. W. Effects of cocaine on methamphetamine-induced neurochemical changes: Characterization of cocaine as a monoamine uptake blocker. J. Pharmacol. Exp. Ther. 242:507–513; 1987.
11. Hill, S. Y.; Powell, B. J. Cocaine and morphine self-administration: Effects of differential nosepoke. Pharmacol. Biochem. Behav. 5:701–704; 1976.
12. Hooks, M. S.; Jones, G. H.; Smith, A. D.; Neill, D. B.; Justice, J. B. J. Response to novelty predicts the locomotor and nucleus accumbens dopamine response to cocaine. Synapse. 9:121–128; 1991.
13. Jones, B. C.; Campbell, A. D.; Radcliffe, R. A.; Erwin, V. G. Cocaine actions, brain levels and receptors in selected lines of mice. Pharmacol. Biochem. Behav. 40:941–948; 1991.
14. Modigh, K. Effects of isolation and fighting in mice on the rate of synthesis of noradrenaline, dopamine and 5-hydroxytryptamine in the brain. Psychopharmacologia 33:1–17; 1973.
15. Oehler, J.; Jahkel, M.; Schmidt, J. Inhibition of isolation-in-

duced changes in aminergic transmission by chronic lithium treatment. Pharmacol. Biochem. Behav. 21:181–184; 1984.
16. Reith, M. A.; Selmeci, G. Cocaine binding sites in mouse striatum, dopamine autoreceptors, and cocaine-induced locomotion. Pharmacol. Biochem. Behav. 41:227–230; 1991.
17. Ross, S. B.; Renyi, A. L. Inhibition of the uptake of tritiated 5-hydroxytryptamine in brain tissue. Eur. J. Pharmacol. 7:270–277; 1969.
18. Ross, S. B.; Renyi, A. L. Uptake of some tritiated sympathomimetic amine by mouse brain cortex in vitro. Pharmacol. Toxicol. 24:297–309; 1966.
19. Sanberg, P. R.; Zoloty, A.; Willis, C. D.; Rhoads, Ticarich, K., et al. Digiscan activity: Automated measurement of thigmotactic and stereotypic behavior in rats. Pharmacol. Biochem. Behav. 27:569–572; 1987.
20. Schenk, S.; Hunt, T.; Malovechko, R.; Robertson, A.; Klukowski, G.; Amit, Z. Differential effects of isolation housing on the conditioned place preference produced by cocaine and amphetamine. Pharmacol. Biochem. Behav. 24:1793–1796; 1986.
21. Schenk, S.; Lacelle, G.; Gorman, K.; Amit, Z. Cocaine self-administration in rats influenced by environmental condition:Implications for the etiology of drug abuse. Neurosci. Lett. 81:227–231; 1987.
22. Taylor, J.; Harris, N.; Vogel, W. H. Voluntary alcohol and cocaine consumption in "low" and "high" stress plasma catecholamine responding rats. Pharmacol. Biochem. Behav. 37:359–363; 1990.
23. Thompson, M. L.; Shuster, L.; Casey, E. Sex and strain differences in response to cocaine. Biochem. Pharmacol. 33:1299–1307; 1984.
24. Tizabi, Y.; Massari, J.; Jacobowitz, D. M. Isolation induced aggression and catecholamine variation in discrete brain areas of the mouse. Brain Res. Bull. 5:81–86; 1980.
25. Welch, A. S.; Welch, B. L. Isolation, reactivity, and aggression: Evidence for an involvement of brain catecholamine and serotonin. In: Eleftheriou, B. E.; Scott, J. P., eds. The physiology of aggression and defeat. New York: Plenum Press; 1971: 91–142.
26. Welch, B. L.; Welch, A. S. Greater lowering of brain and adrenal catecholamines in group-housed than in individually-housed mice administered DL-alpha-methyltyrosine. J. Pharm. Pharmacol. 20:244–246; 1968.
27. Wilmot, C. A.; VanderWende, C.; Speorlein, M. T. Behavioral and biochemical studies of dopamine receptor sensitivity in differentially housed mice. Psychopharmacology (Berl.) 89:364–369; 1986.