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# Open Field, Learned Helplessness, Conditioned Defensive Burying, and Forced-Swim Tests in WKY Rats

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PARÉ, W. P. *Open field, learned helplessness, conditioned defensive burying, and forced-swim tests in WKY rats.* *PHYSIOL BEHAV* 55(3) 433–439, 1994.—Wistar Kyoto (WKY) and Wistar rats were observed in four tests; the open field test (OFT), the conditioned defensive burying (DB) test, and two tests which are considered animal models of depressive behavior, namely the Porsolt forced-swim test (FST) and the shuttlebox escape responding following exposure to inescapable shock, that is, learned helplessness (LH). The four tests were administered according to a semirandomized schedule to control for sequence effects. All rats were later exposed to water-restraint stress and stomachs were subsequently inspected for ulcers. Stress ulcer severity was greater in WKY rats. WKY rats, as compared to Wistar rats, were hypoactive in the OFT, did not engage in DB, rapidly acquired the LH task, and were significantly more immobile in the FST. The FST was positively correlated with behaviors in the LH procedure and, to a lesser degree, with DB, but these relationships were observed only with WKY rats, not Wistar rats. The data suggested that the use of WKY rats represented a more sensitive procedure for detecting possible relationships between putative animal models of depressive behavior.

Stress	Ulcer	Rat	WKY	Wistar	Strain effects	Depression	Open-field test	Forced-swim test
Learned helplessness			Defensive burying		Animal models			

BEHAVIORAL deficits occurring as a result of exposure to an unavoidable stressor are suggestive of human depressive behavior (30,31). The motor deficit, or floating behavior, observed in the forced-swim test is another animal model of depressive behavior (27,28). The former, which is identified as the learned helplessness paradigm, and the Porsolt forced-swim test are two of the most frequently used animal models of depression (35) and represent two examples of stress-induction models of depression. However, there are a few concerns about these stress-induction models. First of all, not all animals that are exposed to inescapable shock fail to acquire the shock escape response 24 h later. Escape failures, or learned helplessness, may occur in only 60 to 80% of animals exposed (3). Acquisition of learned helplessness may depend on the type of the escape task employed (1,16) and the difficulty of the escape response (31). Some studies have reported extreme variability between strains (32) or even a zero incidence of learned helplessness in some strains (34). Another concern is that animals may display a profound disturbance in one task following inescapable stress, but display good performance in a second task (32). This concern reflects the assumption that different animal depression models are essentially measuring the same psychopathological parameters. According to this view, if animals score highly on one depression model, the same an-

imals should score highly on a second model. This assumption may be unwarranted. Symptomatology between depressive patients varies considerably. It is also unreasonable to assume that the mechanisms that mediate one aspect of depressive behavior will also be the same mechanisms that govern another different aspect of depression.

A second approach in animal studies of depressive behavior has focused on genetic studies. This approach may have been prompted by studies that revealed significant strain differences in response to stress-induced behavioral deficits, thereby indicating that genetic factors significantly influence reactivity to stress (32,34). Through selective breeding some investigators have developed rat strains that exhibit responses that model depressive behaviors (12,17). The typical strategy involves observing the responses of these strains in behavioral tests that mimic the vegetative symptoms of the Diagnostic and Statistical Manual, 3rd ed. (DSM-III) criteria for depression. However, there are no animal strain studies in which animals have been observed on multiple tests of depressive behavior.

Recently we reported that Wistar Kyoto (WKY) rats manifested several behaviors that were suggestive of depression. As compared to several other strains, WKY rats are motorically depressed in the open field test, reveal an escape deficit following

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unavoidable shock (i.e., learned helplessness), demonstrate immobility in the forced swim test (19), rapidly acquire a passive avoidance response (25), and freeze in the conditioned defensive burying test (22). The fact that WKY rats are susceptible to restraint-induced stress ulcer (19–21) and also reveal significantly higher levels of adrenocorticotrophic hormone in response to restraint stress (24) suggest that WKY rats are hyperresponsive to stress stimulation. The antidepressant, desipramine, reduced immobility in the forced swim test and also reduced the incidence of stress ulcer in WKY rats (23).

Studies using animal genetic models of depression have not exposed the same animals to multiple tests of depression. Similarly, in most of our studies, WKY rats were exposed to only one task. Given that the genetic factors influence reactivity to stress, it is reasonable to assume that if WKY rats are judged as depressed on one test, then these same animals would be judged as depressed on a second test of depression. While we suggested above that such an analysis might be unwarranted in an unselected rat strain, it is possible that this relationship may be revealed in a strain that is hyperresponsive to stress stimulation.

To investigate this hypothesis, we exposed WKY and Wistar rats to four behavioral tests. These included the open-field test (OFT), shuttlebox escape responding following unavoidable shock, that is, learned helplessness (LH), the Porsolt forced-swim test (FST), and the defensive burying test (DB). The first three tests reveal behaviors that suggest depressive behavior. With regard to DB, we have suggested that freezing behavior in that test reflects depressive behavior (22). All rats were exposed to all four test in a semirandom fashion to control for sequence effects. Following the four tests, all rats were subjected to the water-restraint ulcerogenic procedure. The Wistar strain was chosen as a comparison strain because these rats are not ulcer prone (20,22,25) and are probably less reactive to stress stimulation. The study tested the hypothesis that WKY rats, as compared to the Wistar rats, would score highly on all the tests of depressive behavior and would also be more susceptible to the ulcerogenic procedure.

## METHOD

### Subjects

The study used 24 male WKY rats and 24 male Wistar rats. The WKY rats were provided by Taconic Farms (Germantown, NY) from their outbred line of WKY rats. The Wistar rats were acquired from Charles River Laboratories (Kingston, NY). Rats were housed in our animal facility with ad lib food and water and daylight conditions maintained between 0600 and 1800 h. Rats were 85–95 days old at the beginning of the study.

### Apparatus

*The open-field arena.* This unit was designed after the unit described by Broadhurst (7). The arena was round with a diameter of 82 cm. The circular wall was 30 cm high and was constructed of aluminum sheeting. The arena was situated on a plywood floor. The floor and the wall were painted with black enamel paint. The arena floor was divided by three concentric circles. The smaller inner circle had a diameter of 20 cm; the second circle had a diameter of 50 cm, and the outside circle was defined by the arena wall. Each circle was divided into essentially equal size areas. The number of areas in the inner, middle, and outer circles were 1, 6, and 12, respectively. A ceiling light was situated 132 cm above the arena floor. Five 100-watt bulbs were mounted in the ceiling and served as the illumination for the arena. Cheese cloth was draped from the ceiling and dropped outside the arena wall. The cloth served to diffuse the light and functioned as a one-way screen.

*Learned helplessness equipment.* The inescapable shock cage consisted of a 14 × 17 × 11 cm Plexiglas cage. The rat's tail extended through the rear door and was taped to a Plexiglas rod. The shock source was a Lafayette shock generator, Model 82400. Shock was applied to the tail via two silver electrodes attached with adhesive tape and augmented with electrode paste.

Avoidance/escape training was conducted in a Coulbourn Instruments two-way shuttlebox, Model E10-16, with two adjacent compartments measuring each 18 × 21 × 16 cm. An opening, measuring 11 × 8.5 cm was located in the wall that separated the two compartments. The floor of the shuttlebox consisted of stainless steel rods 0.35 cm in diameter and spaced 1 cm apart. Scrambled shock was provided by a Grason Stadler Model E1064GS shocker-scrambler.

The shock cage and the shuttlebox were both housed in separate sound-attenuated chambers measuring 70 × 53 × 50 cm. The chambers were illuminated by a single 100-watt bulb located at the top of the rear wall. A background 72 dB noise produced by a Grason Stadler Model 901B noise generator served as a masking noise in these enclosures.

*Forced-swim apparatus.* This test used a glass water tank which was 30 cm in diameter and 45 cm tall. The water level was 15 cm from the top. Water temperature was maintained at 25°C.

*Defensive burying.* This apparatus consisted of a clear Plexiglas chamber 45 cm long, 30.5 cm wide, and 45 cm high. The floor was covered with corn cob bedding to a depth of 5 cm. A plastic rod 0.8 cm in diameter and 7 cm long served as the shock prod. Two wires were wrapped around the prod and delivered the 4.0 mA shock generated by the Model E1064 GS Grason Stadler shock generator. The prod protruded from the center of one wall and was 3 cm above the floor bedding. The rod could be removed during habituation and the opening was covered with a 8 × 9 cm piece of plastic. The entire apparatus was illuminated by a 90-watt bulb located 72 cm above the center of the apparatus. The rat was observed in this box from the adjoining room through a one-way mirror.

*Water restraint.* The restraining device for the water immersion procedure (18) was fabricated from PVC tubing 23 cm long and 7.7 cm in diameter (inside dimensions). The tubes had four rows of 1 cm holes drilled through the length of the tube. Once the animal was in the tube, it was closed with a piece of hardware cloth at one end and two bolts at the other end. Tubes were placed in 18.5°C water and suspended so that the water surface was level with the rat's neck.

### Procedure

The rats were housed in single cages 1 week before the beginning of the study. Each rat was tested with all four tasks, but the test sequence was randomized to control for possible test sequence effects. There were 24 possible test sequence combinations. One rat from each strain was assigned to each of these combinations. No two rats, within a strain, were exposed to the same test sequence. With this design, six rats from each strain were tested at any one time on each of the four tasks. The procedures for each test are described below.

*Open-field testing.* The single cage, with the rat inside, was transported to the open-field testing room. Rats were individually placed in the inner circle. Four behaviors were recorded: latency (in s) to leave the inner circle, number of field segments entered, number of rearings, and the number of fecal boluses. The trial lasted 5 min, after which time the rat was returned to its home cage. The arena was wiped with soap and water between each trial.

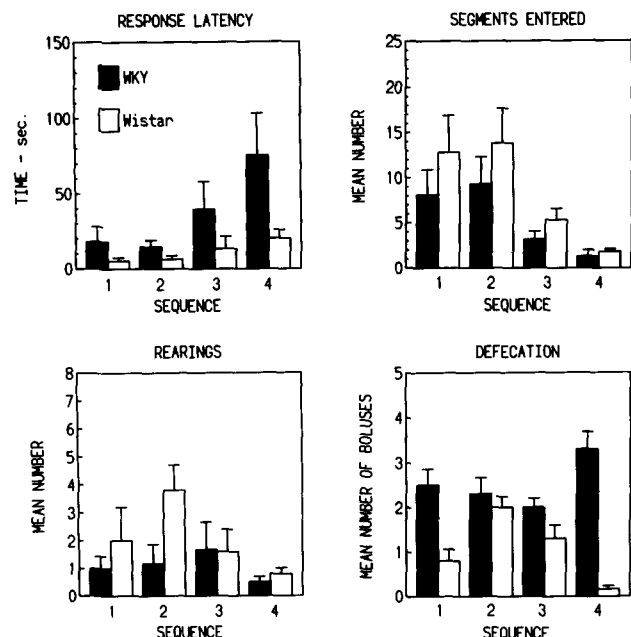


FIG. 1. Means ( $\pm$ SE) for the four dependent variables recorded in the open-field test (OFT) for WKY ( $n = 24$ ) and Wistar ( $n = 24$ ) rats. The behaviors recorded included latency (s) to leave the start area, number of segments entered, number of rearings, and the fecal boluses deposited in the field. The OFT was presented as either the first, second, third, or fourth test within the test battery sequence for each of four subgroups ( $n = 6$ ) within each strain.

**Learned helplessness.** The LH paradigm was adopted from Drugan and his colleagues (9,11). Rats were individually placed in the shock cages and presented with 80 unavoidable 1-s tail shocks on a VI 1-min schedule. Shock intensity was 1.0 mA for shocks 1–35, 1.5 mA for shocks 36–55, and 2.0 mA for shocks 56–80. Twenty-four hours later rats were tested for escape performance in the two-way shuttlebox. Rats were individually placed in the shuttlebox and given a 5-min adaptation period. Thirty trials were administered. A trial was initiated by the onset of a 200 Hz 75 dB tone. Five seconds after tone onset, a 1.5 mA scrambled shock was presented and was terminated when the rat made the appropriate response. For trials 1–5, shock and tone termination required only a single crossing (FR1), but for trials 6–30, the rat had to cross from one side of the shuttlebox to the other side, and then return to the original side (FR2) to terminate the shock and the tone. A trial was terminated after the rat made the appropriate response or 35 s after tone onset. The intertrial interval averaged 45 s with a range of 10–80 s. Response latencies (in s) and response failures (no response within 35 s) were recorded after each trial.

**Forced-swim test.** Rats were individually placed in the water tank and three behaviors were recorded. These included the amount of time spent floating, the number of headshakes, and the number of bobbings. These behaviors were defined as follows: headshakes—shaking head and breaking water surface; bobbing—paddling with forepaws, and/or rear paws with head moving above and below water surface; floating—motionless without moving front or rear paws. Animals remained in the water for 15 min during which time these three behaviors were recorded. Rats were subsequently returned to their home cages.

**Defensive burying.** This was an abbreviated 2-day procedure from one previously reported (22). On the first day, rats in groups of three were placed in the test chamber. The shock prod had

been removed. On the second day the prod was installed in the chamber and activated with a 4 mA shock. Each rat was individually placed in the test chamber. A trial started when the rat touched the prod and a trial lasted 12 min. Data collected included: a) latency to the first DB response, b) the number of DB response, and c) the duration of the DB responses. A DB response was defined as a stereotype response whereby, following prod shock, the rat would quickly retreat to the back of the cage and subsequently, while facing the prod, would start to push, with snout and forepaws, bedding towards the prod. This behavior typically persisted until the prod was covered with bedding materials.

At least 3 days intervened for each rat between the end of one test and the beginning of the next test in the sequence.

**Water-restraint stress.** One week after the fourth and last test, all rats were exposed to the water-restraint ulcerogenic stressor. This procedure is described in detail elsewhere (18). Briefly, rats were food deprived for 24 h and then exposed to water-restraint for 2 h. A 2-h rest period followed before the rats were killed with CO<sub>2</sub> and stomachs removed and inspected for ulcers. The cumulative size of ulcers served as the ulcer severity score.

Strain differences in ulcer were analyzed using a Student's *t*-test. The dependent variables for all the other behavioral tests were analyzed using a two-factor ANOVA design with strain (two levels) comprising one factor, and sequence (four levels) contributing the second factor. To explore the relationship between the behaviors on the various tests, those variables that yielded significant differences between strains were subjected to a correlational procedure using a Pearson Product Moment Correlational Analysis.

## RESULTS

### Open-Field Test

The results of this test are illustrated by Fig. 1. An analysis of the response latency data revealed a significant difference for the main effect of strain,  $F(1, 40) = 5.98, p < 0.01$ . This difference was attributable to the significantly slower response latency measures recorded by the WKY rats. The same analysis disclosed that response latencies increased as a function of test sequence,  $F(3, 40) = 3.08, p < 0.05$ . Thus, rats that received the OFT early in the sequence responded faster than rats which received the OFT late in the sequence. Similar results emerged for the activity measure, segments entered. Wistar rats were more active than WKY rats,  $F(1, 40) = 5.91, p < 0.01$ , and activity diminished when the OFT occurred later in the sequence,  $F(3, 40) = 3.89, p < 0.05$ . The rearing scores also reflected the strain activity pattern. Wistar rats executed significantly more rearing responses,  $F(1, 40) = 3.59, p < 0.05$ , but a significant sequence effect did not emerge with this response,  $F(3, 40) = 2.08, NS$ . WKY rats recorded higher defecation scores as compared to Wistar rats,  $F(1, 40) = 11.19, p < 0.01$ . The main effect of sequence was not significant,  $F(3, 40) = 0.30$ . These data would suggest that, according to the OFT, WKY rats would be judged as more emotional than Wistar rats.

### Learned Helplessness

The response latency scores for the FR2 trials and the response failure data are shown in Fig. 2. These data indicated that LH was more prevalent in WKY rats. Escape response latency scores were significantly longer for WKY rats,  $F(1, 40) = 8.93, p < 0.01$ , and the number of escape response failures was significantly greater for WKY rats,  $F(1, 40) = 5.50, p < 0.01$ . The analysis of these data did not reveal significant sequence effects.

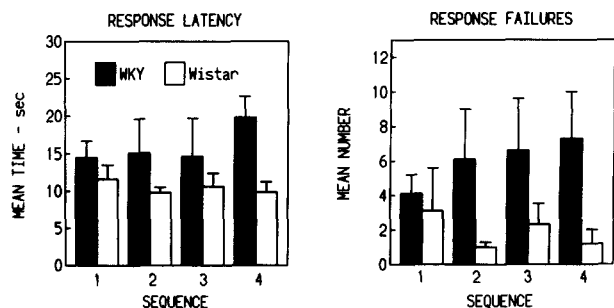


FIG. 2. Means ( $\pm$ SE) for the two dependent variables recorded in the learned helplessness (LH) task for WKY and Wistar rats. Behaviors recorded included avoidance/escape response latency (s) and the number of response failures (not emitting the FR2 response within the 35-s criterion limit). The LH task was presented in a semirandom sequence for each of four subgroups.

### Forced-Swim Test

The three behaviors recorded in the FST are illustrated by Fig. 3. WKY rats were significantly more immobile, and this is reflected by the significant main effect of strain for the floating time scores,  $F(1, 40) = 11.39$ ,  $p < 0.01$ . The difference in floating time scores between the two strains diminished as a function of sequence. A significant strain  $\times$  sequence interaction,  $F(3, 40) = 3.85$ ,  $p < 0.05$ , indicated that the difference in floating time scores between the two strains diminished from the first to the third test sequence. An analysis of the headshake data failed to reveal any significant effects. However, Wistar rats emitted significantly more bobbing responses as compared to WKY rats,  $F(1, 40) = 4.32$ ,  $p < 0.01$ .

### Defensive Burying

WKY rats were significantly more immobile in the DB task. This was reflected by the long response latency scores recorded by WKY rats,  $F(1, 40) = 48.67$ ,  $p < 0.01$ . WKY rats took significantly longer before initiating a DB response and most WKY rats never emitted a DB response. Although response latency increased in Wistar rats as the sequence progressed, this pattern was not significant [strain  $\times$  sequence interaction,  $F(3, 40) = 2.34$ ,  $p > 0.05$ ]. The propensity of WKY rats not to engage in DB was also reflected in the other two behaviors recorded for this task. Response duration was significantly less for WKY rats,  $F(1, 40) = 14.93$ ,  $p < 0.01$ , and the number of DB responses was also significantly less for WKY rats,  $F(1, 40) = 35.85$ ,  $p < 0.01$ . These data are illustrated by Fig. 4.

### Restraint Ulcer

The mean ( $\pm$ SE) ulcer severity scores (i.e., cumulative ulcer size in mm) for WKY rats ( $13.77 \pm 1.73$  mm) significantly exceeded the comparable score for Wistar rats ( $2.70 \pm 0.22$  mm),  $t(46) = 6.45$ ,  $p < 0.01$ .

### Correlational Analysis

Of the 13 dependent variables recorded in this study, six were selected for the purpose of investigating the relationship between the four tasks observed. The variables selected represented those that provided significant differences between the two strains on each task. Accordingly, the responses selected included response latency and segments entered in the OFT, floating time from the FST, escape latency and responses failures from the LH test,

and response latency in the DB task. Cumulative ulcer length was not included in this analysis because the restraint stress procedure was administered as the last testing event for all rats and, thus, differed from all the other tasks that had been randomly scheduled throughout the experiment.

The correlation between the response pairs were achieved by Pearson Product Moment Correlational Analysis. A correlation was provided for each strain. Therefore, the analysis of each response pairing produced a correlation for WKY rats and a correlation for Wistar rats. The correlations so derived are presented in Table 1. All rats were not combined to produce only one correlation between each response pairing because it became obvious that WKY and Wistar rats represented two different populations.

An inspection of Table 1 reveals significant correlations for both strains between the two OFT measures, but this simply reflects the fact that the two responses are related through the test procedure. Thus, rats that quickly leave the start segment (i.e., low response latency scores) will usually have more time to explore (i.e., a high segments entered score), and this relationship is the basis for the negative correlation between these two variables for both WKY and Wistar rats. The same task relationship is also noticeable for the two LH responses. The positive correlations for both strains simply reflect the fact that rats with high escape latency time scores were also the same animals that failed to execute the appropriate escape response within the 35 s time limit.

The more important correlations were those generated between tests. Both OFT variables failed to correlate significantly with any of the other variables except the negative correlation ( $r = -0.68$ ) for WKY rats between the OFT activity measure (segments entered) and the DB latency measure. This correlation implies that inactivity for WKY rats in the OFT is related to long response latency scores in the DB task. The FST and the

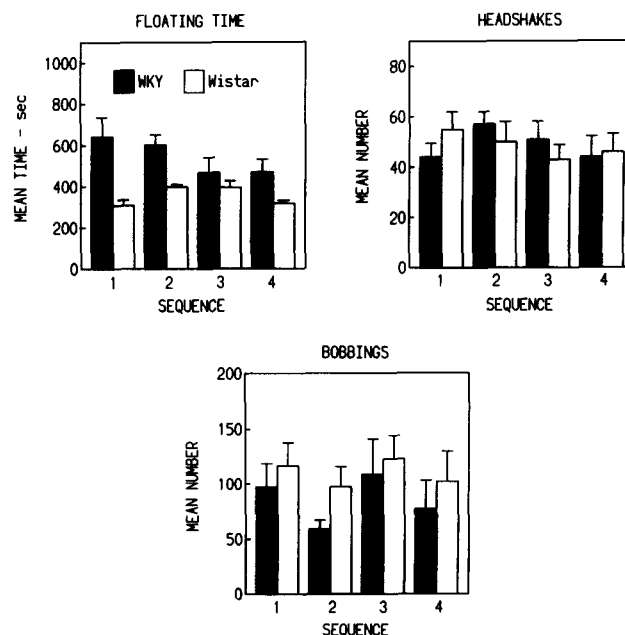


FIG. 3. Means ( $\pm$ SE) for the three dependent variables recorded in the forced-swim test (FST) for WKY and Wistar rats. Behaviors recorded included floating time (s), number of headshakes, and number of bobbings. The FST was presented in a semirandom sequence.

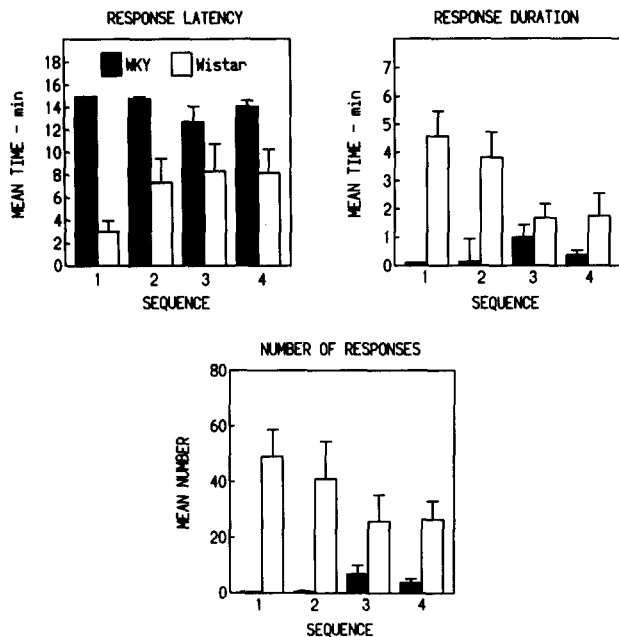


FIG. 4. Means ( $\pm$ SE) for the three dependent variable recorded for the defensive burying (DB) test for both WKY and Wistar rats. Behaviors recorded included latency to initiate the DB response (min), cumulative duration of the DB responses (min), and number of DB responses. A DB trail lasted 15 min. The DB test was presented in a semirandom sequence for subgroups of Wistar and WKY rats.

LH test produced significant correlations, but only for WKY rats. Thus, floating-time behavior was positively correlated to escape latency ( $r = 0.64$ ,  $p < 0.01$ ) and response failures ( $r = 0.59$ ,  $p < 0.01$ ). This suggests that rats judged as exhibiting depressive behavior in the FST will have a high probability of

TABLE 1

PEARSON PRODUCT MOMENT CORRELATION COEFFICIENTS BETWEEN OPEN FIELD, PORSOLT, LEARNED HELPLESSNESS, ND DEFENSIVE BURYING TASKS

		Variables				
		2	3	4	5	6
Open field						
1. Response latency	Wistar	-0.44	0.18	-0.03	-0.08	0.31
	WKY	-0.38	0.11	0.15	0.05	0.14
2. Segments entered	Wistar		-0.17	0.27	0.19	0.09
	WKY		-0.26	-0.13	-0.05	0.68
Forced-swin test						
3. Floating time	Wistar			0.17	-0.20	-0.10
	WKY			0.64	0.59	0.36
Learned helplessness						
4. Escape latency	Wistar				0.69	0.32
	WKY				0.78	-0.04
5. Response failures	Wistar					0.14
	WKY					-0.08
Defensive burying						
6. Response latency						

$p < 0.05$  ( $df = 22$ ), one-tail test requires  $r > 0.32$ .

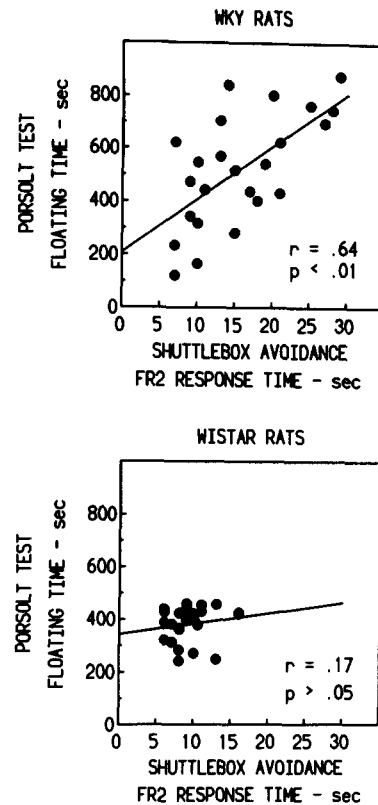


FIG. 5. Floating time scores from the FST test plotted against the shuttlebox FR2 avoidance time from the LH test for WKY rats (upper panel) and Wistar rats (lower panel). Pearson Product Moment Correlational Coefficients are presented for both strains.

being similarly judged when tested with the LH test. However, this relationship prevailed only for the WKY, not Wistar rats. The relationships between floating time in the FST and response time in the LH procedure, for both strains, are illustrated by Fig. 5. These two scatterplots illustrate the presence of a relationship for WKY rats, but the absence of a relationship for Wistar rats. These two plots also support our argument for declining to combine both strains for the purpose of generating a single correlational coefficient between pairs of variables.

Floating time scores also correlated significantly, to a lesser degree, with the DB measure, and again this relationship was observed only with WKY rats ( $r = 0.36$ ,  $p < 0.05$ ).

#### DISCUSSION

A review of the results provides confirmation of findings previously reported with WKY rats. It had already been reported that WKY rats are more immobile in the OFT, record higher floating scores in the FST (19), readily adopt a LH response (19,34), and freeze in the DB test (22). The WKY's susceptibility to stress ulcer has been frequently reported (4,19,20,33), and other responses that suggest heightened emotionality in this strain have also been recorded (6,8,14,15,29). In this regard, this experiment does not present any new information. However, the value of the present study resides in the fact that multiple behavioral measures were obtained from the same animals, thereby allowing us to investigate possible relationships between these behavioral tests. The correlational analysis indicated that no relationship existed between the OFT and either LH or the FST.

Thus, immobility in one measure did not necessarily imply immobility in the others. These data agree with other investigators (2,5,26) who have reported that activity in the OFT and the FST are controlled by different mechanisms. The most interesting outcome was the positive correlation, for WKY rats only, between the FST and the two behaviors recorded for the LH procedure. These data imply that WKY rats that scores highly on depressive behavior in one of these models of depression would also have a high probability of scoring highly on depressive behavior in the second model of depression. These results do not agree with a study by Drugan and colleagues (11) which failed to demonstrate any relationship between LH and the FST. But Sprague-Dawley rats were used in the Drugan study and their negative results agree with the nonsignificant correlations that we recorded with our Wistar rats. However, the addition of a critical factor, a stress-susceptible strain (in our case, WKY rats), produced a positive relationship between the two depression models. It would appear that the use of WKY rats represents a more sensitive organism for examining the relationship between the two tests. It is also interesting that the FST also correlated positively with the latency measure from the DB task. This provides partial support for our earlier study wherein we proposed that the absence of DB, or freezing, behavior in WKY rats "... is another demonstration of this strain's predisposition to depressive behavior ..." [(22), p. 1055]. Unlike the FST, the LH measures failed to correlate with DB. The absence of a relationship here would be critical if depressive behavior were controlled by a solitary mechanism. However, Shanks and Anisman (32) warn that the use of unitary explanations that focus on a single mechanism may be counterproductive in understanding the processes associated with stress-induced behavioral deficits.

The strategy of presenting the four tests in a semirandom sequence to control for presentation effects, produced a few minor effects. There was a tendency towards hypoactivity as tests progressed from the first to the fourth test. However, this sequence effect was significant only with the OFT. When the OFT

was presented as the third or fourth test in the sequence, inactivity increased. Rats were more active in the OFT if that test was presented either as the first or second task in the test sequence. One interpretation of this effect is that the OFT may have been functioning as a measure of cumulative stress. One would expect that repeated handling, from test to test, would produce some habituation, but because each of the four tests presented different stimulus characteristics, this may have produced an unpredictable situation and, consequently, prevented habituation. The possibility of stressor unpredictability may have led to chronic stress in a fashion similar to that observed with chronic stress experimental techniques [see Katz et al. (13)]. Thus, it is possible that the OFT may have been measuring the cumulative stressor reactivity that developed as a function of the number of test experiences. If response latency in the OFT did, indeed, reflect such a process, it is interesting to note that the effect was more emphatic in the hyperactive WKY strain.

An initial reaction to the results of the sequential test strategy was that the freezing behavior of the WKY rats increased as subsequent tests were administered. In the OFT and the LH tests, hypoactivity increased as successive groups of WKY rats were tested. This process was not observed with the DB test, but a ceiling effect with these data may have prevented such an effect to emerge. The suggestion here is that WKY rats may be disproportionately susceptible to chronic stress. This is a suggestion that warrants further study.

The present study provided the following information. It confirmed previous reports concerning the behavior of WKY rats in the OFT, the LH paradigm, the FST, and the DB test. It also provided one more report of the WKY's greater susceptibility to stress ulcer. The most significant outcome was the demonstration that behaviors in the FST and the LH paradigm—two animal models of depressive behavior—were positively correlated, but only in the stress-susceptible WKY strain. These results underline the value of genetic factors in the study of depression and suggest that the WKY strain may be a useful rat strain for studying depressive behavior.

## REFERENCES

- Alentor, A.; Volpicelli, J. R.; Seligman, M. E. P. Debilitated shock escape is produced by both short- and long-duration inescapable shock. *Bull. Psychon. Sci.* 14:337-339; 1979.
- Alonso, S. J.; Castellano, M. A.; Afonso, D.; Rodriguez, M. Sex differences in behavioral despair: Relationship between behavioral despair and open field activity. *Physiol. Behav.* 49:69-72; 1991.
- Anisman, H.; deCantazaro, D.; Remington, G. Escape performance following exposure to inescapable shock: Deficits in motor response maintenance. *J. Exp. Psychol. [Animal Behav.]* 4:197-218; 1978.
- Athey, G. R.; Iams, S. G. Cold-restraint induced gastric lesions in normotensive and spontaneously hypertensive rats. *Life Sci.* 28:889-894; 1981.
- Barrett, R. S.; Ray, O. S. Behavior in the open field, Lashley III maze, shuttlebox, and Sidman avoidance as a function of strain, sex and age. *Dev. Psychol.* 3:73-77; 1970.
- Berger, D. F.; Starzic, J. J. Contrasting lever-press avoidance behaviors of spontaneously hypertensive and normotensive (*Rattus norvegicus*). *J. Comp. Psychol.* 102:279-286; 1988.
- Broadhurst, P. L. Determinants of emotionality in the rat. I Situational factors. *Br. J. Psychol.* 48:1-12; 1957.
- Cierpial, M. A.; Shasby, D. E.; Murphy, C. A.; et al. Open-field behavior of spontaneously, hypertensive and Wistar-Kyoto Normotensive rats: Effects of reciprocal cross-fostering. *Behav. Neurol. Biol.* 51:203-210; 1989.
- Drugan, R. C.; Maier, S. F.; Skolnick, P.; Paul, S. M.; Crawley, J. N. An axiogenic benzodiazepine receptor ligand induced learned helplessness. *Eur. J. Pharmacol.* 113:453-457; 1985.
- Drugan, R. C.; Ryan, S. M.; Maier, T. R.; Maier, S. F. Librium prevents the analgesia and shuttlebox deficit typically observed following inescapable shock. *Pharmacol. Biochem. Behav.* 21:749-754; 1984.
- Drugan, R. C.; Skolnick, P.; Paul, S. M.; Crawley, J. N. A pretest procedure reliably predicts performance in two animal models of inescapable stress. *Pharmacol. Biochem. Behav.* 33:649-654; 1989.
- Henn, F. A.; Johnson, J.; Edwards, E.; Anderson, D. Melancholia in rodents: Neurobiology and pharmacology. *Psychopharmacol. Bull.* 21:443-446; 1985.
- Katz, R. J.; Roth, K. A.; Carroll, B. J. Acute and chronic stress effects on open field activity in the rat: Implications for a model of depression. *Neurosci. Biobehav. Rev.* 5:247-251; 1981.
- Knardahl, S.; Sagvolden, T. Open-field behavior of spontaneously hypertensive rats. *Behav. Neurol. Biol.* 27:187-200; 1979.
- Leaton, R. N.; Cassella, J. V. Locomotor activity, auditory startle and shock thresholds in spontaneously hypertensive rats. *Physiol. Behav.* 31:103-109; 1983.
- Maier, S. F.; Albin, R.; Testa, T. J. Failure to escape in rats previously exposed to inescapable shock depends on the nature of the escape proliferation. *J. Comp. Physiol. Psychol.* 85:581-592; 1973.
- Overstreet, D. Selective breeding for increased cholinergic function: Development of a new animal model of depression. *Biol. Psychiatry* 21:49-58; 1986.
- Paré, W. P. A comparison of two ulcerogenic techniques. *Physiol. Behav.* 44:417-420; 1988.

19. Paré, W. P. Stress ulcer susceptibility and depression in Wistar Kyoto (WKY) rats. *Physiol. Behav.* 46:993-998, 1989.
20. Paré, W. P. Strain, age, but not gender, influence ulcer severity induced by water-restraint stress. *Physiol. Behav.* 45:627-632; 1989.
21. Paré, W. P. Technique and strain comparisons in stress ulcer. *Ann. NY Acad. Sci.* 597:223-230; 1990.
22. Paré, W. P. The performance of WKY rats on three tests of emotional behavior. *Physiol. Behav.* 51:1051-1056; 1992.
23. Paré, W. P. Learning behavior, escape behavior and depression in an ulcer susceptible rat strain. *Integrat. Physiol. Behav. Sci.* 27:130-141; 1992.
24. Paré, W. P.; Redei, E. Depressive behavior and stress ulcer in Wistar-Kyoto rats. *J. Physiol. (Paris)* 87:229-238; 1993.
25. Paré, W. P. Passive-avoidance behavior in Wistar Kyoto (WKY), Wistar and Fischer-344 rats. *Physiol. Behav.* 55(5): 845-852; 1993.
26. Plaznik, A.; Kostowski, W. Modification of behavioral response to intra-hippocampal injections of noradrenaline and adrenoceptor agonists by chronic treatment with desipramine and citalopram: Functional aspects of adaptive receptor changes. *Eur. J. Pharmacol.* 117:247-252; 1985.
27. Porsolt, R. D.; Anton, G.; Blau, N.; Jalfre, M. Behavioral despair in rats: A new model sensitive to antidepressant treatment. *Eur. J. Pharmacol.* 47:379-391; 1978.
28. Porsolt, R. D.; LePichon, M.; Jalfre, M. Depression: A new animal model sensitive to antidepressant treatments. *Nature* 266:730-732; 1977.
29. Rosenwasser, A. M.; Plante, L. Circadian activity rhythms in SHR and WKY rats: Strain differences and effects of clonidine. *Physiol. Behav.* 53:23-29; 1993.
30. Seligman, M. E. P. *Helplessness: On depression, development and death.* San Francisco: Freeman; 1975.
31. Seligman, M. E. P.; Beagley, G. Learned helplessness in the rat. *J. Comp. Physiol. Psychol.* 88:534-541; 1975.
32. Shanks, N.; Anisman, H. Stressor-provoked behavioral changes in six strains of mice. *Behav. Neurosci.* 102:894-905; 1988.
33. Shichijo, K.; Sekine, I.; Nishimori, I.; Ozaki, M. Experimental stress ulcer and gastric catecholamine contents in spontaneously hypertensive rats. *Gastroenterol. Jpn.* 21:567-572; 1986.
34. Wieland, S.; Boren, J. L.; Consroe, P. F.; Martin, A. Stock differences in the susceptibility of rats to learned helplessness training. *Life Sci.* 39:937-944; 1986.
35. Willner, P. The validity of animal models of depression. *Psychopharmacology (Berlin)* 83:1-16; 1984.