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# Environmental Enrichment and Isolation Rearing in the Rat: Effects on Locomotor Behavior and Startle Response Plasticity

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**Background:** *Laboratory rats exhibit behavioral changes that reflect a continuum of early life experience, from isolation-reared to socially reared to enrichment-reared conditions. In this study, we further characterize the behavioral effects of isolation, social, and enriched rearing on locomotor activity, patterns of movement and exploration, startle reactivity, prepulse inhibition (PPI), and habituation in adult rats.*

**Methods:** *Male Sprague-Dawley rat pups (21 days old) were housed under enrichment (three per cage with toys and exposure to enriched environments), normal social (three per cage), or isolation (one per cage) conditions. Eight weeks later, locomotor and exploratory behaviors, acoustic startle reactivity, PPI, and habituation were measured in the three groups.*

**Results:** *Enrichment-reared rats exhibited reduced exploration and rapid habituation of locomotor activity, increased startle reactivity, and normal PPI and startle habituation compared with socially reared controls. Isolation-reared rats exhibited increased exploration and normal habituation of locomotor activity, increased startle reactivity, reduced PPI, and normal startle habituation.*

**Conclusions:** *Isolation- and enrichment-reared rats exhibited opposite changes in some behaviors and similar changes in other behaviors. Specifically, rats raised in enriched conditions appear more efficient at assimilating stimuli from their environment than do rats reared in isolation. Nevertheless, both enrichment- and isolation-rearing conditions increased startle reactivity, whereas only isolation rearing led to disruptions of PPI in adulthood. These results suggest that isolation- and enrichment-rearing conditions produce some common and some differential effects on how rats process environmental stimuli. For studies of isolation-rearing effects on PPI, however, the complex and resource-intensive enrichment condition seems to offer few advantages over the normal social condition. Biol Psychiatry 2000;47:864–873 © 2000 Society of Biological Psychiatry*

**Key Words:** Development, rat, behavior, locomotion, prepulse inhibition, schizophrenia

## Introduction

The development of an animal is influenced by environmental factors, including the amount and quality of contact with other animals (the social environment) and other external environmental factors. To examine the influence and interaction of environmental and developmental factors on behavior, neurochemistry, and neuroanatomy, rats reared under enriched environmental conditions have been compared with those reared in an impoverished environment, usually under conditions of social isolation from other rats. In this context, environmental enrichment involves rearing animals in a socially and physically stimulus-rich environment. Typically, for rats, this enrichment involves housing them in groups to increase social contact and adding stimulating, novel objects into the immediate environment. In contrast, isolation rearing involves raising rats under conditions of isolation—housed singly in a cage from the time of weaning and throughout adulthood. These enriched and isolated conditions are relevant to a spectrum of important issues that relate to the early experiences of mammals and their subsequent neurodevelopment, behavior, and (in humans) potential psychopathologic states.

In comparative studies of behavior and other factors, environmental enrichment-reared and isolation-reared rats displayed profiles at opposite ends of the behavioral spectrum:

1. Enriched-reared rats exhibited enhanced learning compared with socially reared controls in a number of cognitive tasks, whereas isolation-reared rats were impaired in their learning performance (Gardner et al 1975; Park et al 1992; Smith 1972).
2. Enrichment-reared rats displayed reduced locomotor activity, whereas isolation-reared rats were hyperac-

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tive (Bowling et al 1993; Van Waas and Soffié 1996).

3. In a conditioned place-preference task, enrichment-reared rats were more sensitive to the reinforcing effects of amphetamine (Bowling et al 1993), whereas isolation rearing reduced amphetamine reinforcement (Wongwitdecha and Marsden 1995).
4. Extending these studies into the anatomic realm, enriched-reared rats had greater brain weight (Huntley and Newton 1972) and cortical enlargement (Diamond et al 1972; Katz and Davies 1984) and increased dendritic branching (Greenough et al 1973; Venable et al 1989; Volkmar and Greenough 1973) relative to isolation-reared rats.

Thus, the overall picture appears to be one in which enriched-reared pups develop certain enhanced structural and functional advantages: larger brains that are associated with superior learning performance compared with their isolation-reared comparison rats.

Despite these differences, enriched-reared and isolation-reared rats have exhibited similar behaviors in other studies: 1) both enrichment- and isolation-reared rats exhibit increased sensitivity to the locomotor-activating and stereotypy-inducing effects of amphetamine compared with normally reared rats (Bowling and Bardo 1994; Jones et al 1992; Sahakian et al 1977) and 2) both enrichment- and isolation-reared rats have increased cortical dopamine, compared with normally reared rats (Jones et al 1992; Saari et al 1990).

Recently, we have studied the behavioral effects of isolation rearing on locomotion and exploration. These constructs are measured by Behavioral Pattern Monitors (BPMs; see Geyer et al 1986 for detailed description), which provide measures of locomotor activity, habituation to the environment, exploration, and the geometric patterns of locomotion. In one early study, isolation rearing induced hyperactivity in Lister Hooded rats, but had no effect in the Sprague-Dawley strain (Geyer et al 1993). A subsequent study found that isolation-reared specimens of both Lister Hooded and Sprague-Dawley rats exhibited reduced habituation; more straight, predictable movement patterns; and less circumscribed motion compared with socially reared rats (Paulus et al 1998).

Additionally, using the acoustic-startle paradigm, we have examined the effects of isolation rearing on startle reactivity to high-intensity acoustic stimuli and on two forms of startle plasticity: habituation and prepulse inhibition (PPI). Habituation is considered to be the simplest form of learning and refers to the progressive reduction in response to an initially novel stimulus when the stimulus is presented repeatedly to a subject. The rate of startle habituation can be manipulated pharmacologically (Geyer and Tapson 1988) and is

reduced in certain psychiatric disorders, such as schizophrenia (Bolino et al 1992; Braff et al 1992; Geyer and Braff 1982). Prepulse inhibition refers to the reduction in the startle response produced by a low-intensity nonstartling stimulus (the prepulse) when it is presented shortly before the startle stimulus (Hoffman and Ison 1980). Prepulse inhibition provides an operational measure of sensorimotor gating that is present across all mammalian species. Patients with schizophrenia and certain other psychiatric disorders, in which sensorimotor gating deficits and sensory overload appear to be fundamental difficulties, exhibit reduced levels of PPI compared with the case of matched controls (Bolino et al 1992; Braff et al 1978, 1992, 1999).

In accordance with neurochemical hypotheses of schizophrenia, pharmacologic manipulations of dopaminergic, serotonergic, or glutamatergic systems disrupt PPI in rats (Geyer et al 1990; Rigdon and Weatherspoon 1992; Sipes and Geyer 1994, 1995; Swerdlow et al 1994). Furthermore, these drug-induced disruptions of PPI are reversed by typical and atypical antipsychotics (Bakshi et al 1994; Swerdlow et al 1994; Varty and Higgins 1995). We demonstrated that isolation-reared rats display deficits in PPI compared with socially reared controls (Geyer et al 1993). Further studies revealed that this effect is developmentally specific in that similar isolation of adult rats had no influence on PPI (Wilkinson et al 1994). Of potential therapeutic importance is that the deficits in PPI in isolation-reared rats are reversed by both typical and atypical antipsychotics (Bakshi et al 1998; Geyer et al 1993; Varty and Higgins 1995). Thus, the isolation-rearing paradigm may provide a nonpharmacologic and developmentally specific method of inducing schizophreniclike behavioral deficits that has potential utility in the screening of novel antipsychotic drugs.

To further understand the effects of developmental manipulations, we directly compared the behavior of rats reared under enrichment-, normal-, and isolation-rearing conditions. Our specific aims were to compare the effects of enriched, normal, and isolation rearing on the following: 1) exploration and spatial patterns of movement in a novel environment; 2) startle reactivity, PPI, and habituation; and 3) the relationship between measures of motor activity and startle plasticity. We hypothesized that enriched- and isolation-reared rats would display behavioral profiles in both the BPM and PPI paradigms that were at opposite ends of the behavioral spectrum, with socially reared rats being intermediate. Confirmation of this hypothesis would indicate that rats reared in enriched conditions provide important information about the behavioral effects of nonpharmacologic developmental manipulations that span enrichment- to normal- to isolation-rearing conditions.

## Methods and Materials

### Subjects and Housing

Sixty-three male Sprague-Dawley rats (Harlan, San Diego), brought in as weaned 21-day-old pups, were used for all studies. Upon arrival at the holding facility, pups were housed randomly, either one per cage (isolation-reared group,  $n = 23$ ) or three per cage (socially reared and enrichment-reared groups,  $n = 20$  per group), in a holding room controlled for both temperature and humidity, with food and water available ad libitum. All cages were  $25 \times 48 \times 20$ -cm plastic cages with corncob bedding. Three novel objects (durable toys manufactured for cats and dogs bought from local pet stores; e.g., different types of colored, textured balls, rings, and bones) were placed into each cage of enriched rats. Objects were replaced with a new set every day and were cleaned at the end of each week. Objects that became damaged were replaced immediately. As well as receiving novel objects in their home cages, enriched rats were placed into one of three complex and changing environments for 1 hour each weekday, throughout the duration of the study. Each of these complex environments contained different interactive stimuli, including climbing frames, exercise wheels, ladders, tubes, toys, and bells. In the enrichment-rearing condition, rat exposure to each environment was conducted in a counterbalanced manner to ensure that all rats were exposed equally to each environment.

In contrast to the handling associated with the enriched conditions, care was taken to ensure that isolation-reared and socially reared rats received minimal handling, which amounted to once a week for cleaning purposes. Thus, the only environmental difference between the isolation-reared and socially reared groups was a lack of social interaction with cage mates in the isolation-reared rats. Rats were in these rearing conditions for 8 weeks before testing began and then remained in them for the duration of the studies. Locomotor behavior was tested at 11 weeks of age, and startle behavior was tested at 12 weeks of age. All rats were held on a 12-hour reversed light/dark cycle (lights off at 7:30 AM and lights on at 7:30 PM), and all testing occurred between 8:30 AM and 4:00 PM.

### Behavioral Pattern Monitor

To measure locomotion, activity patterns, and exploratory behavior, rats were tested in one of eight BPM chambers, as described previously (Geyer et al 1986). Briefly, each BPM consisted of a black Plexiglas box ( $60 \times 30 \times 30$  cm) with a metal floor, housed within an electrically shielded and ventilated wooden chamber ( $112 \times 55 \times 55$  cm). Within the floor were three floor holes, positioned every 15 cm across the length of the center of the floor. Additionally, there were three wall holes positioned every 15 cm along the length of each of the longer walls, 3.5 cm above the floor. A seventh wall hole was positioned 3.5 cm above the floor, in the center of one of the shorter walls. Each of the 2.5-cm-diameter holes was equipped with an infrared photobeam for the detection of hole pokes by the rats. A  $4 \times 8$ , X–Y array of infrared photobeams, placed 2 cm above the floor, was used to define the X–Y position of an animal, with a resolution of 3.8 cm. Rearing behaviors by the rats against the walls of the chamber were detected by a metal touchplate placed

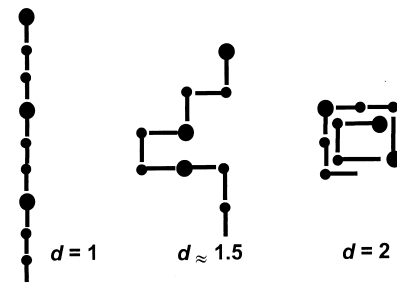


Figure 1. Examples of movement patterns and their approximate spatial  $d$  value. The movement between the examples is quantitatively identical, but each has a different spatial  $d$ .

15 cm above the floor. Every 55 msec a computer sampled the status of all the photobeams and touchplates and stored any changes in patterns of movement and exploration. Data were analyzed across 10-min time bins. All rats were brought to the dark testing room 60 min before testing to acclimatize to the change in environment. Each animal was placed gently into one of the BPM chambers and monitored for 60 min. The chambers were illuminated by 7.5-W red light. Groups were balanced across the BPM chambers to ensure equal exposure to each chamber among the rearing groups. Chambers were cleaned thoroughly between runs.

For the quantitative assessment of spatial patterns of movement sequences, we adopted the scaling hypothesis described by Paulus and Geyer (1993). Briefly, the hypothesis relates the distance traveled between  $k$  microevents to the number,  $k$ , of distinct microevents. From this relationship, patterns of straight movements can be differentiated from circumscribed patterns of movement using the spatial scaling exponent,  $d$ . For example, a  $d$  value of 1 would indicate a perfectly straight, linear pattern of movement, whereas a  $d$  value of 2 would indicate highly circumscribed movement (Figure 1; also, see Paulus and Geyer 1993 for details). The spatial-scaling exponent,  $d$ , was obtained for a segment of 32 consecutive movements. Each movement was divided into three categories: straight movements =  $d < 1.2$ , meandering movements =  $1.2 < d < 1.7$ , and circumscribed movements  $d > 1.7$ . Finally, each movement was categorized according to whether it occurred in the corners, along the short walls, along the long walls, or in the center as defined in Geyer et al (1986). Thus, each movement was categorized by two factors: geometric pattern and location. The frequency of each category was expressed as percentage of total activity. A mixed analysis of variance (ANOVA; within: distribution of  $d$ , location in BPM; between: rearing condition) with Greenhouse–Geisser (GG) corrections for collinearity was used.

### Startle Reactivity, Prepulse Inhibition, and Habituation

Four identical startle chambers were used for measuring startle reactivity and plasticity (SR-LAB system, San Diego Instruments, San Diego). Each chamber consisted of a Plexiglas cylinder (9 cm in diameter) mounted on a frame, supported by four metal pin legs. Sudden movements within the cylinder were

detected by a piezoelectric accelerometer attached directly below the cylinder. A high-frequency loudspeaker mounted 24 cm above the cylinder provided the broadband background noise and acoustic stimuli. An internal 15-W light bulb provided light prepulse stimuli. The whole apparatus was housed in a ventilated chamber (39×38×58 cm). Presentations of the acoustic and light stimuli were controlled by the SR-LAB software and interface system, which also digitized (range, 0–4095), rectified, and recorded responses from the accelerometer. As described elsewhere (Geyer and Swerdlow 1998), sound levels (dB[A] scale) and accelerometer sensitivities within each chamber were calibrated regularly and were found to remain constant over the test period.

The experimental session consisted of a 5-min acclimatization period to a 65-dB background white noise (continuous throughout the session), followed by a 25-min acoustic (20 min) and light (5 min) PPI test session. During the acoustic session, five trial types were presented: a 40-msec, 120-dB startle pulse (P120) and four 20-msec prepulse combinations (set to differing intensities [6 or 12 dB above background noise] and interstimulus intervals [ISI: 100 or 300 msec]; i.e., 6- or 12-dB prepulse before a 100-msec ISI or 6- or 12-dB prepulse before a 300-msec ISI), followed by the P120 stimulus. Trial types were presented in a pseudorandom order (24 presentations of the P120 trial and 12 presentations of each prepulse trial), with an average intertrial interval (ITI) of 15 sec. In addition, six P120 trials were presented at both the beginning (block 1: to familiarize rats to the stimuli) and the end of the acoustic test session (block 2: to separate the acoustic and light PPI sessions). These two blocks of startle stimuli were also used to calculate the amount of acoustic startle habituation (see below). After a 60-sec break at the end of the acoustic test session, the light PPI session began. Startle was measured in response to 12 P120 trials, or 12 trials in which a 100-msec light stimulus was presented immediately before a P120 stimulus. Trials were presented in a random order, with an average ITI of 15 sec.

Mean startle magnitude for each trial-type presentation, the dependent measure, was determined by averaging 100 1-msec readings taken from the onset of the startling stimulus. Startle reactivity was defined as the mean response to the first block of P120 trials. Mean startle response to the P120 trials across both the acoustic and light PPI sessions was also measured. The amount of startle habituation (percentage habituation) was calculated using the formula  $100 - ([\text{mean startle for Block 2}/\text{mean startle for Block 1}] \times 100)$ . The level of PPI (percentage PPI) was determined according to the formula  $100 - ([\text{startle magnitude on acoustic or light prepulse trials}/\text{startle magnitude on P120 trials}] \times 100)$ , such that a 0% value indicated no difference between the responses to prepulse trials and startle trials (i.e., no PPI).

### Data Analysis

Behavioral measures in the BPM, including activity counts, rearing behaviors, hole pokes, and the spatial scaling exponent  $d$ , were analyzed by two-way ANOVA, with rearing condition as the between-subjects factor and with time as the within-subjects factor.

Mean startle reactivity, mean startle magnitudes within the acoustic and light PPI test sessions, and percentage habituation were analyzed by one-way ANOVAs, with rearing condition as the between-subjects factor. Percentage acoustic PPI data was analyzed by a three-way ANOVA, with prepulse intensity and ISI as within-subjects factors and with rearing condition as the between-subjects factor. If there were no significant interactions with intensity and/or ISI, mean percentage acoustic PPI was calculated by collapsing the acoustic PPI over the appropriate prepulse combinations. Mean percentage PPI and percentage light PPI were analyzed by one-way ANOVAs, with rearing condition as the between-subjects factor. When main effects were significant, post hoc analyses were conducted by Tukey's protected  $t$  with an accepted level of significance of  $p < .05$ .

Finally, after the initial ANOVA analyses, selected BPM and startle measures were examined by correlational analyses to determine whether the changes due to rearing conditions were along similar dimensions in the BPM and startle paradigms. Pearson correlation analyses were calculated within each group between activity counts,  $d$ , startle reactivity, and PPI. Bivariate scatterplots were used to ensure that correlation analyses were not affected by the contribution of any abnormal responders and to detect nonlinear relationships. Because few informative correlations were observed, these data are not presented in detail.

## Results

### Locomotor Activity

There were significant main effects attributable to rearing condition [ $F(2,57) = 4.7, p < .02$ ] and time [ $F(5,285) = 379, p < .0001$ ] and to the interaction between rearing condition and time [ $F(10,285) = 3.4, p < .001$ ] on the activity counts measure, indicating that enrichment-reared, socially reared, and isolation-reared rats exhibited differential rates of habituation to the enclosure (Figure 2A). Enrichment-reared rats were significantly less active and habituated faster than did socially reared animals [ $F(1,37) = 6.42, p < .05$ ;  $F(5,190) = 2.39, p < .05$ ]. Isolation-reared rats were not significantly more active than and did not habituate differentially from socially reared rats [ $F(1,38) = 0.14, \text{ns}$ ;  $F(5,190) = 1.90, \text{ns}$ ]. Finally, enrichment-reared rats were significantly less active and habituated significantly faster to the novel environment than did isolation-reared rats [ $F(1,37) = 10.09, p < .01$ ;  $F(5,185) = 6.02, p < .01$ ].

### Locomotor Patterns

Enrichment-reared, socially reared, and isolation-reared rats differed significantly with respect to their patterns of locomotor activity. Specifically, the spatial-scaling exponent,  $d$ , indicating whether the rats engaged in predominantly straight or circumscribed movements, differed significantly among the groups [ $F(2,57) = 7.8, p < .001$ ]. Moreover, there was a significant effect of time

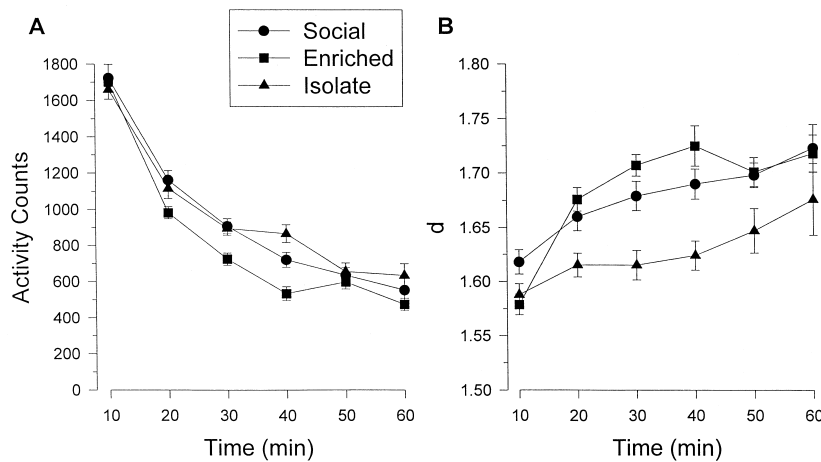


Figure 2. Effects of rearing condition on (A) activity counts and (B) the spatial-scaling exponent, *d*. Values represent mean ± SEM at each time point for each rearing condition.

[ $F(5,285) = 28, p < .0001$ ] and a significant interaction between rearing condition and time [ $F(10,285) = 2.7, p < .01$ ], suggesting that these rats differentially changed their movement patterns over time (Figure 2B). Whereas isolation-reared rats exhibited significantly straighter movements than did socially reared animals, the pattern differences did not result in a differential rate of habituation [ $F(1,37) = 8.47, p < .05$ ;  $F(5,185) = 0.55, ns$ ]. In comparison, isolation-reared rats showed significantly straighter movements, and their movement patterns changed significantly less over time than did those of enrichment-reared rats [ $F(1,37) = 12.51, p < .01$ ;

$F(5,185) = 4.51, p < .01$ ]. In all groups, habituation was characterized by a gradual transition from relatively straight movements to more circumscribed movements.

The proportion of movements in spent in different areas of the BPM was not significantly affected by rearing [ $F_{GG}(3.05,85.42) = 2.07, ns$ ]. Moreover, there was a trend for the rearing to affect the proportion of straight, meandering, or circumscribed movements [ $F_{GG}(3.02,84.6) = 2.30, p < .1$ ]. Finally, there was a trend for the rearing condition to affect the interaction between the proportion of movement patterns initiated in different areas of the BPM [ $F_{GG}(5.86,164.0) = 2.1, p < .1$ ]. As shown in Figure

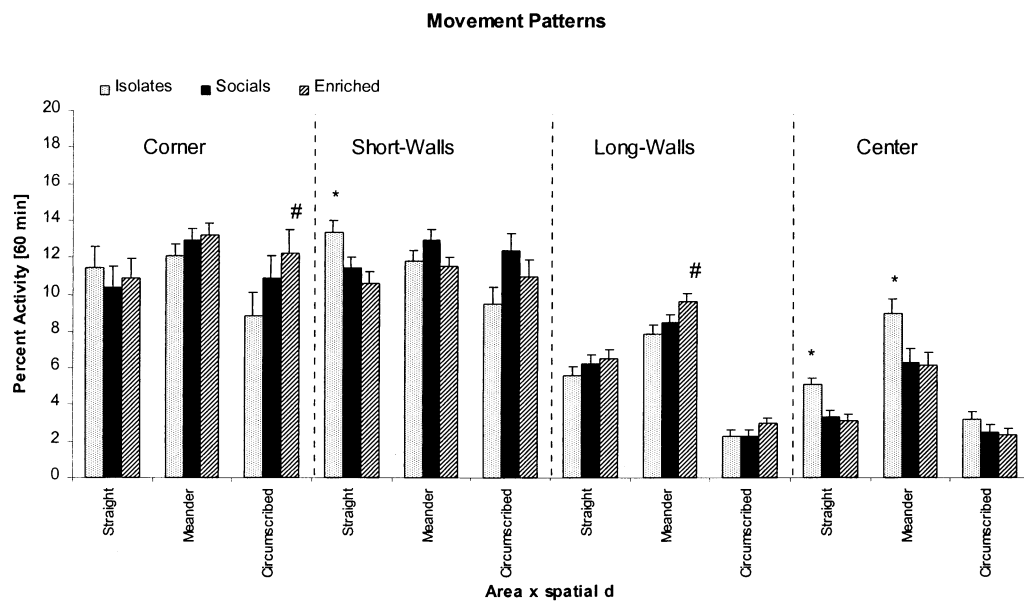


Figure 3. The proportion of different movement patterns initiated by isolation-reared, socially reared, and enrichment-reared rats in the four different areas of the Behavioral Pattern Monitor as group means ± SEM. \*Significant difference between isolation-reared and socially reared or enrichment-reared rats; #significant difference between enrichment-reared rats and isolation-reared or socially reared rats.

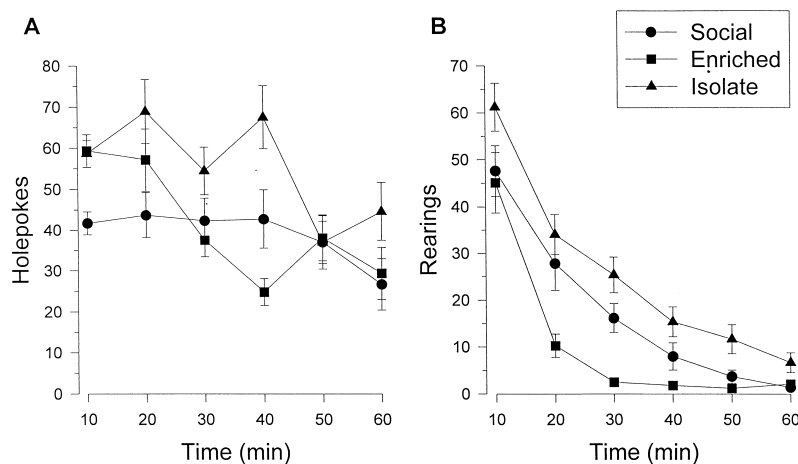


Figure 4. Effects of rearing condition on (A) hole pokes and (B) rearing behavior. Values represent mean  $\pm$  SEM at each time point for each rearing condition.

3, isolates initiated a significantly higher proportion of straight movements from the short walls to the center area than did both socially reared and enrichment-reared rats. In contrast, enrichment-reared rats initiated a higher proportion of circumscribed movements in the corners and along the long walls of the BPM chamber.

#### Exploratory Activity

The effect of rearing condition on hole pokes followed a pattern similar to that observed for the movement patterns of these rats. Specifically, there were significant effects of rearing condition [ $F(2,57) = 5.2, p < .01$ ] and time [ $F(5,285) = 9.8, p < .01$ ] on hole pokes and an interaction between rearing condition and time [ $F(10,285) = 3.6, p < .01$ ], indicating that these rats exhibit different levels of exploratory behavior that habituate at different rates. Compared with socially reared rats, both enrichment- and isolation-reared rats exhibited an increased frequency of hole pokes during the first 10 min in the BPM chamber (Figure 4A). Enrichment-reared rats quickly habituated and exhibited reduced numbers of hole pokes during the remainder of the session. By contrast, isolation-reared rats displayed high levels of hole poking throughout the testing period.

#### Rearing Behavior

The effect of the developmental manipulations on exploratory rearing behavior was similar to that seen with activity counts. There were significant effects of rearing condition [ $F(2,57) = 11, p < .001$ ] and time [ $F(5,285) = 128, p < .0001$ ] on rearing behavior, and there was a significant rearing-by-time interaction [ $F(10,258) = 2.5, p < .01$ ]. Isolation-reared rats displayed a consistently higher level of rearing behavior throughout the test period compared with socially reared and enriched-reared rats.

Although socially reared and enrichment-reared rats had similar levels of rearing in the first 10 min of the session, the two groups differed during the remainder of the test as the enrichment-reared rats quickly habituated to the environment and engaged in minimal amounts of rearing (Figure 4B).

#### Startle Reactivity and Habituation

In the acoustic prepulse session, there was a significant main effect of rearing condition on mean acoustic startle response [ $F(2,60) = 3.1, p = .05$ ]. Enrichment- and isolation-reared rats had higher mean startle responses compared with socially reared rats, but the increase in startle response was only significant in the enrichment-reared rats (Figure 5A). Startle reactivity to the first block of six acoustic startle stimuli was not affected by rearing condition [ $F(2,60) = 1.3, ns$ ], although both enrichment- and isolation-reared rats had higher startle responses than the socially reared group (mean  $\pm$  SEM: socially reared group,  $968 \pm 73$ ; enrichment-reared group,  $1131 \pm 66$ ; isolation-reared group,  $1107 \pm 94$ ). The startle response pattern was similar in the light prepulse session (mean  $\pm$  SEM: socially reared group,  $423 \pm 47$ ; enrichment-reared group,  $549 \pm 48$ ; isolation-reared group,  $529 \pm 59$ ), but the effect of rearing condition was not significant [ $F(2,60) = 1.7, ns$ ].

There was no effect of rearing condition on the percent measure of startle habituation [ $F(2,60) = 0.9, ns$ ], although small differences in group means were observed (mean  $\pm$  SEM: socially reared group,  $53 \pm 6\%$ ; enrichment-reared group,  $57 \pm 5\%$ ; isolation-reared group,  $46 \pm 7\%$ ).

#### Prepulse Intensity

There were significant effects of acoustic prepulse intensity [ $F(1,60) = 189, p < .01$ ] and ISI [ $F(1,60) = 147, p < .01$ ].

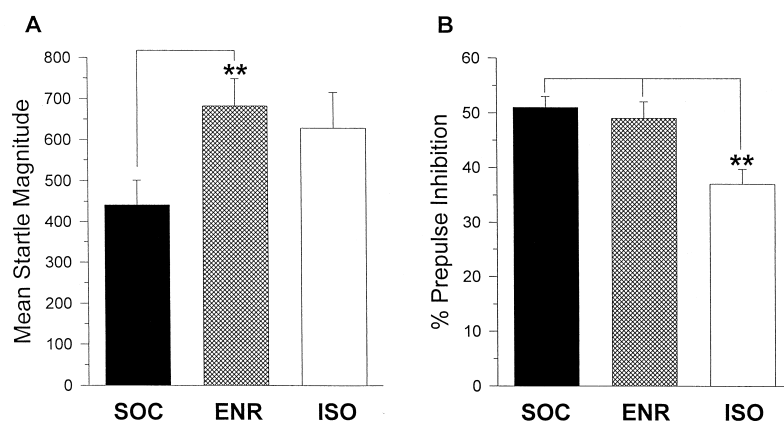


Figure 5. Effects of rearing condition on (A) mean startle magnitude (during the acoustic prepulse session) and (B) mean prepulse inhibition (% prepulse inhibition). SOC, socially reared; ENR, enrichment reared; ISO, isolation reared. Values represent mean percentage prepulse inhibition  $\pm$  SEM for each rearing-condition group.  $**p < .01$ .

.01] on PPI, and there was a significant effect of rearing condition [ $F(2,60) = 7.6, p < .01$ ]. As there were no statistically significant interactions among these factors (see Table 1 for PPI data measured at each prepulse combination), acoustic PPI was collapsed across the prepulse conditions. As shown in Figure 5B, socially reared and enrichment-reared rats had similar levels of PPI, whereas isolation-reared rats had significantly reduced PPI compared with both socially reared and enrichment-reared groups. There was no main effect of rearing condition [ $F(2,60) = 2, ns$ ] on light PPI; however, there was a similar pattern for light PPI across the rearing conditions, with isolation-reared rats exhibiting low levels of light PPI (mean  $\pm$  SEM: socially reared group,  $57 \pm 6\%$ ; enrichment-reared group,  $56 \pm 6\%$ ; isolation-reared group,  $42 \pm 5\%$ ).

### Discussion

This study was designed to examine how the spectrum of environmental manipulations, including enriched, normal, and isolation rearing, affects rats' subsequent behaviors in adulthood, including locomotion, exploration, startle habituation, and PPI. Our findings show that although most of the behavioral effects produced by enrichment and isolation were opposite in nature, other measures were similar. In general, enrichment led to certain behavioral "enhancements," whereas isolation was associated with behavioral deficits. It remains unknown whether similar

changes would be observed in rats exposed to enrichment procedures as adults. Nevertheless, the results lead to a fairly coherent picture of the effects of these differing rearing conditions.

Specifically, in this and other studies of Sprague-Dawley rats (Geyer et al 1993), isolation-reared rats had initial levels of locomotor activity that were similar to socially reared rats and not to the type of isolation-induced hyperactivity that many groups have observed in other strains (Geyer et al 1993; Sahakian et al 1977; Varty and Higgins 1995). Isolation-reared rats engaged in straight movements and maintained increased levels of exploratory hole pokes and rearings throughout the session. In contrast, enrichment-reared rats initially engaged in straight movements, with increased hole pokes and at levels of locomotor activity comparable to those of socially reared rats, and they subsequently habituated rapidly to a pattern of behavior characterized by highly circumscribed movements, reduced hole poking, and low levels of locomotor activity. These findings are consistent with those from previous studies (Bowling et al 1993; Gardner et al 1975; Van Waas and Soffié 1996).

The combination of accelerated habituation to a novel environment and transition from initially straight to circumscribed movements in enrichment-reared rats supports the notion that these animals process the information in a novel environment differently than do the other groups. Specifically, the initial bout of straight movements brings the animal in contact with different areas of the BPM and

Table 1. Effect of Rearing Condition on Percent Prepulse Inhibition Using Four Prepulse Conditions

Rearing condition	Prepulse condition			
	6 dB, 100 msec	6 dB, 300 msec	12 dB, 100 msec	12 dB, 300 msec
Social	$56 \pm 2$	$31 \pm 5$	$65 \pm 2$	$53 \pm 2$
Enrichment	$53 \pm 4$	$27 \pm 4$	$65 \pm 3$	$49 \pm 4$
Isolation	$42 \pm 3$	$19 \pm 4$	$51 \pm 3$	$35 \pm 4$

Values are mean  $\pm$  SEM for each rearing condition.

therefore allows it to explore different parts of the environment. Subsequently, the enrichment-reared rats engage predominantly in circumscribed movements in the corners and along the periphery of the enclosure. Finally, in combination with significant reductions in holepoking and rearing over time, these behavioral changes suggest that processing of the information in a novel environment by enrichment-reared rats leads to a more rapid and extensive behavioral adaptation. These differences are presumably a consequence of the enrichment-reared rats' greater amount of experience with novel and changing environments. In comparison, isolates engaged initially in straight movement patterns but exhibited significantly less behavioral change of these patterns over time than enrichment-reared rats. Thus, in the BPM paradigm, the enrichment-reared rats appeared to be more adaptive in that they quickly adjusted their behavior in accordance with the environmental situation, whereas isolation-reared rats were less adaptive and displayed more perseverative movement patterns. Similar behavioral patterns have been observed in isolation-reared rats in other paradigms (Jones et al 1991; Morgan et al 1977).

Consistent with the theme of isolation-reared maladaptive behaviors, as previously reported (Bakshi et al 1998; Bristow et al 1995; Geyer et al 1993; Varty and Higgins 1995), isolation-reared rats displayed significant deficits in PPI compared with socially reared rats. In these Sprague-Dawley rats, the isolation-rearing-induced deficit in PPI was not accompanied by an increase in initial levels of locomotor activity, confirming previous reports that isolation-induced PPI deficits and locomotor hyperactivity are dissociable (Geyer et al 1993; Varty and Higgins 1995). This replication of the effects of postweaning isolation on PPI in adulthood further supports the potential utility of this paradigm as a nonpharmacologic and developmentally specific model of the similar sensorimotor gating deficits observed in schizophrenic patients. It is important to note that the present finding that enrichment-reared rats have PPI levels similar to socially reared rats indicates that the time-consuming addition of environmental enrichment to the social-rearing condition does not yield increased effects on PPI. Thus, it appears that future studies using the isolation-rearing paradigm to assess the effects of putative antipsychotic treatments on sensorimotor gating need not incorporate the more complex and costly manipulations involved in environmental enrichment.

Interestingly, both isolation- and enrichment-reared rats displayed increased startle reactivity compared with socially reared controls. Therefore, environmental enrichment of rats from the time of weaning increases their reactivity to a startle stimulus but has no independent effect on PPI. The finding of elevated startle responses and normal PPI in enriched rats provides further evidence that

experimental effects on startle and PPI can be dissociated from one another. Furthermore, our finding of reduced PPI in isolation-reared rats is clearly not due to concomitant increases in startle reactivity, because enrichment-reared rats displayed similar increases in startle reactivity even though PPI was not affected. In support of this dissociation, correlation analyses revealed no relationship between startle reactivity and PPI in enrichment-reared, socially reared, or isolation-reared rats, which appears to be clear evidence that the two measures are independent from one another (data not shown). Finally, there was no differential effect of rearing condition on the amount of startle habituation, despite the trend for an opposite effect in enrichment- and isolation-reared rats on startle habituation, which was in the same direction as that measured with locomotor habituation. It should be noted, however, that we measured habituation of startle within the context of a PPI session. Using a session designed specifically to measure habituation by presenting continuous predictable stimuli could reveal startle habituation effects in future studies.

Finally, analyses comparing the locomotor/exploratory measures to the startle plasticity data found no evidence in any of the groups for correlations between locomotor activity/exploratory measures and PPI (data not shown for sake of brevity). This is clear evidence that changes in these two measures are independent from one another. In the socially reared and enrichment-reared groups, we did see evidence for a positive correlation between startle response and the spatial *d* measure, meaning that animals with higher startle reactivity had the highest spatial *d* values. This finding suggests that animals with high levels of startle propensity habituate more quickly to novel environments by transitioning faster from patterns of linear movement to circumscribed movements.

In summary, this study shows that environmental enrichment during development produces a unique profile of behaviors compared with either normal or isolation rearing. Although isolation of adult rats produces hyperactivity without altering PPI (Wilkinson et al 1994), it remains unknown whether exposure of adults rats to enriched environments would produce effects comparable to those observed here. Compared with socially reared rats, enriched rats exhibited accelerated habituation of locomotor activity, investigatory hole pokes, and rearings, resulting in a rapid transition to highly circumscribed patterns of movement. In contrast, isolation rearing did not affect the habituation of motor activity, it increased exploratory hole pokes and rearings, and it led to more predictable, straight patterns of movement. Enrichment had no effect on PPI or startle habituation and actually increased startle reactivity compared with the case of socially reared control rats. Isolation rearing produced a significant reduction in PPI

and no change in startle habituation and produced increased startle reactivity. Thus, relative to socially reared rats, some behavioral differences in the enrichment- and isolation-reared rats are opposite, such as changes in exploration patterns, whereas other behavioral differences are similar, such as increased startle reactivity.

What are the possible neural bases of these behavioral changes? Parallel to the common and diverging behavioral effects of rearing conditions, previous studies have shown that enrichment and isolation-reared rats exhibit some similar changes in neurochemistry, such as increased cortical dopamine (Jones et al 1992; Saari et al 1990). Isolation rearing also alters dopaminergic, serotonin, and adrenergic functions (Bickerdike et al 1993; Fulford et al 1994; Fulford and Marsden 1997; Jones et al 1992; Wilkinson et al 1994). Future studies could examine whether these and other specific neurochemical changes account for these behavioral differences and similarities. For example, is increased startle reactivity in both enrichment- and isolation-reared rats associated with increased cortical dopamine? Are the PPI deficits in isolation-reared rats that are absent in enrichment-reared rats associated with one change in a specific neurotransmitter system? Anatomic studies of cortical and hippocampal regions from these rats would be of interest to examine whether any of these behavioral changes are correlated specifically with any neurochemical and morphological differences between the groups. For example, do isolation-induced deficits in PPI correlate with changes in dendritic branching or cortical volume? Finally, apart from these neural substrate issues, on the basis of these studies, it appears that the complex condition of environmental enrichment has no important advantage over normal social rearing as a control condition when examining isolation-reared rats in the PPI paradigm.

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