The Effects of Environmental Control on Cognition in Rats (Rattus norvegicus)

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The Effects of Environmental Control on Cognition in Rats (*Rattus norvegicus*)

Amber A. Alliger and Peter Moller

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The aim of this study was to allow nonhuman animals to control their environment using operant conditioning procedures and to assess the effect of control on cognitive tasks. The study tested 4 predictions: (a) rats (*Rattus norvegicus*) will control a light stimulus; (b) animals will exhibit preferences for particular stimulus strengths; (c) animals who exert control over environmental stimuli will show improved performance on cognitive tasks compared with animals who lack control; and (d) at the end of the operant phase, experimental subjects will have lower corticosterone levels than animals who lack control. Experimental subjects did show control over a light stimulus and performed significantly better over time in a discrimination task compared with subjects who could not control their environment. There was no difference in corticosterone levels between control and experimental subjects. The results will both contribute to our understanding of how control of environmental stimuli affects the welfare of animals in captive environments and aid in designing experimental conditions that will increase validity and reliability in research.

Nonhuman animals are an integral part of experimental research. They are examined in comparative, developmental, psychophysical, cognitive, and medical...
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studies. The success of pharmaceutical research relies on data from animal studies because of the similarities between humans and subjects in the laboratory. We depend on these similarities for valid and reliable results. Often, however, the standard care provided is not sensitive to the animals’ physiological and behavioral needs; yet, behavioral data are still gathered. There is a wealth of data showing that current housing conditions do not provide sufficient stimulation. In addition, the standard impoverished environments that animals are housed in can potentially interfere with their normal physiological and behavioral development (Benefiel & Greenough, 1998; Rosenzweig & Bennett, 1996). This subsequently raises the issue of whether these animals can serve as valid models (Garner, 2005). Although standard care has led to increased convenience in the husbandry of animals in the laboratory, customary procedures have often led to poor science (Garner, 2005).

Past research on improving captive housing systems has focused on giving laboratory animals objects to interact with: tubes, boxes, or nesting material (van de Weerd, van Loo, van Zutphen, Koolhaas, & Baumans, 1997; Würbel, 2007). A less studied approach addresses the lack of behavioral opportunities in laboratory environments by allowing animals to actively control certain environmental conditions (Dawkins, 1988). Allowing animals to exhibit control mimics important aspects of their natural behavior, such as choice of nesting locations, mates, and the use of foraging sites. Animals in laboratory settings lack such control, potentially leading to frustration and subsequently to abnormal behaviors (Bassett & Buchanan-Smith, 2007; Wiepkema & Koolhaas, 1993). This “active control” approach has allowed gauging the animal’s motivation to gain access to a desired stimulus by having it work under various imposed difficulties (Dawkins, 1988; van de Weerd, van Loo, van Zutphen, Koolhaas, & Baumans, 1998). The outcome of these studies can recommend stimulus conditions to enrich the environment of laboratory animals.

Though the element of control has been well documented (Dawkins, 1980; Kavanau, 1963; Lockard, 1964), the actual nature of the stimulus might not matter as long as the animal can exert some form of control over it (Davis & Levine, 1982). Deer mice used a running wheel only if they themselves could turn on the motor. When the experimenter activated the motor, subjects turned it off—even though it stopped the animal’s access to running (Kavanau, 1962). Having some sort of control over environmental features results in physiological modifications (Weiss, 1971), as neural arborization has been found in animals who were housed in enriched environments (Benefiel & Greenough, 1998). Behavioral changes that accompany these physiological changes were found to improve cognitive skills such as learning and memory (Benefiel & Greenough, 1998; Forgays & Forgays, 1952; Krech, Rosenzweig, & Bennett, 1962; Mohanty & Behera, 1997). Control as a form of enrichment can help in normalizing an animal’s behavior and allowing species-appropriate behaviors to be displayed.
A physiological cause that also affects cognitive performance in laboratory animals is the secretion of corticosteroids. Increased levels of corticosterone induced by either corticosterone treatment (Bodnoff et al., 1995) or physical restraint (Conrad, Galea, Kuroda, & McEwen, 1996) decrease the performance of rats on spatial memory tasks. Spatial memory and novel object recognition involve the hippocampus; thus, when circulating corticosteroids negatively affect the hippocampus (loss of neurons), it is possible that high levels of corticosterone will decrease the subjects’ performance on cognitive tasks (Bardgett, Newcomer, & Taylor, 1996). Enrichment brought about by the animal’s own environmental control may play an important role in the expression of corticosterone. The hypothalamic-pituitary-adrenal axis responds to control in that corticosterone levels were significantly lowered when rhesus monkeys were allowed to control the termination of a shock (Davis et al., 1977; Hanson, Larson, & Snowdon, 1976). Consequently, low levels of corticosterone may increase cognitive skills or prevent cognitive impairment (de Kloet, Oitzl, & Joëls, 1999; Weiss, 1972). Memory consolidation is generally characterized by an inverted-U shaped stress hormone dose-response effect (Yerkes & Dodson, 1908). This has been shown by administration of moderate doses of epinephrine or glucocorticoids leading to improved memory consolidation (Gold & van Buskirk, 1975; McIntyre & Roozendaal, 2007; Roozendaal, Williams, & McGaugh, 1999). Experimentally “optimizing” a subject’s arousal level by identifying and applying the appropriate contingency of reinforcement schedule should result in optimal corticosterone release and subsequent memory consolidation. However, it has been suggested by Mendl (1999) that using the Yerkes-Dodson model may not apply to all conditions that contain features such as stress and cognition as they are multidimensional and may not be identified by this single theory.

Previous research has shown robust findings when testing rats controlling cage illumination levels (Lockard, 1963), and subjects who have control develop physiological features that aid in improved cognitive performance (Benefiel & Greenough, 1998; Weiss, 1971). Allowing animals to display species-typical behavior may result in a less stressed subject and thus affect corticosterone levels (de Kloet et al., 1999). Based on this information, the present study will test the following predictions:

1. Animals will control an environment that contains an adjustable stimulus (light intensity);
2. Animals will exhibit a selected preference for stimulus strength;
3. Animals who have control over their environments will show improved performance on cognitive tasks compared with animals who lack such control; and
4. On completion of the operant phase, experimental subjects will have lower corticosterone levels than animals who lack control.
METHODS

Subjects

Forty-five Long-Evans Hooded male rats (Harlan Laboratories) at the age of 21 days were gentled for a week before testing began by the handling of each subject approximately 2 min every day. In order to tease apart effects between social and environmental enrichment, subjects were singly caged and kept on a 12-hr light cycle with lights on at 1300 hr and fed Harlan 2001 Lab chow™ with water available ad libitum. Selected subjects (n = 24) were food-restricted to 90% body weight for the cognitive testing section of the experiment for 17 days.

All tests were run in the evening, close to the time when lights would turn off in the homeroom, coinciding with the onset of the animals’ active phase. For consistency of handling, only one person cleaned, handled, and tested all subjects throughout the experiment. Homerooms were lit with fluorescent light and were measured at 400 lx (one meter off the ground); temperature remained between 18°C and 23°C, and humidity was kept between 45 and 85 relative humidity units. Animals were kept on paper bedding and cages were cleaned every 5 days.

Materials and Procedure

The order of experiments (Table 1) was conducted as follows.

Object Approach Test

Twenty-four hours before the object approach test began, subjects were habituated to the open field for 5 min. The open field box was constructed of black Plexiglas (61 W × 61 H × 20 D cm³) where a novel object, a soda can with contrasting coloration, was placed in the center for the subject to inspect for 5 min. The following measurements were taken: (a) latency to approach the object, (b) time spent at the object, and (c) number of times touching the object. The test room was free of all extraneous sounds and the ambient light level of the room was 60 lx. As a backup, all behaviors were recorded using an overhead Sony Mini DV™ video camera. The open field box was cleaned with Nolvasan™ between sessions.

<table>
<thead>
<tr>
<th>TABLE 1</th>
<th>Timeline for Experiment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day</td>
<td>1</td>
</tr>
<tr>
<td>Task</td>
<td>Gentling</td>
</tr>
</tbody>
</table>
Operant Conditioning

Individual, naïve rats were tested in an operant cage (Coulbourn Instruments) equipped with five light-emitting diodes (LEDs) located in the ceiling of the chamber. Subjects could control the level of illumination by the use of two levers located on one of the chamber walls. Pressing one lever increased illumination; pressing the second decreased illumination incrementally by affecting on- or offset of one to five LEDs. The rat had only to press a lever once to affect the light intensity (each press would turn on/off one LED). The rat directly controlled the lights. If the rat pressed the lever enough times for all lights to be off, they would stay that way until the rat pressed the other lever to turn on an LED (one with each press). The opposite was true when all lights were on. The average ambient light levels were 0, 26.6, 69, 88, 122, and 140 lx for any one, two, three, four, and five LEDs, respectively (measured from the center of the floor of the cage). The lights were activated by a program written by the staff at Hunter College in Visual Basic™ (Version 6), using a Switch and Sense™ control box connected to a Dell Optiplex™ computer. Three conditions were tested in identically equipped cages: (a) experimental subjects had control over illumination levels \((n = 15)\); (b) yoked subjects experienced the same light levels as the experimental animals in a yoked cage, without having control over illumination levels \((n = 15)\); and (c) control subjects experienced a constant illumination from four LEDs for the duration of the session \((n = 15)\). Both yoked and control animals had levers available; however, pressing them had no consequences. Each session started with four out of five LEDs illuminated in all three cages. Afterward, the positions of the illuminated LEDs were randomized but were identical for the experimental and yoked cages. The number of bar presses, the time the lever was pressed, the number of LEDs in use, and the status (on/off) of each LED was automatically recorded for all cages. Three cages (experimental, yoked, and control) were isolated in a room to reduce light and sound interference from other apparatus. Three complete setups ran at the same time (total of nine cages). Each session ran for half an hour, and the task was completed in 53 days.

Cognitive/Discrimination test. Subjects were tested in the same open field that was used for the object approach test with the addition of a divider fitted with a starting gate operated by a sliding door. Two 15 × 18 cm cards with a 4.4 cm white graphic (a 5-pointed star or square) on a black background served as stimuli. The starting gate was located 46 cm away from the cards, which in turn were located 30.5 cm from each other. Subjects were selected based on their lever-pressing activity in the operant conditioning task. Only the eight most active animals in each group (experimental, yoked, and control) were tested. This selection was based on the assumption that control in the operant
phase would affect those physiological changes that lead to superior performance on the discrimination task. This has been tested by other studies, which found that manipulation of environmental features resulted in neurological changes that lead to improved cognitive performance (Pham et al., 1999; van Praag, Kempermann, & Gage, 2000).

Animals were first target trained (primed) to a graphic that was different from those used in the following discrimination trials. Target training consisted of the subjects’ noses touching the graphic to receive a drop of Nutracal™ for a total of 10 touches. Following the priming session, individual animals were placed in the starting area of the open field and given 2 min to acclimate. Upon opening the gate, subjects could choose from one of the two graphics. Subjects first had to learn to choose, then remember, a particular graphic (star or square) and touch it with their nose in order to get a drop of Nutracal™ reward for a total of 10 trials per session. The cards were pseudorandomly presented in either the left or right position of the open field to ensure a balanced number of presentations of the graphics. Each trial lasted no longer than 3 min with an intertrial-interval of 2 min; sessions were run for 15 consecutive days.

Corticosterone testing. Fecal boli were collected from all subjects at the same time of day once a week during the operant phase and kept frozen at \(-80^\circ\text{C}\). Only samples from weeks 1, 4, and 8 were assayed. The diagnostic kit Corticosterone HS EIA, manufactured by IDS Diagnostics, was used to measure levels of hormone. Instructions that were supplied with the kit were followed for all assays. The sensitivity of hormone detection was 0.17 ng/ml of corticosterone.

Data analysis and approval. Statistical analysis for this experiment was performed using SPSS™ (Version 17) and Microsoft Excel™. The experiment was approved by the Institutional Animal Care and Use Committee of Hunter College (AA/PM 6/09-01).

RESULTS

Object Approach Test

On the object approach test, rats \((n = 45)\) approached the object 5.8 \((SD = 4.7)\) times during the 5-min session, taking an average of 67.2 s \((SD = 59.9)\) s, and spent 15.0 s \((SD = 10.8)\) s at the object. These results are compared with the animals’ performance on the operant conditioning task.
Operant Conditioning

Over the 53-day sampling period, animals in the experimental group pressed the levers, on average, 773.1 times ($SEM = 140.4$); in the yoked group, 688.9 times ($SEM = 129.03$); and in the control group, 204.4 times ($SEM = 26.5$). The number of lever presses was significantly smaller in controls compared with both experimental and yoked animals but did not differ between these two (analysis of variance [ANOVA]; $F(1, 2) = 7.62, p < .001$, least significant difference post hoc test).

Figure 1 illustrates the time course of lever-pressing activity in the three groups and associated best-fit regression functions. Binomial approximations yielded the highest coefficients of determination: experimental animals, $R^2 = 0.48 (y = -0.01x^2 + 0.36x + 14.3)$; yoked animals, $R^2 = 0.84 (y = 0.004x^2 + 0.68x + 27.95)$; and control animals, $R^2 = 0.74 (y = 0.001x^2 + 0.18x + 8.31)$). Although the total number of lever presses did not differ between experimental and yoked animals, there was a distinct difference in the time course of the rats’ activity as expressed by the shape of the regression functions, an inverted parabola for experimental subjects and an almost linear decline in yoked subjects. Experimental animals increased their activity over the first 20 days, followed by a slow decline over the remaining period. On
the other hand, yoked animals started at a higher activity than experimental ones but then immediately decreased their lever-pressing rate, which from about Day 20 consistently remained lower than that of the experimental animals. This was a surprising finding that will be taken up in the Discussion section. The steady decline in lever pressing in yoked subjects mimicked the time course established for control animals, albeit at a much lower activity (Figure 1).

To further detail the experimental subjects' behavior during the operant phase as they manipulated their environment and assessed whether they preferred control or a particular illumination level, only lever presses that changed the light condition were counted; those that maintained the darkest or lightest settings were excluded (Figure 2). Only five lever presses were necessary to sample all illumination levels. Subjects, however, pressed the lever more often than needed, suggesting that they chose control rather than preference for a particular illumination level. But comparable to the drop in their overall activity (Figure 1), by about Day 30, subjects appeared to habituate, no longer exhibiting more than five lever presses.

**FIGURE 2** Mean number of lever presses with $\pm 1\ SEM$ for altering the light stimulus by experimental group. Dotted line represents five lever presses.

**Discrimination Task**

The average number of correct choices performed in the discrimination task by the experimental group ($n = 8$) was $74.5, SEM = 3.19$; for the yoked group ($n = 8$) $71.25, SEM = 3.27$; and for the control group ($n = 8$), $M = 68.0, SEM = 1.95$. There was no significant difference in the total number of correct choices
across groups (one-way ANOVA; $F(2, 14) = 2.85, p > .05$). Over the course of the 15-day sampling period, the experimental subjects learned significantly faster than yoked and control animals, as indicated by the difference in slopes between the experimental group and the other two groups (one-way ANOVA; $F(2, 21) = 4.22, p < .05$; Figure 3).

**Corticosterone Assay**

Levels of corticosterone were not significantly different across the three groups over the three tested time points: Week 0 ($F(1, 2) = 0.20, p > .05$), Week 4 ($F(1, 2) = 0.13, p > .05$), and Week 8 ($F(1, 2) = 1.47, p > .05$; multivariate analysis of variance).

**Correlations Between Object Approach and Operant Tasks**

Animals were rank ordered by their lever-pressing activity during the operant phase. Subsequently, experimental, yoked, and control groups were divided into two subgroups, each by selecting the 5 most active animals within each group (high-performance group; HPG) and the 5 least active animals (low-performance group; LPG). These subgroups were selected assuming that more active subjects in lever pressing in the operant task would show increased performance in the cognitive task.
TABLE 2
Pearson Product-Moment Correlations Between the Number of Times the Subjects Approached a Novel Object and the Number of Lever Presses for the Total Number of Animals in Each Group and the HPG and LPG for Experimental, Yoked, and Control Animals

<table>
<thead>
<tr>
<th>Group</th>
<th>Experimental</th>
<th>Yoked</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total group (n = 15)</td>
<td>.10</td>
<td>.19</td>
<td>.03</td>
</tr>
<tr>
<td>HPG (n = 5)</td>
<td>.92*</td>
<td>.46</td>
<td>−.60</td>
</tr>
<tr>
<td>LPG (n = 5)</td>
<td>−.98*</td>
<td>.72</td>
<td>−.20</td>
</tr>
</tbody>
</table>

*Note. HPG = high-performance group, LPG = low-performance group. Asterisk denotes significance at the .05 level.

The activity of animals in the object approach test was compared with their performance during the operant phase. There was a positive correlation in HPG animals’ performance and a negative correlation in LPG animals’ performance (Pearson’s product-moment correlations; Table 2).

DISCUSSION

Previous research has noted that the lack of control over environmental features is potentially harmful to animals housed in impoverished laboratory settings (Lockard, 1962). Furthermore, robust findings have been obtained when allowing rats to control illumination (Kavanau & Havenhill, 1975; Kish, 1955; Lockard, 1962; McCall, 1965). The present study found similar results; animals given control of a light stimulus in an operant paradigm will press levers more often than control animals to effect changes in ambient illumination, and experimental animals exhibited control over the stimulus rather than preference. Control rather than preference has also been supported in previous studies using rats (Kavanau & Havenhill, 1975; Kish, 1955; Lockard, 1962; McCall, 1965). Further, exerting control during the operant phase improved the animals’ performance on a discrimination task.

Although equal in overall numbers of lever pressing, there was a divergence over time between experimental and yoked animals. Experimental animals showed an initial surge in lever pressing followed by a slow decline that may have been due to what Lockard (1963) suggested: The stimulus change lost novelty, and the subjects decreased lever-pressing activity. Yoked animals experienced the same ambient changes as experimental animals and, although they were not in control, initially pressed the lever more often than experimental subjects. This may have been due to superstitious behavior (Davis & Hubbard, 1972). Yoked animals may have perceived that they were in control...
even though their lever pressing effected no change in illumination. They may have pressed the levers at times similar to the times of experimental subjects and associated changes in illumination with their actions. The nearly linear decline in the performance of both control and yoked subjects may be attributed to the fact that the animals in both these groups learned that there were no consequences to pressing the lever and thus void of any reinforcer. This was not the case with experimental subjects, who continued experiencing and acted on the consequences of their behavior.

When using devices that animals can manipulate in an operant chamber, it is important to realize that the intended experimental reinforcers for an animal’s lever pressing (changing light levels in the context of this research) might not be the only reinforcing stimulus within the animal’s environment. The sound or motion of pressing the lever might be sufficiently reinforcing, even when control of the stimulus is not (Kish, 1955; Kish & Antonitis, 1956). The control animals in the current experiment provide evidence that animals pressed a lever even though there was no reinforcing consequence.

This experiment showed that control rather than preference was more important to experimental subjects. This became apparent when experimental subjects, who needed only five lever presses to be exposed to every possible light level in the operant cage, pressed the lever more often than five times during the operant phase (Figure 2). Control over preference has been tested in several studies using rats (McCall, 1965), mice (Kavanau, 1963), and nonhuman primates (Moon & Lodahl, 1956) with similar results. The rate of lever presses that changed ambient illumination, however, did decrease to an average of five per session during the last few days of the operant phase. Furthermore, as stated in previous papers, variables such as lighting conditions in the homeroom may affect this outcome (Lockard, 1966). Future analysis of the present research will test whether or not light intensities were constant (showing possible preference over control) for the 5 days when the rate of lever pressing fell on or below five times per day.

Although corticosterone levels did not differ significantly among groups in this study, experimental subjects exhibited the lowest, and the yoked animals the highest, levels of the hormone by the last week of the operant phase (Table 3). Further research may find that animals who have control over some aspect of their environment and are able to learn positive consequences of their actions may be less stressed than animals in a yoked situation, who experience uncontrolled changes all the time. Thus, allowing subjects to control aspects of their environment may result in decreased corticosterone production and aid in creating healthier subjects, as found in a study by Davis and Levine (1982).

Prior to dividing subjects into groups at the start of the operant phase, an object approach test was performed to examine whether this task could be used as a predictor of performance on other tasks. Two significant correlations were
of interest, one in HPG and the other in LPG animals during the operant phase. Experimental subjects who approached the object more often also displayed more frequent lever presses. The opposite also held for animals who approached the object less often and who subsequently displayed fewer lever presses. These findings support the concept of animal personality traits (behavioral syndromes) when animals sustain their characteristic behavior regardless of the environmental circumstances (Sih, Bell, & Johnson, 2004). An object approach test may thus be helpful in selecting experimental subjects who will in all likelihood perform at chosen levels of activity on operant and other locomotor tasks.

Renner and Rosenzweig (1987) noted that when behavioral changes such as higher level cognitive abilities are induced by enrichment, they are likely to be found in higher level functioning areas of the brain such as the hippocampus and/or the cerebral cortex. A common method of trying to understand the effects of pharmaceuticals within clinical trials is testing animals in behavioral tasks, which often have little relevance to human conditions. It has been suggested that the tasks used in human cognitive research should be adapted to animal subjects, which might result in higher test validity (Garner, Thogerson, Würbel, Murray, & Mench, 2006). It was hypothesized in the current study that the discrimination task would produce results analogous to those found in tasks performed by humans (Garner et al., 2006).

Although the experimental animals did not outperform yoked or control subjects in the total number of correct choices in the discrimination task, the experimental animals, over time, increased the number of correct choices. Krech et al. (1962) found that rats raised with access to environmental enrichment were able to discriminate between doors that would lead to goal boxes with reward and goal boxes without reward. In addition, Rothblat and Hayes (1987) were able to successfully train rats to discriminate between three-dimensional cues. Results in the present study might have been more robust had subjects been presented with a spatial discrimination task as in the Krech et al. study or with three-dimensional objects as in the Rothblat and Hayes study.
The current research used a two-dimensional card with a graphic that might not have been easily discernible. Using a three-dimensional object may have represented a naturalistic stimulus with ethological validity (Gerlai & Clayton, 1999). However, in support of the use of two-dimensional graphics, Bussey, Saksida, and Rothblat (2001) found that mice could successfully discriminate between graphic images on a computer screen.

CONCLUSION

Applying these procedures will allow caretakers of animal maintenance facilities to understand their subjects' preferences and, when applied, will ultimately result in improved husbandry practices. Guided by this plan, results of future experiments not only will be important for the welfare of animals in captive environments but also will aid in designing better scientific methods, yielding animal models with increased research validity and reliability. Animals raised and maintained in improved conditions will provide better substitutes for human conditions.

ACKNOWLEDGMENTS

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