References and Notes

1. G. E. Hutchinson, *An Introduction to Population Ecology* (Yale Univ. Press, New Haven, Conn., 1978).
2. J. L. Harper, *Population Biology of Plants* (Academic Press, London, 1977); ______ and A. D. Bell, in *Population Dynamics*, R. M. Anderson and B. D. Turner, Eds. (Blackwell, Oxford, 1979), p. 29.
3. H. M. Jahns, in *The Lichens*, V. Ahmadjian and M. E. Hale, Eds. (Academic Press, New York, 1973), p. 3.
4. J. B. C. Jackson, *Am. Nat.* **111**, 743 (1977); ______, in *Biology and Systematics of Colonial Organisms*, G. Larwood and B. Rosen, Eds. (Academic Press, London, 1979), p. 499.
5. J. H. Connell, in *Biology and Geology of Coral Reefs*, O. A. Jones and R. Endean, Eds. (Academic Press, New York, 1973), vol. 2, p. 205.
6. R. W. Buddemeir and R. A. Kinzie, *Oceanogr. Mar. Biol.* **14**, 183 (1976); I. G. MacIntyre and S. V. Smith, *Proc. Int. Coral Reef Symp. 2nd* **2**, 277 (1974).
7. J. B. Lewis, *Proc. Int. Coral Reef Symp. 2nd* **1**, 201 (1974); J.. W. Scatterday, *ibid.*, p. 85.
8. W. H. Hildemann, D. S. Linthicum, D. C. Vann; *Immunogenetics* **2**, 269 (1975); W. H. Hildemann, R. L. Raison, C. J. Hull, L. Akaka, J. Okumoto, G. Cheung, *Proc. Int. Coral Reef Symp. 3rd* **1**, 537 (1977); D. C. Potts, in *Coelenterate Ecology and Behavior*, G. O. Mackie, Ed. (Plenum, New York, 1976), p. 79; R. L. Raison, C. J. Hull, W. H. Hildemann, in *Phylogeny of T and B Cells*, R. K. Wright and E. L. Cooper, Eds. (North-Holland, Amsterdam, 1976), p. 3.
9. H. M. Reiswig, *Bull. Mar. Sci.* **23**, 191 (1973); P. K. Dayton, G. A. Robilliard, R. T. Paine, L. B. Dayton, *Ecol. Monogr.* **41**, 351 (1974).
10. K. B. Clark, *Helgol. Wiss. Meeresunters.* **27**, 28 (1975).
11. C. Birkeland and B. Gregory, *Nat. Hist. Mus. Los Angeles Cty. Sci. Bull.* **20**, 57 (1975); R. A. Kinzie, *Stud. Trop. Oceanogr.* **12**, 29 (1974).
12. J. S. Ryland, *Adv. Mar. Biol.* **14**, 285 (1976).
13. W. H. Hildemann, I. J. Johnson, P. L. Jokiel, *Science* **204**, 420 (1979).
14. F. B. Ivker, *Biol. Bull.* **143**, 162 (1972).
15. J. Theodor, *Bull. Inst. Oceanogr. Monaco* **66**, 1 (1966); *Nature (London)* **227**, 690 (1970).
16. A. E. D. Stebbing, in *Living and Fossil Bryozoa*, G. P. Larwood, Ed. (Academic Press, London, 1973), p. 173.
17. F. W. Bancroft, *Proc. Calif. Acad. Sci. Ser. 3* **3**, 137 (1903); G. Freeman, *Transplant. Proc.* **2**, 236 (1970); S. Karakashian and R. Milkman, *Biol. Bull.* **133**, 473 (1967); F. M. Burnet, in *Contemporary Topics in Immunobiology*, E. L. Cooper, Ed. (Plenum, New York, 1974), vol. 4, p. 13.
18. J. D. McLeod, *Science* **200**, 771 (1978).
19. F. M. Broadhurst, *Nor. Geol. Tidsskr.* **46**, 401 (1966); J. St. Jean, Jr., in *Proceedings of the North American Paleontological Convention*, E. L. Yochelson, Ed. (Allen Press, Lawrence, Kans., 1971), vol. 2, part J, p. 1389; S. Kershaw and R. Riding, *Lethaia* **11**, 233 (1978).
20. M. E. Philcox, *J. Paleontol.* **45**, 338 (1971); J. H. Stel, *Studies on the Paleobiology of Favositids* (Stabo/All-Round, Groningen, 1978).

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Environmental Influences on Body Weight and Behavior in Developing Rats After Neonatal 6-Hydroxydopamine

Abstract. *There is less hyperactive motor activity and better avoidance performance in rat pups treated with 6-hydroxydopamine as neonates and reared with vehicle-treated littermates than in pups reared in litters composed solely of other 6-hydroxydopamine–treated animals. Thus, in this experimental model of hyperactivity, an environmental manipulation provides an alternative to pharmacologic agents in reducing activity and improving learning performance.*

In recent years, evidence from several lines of investigation has indicated that both genetic endowment and environmental determinants contribute to the behavioral repertoire of the developing mammalian central nervous system. Although such environmental alterations as modification in litter size have been shown to produce enduring effects on behavior (*1*), the consequences of other aspects of litter composition on subsequent development have received less attention. One such aspect has been the behavioral effects of rearing developing mice with foster mothers of a different species or strain. Denenberg *et al.* (*2*) noted reductions in open-field activity and aggression in mice reared by rat foster mothers. McCarthy and Southwick (*3*) showed that reciprocal cross-fostering of mice of an aggressive strain with a more passive strain decreased the aggressive behavior of the more aggressive pups but had no effect on the more passive strain.

Administration of 6-hydroxydopamine (6-OHDA) to the neonatal rat pup results in hyperactive motor activity that abates with maturity and cognitive deficits that persist into adult life (*4, 5*). In recent studies we were able to attenuate such hyperactivity by placing the pups with their anesthetized mother (*6*). The subsequent reduction in activity was even more pronounced than that observed after administration of amphetamine or methylphenidate. Furthermore, Randall and Campbell (*7*) noted that hyperactivity in the developing rat pup may be attenuated by the presence of an anesthetized lactating female, and Smith and Spear (*8*) showed that home environmental cues, such as litter shavings, are critical determinants of early learning and retention. These findings suggest a complex interaction between biological factors and environmental influences during early development.

In the present experiment, we examined the effects of varying the litter composition on activity and cognitive performance in normal and 6-OHDA-treated rat pups. Sprague-Dawley rat pups (Charles River) were cross-fostered at 2 days of age and maintained with the same mother in litters of nine to ten animals throughout the 33-day experiment. They were divided into four distinct groups: (i) vehicle homogeneous (V-Hom), pups administered saline and reared with similarly treated pups; (ii) treated homogeneous (T-Hom), pups treated with 6-OHDA at 5 days of age and reared with similarly treated pups; (iii) vehicle heterogeneous (V-Het), pups given vehicle and reared in litters in which 50 percent of the pups received vehicle and 50 percent 6-OHDA; and (iv) treated heterogeneous (T-Het), pups treated with 6-OHDA and reared in litters in which, again, 50 percent of the pups received vehicle and 50 percent 6-OHDA. There were 12 litters in all (three litters for each of the four groups), with 22 to 26 animals in each experimental group. Brain dopamine was selectively depleted at 5 days of age by administering desmethylimipramine (20 mg/kg, intraperitoneally) followed 1 hour later by intracisternal 6-OHDA (100 μg in 20 μl of saline, calculated as the free base; Regis Chemical).

Activity was recorded in a soundproof room when the pups were 12, 15, 19, 23, 27, and 30 days of age. Each pup was randomly assigned to one of ten plastic cages placed on the floor of the room, and recording was begun immediately with a television camera coupled to a time-lapse tape recorder. Activity was scored by playing the tape back at a speed equivalent to six times that of real time, and was determined for alternate 5-minute periods throughout a 60-minute observation period. Activity was defined as any detectable movement. Duration was determined by activating an electric timer at the onset of any movement and stopping it when the movement ceased. The cumulative duration of movements for each 5-minute interval was thus obtained, and the percentage of time in which the pup was active during each 60-minute observation period was then calculated and recorded. Avoidance performance was determined in a shuttle box at 27 days (*9*). All animals were killed at 33 days, and their brains were analyzed for dopamine and norepinephrine by high-pressure liquid chromatography (*10*). Activity and avoidance learning data were then subjected to analyses of variance, with age and trial blocks representing within-group factors and 6-OHDA (or vehicle) and litter composition representing between-group factors.

Figure 1 shows the effect of 6-OHDA

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and litter composition on body weight. Treatment with 6-OHDA produced a significant effect on weight, $F(1, 106) = 28.8$, $P < .001$, as did litter composition, $F(1, 106) = 25.0$, $P < .001$. The 6-OHDA times litter composition interaction was also significant, $F(1, 106) = 10.4$, $P < .005$. Scheffé post hoc comparisons indicate that beginning at 15 days of age pups in the V-Het group were significantly heavier than those in the three other groups. The weight of the V-Hom pups was similar to that of pups in both 6-OHDA groups until 27 days, when the V-Hom group began to diverge from the T-Hom group (although the weights of the V-Hom pups were not significantly different from those of the T-Het pups). Both 6-OHDA-treated groups were similar in weight until 30 days of age, when the T-Het pups weighed significantly more than the T-Hom pups.

Analysis of activity indicated a significant main effect for 6-OHDA treatment, $F(1, 106) = 20.1$, $P < .001$, and age, $F(5, 530) = 25.7$, $P < .001$, but not litter composition, $F(1, 106) = 1.69$, $P > .05$. As shown in Fig. 2, the interaction of age, 6-OHDA treatment, and litter composition had significant effects on activity during the first month of postnatal life, $F(5, 530) = 3.44$, $P < .005$. Comparing treated pups with their controls reared in mixed litters, we observe that hyperactivity in T-Het pups first became evident at 15 days, began to decline by day 23, and was no longer statistically significant on days 27 and 30, an activity pattern consonant with our previous findings (*4, 5*), but which may be confounded by the significant differences in body weight. On the other hand, if we compare 6-OHDA-treated pups with controls raised in homogeneous litters, we observe that hyperactivity was not present at 15 days. Indeed, a sharp activity peak seen in normally reared controls at 15 days (*11*) was markedly attenuated in controls raised in heterogeneous litters ($P < .025$, Scheffé test). However, activity in V-Hom pups declined by day 19 and remained uniformly low from that point on. Activity levels of the T-Hom pups also increased on day 15 but failed to decline during subsequent testing. Thus, for T-Hom pups, hyperactivity began at 19 days of age and remained present until at least 30 days, a pattern paralleling that found by Erinoff *et al.* (*5*). Furthermore, whereas both groups of 6-OHDA-treated pups were more active than both control groups at 19 and 23 days of age, there was no discernible difference in body weight among the T-Hom, T-Het, and V-Hom groups. This finding suggests that reduced body weight is not necessary to produce hyperactivity.

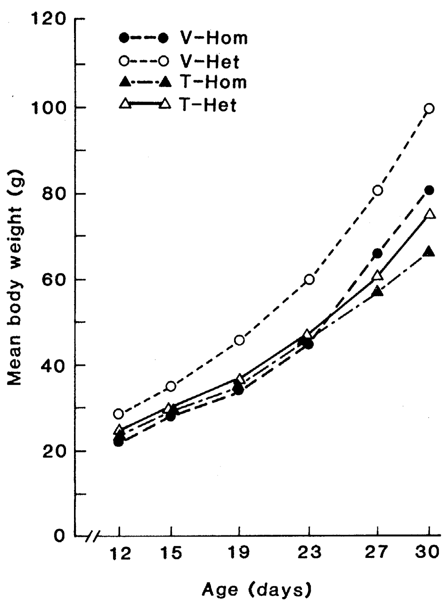

Fig. 1. Effect of litter composition and 6-OHDA on body weight in the rat pups. Each point represents the mean body weight for each group (22 to 26 pups per group).

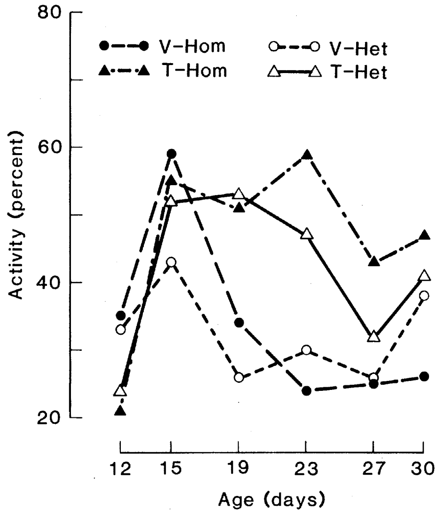

Fig. 2. Activity during the first month of postnatal life in normal and 6-OHDA-treated rat pups reared in homogeneous or heterogeneous litters. Each point represents the mean activity for each group (22 to 26 pups). Activity represents the percentage of time active during a 60-minute observation period.

The interaction of litter composition and 6-OHDA treatment produced a significant effect on avoidance learning as measured in a shuttle box at 27 days of age, $F(1, 109) = 4.08$, $P < .05$; this effect was also observed in the interaction between litter composition, 6-OHDA treatment, and avoidance learning over blocks of four trials, $F(4, 440) = 4.23$, $P < .005$. As shown in Fig. 3, both control groups rapidly learned to avoid shock: they required 80 to 90 seconds in the first block of trials, but by the fourth block they traversed the maze in 10 to 20 seconds. Both experimental groups required significantly more time to traverse the maze ($P < .001$, Scheffé test), but of greater interest is the difference between the experimental groups themselves. In the initial trial block the escape latencies of the T-Hom and T-Het groups were similar, but by the second trial block they began to diverge ($P < .025$). The T-Het group continued to exhibit shorter escape latencies at the third ($P < .005$), fourth ($P < .005$), and fifth trial block ($P < .001$).

Brain catecholamine concentrations were similar in all four groups. Brain dopamine, however, was reduced 86 percent after treatment with 6-OHDA, and norepinephrine was reduced 11 percent.

Despite the corroboration of separate investigative groups utilizing diverse methods for measuring activity (*4, 5*), Loch *et al.* (*12*) have suggested that the locomotor hyperactivity observed after neonatal administration of 6-OHDA could be confounded by growth retardation or undernutrition. In recent experiments we were unable to document significant alterations in suckling behavior in food-deprived, 6-OHDA-treated pups, nor did we observe any differences in food consumption between pups treated with 6-OHDA at 5 days of age and control littermates when both groups were examined between 18 and 45 days postnatally. The results of the present experiment, however, provide more compelling evidence that the hyperactive

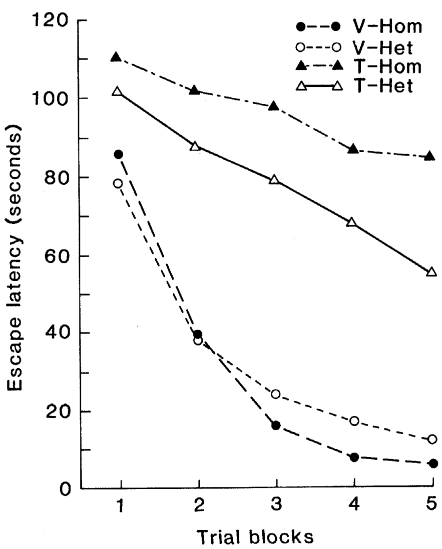

Fig. 3. Avoidance learning in a shuttle box at 27 days of age. Each point represents the mean escape latency for a block of four trials for each group (22 to 26 pups).

behavior and impaired avoidance performance observed after neonatal administration of 6-OHDA is related to reduction in brain dopamine rather than simply being a nonspecific effect of malnutrition.

Thus, although the weight of the V-Hom pups paralleled that of the T-Hom and T-Het pups, the V-Hom pups manifested activity and avoidance learning patterns similar to those of the V-Het group—behaviors clearly different from the hyperactivity and impaired avoidance performance noted in both 6-OHDA-treated groups. This finding appears to resolve the confusion surrounding the effect of 6-OHDA on body weight.

Of perhaps even greater interest, the results of this experiment support the belief that biological factors (such as the route of 6-OHDA administration) and environmental influences (such as litter composition) interact to produce significant effects on body weight, locomotor activity, and avoidance performance. Studies such as the present one assume particular relevance when we consider the etiology and treatment of the hyperactive child syndrome, the most common health problem affecting schoolchildren (*13, 14*). Recent clinical studies indicate that alterations in the metabolites of brain catecholamines may be found in affected children (*15*), and there is abundant evidence that pharmacologic stimulants (amphetamine and methylphenidate) often ameliorate many of the cardinal symptoms of the disorder (*14, 16*). Less appreciated are reports suggesting that particular modifications of the environment may also be effective in improving many of the symptoms (*17*). In this context, our findings support the notion that environmental manipulations may be used effectively to treat abnormal behaviors resulting from biological causes such as depletion of brain dopamine. Furthermore, these environmental modifications may be equal to or even superior to pharmacologic intervention in ameliorating specific symptoms. For example, the improvement in avoidance performance observed in T-Het pups relative to T-Hom pups was comparable to that observed in pups after treatment with methylphenidate (*18*).

Although extrapolation from animal study models to human disorders must be done with caution, such findings suggest that environmental manipulation could serve as an alternative to the administration of methylphenidate and amphetamine in hyperactive children. More importantly, these findings suggest that future studies should focus not on whether hyperactivity is related to biological factors or environmental factors, but rather on the contribution of each to the behavioral repertoire of the developing organism.

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References and Notes

1. F. Wehmer and K. L. C. Jen, *Dev. Psychobiol.* **11**, 353 (1978); P. F. D. Seitz, *Am. J. Psychol.* **110**, 916 (1954); J. Lat, E. M. Widdowson, R. A. McCance, *Proc. R. Soc. London* **153**, 347 (1960); R. Priestnall, *Dev. Psychobiol.* **6**, 217 (1973); S. Franhova, *Nutr. Metab.* **12**, 228 (1970); M. H. Teicher and J. T. Kenny, *Nature (London)* **275**, 644 (1978).
2. V. H. Dennenberg, G. A. Hudgens, M. X. Zarrow, *Science* **143**, 380 (1963).
3. R. McCarty and C. M. Southwick, *Dev. Psychobiol.* **12**, 269 (1979).
4. B. A. Shaywitz, R. D. Yager, J. H. Klopper, *Science* **191**, 305 (1976); J. C. Stoof, H. Dijkstra, J. P. M. Hillegers, *Psychopharmacology (Berlin)* **57**, 163 (1978); S. M. Eastgate, J. J. Wright, J. S. Werry, *ibid.* **58**, 157 (1978); C. A. Sorenson, J. S. Vayer, C. S. Goldberg, *Biol. Psychol.* **12**, 133 (1977).
5. L. Erinoff, R. C. MacPhail, A. Heller, L. S. Seiden, *Brain Res.* **164**, 195 (1979).
6. M. H. Teicher, H. L. Kootz, D. J. Cohen, B. A. Shaywitz, *J. Comp. Physiol. Psychol.*, in press.
7. P. K. Randall and B. A. Campbell, *ibid.* **90**, 453 (1976).
8. G. J. Smith and N. E. Spear, *Science* **202**, 327 (1978).
9. B. A. Shaywitz and D. E. Pearson, *Pharmacol. Biochem. Behav.* **9**, 1973 (1978); B. A. Shaywitz, G. G. Griffieth, J. A. Warshaw, *Neurobehav. Toxicol.* **1**, 113 (1976).
10. G. W. Anderson, D. K. Batter, J. G. Young, B. A. Shaywitz, D. J. Cohen, *J. Chromatogr.* **181**, 453 (1980).
11. B. A. Campbell, L. D. Lytle, H. C. Fibiger, *Science* **166**, 635 (1969).
12. R. K. Loch, L. S. Refales, I. A. Michaelson, R. L. Bornschein, *Life Sci.* **22**, 1963 (1978).
13. P. H. Wender, *Minimal Brain Dysfunction in Children* (Wiley, New York, 1971), pp. 59–61.
14. G. Weiss and L. Hechtman, *Science* **205**, 1348 (1979).
15. T. Shetty and T. N. Chase, *Neurology* **26**, 1000 (1976); B. A. Shaywitz, D. J. Cohen, M. B. Bowers, Jr., *J. Pediatr.* **90**, 67 (1977); W. Shekim, H. Dekirmenjian, J. Chapel, *Am. J. Psychiatry* **134**, 1276 (1977).
16. R. A. Barkley, *J. Child Psychol. Psychiatry Allied Discip.* **18**, 137 (1977).
17. S. G. O'Leary and W. E. Pelham, *Pediatrics* **61**, 211 (1978); J. H. Satterfield, D. P. Cantwell, B. T. Satterfield, *Arch. Gen. Psychiatry* **36**, 965 (1979).
18. B. A. Shaywitz, J. H. Klopper, J. W. Gordon, *Arch. Neurol.* **35**, 463 (1978).
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Minimal Conditions for the Visual Detection of Structure and Motion in Three Dimensions

Abstract. *Human observers detected the global three-dimensional organization of visual patterns consisting of only two successive frames of randomly positioned dots, corresponding to projections of a rotating sphere. A perfectly coherent sphere yielded a stable perceptual organization that was detected more accurately than other slightly less organized patterns.*

One of the impressive achievements of the visual nervous system is the perception of stable structures moving in three-dimensional space. Even though the metric properties of the stimulus patterns projected onto the two-dimensional surface of photoreceptors are continually changed by movements of the observer and movements of environmental objects, the perceived structure of three-dimensional space remains invariant under these projective transformations.

Psychophysical research on the "kinetic depth effect" (*1, 2*) has suggested that perceptual stability of three-dimensional space arises directly from the optical projections of dynamic patterns without requiring the intervention of cognitive processes (*3*). A small number of lines or spots that form no recognizable pattern in a stationary two-dimensional projection yield a compelling impression of a solid object when the projection is moved as if rotating in three-dimensional space. Most of this evidence, however, has relied upon subjective judgments; objective and quantitative determinations of observers' sensitivities to structural details have been lacking. Additionally, most experiments have used patterns of relatively small numbers of elements, usually displayed in motion over several seconds (*4*). As a result, the dependence of this perceptual sensitivity on the complexity of the pattern and the duration of observation remains unclear.

Our experiments provide objective evidence for the perception of global three-dimensional structure and motion in stimulus patterns consisting of only two successive frames of several hundred randomly positioned dots. We used a temporal variant of Julesz's "cyclopean" method (*5*), in which the geometric information for this perception was provided only by the space-time