Effects of prenatal hypoxia upon activity and emotionality of the rat[1]

CHARLES J. VIERCK, JR., FREDERICK A. KING AND VERGIL H. FERM[2]
CENTER FOR NEUROBIOLOGICAL SCIENCES, UNIVERSITY OF FLORIDA

Gravid female rats were made hypoxic on the eighth or twentieth day of term. Their progeny were found to be more active in an avoidance shuttle box. These results are contrasted to similar studies measuring activity in non-noxious circumstances. Also, the experimental Ss were found to be hypoemotional in comparison to their controls as measured by a rating scale and weight loss during avoidance training. The offspring of animals treated on the eighth day of gestation were less emotional than those receiving treatment on the twentieth day, confirming other studies demonstrating behavioral differences linked to prenatal age at treatment.

Recent evidence indicates that the behavioral dimensions of emotionality and activity are extremely sensitive to various perinatal treatments, including the following: oxygen deprivation (Saxon, 1961a, 1961b; Becker, 1958; Vierck & Meier, 1963), X-irradiation (Werboff et al, 1962), drug injection (Werboff et al, 1961; Werboff & Havlena, 1962), and even water vs. saline or intraperitoneal vs. subcutaneous injection (Werboff & Havlena, 1962).

Hypoxia, administered neonatally to monkeys (Saxon, 1961a, 1961b) renders the experimental animals hyperactive in a novel environment, hypoactive after adaptation to the testing environment, and generally hypoemotional. Prenatal hypoxia in mice, if given late in gestation, produces identical activity results, but the animals treated early become generally hypoactive (Vierck & Meier, 1963). The present study extends these findings to prenatal hypoxia of the rat.

Method

Two groups of four, gravid, female rats of the Wistar strain were made hypoxic on the eighth (H8) and twentieth (H20) days of term, and their progeny comprise the experimental animals of this study (H8, N=10; H20, N=25). The control group (C) consisted of four litters from untreated mothers (N=23). Hypoxia was induced by evacuating air from a dessicator at a rate which maintained a simulated altitude of 33,000 ft. for 6 hr. (including 20 min. rise and fall times).

Emotional behavior was rated numerically by assigning a value of from zero to five according to strength of reaction to each of six components. As described by King (1958, p. 58), the emotional components are: (a) attack or flight reaction to a pencil presented visually to the S's face, (b) startle and flight reaction to tactile stimulation of the animal's back, (c) resistance to capture, (d) muscular tension and resistance to handling, (e) vocalization during testing, (f) urination and defecation during testing. A further measure related to emotionality was obtained by recording the amount of weight lost during five 1/2-hr. avoidance conditioning sessions. Forty conditioning trials per day were randomly presented in time and consisted of the sounding of a tone until the animal crossed into the opposite compartment of the shuttle box. If the animal did not respond correctly within a 5-sec. avoidance period, shock was applied to its feet until crossing occurred. Efficiency of learning was measured as percent avoidance responses, and level of activity was assessed by recording the total number of crossings between compartments of the shuttle box. The latter measure included 40 avoidance or escape crossings in each daily session.

Results

As seen in Fig. 1B, both groups H8 and H20 exhibited consistent hyperactivity as compared to the control group. These differences were frequently significant (solid symbols in Fig. 1) and were maintained over five consecutive days of avoidance testing, even

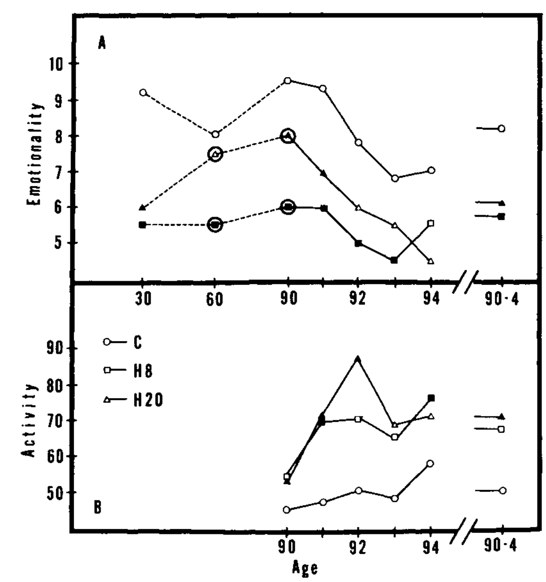

Fig. 1. Median emotionality ratings (A) and mean activity scores (B) for the three groups at different ages of testing. Solid symbols indicate statistically significant differences between control and experimental groups (5% level). Encircled symbols denote significant differences between groups H8 and H20. The statistical tests used were the Mann-Whitney U for emotionality and t-test for activity. The number of subjects was as follows: 30 and 60 days, C = 23, H8 = 10, H20 = 25; 90 - 94 days, C = 10, H8 = 7, and H20 = 7. Animals in the smaller groups (90 - 94 days) were randomly selected from the larger groups with the provision that all litters be represented.

though the experimental groups received fewer shocks in the shuttle box. The mean percent conditioned responses over 200 trials were: C = 40.8, H8 = 52.2, H20 = 51.0 (differences between groups not significant).

The emotionality rating scale revealed consistent hypoemotionality for groups H8 and H20 (Fig. 1A). These differences were maintained from 30 to 90 days of age and held up over five consecutive days of testing (90-94 days). In addition, group H8 was consistently less emotional than group H20 (circled symbols in Fig. 1 indicate significant differences on days 60 and 90). In support of the emotionality rating data, groups H8 and H20 lost significantly less weight than the control group during individual avoidance conditioning sessions, indicating less urination and defecation in response to stress. The weight loss data were adjusted by the analysis of covariance procedure (Cochran & Cox, 1950) to control for the number of shocks received by each animal. The mean weight losses in grams before and after adjustment were: C = 7.2, 2.3; H8 = 3.2, -0.9; H20 = 3.6, -0.6.

Neurological examination revealed no differences between groups, except that a greatly attenuated startle response to an intense auditory stimulus (hand clap) was observed for group H8. The H8 rats were not deaf as indicated by efficient responding to an auditory CS in the shuttle box.

Discussion

The results of this study lend a good deal of generality toward identification of an hypoxic behavioral syndrome involving activity and emotionality. Some part of the emotionality-activity pattern has now been demonstrated with neonatal treatment of monkeys (Saxon, 1961a, 1961b) and guinea pigs (Becker, 1958) and prenatal treatment of mice (Vierck & Meier, 1963) and rats. In these studies, hypoemotionality among treated animals has been demonstrated with the following measures: observation of behavior in an open field, reaction to electric shock, reaction to handling and prodding, and excretion under stress. In the present study, hypoemotionality of group H8 with respect to group H20 extends previous findings that Ss deprived of oxygen early in gestation learn a maze faster (Meier et al, 1960) and are less active (Vierck & Meier, 1963) than late deprived animals.

All hypoxic Ss maintained hyperactivity over five consecutive days of testing, in contrast to previous studies showing consistent hypoactivity (early treated group) or reversal from hyper- to hypoactivity within this period (late treated groups). Possibly the intense stress conditions created by electric shock were responsible for hyperactivity of the early treated group (H8) in this study, environmental novelty not providing sufficient activation in the previous study. The same explanation would apply to consistent hyperactivity among the late treated group (H20), environmental novelty being an adequate activator to comparable groups in the other studies. Thus, hypoxic animals may be characterized as somatically energized under stress (novel environment or electric shock conditions) and sluggish in familiar surroundings. This pattern corroborates the clinical findings of Preston (1945), who studied children with histories of hypoxia at birth and noted hyperreactivity under stress but otherwise profound lethargy. Strikingly similar results have also resulted from prenatal irradiation (Werboff et al, 1962), all experimental groups exhibiting hypoemotionality, early irradiated groups demonstrating hypoactivity, and late irradiated groups showing hyperactivity.

References

Becker, R. F. Learning ability after asphyxiation at birth, especially as it concerns the guinea pig. In W. F. Windle (Ed.), *Neurological and psychological deficits in asphyxia neonatorum.* Springfield, Ill.: Charles C. Thomas, 1958.

Cochran, W. G., & Cox, G. M. *Experimental designs.* New York: John Wiley and Sons, Inc., 1950.

Havlena, J., & Werboff, J. Postnatal effects of control fluids administered to gravid rats. *Psychol. Rep.*, 1963, 12, 127-131.

King, F. A. Effects of septal and amygdaloid lesions on emotional behavior and conditioned avoidance responses in the rat. *J. nerv. ment. Dis.*, 1958, 126, 57-63.

Meier, G. W., Bunch, M. E., Nolan, C. Y., & Scheidler, C. H. Anoxia, behavioral development, and learning ability: a comparative-experimental approach. *Psychol. Monogr.*, 1960, 74, (Whole No. 448).

Preston, M. I. Late behavioral aspects found in cases of prenatal, natal and postnatal anoxia. *J. Pediat.*, 1945, 26, 353-366.

Saxon, S. V. Effects of asphyxia neonatorum on behavior in the rhesus monkey. *J. genet. Psychol.*, 1961a, 99, 277-282.

Saxon, S. V. Differences in reactivity between asphyxial and normal rhesus monkeys. *J. genet. Psychol.*, 1961b, 99, 283-287.

Vierck, C. J., Jr., & Meier, G. W. Effects of prenatal hypoxia upon locomotor activity of the mouse. *Exp. Neurol.*, 1963, 7, 418-425.

Werboff, J., Gottlieb, J. S., Havlena, J., & Word, T. J. Behavioral effects of prenatal drug administration in the white rat. *Pediatrics*, 1961, 27, 318-324.

Werboff, J., & Havlena, J. Postnatal behavioral effects of tranquilizers administered to the gravid rat. *Exp. Neurol.*, 1962, 6, 263-269.

Werboff, J., Havlena, J., & Sikov, M. R. Effects of prenatal X-irradiation on activity, emotionality, and maze-learning ability in the rat. *Radiat. Res.*, 1962, 16, 441-452.

Notes

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2. Now at Department of Pathology, Dartmouth Medical School.