The effect of carbon dioxide on spontaneous locomotor activity in normoxic and hypoxic atmospheres

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Eleven male Sprague-Dawley rats were run in an activity wheel for three 20 min sessions under each of four atmospheres varying in O₂ concentration (21% or 8%) and CO₂ concentration (0% or 5%), remainder N₂. Results indicated an interaction of CO₂ and O₂ levels. The addition of 5% CO₂ to a normoxic atmosphere reduced spontaneous locomotor activity. The addition of 5% CO₂ to a hypoxic atmosphere increased the level of activity. These data are consistent with the findings of other investigators concerning the effects of CO₂ and O₂ on the central nervous system.

Inspiration of atmospheres containing either high concentrations of CO₂ or low concentrations of O₂ individually tend to depress central nervous system (CNS) function, although evidence of transient excitation has sometimes been observed (Creutzfeldt, Kasamatsu, & Vaz-Ferriera, 1957; Dunlop, 1957; Everett, Goodsell, & Toman, 1952; Gellhorn & Ballin, 1950; Gibbs, Gibbs, Lennox, & Nims, 1943; Woodbury, Rollins, Henrie, Jones, & Sato, 1956). However, inspiration of atmospheres containing the combination of both high concentrations of CO₂ and low concentrations of O₂ tends to normalize CNS function and behavior rather than to compound the depressant effects of high CO₂ and low O₂ individually (Annau & Weinstein, 1967; Childs, Hamlin, & Henderson, 1935; Gibbs et al, 1943).

Activity level of rats has been used as an indication of CNS function (e.g., Kinnard & Carr, 1957). Gerben (in press) has demonstrated that the running behavior of rats in an activity wheel is sensitive to the effects of hypoxia. Locomotor activity generally decreased with hypoxia, although initial increases were sometimes observed.

If it is assumed that the effects of hypoxia on spontaneous activity were related to its CNS effects, it would be expected that the above described interaction between CO₂ and O₂ levels in the inspired atmosphere would be reflected in running behavior. The present experiment was designed to investigate this interaction.

Subjects

Eleven male albino rats from the Sprague-Dawley strain were housed singly in home cages with food and water continuously available. Ss were approximately 70 days old at the beginning of pretraining (see below).

Apparatus

The activity wheel, gas chamber, and recording apparatus were previously described in detail (Ger-

ben, in press). Essentially, this apparatus consisted of an activity wheel mounted in a gas chamber with a volume of approximately 10 liters. Electromechanical counters recorded the number of 1/8 revolutions (responses) of the wheel in either direction. Cylindrical O₂-N₂-CO₂ mixtures provided the experimental atmospheres. The mixtures were calibrated to be within 0.5% of the stated values.

Design

A treatments by treatments by runs by subjects design (Lindquist, 1953) was used with two levels of O₂ (21 and 8 percent) and two levels of CO₂ (0 and 5 percent). Each of the four resulting atmospheric conditions was presented on one of four consecutive days. Three runs through the four atmospheric conditions were presented with three days intervening between each run. Within each run, the order of presentation of atmospheres was randomly determined for each S.

Procedure

Ss were given 20 days of pretraining in order to adapt them to the activity wheel. Each pretraining session consisted of 5 min of exposure to the activity wheel during which running was prevented by a braking system on the wheel, immediately followed by a 20 min period during which running was allowed. The atmosphere during pretraining was room air.

Experimental sessions were identical to pretraining sessions except for the manipulation of atmospheric conditions. During the 5 min initial exposure period, the experimental atmosphere was introduced into the chamber at a rate of 15 liters per min (see Gerben, in press). After 5 min had elapsed, the flow rate was reduced to 5 liters per min and the brake was released, thus allowing running to begin. Activity was measured by counting the number of 1/8 revolutions of the wheel in either direction within the 20 min running period.

Results

Figure 1 shows mean responses (1/8 revolutions) under each of the four atmospheric conditions in each of the three runs. Inspection of this figure suggests an interaction between the effects of O₂ and CO₂. Analysis of variance yielded a statistically significant interaction between these variables ($F = 31.39$, $df = 1/10$, $p < .05$). The main effect attributable to oxygen level was also statistically significant ($F = 14.50$, $df = 1/10$, $p < .05$). Subsequent t tests on the

Fig. 1. Mean responses (1/8 revolutions) as a function the percentage of oxygen and the percentage of carbon dioxide. The number to the left of each function refers to the run from which the data were taken.

total activity during the three runs indicated that CO₂ significantly decreased activity under conditions of normal O₂ concentration ($t=5.67$, $df=10$, $p<.05$) and significantly increased activity under hypoxic conditions ($t=2.79$, $df=10$, $p<.05$).

Discussion

The results of the present experiment indicate that running behavior of rats is sensitive to the effects of high CO₂ and low O₂ concentration both individually and in combination. In addition, the interaction of these conditions observed by previous investigators was verified using spontaneous activity.

The data suggest that the depressant effects of CO₂ on activity under normoxic conditions may be related to its depressant effects on the CNS. Woodbury & Karler (1960), in a review of experiments involving the effects of CO₂ on seizure thresholds, conclude that CO₂ has a triphasic effect on CNS excitability. Low concentrations of CO₂ (approximating the 5% level used in the present study) depress cortical function. With progressively higher concentrations (10-30%), subcortical structures are stimulated and overcome cortical depression. At concentrations of CO₂ above 30%, both cortical and subcortical depression occurs. The decrease in locomotor activity in the present experiment may reflect cortical depression. Whether this behavior is correlated with seizure measures of cortical excitability over a wider range of CO₂ concentrations is not known.

The increase in activity resulting from the addition of CO₂ to a hypoxic atmosphere may be related to the normalizing action of CO₂ on cerebral function under hypoxic conditions. Hyperventilation stimulated

by hypoxia causes a loss of CO₂ via the lungs. This may cause cerebral vasoconstriction and reduced cerebral blood flow. Inhalation of CO₂ compensates for the loss of CO₂, causing cerebral vasodilation and increased cerebral blood flow. In addition, CO₂ stimulates ventilation and shifts the hemoglobin dissociation curve so that more oxygen is delivered to the tissues (Gellhorn, 1937). Carbon dioxide was found to greatly reduce the effects of hypoxia on direct measures of cortical function (Gibbs et al, 1943). Gibbs has suggested that CO₂ is as important to normal cerebral function as is oxygen.

Thus, there is considerable neurophysiological evidence consistent with the present results. That is, to the extent that the level of spontaneous locomotor activity is related to CNS function (Kinnard & Carr, 1957; Pirch & Norton, 1967; Sutton, 1967), the present experiments suggest that O₂ and CO₂ have interacting effects on brain mechanisms which mediate voluntary activity.

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