NITROGEN-INDUCED BRADYCARDIA IN ANESTHETIZED RATS

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ABSTRACT

In order to differentiate the overall effect of pressure and the type and partial pressure of the component gases of the gas mixture 10 anesthetized, male Wistar rats average weight 400 g. and aged 6 months were exposed to 4 conditions of gas pressure and composition in a pressure chamber for periods of 2 hours on separate occasions. Heart rate, ECG, respiration, rectal temperature, chamber pressure and temperature, O_2 and CO_2 partial pressures were measured continuously. Both the character and time of onset of the developed bradycardia in the 4.2 ata condition differed from the other conditions. Manipulation of the composition of the gaseous environment at the point of the maximally developed bradycardia while keeping the overall pressure constant always produced a sustained tachycardia. Pharmacological interventions with vagus blocking (atropine) and a B blocking drug propranalol were also studied.

INTRODUCTION

One early manifestation of depressed metabolism resulting from increased air pressures of from 1 to 10 ata before stupefaction and motor control is lost is the pronounced bradycardia which develops both in men and animals (1). It was easy to ascribe this observation to the increased partial O_2 pressure since breathing pure O_2 had been shown to have similar consequences as early as 1912 (2), a result confirmed later several times (3,4). It was subsequently shown that the O_2 effect is mediated through the vagus (5). Recently (6) it was observed that a part of diving bradycardia may also be ascribed to the effect of increased N_2 partial pressure alone. This N_2-induced bradycardia seemed not to be abolished in man by vagus blocking (8). The experiments described below were intended to study the mechanism of N_2-induced bradycardia.

METHODS

Experiments took place in a small vertical animal chamber 1 1/2 feet in diameter and 3 feet deep which could be pressurized to 10 ata.

ANIMALS AND ANESTHESIA

Rats were exposed on separate occasions to 4 conditions of gas pressure and composition for periods up to 2 hours. Each exposure was not more frequent than 2 days. Animals were anesthetized with 60 mg/Kg sodium pentobarbital ip.

CONDITION I (1 ata air)

The anesthetized animal was placed in the chamber and aerated for 5 minutes. It remained there for 2 hours.

CONDITION II (5 ata air)

The anesthetized animal was compressed to 5 ata with air.

CONDITION III 4.2 ata (4 ata N_2 and .2 ata O_2)

The animal was compressed to 4.2 ata with N_2.

CONDITION IV 1.8 ata (1 ata O_2 + .8 ata N_2)

The animal was compressed from 1 ata air to 1.8 ata with 100% O_2. In all cases carbon dioxide tension was allowed to accumulate throughout. The final concentration were never greater than 2%.

PHARMACOLOGICAL MANIPULATION

Subsequently in several animals the effects of raised ambient pressure were studied in atropinized rats and in beta receptor blocked animals (propanalol).

RESULTS

Mean decrements in heart rate, rectal temperature and increments in respiration, between the start and end of the compression period were calculated for the group of animals in each condition. Table 1 shows the t-ratio of the difference between correlated means among the various conditions. Significant differences occur between the 4.2 ata condition and the 1 ata and 5 ata conditions in mean heart rate decrements and between the 1.8 ata and 5 ata condition. The time course of the heart rate decrement in the various conditions is shown in Figure 1. The qualitative aspects of the 4.2 ata decrement curve may be seen to be very different from the others. Actual records of some experiments are shown in Figures 2,3, and 4. Figure 2 shows that when nitrogen is replaced by oxygen at 4.2 ata although the heart rate is increased the usual ventilatory response to oxygen breathing is observed. Figure 3 and 4 show the effect of vagus blocking with atropine and beta blockage with propanolol respectively. Vagus blocking does not alter the heart rate-pressure response.

DISCUSSION

These data confirm the separate effect of raised ambient nitrogen pressure on heart rate decrement distinguishing it from the decrement due to high inspired oxygen tensions mediated through the vagus nerve. A similar bradycardia has been observed in man in response to elevated nitrogen tensions - an effect not abolished by atropine (7). The mean latent period of exposure to raised ambient nitrogen pressure before the onset of steep heart rate decline of 25-30 min. is similar to the time interval previously noted for cessastion of brain waves in mice subjected to high pressure. This reflects possible involvement of the CNS (8). Nitrogen molecules in vivo may also be involved in supression of metabolic activity at cellular sites by inhibiting molecular transport across the cell membrane (9). Previous evidence for this effect from in vitro studies on oxygen consumption in tissue slices is controversial indicating both lower and unchanged $\dot{V}O_2$ ml/mg/hr in N_2 atmospheres compared to O_2-Ne or O_2-He mixtures (10, 11, 12). However even if respira-

tion falls severely in the cell due to such molecular interactions the cell function can be suspended so that it may take up its function again later when oxygen is available (13). In this respect the fall in metabolic function, relected in the heart rate decrement, is qualitatively similar, although considerably abbreviated, to the time course of this parameter in hibernating animals at the onset of hibernation (14). The recently observed critical role of core temperature in the balance of sympathetic and parasympathetic level (15) seems not important in these experiments. The exact mechanism of N_2 - induced bradycardia, is still undetermined but since the effect of increasing oxygen tension on the developed nitrogen-bradycardia is a tachycardia it is possible that tissue respiration at the cellular level is inhibited either in the nerve itself or its receptor sites.

TABLE 1. t-ratio of differences in paired means between groups.

		t-ratio of paired mean differences				
Ata	1-5	1-4.2	1-1.8	5-4.2	5-1.8	4.2-1.8
Heart Rate	0.29	-3.60	-1.58	-2.53	-2.39	1.92
Rectal Temp.	0.57	0.10	0.40	1.89	1.25	0.90
Respir-ation	0.87	0.72	-1.47	-0.61	1.21	-0.43

* t-ratio 2.26 significant at .05 level; 3.25 significant at .01 level.

FIG. 1 Heart rate decrement in anesthetized rats under pressure.
FIG. 2 Oxygen manipulation effect.
FIG. 3 Vagus blocking effects.
FIG. 4 β-blocking effects.

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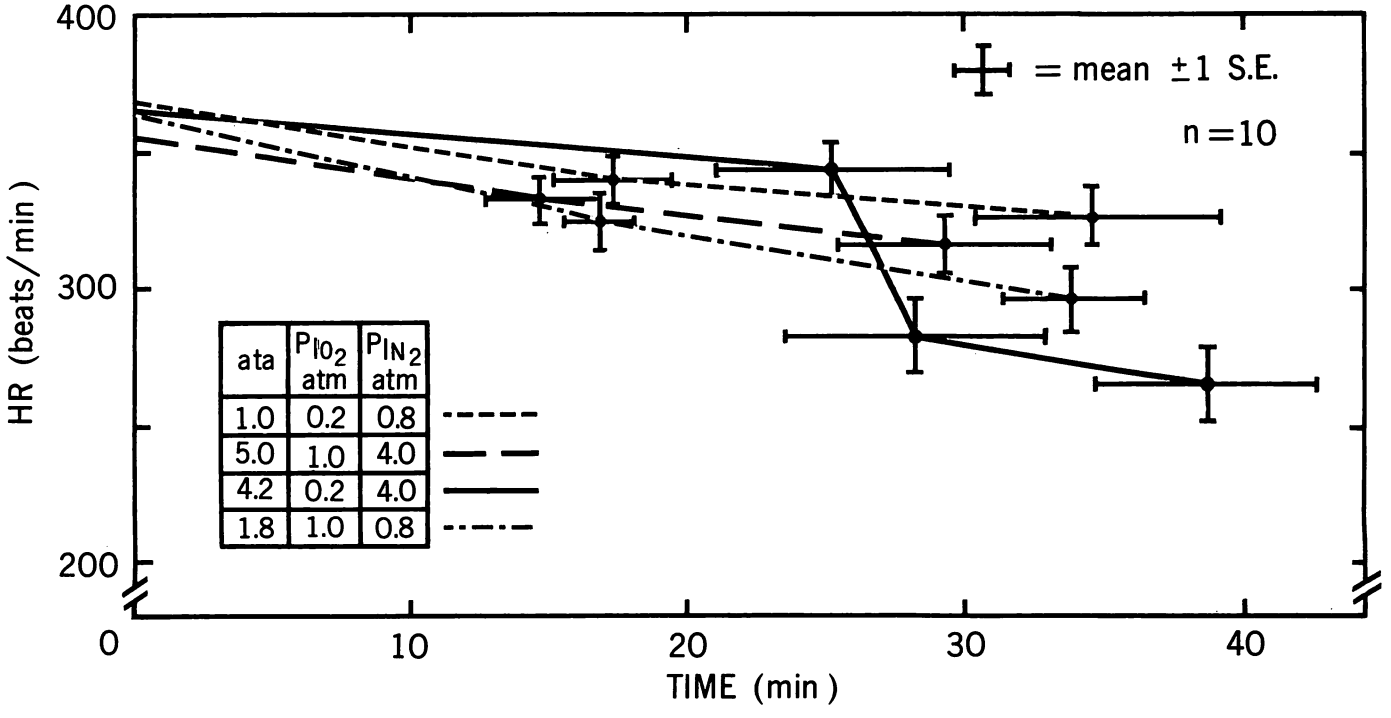
BIBLIOGRAPHY

1. Shilling, C.W., Hawkins, J.A., and Hansen, R.A. Naval Med. Bul. Wash., 34: 39-47, 1936.
2. Parkinson, J., J. Physiol.(Lond.) 44:54, 1912.
3. Dautrebande, L., and Haldane, J.S., J. Physiol. (Lond.) 55: 296, 1921.
4. Barratt-Boyes, B.G., and Wood, E.H., J. Lab. Clin. Med. 51: 72, 1958.
5. Daly, W.J., and Bordurant, S., J. Clin. Invest. 41: 126-132, 1962.
6. Hesser, C.M., Proc. Int. Union Physiol. Sci. 7: 191, 1968.
7. Fagraeus, L., Unpublished Observations.
8. Bennett, P.B., and A. Glass. Electroencephalog. Clin. Neurophysiol., 13: 91-98, 1961.
9. Schreiner, H.R., Fed. Proc. 27: 3, 1968.
10. Maio, D.A. and J.R. Neville, Aerospace Med. 38: 1049, 1967.
11. Ho Lee Young, and P.R. Lundgren, Aerospace Med. Assoc. 190-191, 1970.
12. Rodgers, S.H., W.O. Fenn and A.B. Craig, Jr. Respiration Physiology. 6: 168-177, 1969.
13. Lubbers, H., In A Symposium on O_2 Measurements in Blood and Tissues, Eds. J.P. Payne and P.W. Hill, London, J.A. Churchill. p. 199, 1966.
14. Lyman, C.P. and R.C. O'Brien, Bull Museum Camp Zool. Harvard Coll. 124: 353-372, 1960.
15. Walsh, R.R., Am.J.Physiol. 217(4): 1139-1143, 1969.



EFFECT OF RAISED AMBIENT PRESSURE ON HEART RATE IN ANESTHETIZED RATS