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Influence of nitrous oxide, nitrogen, neon, and helium on the beating frequency of the mouse sinus node at high pressure

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Örnhagen, H. Ch. 1979. Influence of nitrous oxide, nitrogen, neon, and helium on the beating frequency of the mouse sinus node at high pressure. Undersea Biomed. Res. 6(1): 27–39.—The beating frequency (BF) reducing effect of 150 atm of hydrostatic pressure on mammalian cardiac pacemaker tissue (hyperbaric bradycardia) was counteracted by dissolved gas only if the gas was added after hydrostatic compression. The effect on BF seemed to be related to the narcotic potency of the gas and the effect was reversible. The gases tested were N_2O, N_2, Ne, and He, in decreasing order of potency. If N_2O was added at a moderately raised ambient pressure prior to hydrostatic compression to 150 atm, there was no difference in the degree of hyperbaric bradycardia, compared to compression without gas. During decompression, however, experiments performed with gas showed a significantly higher gain in BF compared to experiments without gas. Autonomic blockade seemed to eliminate the difference between decompression with and without N_2O. The results demonstrate that N_2O, N_2, and Ne, and to a small extent He, may counteract the retarding effect that increased hydrostatic pressure has on cardiac pacemaker activity. These effects on the cardiac pacemaker are similar both to the effects of increased hydrostatic pressure and of gases at elevated pressures on the central nervous system, but some important differences remain to be explained.

hyperbaric bradycardia
hydrostatic pressure
heart rate
inert gas
dissolved gas
nitrous oxide
nitrogen
neon
helium
sinus node

Elevation of the ambient pressure reduces the beating frequency (BF) of mammalian cardiac pacemakers (Örnhagen and Hogan 1976; Lundgren and Örnhagen 1976; Örnhagen and Hogan 1977). This slowing of the BF caused by hydrostatic pressure has been called hyperbaric bradycardia. The properties of the excitable membrane of the cardiac pacemaker cell have similarities with the nerve cell membrane, and it has been speculated that the mechanism leading to hyperbaric bradycardia might be of the same nature as that of the high pressure

nervous syndrome (HPNS) (Lundgren and Örnhagen 1976). HPNS has been shown to be caused by increased hydrostatic pressure on the cells of the central nervous system (Kylstra, Nantz, Crowe, Wagner, and Saltzman 1967). More recent studies have shown that narcotic gases in the breathing medium mitigate these symptoms of HPNS both in animals (compare Brauer, Way, Jordan, and Parrish 1971) and in man (Bennett, Blenkarn, Roby, and Youngblood 1974). The present study was undertaken to find out if the BF- reducing effect of hydrostatic pressure could be counteracted by N_2O, N_2, Ne, and He.

MATERIAL AND METHODS

Mice (NMRI) weighing approximately 30 g were killed through cervical dislocation. The sinus node and surrounding atrial muscle was immediately excised from the beating heart and maintained at room temperature in Tyrode's solution having the following millimolar composition: NaCl 137.0, dextrose 5.5, $NaHCO_3$ 12.0, KCl 2.7, MgCl 0.5, and $CaCl_2$ 1.8. In a 2000-ml stainless steel bottle, 700 ml of this solution was equilibrated at 1 atm with a mixture of 98% O_2 and 2% CO_2 to give a pH of 7.46. Tyrode's solution equilibrated with this gas mixture will hereafter be referred to as standard Tyrode's solution. When the bottle was pressurized with the special test gases, the O_2 and CO_2 partial pressures remained largely unchanged. The accuracy of the pressure measurement of the test gases He, Ne, and N_2 was ± 5 atm, and for N_2O ± 0.5 atm. The bottle was shaken repeatedly and kept for at least 12 h in a horizontal position to maximize the gas-liquid interface. After the experiments, the amount of gas in the Tyrode's solution in the stainless steel bottle was measured by decompressing a measured volume of solution in a syringe to 1 atm. In some experiments the gas phase on top of the Tyrode's solution was analyzed by mass spectrometer. Results of these analyses were all in good agreement with expected values.

The tissue preparation in Series A through C was kept in a small Lucite® bath placed in a steel pressure chamber (Fig. 1) having an internal volume of 7 liters. Helium was used to pressurize the chamber and the compression-decompression rate was 10 atm × min^{-1}. The tissue bath in the chamber was covered with a glass lid to minimize contamination of the bathing solution by the He used for compression or loss of test gas to the chamber atmosphere. The perfusion network inside the chamber included short pieces of latex tubing, creating a possible pathway for diffusion of gases out of or into the perfusing medium. However, with respect to the high flow of solution through the tubing, the loss of dissolved gases could not be of any major importance. The Tyrode's solution perfusing the bath exited via perforation and stand pipe mounted on the glass lid. This design allowed for pure hydrostatic compression of the tissue contained within the bath. The solution was pumped (pump: Constametric II, Laboratory Data Control, Riviera Beach, Florida) to the tissue bath from the external reservoirs at a constant flow rate selectable between 5–10 ml × min^{-1} regardless of changes in chamber pressure. Bath temperature was maintained constant with a control network employing thermoelectric Peltier units (601-400U Cambridge Thermionic Corp., Cambridge, Mass.) and a thermistor probe (44202 YSI, Yellow Springs, Ohio). Temperature regulation during steady-state conditions was kept within 0.05°C of the set point (27°C). The response of the system to adiabatic temperature changes was such that only minor temperature transients of less than 0.5°C lasting less than 1 min occurred at the onset and conclusion of the compression and decompression phases. Changes in BF occurring during these short temperature transients were disregarded. The chamber was fitted with a precision pressure gauge (Heise, Model 17289, Newtown, Conn., accuracy ± 0.1 atm) that provided continuous monitoring of chamber pressure. Spontaneous BF of each preparation was manually counted over 30-s

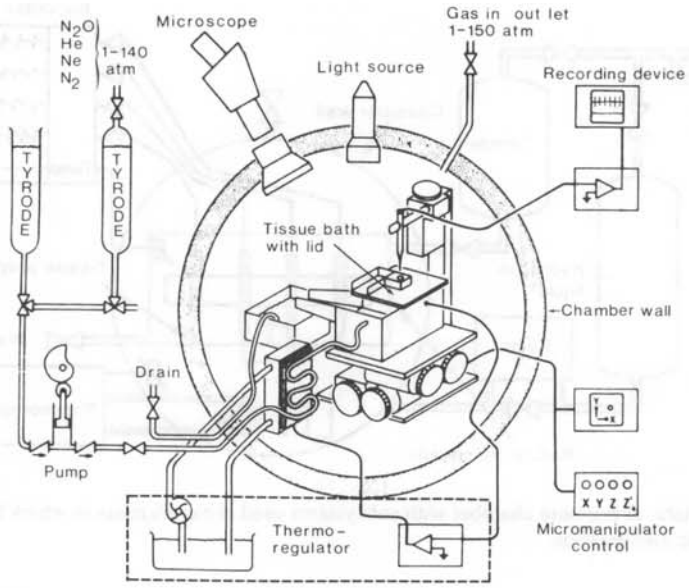

Fig. 1. Schematic of chamber and subsystem used in series A through C.

periods from unipolar surface electrode signal recordings. The silver/silver-chloride electrode coupled to a Grass EKG-tachometer (Mod. 1P4D, Grass, Quincy, Mass.) made contact with the tissue through the perforation in the bath lid that served as the bath outflow port. Precise positioning of the electrode was accomplished using motorized micromanipulators remotely controlled from the outside of the chamber. Signals from the thermistor probe, pressure gauge, and surface electrogram electrode were recorded simultaneously on a Grass polygraph machine (Mod. 7 WC SPA, Grass, Quincy, Mass.). The chamber, tissue bath, temperature control, and micromanipulator systems were designed and built in the Department of Physiology, State University of New York at Buffalo, Buffalo.

For technical reasons, only three test gases could be used in each experimental series. The protocols for the three experimental series A, B, and C, employing different gases at different partial pressures at a constant hydrostatic pressure of 150 atm, are given along the abscissa in Figs. 3, 4, and 5. In principle, a constant high (150 atm) hydrostatic pressure was first established, and the preparation was then exposed to dissolved gases at different partial pressures.

In a separate series of experiments employing a different technique, the effect of 5 atm of N_2O on the BF at a hydrostatic pressure of 6 atm was tested. Furthermore, these experiments dealt with the BF response to hydrostatic compression to 150 atm under a constant N_2O pressure of 5 atm. For blocking of autonomic nerve endings in the tissue preparations, 1 mg of atropine and 4 mg of practolol per liter of Tyrode's solution were used according to the method of Wit and Cranefield (1974). In the earlier experiments on liquid-breathing mice (Lundgren and Örnhagen 1976) and on cardiac pacemaker preparations (Örnhagen and Hogan 1977), sympathetic blockade was obtained with propranolol. In the present series of experiments practolol was used because it lacks anesthetic effects (Barrett 1971) and was therefore preferred to avoid a possible interaction with anesthetic gases.

Four preparations were mounted in a tissue bath filled with Tyrode's solution (Fig. 2). The beating activity was monitored via fixed unipolar silver/silver-chloride electrodes and recorded on a Mingograf 800 (Siemens-Elema, Stockholm, Sweden). The tissue bath, made of

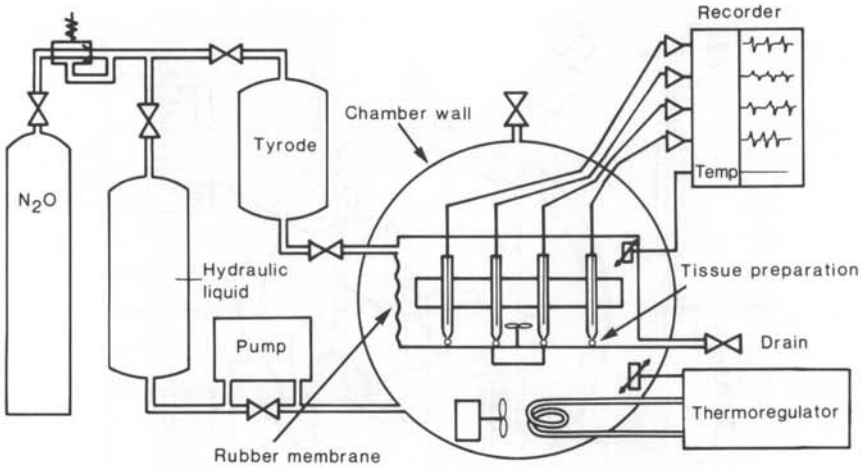

Fig. 2. Schematic of pressure chamber with subsystems used in experiments in which N_2O was added before hydrostatic compression.

Plexiglas, had a volume of 100 ml and was fitted with a propeller for stirring. When the Tyrode's solution in the bath was changed, a constant pressure head for the Tyrode's solution inside the tissue bath and the hydraulic liquid outside the bath was created by compressed N_2O from a cylinder, which was convenient since this gas was often required to saturate the Tyrode's solution. When the gas was used only to provide the pressure head, special care was taken not to get any dissolved N_2O into the tissue bath. The volume decrease of the Tyrode's solution in the bath caused by the compression was compensated for by the displacement of a rubber membrane in one of the sides of the tissue bath. The bath was placed in a small liquid-filled (FC 75 Fluorocarbon, 3M Company, St. Paul, Minn.) pressure chamber that was thermoregulated to maintain bath temperature at 27 ± 0.3°C.

Results are given as means ± 1 SD. For clarity, only mean values are plotted in the graphs. Tests for statistical significance were made with Student's *t*-test and paired *t*-test.

RESULTS

Effects of test gases added at high hydrostatic pressure

Compression of the six preparations of series A (Fig. 3) from 1 to 150 atm gave a change of the mean BF from 173 ± 19.3 to 127 ± 13.7 beats × min^{-1}. When, at a hydrostatic pressure of 150 atm, the preparations were perfused with Tyrode's solution saturated with N_2 at 140 and 70 atm and N_2O at 10 atm, the BF was increased significantly. A change back to standard Tyrode's solution after exposure to a test gas reduced the frequency significantly. The decompression during perfusion with standard Tyrode's solution gave a mean increase in BF of 38 beats × min^{-1} to 140 ± 31.5.

In Series B (n = 6), results of which are displayed in Fig. 4, the experimental protocol was the same as in Series A except for the test gases and the decompression procedure. Helium and Ne were tested and decompression was made to 10 atm while perfusing the preparations with Tyrode's solution containing N_2O at 5 atm. The intention of this procedure was to test whether the presence of a test gas, which had distinct effects at pressure, would alter the BF

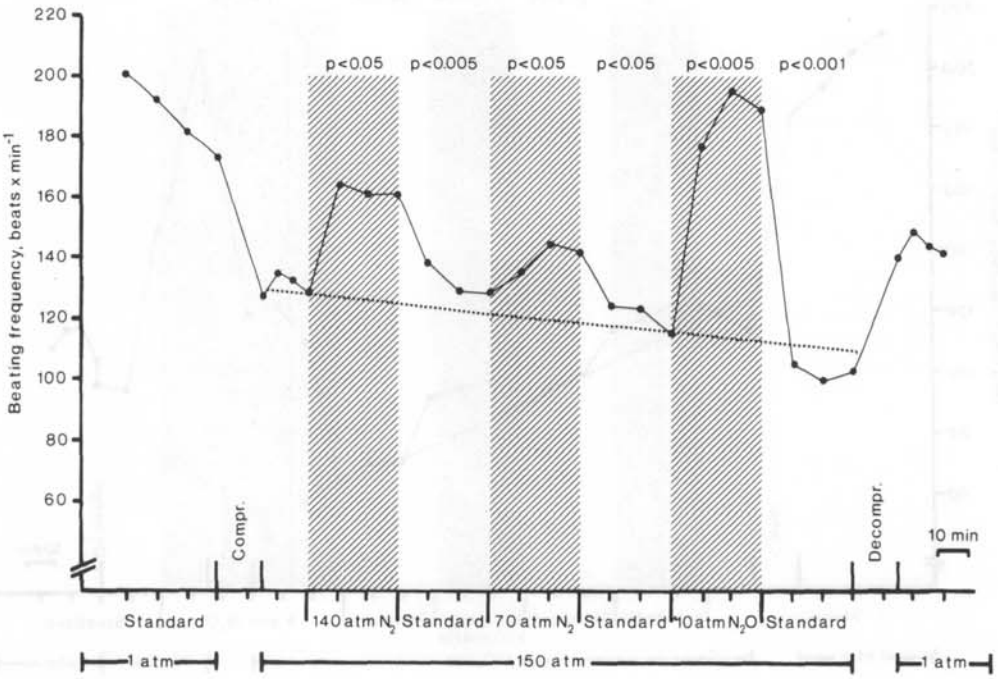

Fig. 3. Mean beating frequencies of 6 mouse sinus node preparations at 1 atm and 150 atm (temperature 27°C). At a constant hydrostatic pressure of 150 atm, perfusion was made with Tyrode's solution containing either 140 atm or 70 atm of N_2 or 10 atm of N_2O, as indicated by shaded columns. Dotted regression line shows fall in beating frequency with time during perfusion with standard Tyrode's solution at 150 atm. *P*-values are obtained from paired *t*-tests of BFs before and after 30 min of a new environment. BF values have been corrected for time-dependent decay (see text for details).

response to decompression. The mean BF of 5 preparations fell from 186 ± 23.2 to 114 ± 15.3 beats × min^{-1} when 150 atm of hydrostatic pressure was applied. (One preparation developed arrhythmia and was therefore excluded.) Introduction of 140 atm of He in Tyrode's solution gave a non-significant change in BF. However, the drop in BF as a result of washing out the He solution with standard Tyrode's solution was significant. The introduction and elimination of Tyrode's solution saturated with a mixture[1] of 120 atm of Ne and 20 atm of He gave significant changes in BF, as did 5 atm of N_2O. Decompression to 10 atm while the preparations were simultaneously exposed to 5 atm of N_2O made the mean BF reach a top value of 208 ± 27.3 beats × min^{-1} immediately after arriving at 10 atm. During 15 min at this pressure, the BF then fell to 148 ± 53.7 beats × min^{-1}. Twenty minutes of perfusion with standard Tyrode's solution at 10 atm reduced the BF to 98 ± 14.5 beats × min^{-1}, while the following decompression to 1 atm increased the rate to 108 ± 18.8 beats × min^{-1}.

Series C (Fig. 5) was run on 6 preparations to explore the effects of relatively low pressures of N_2 and N_2O. The initial hydraulic compression to 150 atm gave a reduction of the mean BF in the six preparations from 162 ± 20.2 to 113 ± 17.3 beats × min^{-1}. The perfusion with Tyrode's solution containing 35 atm of N_2 and 2.5 atm of N_2O did not cause any significant changes of the BF. The following decompression to 10 atm yielded an increase to 127 ± 27.0 beats × min^{-1}.

[1]This particular mixture, left over from other experiments, was used instead of pure Ne for economic reasons.

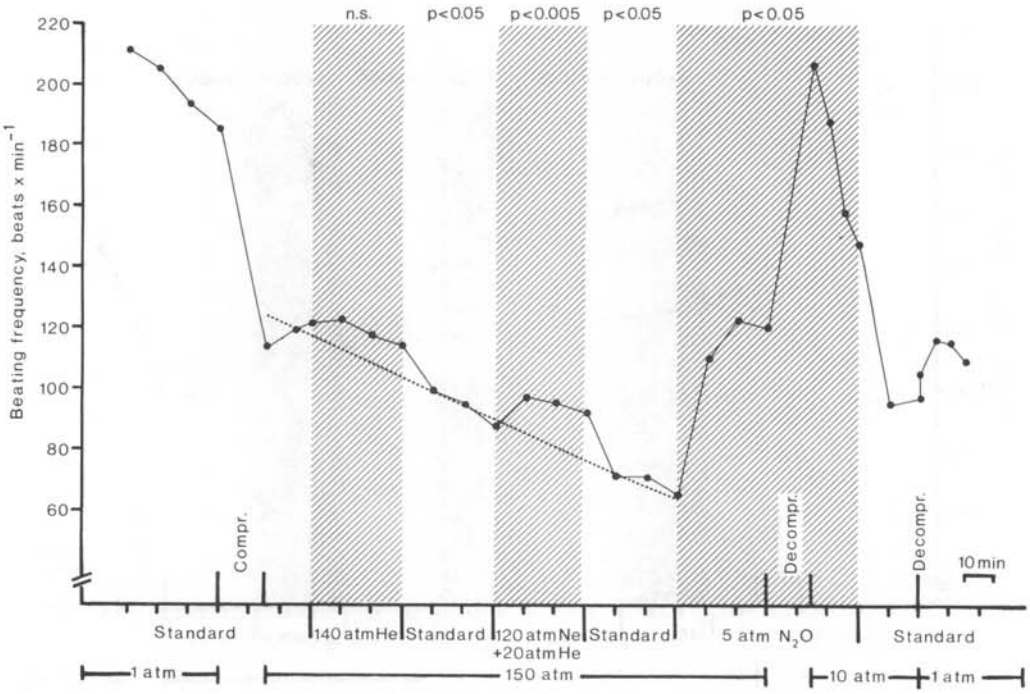

Fig. 4. Mean beating frequencies of 6 mouse sinus node preparations at 1 and 150 atm (temperature 27°C). Periods of perfusion at 150 atm with Tyrode's solution containing 140 atm of He, a mixture of 120 atm Ne and 20 atm of He, or 5 atm N_2O are indicated as shaded areas. During later part of perfusion with 5 atm N_2O, chamber was decompressed to 10 atm. Dotted regression line shows fall in beating frequency with time during perfusion with standard Tyrode's solution at 150 atm. *P*-values are obtained from paired *t*-tests of BFs before and after 30 min of a new environment. BF values have been corrected for time-dependent decay (see text).

Correction of BF values

Regression lines were calculated for each preparation in Series A, B, and C from the individual frequency values obtained during the intervals of perfusion with standard Tyrode's solution at 150 atm. A time-related fall in BF was found and corrected for in the paired *t*-tests. Thus, each raw value was increased by the number of beats corresponding to the time-related drop calculated for each preparation. In Figs. 3–5, the significance levels from the paired *t*-tests are given over each 30-min period tested.

The mean drop in BF with time was found to be 11 beats $\times$ min^{-1} $\times$ h^{-1} in Series A and C and 27 beats $\times$ min^{-1} $\times$ h^{-1} in Series B. The time-related fall observed in 9 preparations kept at control conditions at 1 atm for 6 h was 9 beats $\times$ min^{-1} $\times$ h^{-1}. A regression line was also calculated on the mean BF values obtained during perfusion with Tyrode's solution at 150 atm. This is the dotted line in Figs. 3, 4, and 5. A line may also be drawn through the last frequency value at 1 atm before compression and the value after decompression to 1 atm in Fig. 3. Such a line will run parallel to the regression line just mentioned, which indicates that pressure did not affect the time-related fall in BF.

The maximum response to the test gases or to their elimination developed within 10 to 20 min. The delay of the BF response was of the same order of magnitude as was found for the

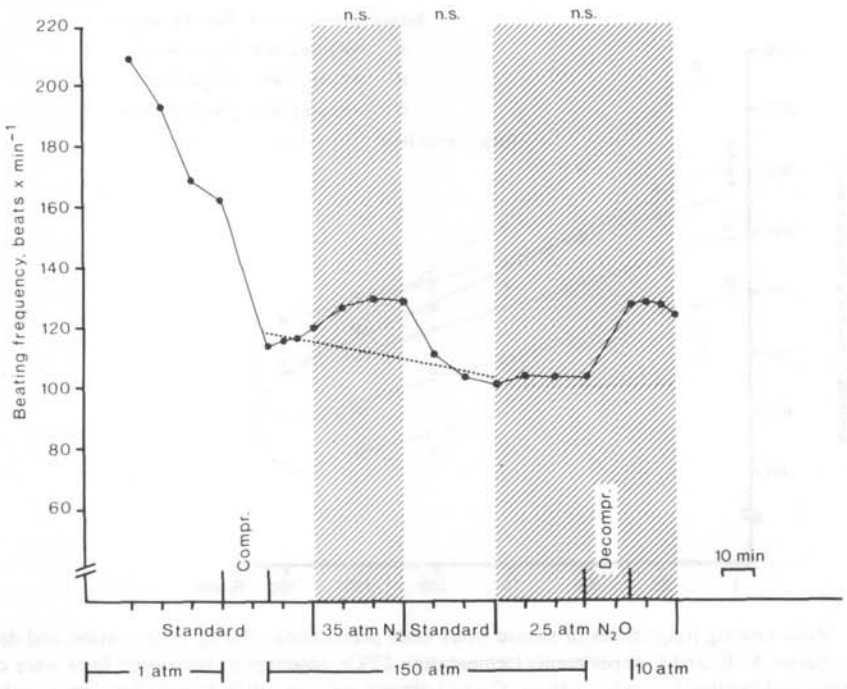

Fig. 5. Mean beating frequencies of 6 mouse sinus node preparations at 1 and 150 atm (temperature 27°C). Periods of perfusion with 35 atm N_2 and 2.5 atm N_2O are indicated as shaded areas. Dotted regression line shows fall in beating frequency with time during periods of perfusion with standard Tyrode's solution. During later part of perfusion with 2.5 atm N_2O, decompression to 10 atm was made. *P*-values are obtained from paired *t*-tests of BFs before and after 30 min of a new environment. BF values have been corrected for time-dependent decay (see text).

response in some separate experiments in which drugs, e.g., adrenaline, were added to the perfusing Tyrode's solution. Therefore, it may be concluded that the response to the dissolved gases was rapid, and that the delay was caused mainly by the time required to wash out the dead space of the perfusion system. In three preparations, periods of severe arrhythmia developed during the experiment, and these parts of the experiments were excluded.

Figure 6 illustrates how the presence of N_2O influenced the response to decompression. In this figure, the mean BFs from Series A, B, and C, respectively, were plotted versus pressure during compression and decompression. All compression values were obtained in the absence of N_2O. During the decompression in Series A, standard Tyrode's solution was used as the perfusing medium. In Series B, the decompression was undertaken with 5 atm N_2O in the Tyrode's solution, and in Series C the N_2O pressure was 2.5 atm. For Series A and C the fall in BF during the period spent at 150 atm is indicated by the curved arrows in the figure. The addition of 5 atm of N_2O at the end of Series B increased the BF enough to mask the time-related reduction in BF. The changes in BF with pressure were treated as linear functions for each of the three series of experiments. The decompression in Series A gave a slope of the regression line (-0.2855, SE = 0.037) that was almost identical with the slope of the line for values obtained during compression (-0.2877, SE = 0.024). The presence of N_2O at a low pressure (2.5 atm) in Series C did not affect the slope of the regression line of decompression (-0.2694, SE = 0.039) compared to the slope during compression (-0.2990, SE = 0.021). In

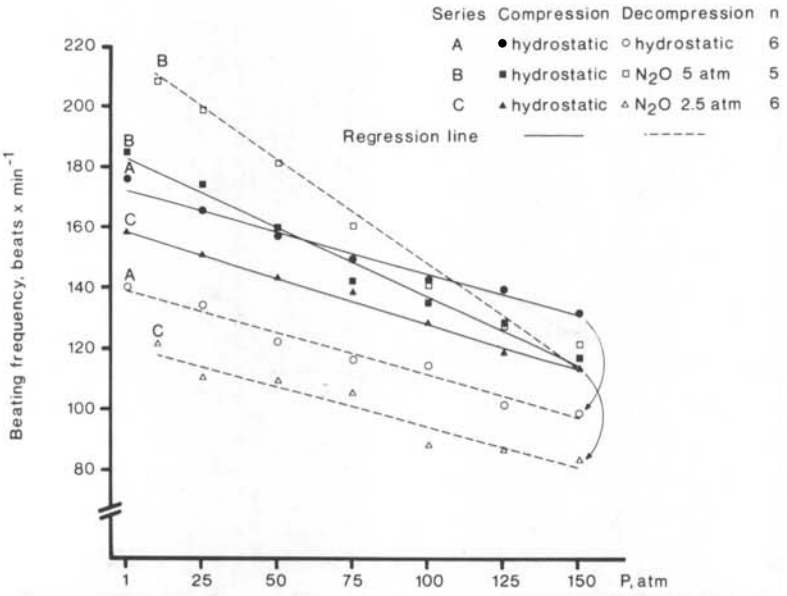

Fig. 6. Mean beating frequencies of mouse sinus node preparations during compression and decompression in Series A, B, and C experiments (temperature 27°C). Interrupted regression lines were calculated on individual beating frequency values. Curved arrows indicate fall in beating frequency with time during stay at 150 atm (compare Figs. 3, 4, and 5).

Series B, in which the N_2O partial pressure was 5 atm, the slope (-0.6638, SE = 0.048) of the decompression was, however, steeper ($P<0.005$) than the slope of the compression (-0.4653, SE = 0.040).

Effects of N_2O added at low hydrostatic pressure

In the preceding sections, the effects of adding N_2O, N_2, Ne and He to the preparation after compression were described. This section deals with experiments on 19 sinus node preparations in which perfusion with Tyrode's solution containing N_2O was begun before compression. Experiments were also made with atropine (1 mg × liter^{-1}) and practolol (4 mg × liter^{-1}) added in addition to N_2O. Because the drugs themselves caused an increase in BF, these values were expressed as percent of the BF immediately before compression, which allows a direct comparison of BF values obtained under different experimental conditions (Fig. 7). In contrast to the observation at 150 atm, the introduction or elimination of 5 atm of N_2O in Tyrode's solution at an ambient pressure of 6 atm (n = 8) did not produce any significant change in the mean BF, nor did the addition of atropine and practolol (n =8) make any difference in this respect. Figure 7 further illustrates the relative BF as a function of pressure and time in experiments in which 8 non-blocked (open circles) and 8 blocked (closed circles) preparations were compressed and decompressed at 10 atm × min^{-1} while exposed to 5 atm of N_2O. The dashed and dotted lines give the relative BF for sinus node preparations in standard Tyrode's solution with blockers and without blockers, respectively.

As can be seen, there were no differences in the degree of bradycardia between preparations exposed to 5 atm of N_2O and preparations in standard Tyrode's solution. Thus, the relative BF of non-blocked preparations in standard Tyrode's solution was 73.4 ± 14.0% immediately

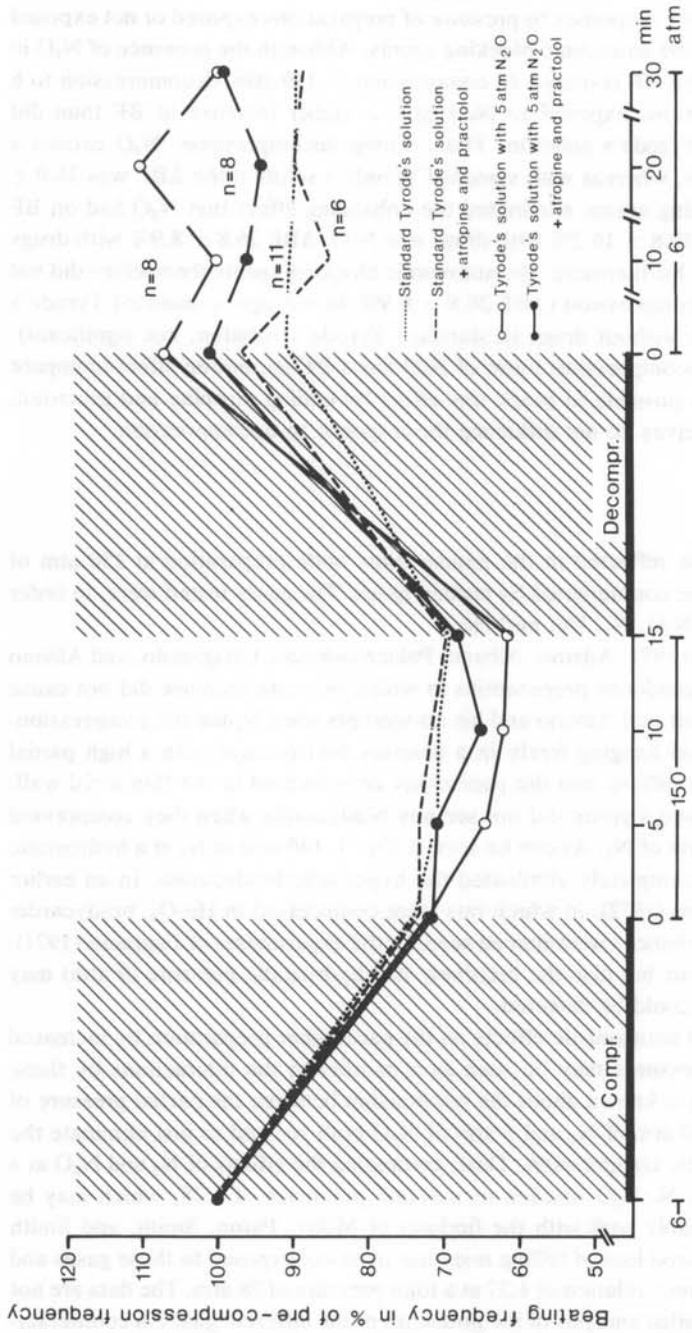

Fig. 7. Mean beating frequencies in percent of precompression beating frequencies of 8 blocked (atropine, 1 mg × liter^{-1} and practolol, 4 mg × liter^{-1}, filled circles) and 8 non-blocked (open circles) mouse sinus node preparations compressed at 10 atm × min^{-1} in Tyrode's solution saturated with 5 atm of N_2O (temperature 27°C). Dashed line shows corresponding beating frequency responses for 6 preparations in standard Tyrode's solution with blockers. Dotted line shows beating frequency responses for 11 preparations in standard Tyrode's solution without blockers.

upon arrival at 150 atm, and the corresponding value in the presence of 5 atm of N_2O was 72.0 ± 20.1%. After 15 min at pressure there was still no difference (BF 68.8 ± 12.7% for preparations in standard solution; BF 61.4 ± 10.8% for preparations exposed to N_2O). The above-mentioned similarities in the BF responses to pressure of preparations exposed or not exposed to N_2O were not changed by the autonomic blocking agents. Although the presence of N_2O in the perfusate did not affect the BF response to compression to 150 atm, decompression to 6 atm of non-blocked preparations exposed to N_2O gave a higher increase in BF than did decompression in standard Tyrode's solution. Thus, during decompression, N_2O caused a relative ΔBF of 49.4 ± 15.5%, whereas with standard Tyrode's solution the ΔBF was 24.0 ± 15.8% ($P<0.005$). The blocking agents eliminated the enhancing effect that N_2O had on BF during decompression (ΔBF 32.8 ± 16.2% with drugs and N_2O, ΔBF 26.8 ± 8.9% with drugs and no N_2O; not significant). Furthermore, the autonomic blocking agents themselves did not influence the response to decompression (ΔBF 26.8 ± 8.9% with drugs in standard Tyrode's solution, ΔBF 24.0 ± 15.8% without drugs in standard Tyrode's solution; not significant). Thus, it seems that during decompression 5 atm of N_2O has a BF-increasing effect (compare Series B in Fig. 6), and it is possible to block this effect by adding atropine and practolol, although these agents themselves do not influence the response to decompression.

DISCUSSION

Hyperbaric bradycardia, as reflected in the mouse sinus node preparation at 150 atm of hydrostatic pressure, could be counteracted by certain gases. The gases tested were, in order of decreasing effectiveness, N_2O, N_2, Ne, and He.

Two publications (Fagraeus 1971; Albano, Albano, Palazzoadriano, Guagliardo, and Albano 1973) describe work on Langendorph preparations in which pressure increase did not cause bradycardia. Fagraeus used air and Albano and his co-workers used N_2 for the compression. In a Langendorph preparation hanging freely in a gaseous environment with a high partial pressure of N_2, the N_2 might diffuse into the pacemaker cells located in the thin atrial wall. This might explain why Albano's group did not see any bradycardia when they compressed their preparations with 150 atm of N_2. As can be seen in Fig. 3, 140 atm of N_2 at a hydrostatic pressure of 150 atm almost completely eliminated the hyperbaric bradycardia. In an earlier study by Criscuoli and Albano (1972), in which rats were compressed in He-O_2, bradycardia and cardiac conduction disturbances were indeed seen. In the experiments of Fagraeus (1971), not only the nitrogen in the air but also the relatively low hydrostatic pressure (9 atm) may explain why no bradycardia could be detected.

The present observation of antagonistic effects on the pacemaker preparation by increased hydrostatic and inert gas pressures may be seen as a parallel to the interactions by these factors on the CNS. Nothing is known about the relationship between the partial pressure of gas and BF response, but 140 atm of N_2 and 5 atm of N_2O both seemed to just eliminate the effect of 150 atm of hydrostatic compression. Thus, comparing the effects of N_2 and N_2O at a point of equal effect gives a N_2:N_2O relation of narcotic potencies of 1:28, which may be fortuitous but agrees remarkably well with the findings of Miller, Paton, Smith, and Smith (1973). These workers compared loss of rolling response in newts exposed to these gases and found a N_2:N_2O narcotic potency relation of 1:27 at a total pressure of 78 atm. The data are not sufficient to allow a more detailed analysis of the potencies of the different gases in counteracting hyperbaric bradycardia, but it seems as if the order among the gases corresponds to that of their narcotic potencies, with N_2O most potent, followed by N_2 and Ne, and with He having the lowest, if any, potency.

Irrespective of whether N_2O was added at the start of an experiment or when the preparation was kept at 150 atm, the gas made the recovery of the BF upon decompression more pronounced (Figs. 6 and 7). In contrast, though N_2O introduced at 150 atm markedly counteracted hyperbaric bradycardia, this was not the case when the preparations were exposed to the gas before compression. Similarly, the introduction or elimination of N_2O in preparations kept at stable low (6 atm) pressure did not have any significant effect on BF. It thus appears that under the present conditions, N_2O has a positive chronotropic effect only if the BF has first been depressed by high hydrostatic pressure. On the other hand, N_2O not only blocks the effect of hydrostatic pressure but seems to act as a stimulant on BF, since 10 atm of N_2O gave an overshoot (higher BF than the initial values) in Series A. There are other similar examples in the field of high pressure physiology. For example, the amplitude of the action potential in nerve axons is not reduced (or only slightly so) by hydrostatic pressure, although it counteracts the reduction of action potentials caused by anesthetics such as alcohol and N_2O (Spyropoulos 1957; Henderson 1975).

The present results do not explain how pressure and narcotic gases exert their influences on the cardiac pacemaker; however, these may be discussed in relation to current concepts of anesthesia mechanisms. When anesthetics are dissolved in a cell membrane, they seem to expand membranes and artificial bilayers (Roth and Seeman 1971; Miller et al. 1973; Trudell, Hubell, and Cohen 1973), while increased pressure reduces their volume (Macdonald 1978). On the other hand, anesthetics have been reported to cause a fluidization or disordering of lipid bilayer membranes that can be counteracted if ambient pressure is increased (Trudell, Hubell, Cohen, and Kendig 1973). Again, anesthetics also reduce the sodium conductance and thus affect the action potential, while the resting membrane potential is not influenced (Spyropoulos 1957; Gershfeld and Shanes 1958; Henderson 1975). In summary, anesthetics have been called "electrical stabilizers" (Seeman 1972). Any of these phenomena, if applicable to cardiac pacemaker cells, could interfere with the changing potassium conductance claimed to be responsible for slow spontaneous diastolic depolarization (Noble 1975), and could consequently influence the BF.

The relatively high BF in the beginning of the experiments compared to the steady-state BF recorded later was probably caused by mechanical stretch during the preparation (compare Deck 1963; Pathak 1972). The frequency dropped rapidly during the first 30 min after preparation. Thereafter, the base-line slope was more moderate and linear. The unusually steep slope of the base line in Series B compared to those of Series A and C may have been due to inherent properties of the Series B hearts. However, some kind of action specific to He and Ne, not seen in N_2 and N_2O, cannot be excluded. There are reports indicating that He may have a direct effect on the heart. In fact, He at 1 atm has been shown to counteract arrhythmia in hypoxic hearts (Pifarré, Cox, Jasuja, and Neville 1969; Toltzis and Scott 1972; Raymond, Weiskopf, Halsey, Goldfien, Eger, and Severinghaus 1972). However, other investigators have been unable to show this effect of He (Holland, Wolfe, and Kylstra 1973; Nicholas, Hart, and Kim 1974). Whether a specific effect of He at 1 atm has any relationship to the relatively steep slope of the base line in Series B is impossible to say. It is remarkable, though, that no arrhythmias were observed in the preparations exposed to He, while episodes of arrhythmia occurred in one preparation in each of Series A and C. Moreover, in one case in Series B, compression-induced arrhythmia was immediately relieved by the introduction of He.

The undershoot and overshoots of BF at compression and decompression (described earlier in Örnhagen and Hogan 1977) were much smaller in these experiments, probably due to the slower compression and decompression rate used in these experiments.

The effect of N_2O during decompression was to enhance the increase in BF that always accompanied decompression. However, autonomic blockade (atropine and practolol) eliminated this effect of N_2O, which may indicate either that the N_2O depended on autonomic receptors for its effect or, alternatively, that the gas and the blocking agents interacted directly at the site of a BF-regulating mechanism in the pacemaker cell membrane. The positive chronotropic effect of 1.4 atm of N_2O in rats found by Stetzner and De Boer (1972) was suggested by them to be an effect of increased catecholamines in the intact animal. This notion gains support from the present experiments, in which no chronotropic effect was found in sinus node preparations when 5 atm of N_2O were added at low hydrostatic pressure.

In conclusion, there seems to be a similarity between the way in which high inert gas pressures counteract hyperbaric bradycardia and the manner in which HPNS is induced by increased hydrostatic pressures, suggesting that they are functionally related. However, that gas at relatively low ambient pressure can also have a narcotic effect on the CNS that can be counteracted by pressure demonstrates a difference. In the sinus node preparation, N_2O had no BF-increasing effect at relatively low pressures, while it counteracted the effects of high hydrostatic pressures if added after compression. The absence of this reciprocity in the sinus node tissue remains to be explained.

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Örnhagen, H. Ch. 1979. Effets de l'azote, du protoxyde d'azote, du néon, et de l'hélium sur la fréquence de battement du noeud sinu-atrial de la souris, à des hautes pressions. Undersea Biomed. Res. 6(1): 27–39.—La réduction de la fréquence de battement provoquée par l'exposition à la pression hydrostatique (150 ATA) ne se laisse contrôler par le gaz dissous que si le gaz est ajouté au mélange après la mise en pression. L'effet sur la fréquence paraît se rapporter à la puissance narcotique du gaz. Les gaz testés, rangés selon la puissance, sont: N_2O, N_2, Ne, et He. Si on ajoute le gaz à une pression un peu élevée, avant la compression jusqu'à 150 atm, la bradycardie hyperbare ne diffère point de celle qu'on observe sans gaz. Pendant la décompression, cependant, la fréquence augmente significativement, par rapport aux expériences sans gaz. Le blocage autonome paraît supprimer la différence entre les décompressions avec et sans N_2O. Ces résultats montrent que le protoxyde d'azote, l'azote, le néon, et jusqu'à un certain degré aussi l'hélium peuvent s'opposer à l'effet retardateur de la pression accrue sur l'activité du système de conduction du coeur. Ces effets sur le système de conduction ressemblent aux effets d'une augmentation de pression et aux effets des gaz sur le système nerveux central à des pressions élevées. Il nous reste cependant plusieurs différences importantes à elucider.

bradycardie hyperbare
pression hydrostatique
fréquence cardiaque
gaz inerte
gaz dissous
protoxyde d'azote
azote
néon
hélium
noeud sinu-atrial

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