Cardiovascular response to acute hypoxemia in adult rats hypoxemic neonatally

C.V. Rohlicek*, T. Matsuoka1, C. Saiki2

Department of Pediatrics McGill University & Division of Cardiology Montréal Children’s Hospital, 2300 Tupper Street, Montréal, Quebec, Canada H3H 1P3

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Abstract

Objective: To determine the effects of chronic hypoxemia neonatally on the cardiovascular response to acute hypoxemia in adulthood.

Methods: Experiments were conducted on adult rats (82 ± 2 days) which had been made chronically hypoxemic (hypobaric hypoxia equivalent to FiO2 0.14) during the first ten days of life but raised in room air (Neonatally Hypoxemia) as well as on adult rats never previously hypoxemic (Control). The animals were instrumented with catheters in the right common carotid artery and superior vena cava for measurements of mean systemic arterial pressure (MAP), central venous pressure, heart rate (HR), arterial blood gases, and arterial as well as mixed venous O2 saturation. Oxygen consumption (VO2) was measured allowing calculation of cardiac index (CI), stroke volume index (SVI) and systemic vascular resistance index (SVRI). The rats were made acutely hypoxemic by exposure to FiO2 0.10 for 20 min.

Results: HR increased and MAP decreased to similar extents in both groups during acute hypoxemia. However, SVI and CI increased significantly (P < 0.05) during acute hypoxemia in the Neonatally Hypoxemic group (24 ± 6%, 41 ± 8%) but respectively decreased and did not change in the Control animals (−13 ± 6%, 2 ± 6%). SVRI fell significantly more during hypoxemia in the Neonatally Hypoxemic animals than in the Control group (36 ± 4% vs. 14 ± 5%).

Conclusions: Hypoxemia experienced in early life has long-term effects on the cardiovascular response to acute hypoxemia at maturity. This may have important implications for individuals hypoxemic in early life due to congenital cyanotic heart defects or pulmonary disease secondary to prematurity.

Keywords: Hypoxia/anoxia; Developmental biology; Hemodynamics; Ventricular function; Vasoconstriction/dilation

1. Introduction

Persistent hypoxemia in early life is often due to a congenital cyanotic heart defect or pulmonary disease secondary to prematurity. Such hypoxemia may persist for several weeks or months until surgical repair of the structural cardiac defect or improvement in pulmonary function makes the individual normoxemic. Previous investigations have shown that ventilatory control may be abnormal after repair of Tetralogy of Fallot in humans [1] while long-lasting effects on ventilatory mechanics and control have been demonstrated in post-pubertal rats following chronic hypoxemia neonatally [2–4]. However, it remains unclear whether there are also long-term effects of chronic hypoxemia in early life on cardiac function and cardiovascular control which might alter the cardiovascular response to stresses such as acute hypoxemia in adulthood.

The cardiovascular response to acute hypoxemia consists of an increase in cardiac output and a neurogenically mediated redistribution of peripheral blood flow which favor oxygen delivery to the central nervous system and myocardium [5,6]. Alterations in this response could be advantageous or disadvantageous in this regard. Either a
decreased cardiac output response or inadequate vasoconstriction in less essential tissues with acute hypoxemia could impair oxygen delivery to the brain and heart. Alternatively an augmented cardiac output response or a greater peripheral vasoconstriction in less essential tissues could further favor oxygen delivery to the brain and heart. These possibilities might have important implications for individuals who have experienced prolonged hypoxemia in early life if they are challenged by an acute hypoxic stress perioperatively when cardiac re-operation is required or alternatively during an intercurrent respiratory illness.

There is evidence to suggest the possibility that there are long-lasting effects of chronic hypoxia experienced in early life which may make the myocardium more resistant to an acute hypoxic stress in later life. It is well known that myocardial contractility is decreased during episodes of acute oxygen lack [7]. Previous investigators have shown that following chronic hypoxemia in the adult rat the contractile function of isolated ventricular myocardium is more resistant to an acute hypoxic stress [8] and recovers better on subsequent reoxygenation [9,10]. Ostadal et al. [11] have shown in adult rats that this protective effect lasts several weeks. A protective effect of chronic hypoxemia has also been demonstrated in the myocardium of newborn rats [12]. However, it is not known whether such an effect persists to maturity nor whether such an effect is of significance in the intact animal.

The possibility of a persistent effect of chronic hypoxemia experienced in early life on the central nervous system control of cardiovascular function also exists. Several investigators have shown that during exercise even some years after repair of Tetralogy of Fallot cardiac output increases less than in normal individuals [13–16] even in the absence of residual structural defects [17,18]. This impairment may be due to alterations in autonomic output to the heart as a consequence of chronic hypoxemia in early life as is suggested by the finding of a decreased heart rate response to exercise after repair of Tetralogy of Fallot [19] as well as by investigations in Tibet that indicate greater parasympathetic tone and less sympathetic activation during exercise in lifetime high altitude Tibetan nates compared to recently arrived lowland ethnic Chinese [20]. Previous investigations of central respiratory control in high altitude natives residing at sea level for some time [21], individuals who have undergone repair of cyanotic heart defects [1], as well as in adult rats made hypoxic for the first week of life [4] have shown that that such subjects exhibit a blunted hypoxic stimulation of ventilation. The close links which exist between the central nervous control of respiratory and cardiovascular function [22] also support the possibility that there may be long-term effects of hypoxemia experienced in early life on central cardiovascular control in later life. Finally work by Soulier et al. [23,24] on catecholamine content and turnover in the carotid bodies, brainstem cell groups involved in cardio-respiratory control, sympathetic ganglia, and the adrenal glands of adult rats exposed to several days of hypoxemia neonatally suggests a decreased arterial chemoreceptor sensitivity to acute hypoxemia as well as a decreased potential for sympathoadrenal activation.

Thus there is a basis to postulate alterations in cardiac function and/or cardiovascular control after chronic hypoxemia experienced in early life. Such changes might have important effects on the ability to deal with stresses such as acute hypoxemia in later life that require increases in cardiac output and a redistribution of peripheral blood flow to ensure adequate oxygen delivery to key tissues. In this regard we have studied the cardiovascular response to acute hypoxemia in unanesthetized adult rats which had been made hypoxic during the first ten days of life and compared these responses to those in adult rats never previously hypoxic. The hypothesis tested is that hypoxic exposure in early life in the rat alters the cardiovascular response to acute hypoxemia in adulthood.

2. Methods

Experiments were conducted on 34 unanesthetized adult male Sprague–Dawley rats weighing 437±8 (S.E.M.) g and aged 82±2 days. The investigation was approved by the McGill University animal care committee and conforms with the Guide for the Care and Use of Laboratory Animals published by the US National Institutes of Health (NIH publication No. 85-23, revised 1996). Seventeen animals had experienced hypobaric hypoxia (500 mmHg, inspired PO2 105 mmHg equivalent to FiO2=0.14 under normobaric conditions) from day 1 to day 10 of life (Neonatally Hypoxic) using a hypobaric chamber. Following this period of chronic hypoxia these animals were reared in normoxia at ambient atmospheric pressure (Montréal, 50 m above sea level). The other 17 rats were not made hypoxic prior to the experiments outlined below (Control).

Early on the day of the experiment the animals were instrumented under Althesin (alphaxalone–alphadolone) anesthesia administered intravenously (4 mg/kg bolus followed by a continuous infusion of 5–15 mg/kg per hour) by way of an angio-catheter placed percutaneously into a tail vein. The right common carotid artery and right internal jugular vein were exposed through a midline incision in the neck. Catheters were placed in the aorta and in the superior vena cava from these vessels and the incision closed with sutures. A colonic temperature probe was also placed by way of the rectum at this time. During the recovery from anesthesia colonic temperature (Tc) was maintained at 37.5–38.5°C by radiant heat. Experiments were performed 4 h after termination of anesthesia at which time the animals were fully awake without any evident signs of pain or distress.

At the time of experimentation the rat was placed in a cylindrical plexiglass chamber measuring 9×30 cm
through which air flowed at a constant rate of 1.8 l/min. The ambient temperature of the chamber was maintained at 25°C by means of a surrounding water bath. Systemic arterial pressure (SAP) and central venous pressures were measured continuously with Hewlett-Packard pressure transducers and displayed on a Gould polygraph. Arterial oxygen saturation (SaO₂), superior vena cava oxygen saturation as an index of mixed venous oxygen saturation (SvO₂), and hemoglobin concentration (Hb) were determined from 200 µl arterial and venous blood samples using a Radiometer model OSM2b hemoximeter. In eight Neonatally Hypoxic and 14 Control animals arterial blood gases were also determined from 200 µl arterial blood samples using an Instrumentation Laboratories model 1302 blood gas analyzer. Arterial blood gas values were corrected according to the condition (normoxia vs. hypoxia, with groups either during normoxia or hypoxia (Fig. 1). Central venous blood oxygen contents (CaO₂, CvO₂) were calculated ventricular weights of the Neonatal Hypoxemic rats were corrected according to the model of blood gas analyzer. Arterial blood gas values were greater than those of the Control animals (2.98±0.07 vs. 2.62±0.08 g/l), due to a larger right ventricular mass in the former animals (0.79±0.05 vs. 0.53±0.03 g/l), with no significant difference in left ventricular weight between the two groups (2.18±0.06 vs. 2.10±0.10 g).

3. Results

3.1. Age, body weight, heart weight and hemoglobin concentration

There was no significant difference between Neonatally Hypoxic and Control groups in regard to weight, age or hemoglobin concentration respectively (Neonatally Hypoxic: 431±7 g, 84±3 days, 145±4 g/l vs. Control: 443±17 g, 79±3 days, 154±3 g/l). However, the combined ventricular weights of the Neonatal Hypoxic rats were greater than those of the Control animals (2.98±0.07 vs. 2.62±0.08 g/l, P<0.05) due to a larger right ventricular mass in the former animals (0.79±0.05 vs. 0.53±0.03 g/l, P<0.05) with no significant difference in left ventricular weight between the two groups (2.18±0.06 vs. 2.10±0.10 g).

3.2. SaO₂, SvO₂, O₂, arterial blood gases, VO₂, and colonic temperature

During normoxia arterial oxygen saturation (SaO₂), mixed venous oxygen saturation (SvO₂), arteriovenous oxygen content difference (Cₐv,O₂), arterial blood gases, VO₂, and colonic temperature (Tc) values did not differ between the Neonatally Hypoxic and Control groups (Table 1). In both groups exposure to 10% inspired O₂ was associated with a significant fall in SaO₂, SvO₂, PaO₂, and PaCO₂: an increase in arterial pH; and no change in VO₂ or colonic temperature (Table 1). There was no significant difference in the arterial blood gases, VO₂ or Tc during hypoxia between rats of the two groups. During hypoxia SaO₂ was slightly lower in the Neonatally Hypoxic animals compared to the Control rats while SvO₂ was significantly less (Table 1). The Cₐv,O₂ did not change with acute hypoxemia in the control rats but decreased significantly in the Neonatally Hypoxic animals and as a result was significantly less during hypoxia in the latter rats compared to the Control group (Table 1).

3.3. Mean systemic arterial pressure, heart rate, cardiac index, stroke volume and systemic vascular resistance index

In both the Neonatally Hypoxic and Control groups mean systemic arterial pressure (MAP) decreased and heart rate (HR) increased during hypoxemia (Fig. 1). There was no difference in these variables between the two groups either during normoxia or hypoxia (Fig. 1). Central
Table 1

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<thead>
<tr>
<th></th>
<th>21% O₂</th>
<th>10% O₂</th>
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<tr>
<td>SaO₂</td>
<td>96±1%</td>
<td>58±2%*</td>
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<tr>
<td></td>
<td>95±1%</td>
<td>50±2%*</td>
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<tr>
<td>SvO₂</td>
<td>57±2%</td>
<td>21±1%*</td>
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<td></td>
<td>52±2%</td>
<td>15±2%*</td>
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<tr>
<td>Cvo₂O₂</td>
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<td>7.9±0.3 ml O₂ 100 ml⁻¹</td>
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<td></td>
<td>8.5±0.5 ml O₂ 100 ml⁻¹*</td>
<td>6.2±0.5 ml O₂ 100 ml⁻¹*</td>
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<tr>
<td>PaO₂</td>
<td>90±2 mmHg</td>
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<td></td>
<td>85±4 mmHg</td>
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<td>PaCO₂</td>
<td>38±1 mmHg</td>
<td>25±1 mmHg*</td>
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<tr>
<td></td>
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<td>pH</td>
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<td></td>
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<tr>
<td>VO₂</td>
<td>18.6±0.4 ml min⁻¹ kg BW⁻¹</td>
<td>19.2±0.5 ml min⁻¹ kg BW⁻¹</td>
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<td>19.2±0.5 ml min⁻¹ kg BW⁻¹</td>
<td>19.4±0.7 ml min⁻¹ kg BW⁻¹</td>
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<tr>
<td>Tc</td>
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<td></td>
<td>38.5±0.2°C</td>
<td>38.3±0.1°C</td>
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*P<0.05 21% O₂ vs. 10% O₂; †P<0.05 Control vs. neonatal hypoxia.

Venous pressure did not change on exposure to hypoxia ranging between 1 and 3 mmHg.

In normoxia cardiac stroke volume normalized by body mass (SVI), Cardiac index (CI) and systemic vascular resistance index (SVRI) did not differ between the two groups (Fig. 2). With exposure to hypoxia of the Control animals CI and SVRI did not change while SVI decreased significantly (Fig. 2). In contrast acute hypoxic exposure of the Neonatally Hypoxic group was associated with a significant increase in CI and SVI as well as with a fall in SVRI (Fig. 2). As a consequence of these changes the CI and SVI were significantly greater during hypoxia in the Neonatally Hypoxic group compared to the Control group while SVRI was significantly less (Fig. 2).

3.4. Cardiovascular responses to FiO₂=0.085

As noted above (Table 1), the Neonatally Hypoxic
4. Discussion

Previous work in awake rats [5,26] has shown that with exposure to acute systemic hypoxia heart rate increases and systemic arterial pressure falls. These changes are accompanied by a moderate increase in cardiac output. We have found such a response in our Control animals. However, rats which had been made hypoxemic neonatally for 10 days showed a markedly greater cardiac output response to acute hypoxia than Control rats although their heart rate increased and systemic arterial pressure fell as in the Control animals.

The increased cardiac output response to acute systemic hypoxia in the Neonatally Hypoxemic rats may be due to alterations in myocardial function. As is reviewed in the Introduction previous investigators have shown that prior adaptation to chronic hypoxia in adult [9,10] and infant rats [12] increases myocardial resistance to subsequent acute hypoxemic stress. In adult rats this protective effect appears to last several weeks [11]. Our results support the possibility of a similar long lasting effect of chronic hypoxemia experienced neonatally. The mechanisms involved in the protective effect of hypoxic adaptation are not known although there is some evidence for the possibility of adjustments in energy metabolism and neurohumoral regulation [27].

An alternate explanation for the increased cardiac output response to acute systemic hypoxia is a modification of neurohumoral cardiovascular control during acute hypoxemia by the prior exposure to chronic neonatal hypoxemia resulting in impaired neurogenic vasoconstriction necessitating a greater cardiac output in order to maintain systemic arterial pressure. There is evidence indicating that there are maturational changes in a number of the neurally mediated cardiovascular reflexes during early life [28,29]. This suggests that these reflexes are not preset at birth and that the potential of their usual maturation being altered by abnormal circumstances exists. In this regard the work of Soulier and coworkers [23,24] on various components of the arterial chemoreceptor arc suggests that neonatal hypoxemia in rats may have long-lasting depressant effects on the sympathoadrenal activation by an acute hypoxic stimulus. These investigators have shown that noradrenaline and dopamine content of the carotid bodies in adult rats made chronically hypoxemic for the first few days of life are significantly increased [23]. Both dopamine and norepinephrine have inhibitory effects on carotid body sensory function [30]. Soulier et al. [23,24] have also found in adult rats made hypoxic neonatally that noradrenaline content and turnover are decreased in brain-stem cell groups involved in the integration cardiorespiratory chemoreflex activity, sympathetic ganglia, and the adrenal medulla. This implies that sympathoadrenal activation is more difficult in adult rats hypoxemic neonatally. These changes could result in an alteration of the usual cardiovascular response of the adult animal to acute hypoxia.

Rats became more desaturated during exposure to FiO$_2$ = 0.10 than the Control rats. In order to test the possibility that the greater cardiac output and stroke volume index as well as lower systemic vascular resistance index exhibited by the former animals during hypoxia were the result of this difference in SaO$_2$, seven Control animals were further exposed to FiO$_2$ = 0.085 for 20 min. This resulted in a decrease in SaO$_2$ from 59±3% to 46±2% ($P<0.002$) which level was not significantly different from that observed in the Neonatally Hypoxemic rats during exposure to FiO$_2$ = 0.10 (50±2%). This additional decrease in SaO$_2$ was associated with a further fall in MAP (−14±4 mmHg, $P<0.02$) but no more change in HR, SVI, CI or SVRI.

![Fig. 2. Cardiac index (a), stroke volume index (b), and systemic vascular resistance index (c) during normoxia (FiO$_2$ = 0.21) and hypoxia (FiO$_2$ = 0.10) in control animals and in rats hypoxemic neonatally. Values shown are ±S.E.M. Significant differences are indicated (*$P<0.05$).](https://academic.oup.com/cardiovascres/article-abstract/53/1/263/432668)
pressure. that abnormal conditions in fetal and infant life are a cause impaired vasoconstriction in turn obligating an increased ments. Hypoxic rats during acute hypoxia as a result of severe degree of neonatal hypoxic exposure in our experi-
peripheral vascular resistance seen in the adult Neonatally be due to the greater age of our animals and / or the less vascular smooth muscle following neonatal hypoxemia it baseline conditions or during acute hypoxemia. This could contribute to the greater decrease in systemic vascular resistance in normoxia with an augmented pulmonary vasoconstriction on exposure to acute hypoxia. However, such changes seem unlikely to explain our findings of an increased cardiac output and decreased systemic vascular resistance during acute hypoxia in our adult Neonatally Hypoxic rats compared to the Control animals.
We have found that the right ventricular mass of adult rats hypoxic neonatally was increased compared to control animals. The left ventricular mass was not different from control animals. Previous investigators have also noted a persistent right ventricular hypertrophy in adult rats that had experienced a similar degree of chronic hypobaric hypoxia in early life [34–36] along with persistent elevation of pulmonary artery pressure and pulmonary vascular resistance. Experiments in rats [37] and humans [38] have further suggested that pulmonary arterial vasoconstriction in response to acute hypoxia may be increased in adults hypoxic in early life. Thus it is likely that our adult Neonatally Hypoxic rats similarly had elevated pulmonary artery pressure and pulmonary vascular resistance. Of note in this regard is the fact that the cardiac output observed could have been a compensatory mechanism to maintain systemic arterial pressure and thus blood flow as well as oxygen delivery to the brain and myocardium.
Recent work by Ruijtenbeek et al. [31] has shown biochemical and histological evidence of sympathetic hyperinnervation of the femoral arteries following chronic prenatal hypoxia in chick embryos. These authors suggest that this hyperinnervation may persist to adulthood on the basis of the observation in spontaneously hypertensive rats that once established sympathetic hyperinnervation persists. This would be inconsistent with the hypothesis outlined above. However, these investigators did not demonstrate that following prenatal hypoxia and subsequent normoxia that the sympathetic hyperinnervation which they found persists to maturity. Of note in this regard is that the work of Soulier et al. [24] indicates that the catecholamine content of various sympathetic ganglia and cardiovascular effector tissues is decreased in adult rats made chronically hypoxic in early life. Thus, while chronic hypoxemia perinatally may well lead to sympathetic hyperinnervation in early life, the available evidence suggests that such a hypoxic experience actually leads to decreased sympathetic cardiovascular effector input at maturity.
There has been little investigation of systemic vascular smooth muscle function following neonatal hypoxia. However, there is evidence that the pulmonary vascular smooth muscle of adult rats hypoxic neonatally is less responsive than that of control rats to various vasoconstrictor stimuli such as K+, serotonin, and norepinephrine [32]. If such a decreased responsiveness is also present in systemic vascular smooth muscle following neonatal hypoxemia it could contribute to the greater decrease in systemic peripheral vascular resistance seen in the adult Neonatally Hypoxic rats during acute hypoxia as a result of impaired vasoconstriction in turn obligating an increased cardiac output in order to maintain systemic arterial pressure.
Of interest is the finding that heart rate increased to the same extent in both groups of animals with acute hypoxemia yet cardiac output increased to a greater extent in the animals hypoxic neonatally. This implies that the increase in cardiac output was the result of an increase in cardiac stroke volume. Previous investigators have demonstrated in rats an augmented stroke volume with exercise following a period of training [33], indicating that it is possible to modulate stroke volume in rats despite their extremely fast heart rates. Whether the ability to increase stroke volume is due to increased autonomic drive, myocardial changes, or a combination of these is not clear.
We have found that the right ventricular mass of adult rats hypoxic neonatally was increased compared to control animals. The left ventricular mass was not different from control animals. Previous investigators have also noted a persistent right ventricular hypertrophy in adult rats that had experienced a similar degree of chronic hypobaric hypoxia in early life [34–36] along with persistent elevation of pulmonary artery pressure and pulmonary vascular resistance. Experiments in rats [37] and humans [38] have further suggested that pulmonary arterial vasoconstriction in response to acute hypoxia may be increased in adults hypoxic in early life. Thus it is likely that our adult Neonatally Hypoxic rats similarly had elevated pulmonary artery pressure and pulmonary vascular resistance in normoxia with an augmented pulmonary vasoconstriction on exposure to acute hypoxia. However, such changes seem unlikely to explain our findings of an increased cardiac output and decreased systemic vascular resistance during acute hypoxia in our adult Neonatally Hypoxic rats compared to the Control animals.
We have found that the adult rats made chronically hypox-
emiac neonatally became more desaturated on exposure to an FiO2 of 0.10. This greater arterial oxygen desaturation was not a factor in the observed differences in CI, SVI, or SVRI between the Neonatally Hypoxic and Control animals as exposure of the latter animals to a more hypoxic gas mixture to achieve an equivalent degree of desaturation had no further effect on these variables. The cause of the apparent greater arterial oxygen desaturation in the Neonatally Hypoxic animals is not evident. One possible explanation would be a relative impairment of the ventilatory response to acute hypoxemia in the Neonatally Hypoxic rats as has been previously demonstrated by Okubo and Mortola [4]. However, our results do not suggest such an impairment in the present experiments as we found no difference in PaCO2 or VO2 between the Neonatally Hypoxic and Control animals either under baseline conditions or during acute hypoxemia. This discrepancy from the work of Okubo and Mortola [4] may be due to the greater age of our animals and/or the less severe degree of neonatal hypoxic exposure in our experiments.
Human population studies have indicated the possibility that abnormal conditions in fetal and infant life are a cause of various chronic diseases in adulthood as a result of
altered physiologic or metabolic programming at critical periods of early development [39]. In particular, the work of Barker and associates has suggested that low birth weight is associated with an increased risk of coronary heart disease and disorders related to it [40]. More recent work suggests that those individuals who experience low weight gain during infancy are also at risk of developing coronary artery disease in later life [41]. Of interest in this regard is that weight gain in the infant rat is reduced during chronic hypoxia with subsequent compensation in body growth on the return to normoxia [32,42,43]. It is possible that our results represent an example of abnormal physiologic programming resulting in altered cardiovascular control due to hypoxemia and/or poor weight gain during early life.

The major limitations of this study concern the accurate determination of cardiac output and the extrapolation of our results in a rat model to human physiology. We have measured cardiac output using the Fick principle [44]. The underlying assumptions are that oxygen consumption, and mixed venous as well as systemic arterial oxygen content can be accurately determined. We have previously applied the flow through method of determining oxygen consumption [25] in newborn cats and dogs [45,46]. Our results in awake adult rats in the present investigation are in agreement with previous reports [47]. Both blood oxygen saturation and hemoglobin concentration can be accurately determined for small sample volumes [48] allowing for the calculation of blood oxygen content. We have used superior vena cava blood oxygen saturation as an index of mixed venous oxygen saturation as has been validated in human children [49]. Work by Musch and Larach [50] in anesthetized, ventilated and open-chested adult rats indicates that while the oxygen content of blood samples from the right atrium, right ventricle and pulmonary artery are not different the blood oxygen content of the inferior vena cava is less than that of the pulmonary artery. This would suggest that the blood oxygen content of the superior vena cava is greater than that of the pulmonary artery (i.e. ‘true’ mixed venous blood) in this preparation. If this is also true of awake and spontaneously breathing rats then this would have lead to overestimation of cardiac output in our experiments. However, our values for cardiac output are very similar to those of numerous previous investigators using a variety of different techniques to determine cardiac output in the rat [44]. This would suggest that the potential error introduced by our use superior vena cava blood oxygen saturation as an index of mixed venous blood oxygen saturation was not great. We have used a small rodent model to study the effects of neonatal hypoxemia on the cardiovascular response to acute hypoxia at maturity. Extrapolation of our findings in this model to humans must be done cautiously. Our animals were made chronically hypoxic for the first 10 days of life. Differences in the degree of maturity at birth and the rate of subsequent development between rats and humans make it hard to establish a precise human parallel in regard to the age at hypoxic exposure and length of such exposure. While there are significant similarities in the cardiovascular systems of rats and humans, differences certainly exist as a consequence of the types of demands placed on the cardiovascular systems of these species. As a result, direct comparisons of the effects of neonatal hypoxemia on the adult response to acute hypoxia in the rat and human may be difficult.

In conclusion, a prolonged period of hypoxemia experienced during early life in rats has long-lasting effects on the cardiovascular response to acute systemic hypoxemia at maturity. This may be due to altered myocardial function and/or changes in the autonomic nervous system response to acute hypoxemia. One interpretation of our results would suggest a greater cardiac resistance to such a hypoxic stress. However, it is also possible that during an acute hypoxic stress a greater than normal increase in cardiac output may become necessary in order to maintain oxygen delivery to vital tissues and offset a suboptimal redistribution of blood flow. Whether our findings are of clinical relevance must await human investigations. Either a greater cardiac resistance to a hypoxic stress or a suboptimal redistribution of blood flow during acute hypoxemia would have important implications for individuals who have experienced prolonged hypoxemia in early life.

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References


