Effects of hypoxia on the venous circulation in rainbow trout (Oncorhynchus mykiss)

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Abstract

Hypoxia in fish is generally associated with bradycardia while cardiac output (\(\dot{Q}\)) remains unaltered or slightly increased due to a compensatory increase in stroke volume (SV). Rainbow trout (Oncorhynchus mykiss) were subjected to severe (\(P_{O2}=7.3\pm0.2\) kPa) or mild (\(P_{O2}=11.5\pm0.2\) kPa) hypoxia. Central venous pressure (\(P_{ven}\)), dorsal aortic pressure (\(P_{da}\)), heart rate (\(f_H\)) and \(\dot{Q}\), were recorded in vivo. Both levels of hypoxia triggered a significant increase in \(P_{ven}\). Severe hypoxia was associated with bradycardia and unaltered \(\dot{Q}\), whereas mild hypoxia was associated with a small but significant increase in \(\dot{Q}\) and no bradycardia. These findings indicate that an increase in \(P_{ven}\) promotes an increase in SV during hypoxia. Since mild hypoxia increased \(P_{ven}\), \(\dot{Q}\) and SV without bradycardia or reduced systemic resistance (\(R_{sys}\)), we hypothesize that an active increase in venous tone serving to mobilize blood to the central venous compartment in order to increase cardiac preload and consequently SV, is an important cardiovascular trait associated with hypoxia. Pharmacological pre-treatment with prazosin (1 mg kg\(^{-1}\)) did not conclusively reveal the underlying mechanisms to the observed changes in \(P_{ven}\). This study discusses the influence of venous pooling, reduced \(R_{sys}\) and altered venous tone on changes in \(P_{ven}\) observed during hypoxia.

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1. Introduction

Many fish live in an environment that is highly variable in terms of physical as well as chemical properties. Particularly, coastal and fresh water environments show large temporal and spatial fluctuations in oxygen availability. To cope with varying levels of oxygen in the water, a number of physiological adaptations have evolved in fish. An increased vagal tone on the heart, inducing bradycardia is commonly seen as a response to hypoxia (Holeton and Randall, 1967; Wood and Shelton, 1980; Randall, 1982). In spite of the reduced heart rate (\(f_H\)), cardiac output (\(\dot{Q}\)) is often maintained unaltered or increased due to a compensatory increase in stroke volume (SV). Since fish have an end-systolic volume close to zero, the end-diastolic volume is the major determinant of SV (Farrell, 1991; Franklin and Davie, 1992; Forster and Farrell, 1994). Venous filling pressure is one of the most important factors controlling filling, and consequently SV of the teleostean heart.

It was earlier assumed that fish lack the ability to actively alter venous tone and the role of cardiac suction filling, vis a fronte, has probably also been exaggerated (Satchell, 1970, 1992). Hence, the view that veins serve as passive conduit vessels, where venous return is more or less exclusively regulated by events occurring upstream of the venous circulation (i.e. primarily arterioles) and due to the negative pericardial pressures created by cardiac contraction, is today strongly questioned. Growing evidence for an active control of venous tone in vivo in fish has accumulated during the last years (Conklin et al., 1997; Olson et al., 1997; Zhang et al., 1998; Hoagland et al., 2000; Sandblom and Axelsson, 2005). These studies indicate that the mechanisms controlling venous return, hence cardiac filling and cardiac output, in the piscine circulation are overall quite similar to the mammalian circulation.

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Although, venous tone is actively controlled in trout at rest, a number of other factors could potentially affect $P_{\text{ven}}$ during hypoxia. These factors can be summarized as follows: 1) Hypoxic bradycardia promoting central venous pooling of blood (Altirimas and Axelsson, 2004). 2) Reduced $\dot{Q}$, due to reduced myocardial force development during hypoxia (Arthur et al., 1992; Vornanen and Tuomennoro, 1999). 3) Hypoxic vasoconstriction in the gills leading to increased cardiac afterload (Sundin and Nilsson, 1997; Perry et al., 1999). 4) Local vasodilatation resulting in reduced systemic resistance ($R_{\text{sys}}$) and a decreased arterio-venous pressure gradient (Axelsson and Fritsche, 1991; Smith et al., 2001).

The present study has focused on the importance of changes in $P_{\text{ven}}$ and the associated changes in SV that occurs during hypoxia in rainbow trout. By using two different levels of hypoxia, one that did induce bradycardia and one that did not, we investigated the effects of vasoconstriction, bradycardia, reduced $\dot{Q}$ and $R_{\text{sys}}$ on the changes in $P_{\text{ven}}$.

2. Material and methods

2.1. Animals

Rainbow trout (Oncorhynchus mykiss) of mixed sexes (400–770 g) were purchased from a local fish farm and kept at the department. Fish were held at 15 °C in 2 m³ tanks, supplied with circulating water from a semi-open system. A maintenance diet of commercial trout pellets was fed and the photoperiod was adjusted to natural conditions. Ethical permits covered all experiments (96/2001).

2.2. Surgical procedures

Fish were collected from the holding tanks and anaesthetized in MS-222 solution (150 mg L⁻¹) buffered with sodium bicarbonate (300 mg L⁻¹). After anaesthesia, the fish were weighed and transferred to an operating table, covered with water-soaked foam rubber. A closed recirculating system at 10 °C irrigated the gills with water containing sodium bicarbonate buffered MS-222 (150 mg L⁻¹ and 75 mg L⁻¹ respectively). All catheters were custom made from polyethylene tubing (PE-50) and filled with heparinized (50–100 IU mL⁻¹) saline (0.9%) before surgery. To record venous pressure, the sinus venous was non-occlusively cannulated as follows. The fish was positioned on its side and the left operculum and the gills were carefully retracted by a piece of plastic that was held in place with a piece of string, attached to the foam rubber. A less than 10 mm incision, running approximately 45° dorsoventrally was made. Starting point was on top of the cleithrum ending posterior to the Vth gill arch. The lateral part of the left ductus of Cuvier was dissected free, using blunt dissection. The vessel was gently pulled, ideally ~5 mm, and secured in this position. A small hole was cut and a bubbled PE-50 catheter was carefully inserted until the bubble was located inside the vessel (approx. 10 mm). A 4-0 suture was tied around the catheter and the vessel wall, tightly above the bubble. The catheter was additionally attached with two lateral skin sutures. For further details see Altirimas and Axelsson (2004). Systemic blood pressure was recorded from the dorsal aorta. Cannulation was performed via the roof of the buccal cavity, as described by Axelsson and Fritsche (1994). The catheter was exteriorized through the snout and attached with a dorsal suture. To record changes in cardiac output (i.e. ventral aortic flow) a cuff-type flow probe (i.d. 1.8–2.2 mm) custom-made from perspex, was placed around the ventral aorta. An incision was made on the left side of the isthmus and the aorta was exposed using blunt dissection. The lead from the probe was secured with lateral skin sutures. After surgery the fish was transferred to a holding chamber, or immediately to the experimental chamber. Both type of chambers were connected to the same circulating water system with a temperature of 15 °C. The fish were allowed to recover for at least 48 h after surgery, and were moved to the experimental chambers at least 24 h prior to experiments. All chambers were thoroughly covered to minimize stress from visual stimuli.

2.3. Experimental protocols

The experimental protocols started with a 2-min recording of normoxic control conditions, followed by an 8-min hypoxic period. 8 min of hypoxia was chosen in accordance with the experimental protocols used in previous studies with an identical experimental set-up (Fritsche and Nilsson, 1989, 1990). Two levels of hypoxia were used in the chambers, hereafter referred to as severe ($P_{W}O_{2}=7.3±0.2$ kPa) and mild ($P_{W}O_{2}=11.5±0.2$ kPa). The protocols were subsequently repeated after pharmacological treatment with the α-adrenergic antagonist prazosin (1 mg kg⁻¹, Pfizer, Sandwich, England). 1 mg of prazosin was dissolved in 1 mL of saline resulting in a volume of 0.5 mL in a 500 g fish. The catheter was flushed with heparinized (50–100 IU mL⁻¹) saline (0.9%) after drug administration to ensure that the entire dose of the drug would reach the circulation. Control experiments with sham-injections of equal volumes of physiological saline (0.9%) revealed that repeated exposures to severe hypoxia and injections neither altered resting cardiovascular variables, nor the responses to hypoxia (Table 1). The first and the second hypoxic exposure (after prazosin or sham treatment) were separated by 1.5–2.0 h since this time is sufficient for complete blockade and at the same time sufficient for the acute side-effects of prazosin to wear off. $P_{\text{dan}}$, $P_{\text{veno}}$, $f_{1}$ and $\dot{Q}$ were continuously recorded in both series.
Table 1
Resting cardiovascular variables and the effects of repeated exposures to severe hypoxia and sham-injection with physiological saline in rainbow trout (Oncorhynchus mykiss)

<table>
<thead>
<tr>
<th>Untreated</th>
<th>Normoxia</th>
<th>Hypoxia</th>
<th>Saline</th>
<th>Normoxia</th>
<th>Hypoxia</th>
</tr>
</thead>
<tbody>
<tr>
<td>( P_{\text{ven}} ) (kPa)</td>
<td>9</td>
<td>0.06±0.03</td>
<td>0.18±0.03*</td>
<td>8</td>
<td>0.06±0.05</td>
</tr>
<tr>
<td>( P_{\text{da}} ) (kPa)</td>
<td>7</td>
<td>3.44±0.25</td>
<td>3.28±0.29</td>
<td>7</td>
<td>3.16±0.21</td>
</tr>
<tr>
<td>( f_{\text{H}} ) (beats min(^{-1}))</td>
<td>9</td>
<td>64.2±3.5</td>
<td>54.5±3.5*</td>
<td>8</td>
<td>62.6±4.2</td>
</tr>
<tr>
<td>( Q ) (%)</td>
<td>7</td>
<td>99.7±0.9</td>
<td>100.2±6.8</td>
<td>6</td>
<td>99.1±1.2</td>
</tr>
</tbody>
</table>

Data are presented as means±SE, where the hypoxic values are taken from the last 2 min of the 8 min hypoxic period (\( P_{\text{W}O_2}=6.8±0.2 \) kPa).

* Statistically significant difference between pairs. No significant difference between normoxic values before and after sham-injection with physiological saline (1 mL kg\(^{-1}\) bw) was found.

2.4. Equipment and data acquisition

Hypoxic water was prepared in a separate 50-L barrel connected to the experimental chambers. The temperature difference between the two compartments never exceeded 0.8 °C. A gas mixing flow meter (model GF-3MP, Cameron Instruments, USA) supplied the hypoxic system with a gas mixture of air and \( N_2 \) balanced to obtain the desired level of oxygenation. The switch to hypoxic water reduced the oxygen tension to the final value within approximately 1 min. Thereafter, the oxygen level remained stable during the entire length of the hypoxic period. Water oxygen tension of the experimental chamber was continuously measured with an oxygen electrode (Oxi340i/SET, WTW, Germany or model 781, Strathkelvin Instruments, Scotland) located at the inlet of the chamber. The equipment was calibrated daily against the current barometric pressure. Catheters were connected to pressure transducers (model P23ID, GOULD Statham, USA or DPT-6100, pvb medizintechnik, Germany) connected to a Grass Recorder (model 7P1JK, Grass instruments, USA) or 4ChAmp amplifier (Somedic, Sweden). Calibration of pressure was done against a static water column, with the water surface of the experimental chamber serving as baseline. The ventral aortic flow probe was connected to a directional-pulsed Doppler flow meter (model 545C-4, University of Iowa, USA). Heart rate was either directly recorded from the pulsatile signal of the cardiac output or dorsal aortic pressure signals using a Tachograph Recorder unit (model 7P44D, Grass Instruments, USA), or subsequently calculated from the pulsatile pattern of stored dorsal aortic or venous pressure recordings. Data was continuously stored on a PC running a custom made program, General Acquisition (Labview version 6.01, National Instruments, USA).

2.5. Statistical analysis

The values compared statistically are mean values of the normoxic control period and mean values of the last 2 min of the corresponding 8-min hypoxic period. The last 2 min of the hypoxic period was chosen as the representative hypoxic value due to the following conditions. 1) Approximately 1 min was required after the switch to hypoxic water before a low and stable oxygen level was reached in the experimental chamber. 2) Since the interaction between \( f_{\text{H}} \) and \( P_{\text{ven}} \) was one of the main objectives of the present study and experiments on cod (Gadus morhua), using an identical experimental set-up, has revealed that the bradycardic response to hypoxia develops quite slowly and reaches the lowest level after 6–8 min (Fritsche and Nilsson, 1989). Differences between pairs (\( P<0.05 \)) were evaluated using a two-tailed Wilcoxon matched-pairs signed-ranks test. Statistics for \( \dot{Q} \), \( R_{\text{sys}} \) and SV were calculated using raw data but are expressed as percentage values in graphs where the initial untreated normoxic value was set to 100%.

3. Results

3.1. Severe hypoxia

In untreated fish severe hypoxia (Fig. 1, \( P_{\text{W}O_2}=7.3±0.2 \) kPa) induced a significant increase in \( P_{\text{ven}} \) from 0.07±0.01 to 0.14±0.03 kPa, while \( P_{\text{da}} \) dropped from 3.3±0.1 to 2.6±0.1 kPa. The changes in blood pressure were accompanied by a significant reduction of \( R_{\text{sys}} \) by 18.9%. Although severe hypoxia triggered a bradycardia (67.7±5.5 to 51.7±4.3 beats min\(^{-1}\)) \( \dot{Q} \) remained unaltered due to a compensatory increase in SV by 29.9%.

3.2. Mild hypoxia

Mild hypoxia (Fig. 2, \( P_{\text{W}O_2}=11.5±0.2 \) kPa) also resulted in an increased \( P_{\text{ven}} \) from a normoxic value of 0.06±0.03 to 0.10±0.03 kPa. In contrast to the severe hypoxia; \( P_{\text{da}} \), \( R_{\text{sys}} \) and \( f_{\text{H}} \) were unchanged at the end of the mild hypoxic period and \( \dot{Q} \) increased significantly by 6.4% due to a significant increase in SV by 7.7%.

3.3. Effects of \( \alpha \)-adrenergic receptor blockade

Blockade of \( \alpha \)-adrenoceptors with prazosin altered resting cardiovascular variables in both the severe (Fig. 1) as well as in the mild hypoxic series (Fig. 2). \( R_{\text{sys}} \) and \( P_{\text{da}} \) decreased significantly by 13.2% and 3.3±0.1 to 2.9±0.2
kPa and by 12.3% and 3.3% to 2.8 kPa respectively. SV and Q at rest increased in the mild hypoxic series by 47.4% and 54.8% respectively but were not significantly changed in the severe hypoxic series. Pven only increased significantly in the severe hypoxic series from 0.07±0.01 to 0.15±0.04 kPa.

Fig. 1. Summary of cardiovascular effects of 8 min of severe hypoxia between hatched lines (PAO2=7.3±0.2 kPa), in untreated (left-hand panels) and after treatment with prazosin (1 mg kg⁻¹) (right-hand panels). (A) central venous blood pressure (Pven, N=8); (B) dorsal aortic blood pressure (Pda, N=8); (C) heart rate (fH, N=8); (D) cardiac output (Q, N=7); (E) systemic resistance (Rsys, N=7) and F, stroke volume (SV, N=7) in rainbow trout (Oncorhynchus mykiss). For Q, Rsys and SV the initial untreated normoxic value is normalized to 100%. The time between hatched vertical lines represent 480 s of hypoxia. The values are means±S.E.M. *Statistically significant difference between an average value of the normoxic period and an average value of the last 2 min of the hypoxic period (right-and left-hand panels). #Significant difference in resting values after prazosin treatment (right-hand panels).

Fig. 2. Summary of cardiovascular effects of mild hypoxia (PAO2=11.5±0.2 kPa) in untreated (left-hand panels) and prazosin treated (1 mg kg⁻¹) (right-hand panels) rainbow trout (Oncorhynchus mykiss). For abbreviations and details see Fig. 1.
Both severe as well as mild hypoxia after prazosin treatment resulted in a significantly increased $P_{\text{ven}}$ from 0.15±0.04 to 0.22±0.04 kPa and from 0.10±0.03 to 0.12±0.03 kPa respectively and a significantly reduced $P_{\text{da}}$ from 2.9±0.2 to 1.4±0.2 kPa and 2.8±0.1 to 2.5±0.1 kPa respectively. The changes in blood pressure during severe and mild hypoxia were associated with significant reductions in $R_{\text{sys}}$ by 44.6% and 9.8% respectively. Similarly to the responses in untreated fish, only the severe hypoxia triggered a significant bradycardia (72.6±5.8 beats min$^{-1}$ to 33.3±5.5 beats min$^{-1}$). Despite a significant increase in SV by 43%, the drop in $f_H$ during severe hypoxia resulted in a significantly reduced $\dot{Q}$ by 48.7%. Although no significant change in SV or $f_H$ was seen during mild hypoxia, $\dot{Q}$ increased significantly by 14.3%.

4. Discussion

Resting $f_H$ in this study is comparable to values obtained from previous studies with similar instrumentation. For example, Conklin et al. (1997) reported a $f_H$ of 68.7±1.8 beats min$^{-1}$ during normoxic resting conditions at 12 °C, compared to 66.2±5.5 beats min$^{-1}$ (Fig. 1C) and 53.3±4.7 beats min$^{-1}$ (Fig. 2C) at ~15–16 °C in the present study. Our recordings of $P_{\text{ven}}$ are comparatively lower, 0.07±0.01 and 0.06±0.03 kPa (Figs. 1A and 2A respectively) compared to 0.27±0.08 kPa reported by Conklin et al. (1997). The surgical technique used by Conklin et al. (1997) involved puncturing of the pericardium, which may have affected $P_{\text{ven}}$ (see Farrell et al., 1988 for discussion). In a recent study from the same laboratory a less invasive technique was employed, where the ductus of Cuvier was percutaneously cannulated (Minnerick et al., 2003). As judged from venous pressure recording traces (no absolute values given) $P_{\text{ven}}$ was lower, in fact possibly subambient, in these experiments. These findings are important since they emphasize that an intact pericardium is vital for proper measurements of $P_{\text{ven}}$ in vivo.

4.1. Cardiovascular responses to hypoxia in untreated fish

Farrell (1991) claimed that venous filling pressure is a strong determinant of stroke volume in fish. We conclude that the increase in SV during both levels of hypoxia was mediated by the observed increase in $P_{\text{ven}}$. This resulted in an unaltered or increased $\dot{Q}$ during hypoxia depending on the heart rate response. It is tempting to speculate that the increase in $P_{\text{ven}}$ is the result of an active venoconstriction due to $\alpha$-adrenoceptor stimulation, as has previously been reported for resting trout by Zhang et al. (1998), thus promoting vis a tergo filling of the heart. Although attractive, venoconstriction is not the only potential mechanism whereby hypoxia could raise venous pressure.

In the present study the increase in $P_{\text{ven}}$ during severe hypoxia was associated with bradycardia, reduced $R_{\text{sys}}$ and a drop in $P_{\text{da}}$. These findings could all suggest that the hypoxic change in venous pressure was due to pooling and (or) reduced peripheral resistance. The rationale for exposing fish to a milder level of hypoxia was the observation that previous studies have shown that mild hypoxia can serve to increase SV without an accompanying bradycardia, thus serving to increase $\dot{Q}$ (Wood and Shelton, 1980; Gamper et al., 1994). Indeed, this was the case in the present study and the increase in $P_{\text{ven}}$ during mild hypoxia was, in contrast to the severe hypoxia, associated with an unaltered $P_{\text{da}}$ and no change in $R_{\text{sys}}$ (Fig. 2). These findings strongly refute the possible roles of venous pooling and (or) reduced $R_{\text{sys}}$ and indicates that an active increase in venous tone is responsible for the mobilization of blood to the central venous compartment in order to increase cardiac preload and hence SV during mild hypoxia.

To our knowledge there is only one previous report of venous blood pressure recordings in fish during hypoxia (Perry et al., 1999). In that study the most severe hypoxia used (2.6±2.4 kPa) elicited a significant increase in $P_{\text{ven}}$ in conformity with our results. On the contrary, a slightly milder hypoxia (8.5±0.6 kPa) did not result in any significant change in $P_{\text{ven}}$. Although $\dot{Q}$ was significantly reduced and a significant bradycardia was observed, the authors did not discuss the potential effects of venous pooling on $P_{\text{ven}}$. The discrepancy in response to various levels of hypoxia between these two studies is not known. It could be hypothesised that the time-course of the hypoxic exposure might play a role since hypoxia was induced very quickly (within 1 min) in the present study and much slower (within 15–20 min) in the study by Perry et al. (1999). The surgical method for implantation of the venous catheter might also have affected the result.

In spite of the fact that Randall (1982) stated that hypoxia is generally not associated with changes in gill resistance, branchial hypoxic vasoconstriction has been reported, although at oxygen levels much lower than the mild hypoxia in the present study. Perry et al. (1999) reported branchial resistance to increase at 8.7 kPa but not at 12.7 or 16.3 kPa, whereas Sundin and Nilsson (1997) reported hypoxic branchial vasoconstriction to occur in trout after 4 min of very severe hypoxia (1.07–1.33 kPa). An increase in branchial resistance during hypoxia would be expected to be associated with a reduced $P_{\text{da}}$. This was not the case during mild hypoxia in the present study, suggesting that branchial vasoconstriction did not occur (Fig. 2). However, we cannot exclude the possibility that branchial vasoconstriction could have been partly responsible for the increase in $P_{\text{ven}}$ observed during severe hypoxia.

4.2. Cardiovascular effects of hypoxia after $\alpha$-adrenergic receptor blockade

The influence of an $\alpha$-adrenergic tonus on the venous vasculature at rest has been established for trout (Zhang...
et al., 1998). In the present study prazosin was used in an attempt to abolish the increase in $P_{\text{ven}}$ observed during hypoxia. However, the $P_{\text{ven}}$ responses after $\alpha$-adrenoceptor blockade were qualitatively similar to pretreatment responses. The persistent increase in $P_{\text{ven}}$ during both levels of hypoxia after prazosin treatment is probably best explained by the dramatic decrease in $R_{\text{sys}}$. In contrary to the unaltered $R_{\text{sys}}$ in untreated fish during mild hypoxia (Fig. 2), $\alpha$-adrenoceptor blockade caused $R_{\text{sys}}$ to drop significantly during the hypoxic exposure, as has been observed previously (Axelsson and Fritsche, 1991; Smith et al., 2001). The drop in $R_{\text{sys}}$ during hypoxia reduces the pressure gradient between the arterial and the venous circulations with a resultant increase in $P_{\text{ven}}$ and a drop in $P_{\text{da}}$. However, the potential role of vasoactive substances others than catecholamines that could influence $P_{\text{ven}}$ cannot be ruled out (Conklin et al., 1997; Olson et al., 1997; Hoagland et al., 2000).

By reducing $R_{\text{sys}}$ and $P_{\text{da}}$ prazosin treatment probably also increased capillary fluid retention leading to an increased blood volume and a reduced hematocrit and blood viscosity. The increase in normoxic resting levels of $P_{\text{ven}}$ after $\alpha$-adrenergic blockade (right-hand panel Fig. 1A) is probably due to these factors or possibly a compensatory up-regulation of some other vasoactive systems. Zhang et al. (1998) concluded that the venous system in fish is subjected to an adrenergic tonus at rest. Indeed, $P_{\text{ven}}$ dropped after an injection of prazosin (0.47 mol/kg bw) in that study, but only the first 30–35 min after the injection was shown. This period might be too short to obtain a steady state after $\alpha$-adrenoceptor blockade. Also in our study an initial decrease in both $P_{\text{ven}}$ and $P_{\text{da}}$ was generally observed following prazosin injection, but 1.5–2 h later when the experiments were performed, $P_{\text{ven}}$ had recovered to or above the initial value.

4.3. Concluding remarks

Summarizing the data from the two series shows that increasing cardiac preload by an active mobilization of venous blood to central venous compartments probably is an important trait of the cardiovascular response to hypoxia in fish. Depending on the $f_{\text{th}}$ response this serves to increase SV and counteract the bradycardia during severe hypoxia thus leaving $Q$ unaltered or increases SV and $Q$ during mild hypoxia. Future studies to evaluate from where in the venous vasculature blood is being shifted during hypoxia could indeed be fruitful. Studies on mammals point out the splanchnic vasculature as an important blood volume reservoir that is mobilized during hypoxia (Pang, 2001). If this is also true for fish remains to be substantiated. The fact that pharmacological treatment with prazosin did not succeed to unfold the regulatory mechanisms underlying the changes in venous pressure, emphasize the complexity of venous hemodynamics in live animals. The fact that $P_{\text{ven}}$ increased during hypoxia after prazosin treatment indicates that factors outside the venous system, such as changes in $Q$ and $R_{\text{sys}}$ also affect $P_{\text{ven}}$ in vivo. The inherent problems with hemodynamic measurements of the venous circulation, is probably part of the reason why its role has so far been largely neglected by researchers in the field of comparative cardiovascular physiology.

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