Transmission of arterial oxygen partial pressure oscillations to the cerebral microcirculation in a porcine model of acute lung injury caused by cyclic recruitment and derecruitment

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Editor’s key points

- Cyclic recruitment and derecruitment of lung units lead to oscillations in arterial oxygen partial pressure and are involved in the pathophysiology of acute lung injury.
- In this experimental study in a pig model, oscillations were also observed in cerebral oxygen partial pressure and blood flow.
- Oscillations in cerebral and systemic oxygenation might contribute to the interaction between acute lung and brain injury.

Background. Cyclic recruitment and derecruitment (R/D) play a key role in the pathomechanism of acute lung injury (ALI) leading to respiration-dependent oscillations of arterial partial pressure of oxygen (Pao2). These Pao2 oscillations could also be forwarded to the cerebral microcirculation.

Methods. In 12 pigs, partial pressure of oxygen was measured in the thoracic aorta (Pao2) and subcortical cerebral tissue (PbrO2). Cerebral cortical haemoglobin oxygen saturation (SbrO2), cerebral blood flow (CBF), and peripheral haemoglobin saturation (SpO2) were assessed by spectroscopy and laser Doppler flowmetry. Measurements at different fractions of inspired oxygen (FiO2) were performed at baseline and during cyclic R/D. Statistics: frequency domain analysis, the Mann–Whitney test, linear models to test the influence of Pao2, and systolic arterial pressure (SAP) oscillations on cerebral measurements.

Results. Parameters [mean (SD)] remained stable during baseline. Pao2 oscillations [10.6 (8) kPa, P phase reference], systemic arterial pressure (SAP) oscillations [20 (9) mm Hg, phase Pao2−SAP 33 (72)], and SpO2 oscillations [1.9 (1.7)%, phase Pao2−SpO2 264 (72)] were detected during lung R/D at Fio2 1.0. Pao2 oscillations decreased [2.7 (3.5) kPa, P = 0.0008] and SpO2 oscillations increased [6.8 (3.9)%]. P = 0.0014 at Fio2 0.3. In the brain, synchronized PbrO2 oscillations [0.6 (0.4) kPa, phase PbrO2−Pao2 90 (39)8], SbrO2 oscillations [4.1 (1.5)%, phase PbrO2−SbrO2 182 (54)], and CBF oscillations [198 (176) AU, phase PbrO2−CBF 201 (63)] occurred that were dependent on Pao2 and SAP oscillations.

Conclusions. Pao2 oscillations caused by cyclic R/D are transmitted to the cerebral microcirculation in a porcine model of ALI. These cyclic oxygen alterations could play a role in the crosstalk of acute lung and brain injury.

Key words: brain, blood flow; brain, oxygen consumption; lung, respiratory distress syndrome; measurement techniques, oximeters; oxygen, partial pressure

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Mechanical ventilation is critical for the survival of patients with acute lung injury (ALI) or acute respiratory distress syndrome (ARDS). A protective ventilator strategy using low tidal volumes (VT) and limited inspiratory plateau pressure (Pplat) has been associated with a reduction in mortality.1 This approach, however, may result in increased recruitment and derecruitment (R/D) and aggravate ventilator-induced lung injury (VILI).2 It has been demonstrated that varying pulmonary shunt fraction attributed to R/D within the respiratory cycle (cyclic R/D) leads to aortic Pao2 oscillations. This mechanism has been described at high temporal resolution using novel fast oxygen-sensing technology.3 4

The impact of cyclic R/D and consequent Pao2 oscillations on vital organs such as the heart, kidney, and brain is unknown. Alterations in oxygen supply to the brain could affect neuronal tissue integrity. This hypothesis is consistent with the observation that the majority of patients with ALI/ARDS develop neurological dysfunction associated with morphological brain damage.5 6 Furthermore, evidence from sleep apnoea research suggests that cyclic alterations in oxygenation can promote neuronal dysfunction.7 8 However, the influence of cyclic R/D-associated Pao2 oscillations on cerebral microcirculation has not been investigated.

In the present study, we investigated the following hypotheses: (i) cyclic R/D induces respiratory-dependent oscillations of the following parameters: arterial partial pressure of oxygen (Pao2), peripheral haemoglobin oxygen saturation (SpO2), cerebral subcortical partial pressure of oxygen
(PbrO2), cerebral cortical haemoglobin oxygen saturation (SbrO2), and cerebral cortical blood flow (CBF) at the capillary-venous level; (ii) altered fractions of inspired oxygen affect the amplitude of these oscillations; and (iii) variations in systolic arterial pressure (SAP) influence cerebral oscillations.

**Methods**

After approval by the governmental animal care committee (Rhineland-Palatinate, Germany, approval number 23177-07 / G09-1-037), 12 juvenile pigs (German country race, weight 25–27 kg) were investigated. These studies conformed to ARRIVE guidelines.

**Anaesthesia and preparation**

After i.m. sedation (ketamine 8 mg kg⁻¹ and midazolam 0.2 mg kg⁻¹) and vascular access via ear vein, anaesthesia was induced i.v. (fentanyl 4 μg kg⁻¹, propofol 4 mg kg⁻¹, atracurium 0.5 mg kg⁻¹) to facilitate tracheal intubation (tube inner diameter 8.0 mm). Anaesthesia was maintained by continuous infusion (fentanyl 0.1–0.4 mg kg⁻¹ h⁻¹ and propofol 8–12 mg kg⁻¹ h⁻¹). A standard pressure-controlled ventilatory regimen was initiated with a tidal volume (Vt) of 10–12 ml kg⁻¹, PEEP of 5 cm H2O, FIO2 of 0.3–0.4, inspiration to expiration ratio (I:E) of 1:2, and variable respiratory rate (RR) to maintain normocapnia (Servo 900 C, Siemens, Erlangen, Germany). Sterofundin solution (Braun, Melsungen, Germany) was infused continuously (5 ml kg⁻¹ h⁻¹). The following vascular catheters were placed by surgical cut-down: an arterial line and a PICCO catheter (Pulsion Medical Systems, Munich, Germany) via the right femoral artery; a central venous line via the right femoral vein; an arterial introducer for fast measurements for PO2, via the left femoral artery. Haemodynamic and spirometric measurements were sampled at 100 Hz using Philips S5 monitoring software (S5 Collect, Datex Ohmeda GmbH, Duisburg, Germany). Fast haemoglobin oxygen saturation (SpO2) measurement was performed at the pig tail.

A craniotomy (20 × 10 mm) was performed 5 mm from the midline and 5 mm behind the coronal suture for positioning of the cerebral subcortical PO2 probe (PbrO2) and the combined cerebral cortical haemoglobin oxygen saturation (SbrO2) and CBF monitoring probe. Because the dura was opened for positioning of the probes, intracerebral pressure was not measured. The head was wrapped in plastic foil to fixate the experimental setting. The time to prepare the experiments took about 4–6 h including craniotomy and positioning of probes. Postmortem the brain was removed, correct positioning of the probes was verified, and the surrounding tissue was examined for cerebral haemorrhage. A Rapidlab 248 device (Bayer Healthcare, Leverkusen, Germany) was used for arterial blood gas analysis (BGA). Temperature was measured by a pericranial temperature probe (Temp) placed in the temporal muscle. Body surface warming was performed by a heating blanket system. Cardiac index was assessed by single-indicator transpulmonary thermodilution using the PICCO system.

**10 Hz fluorescence quenching of oxygen (Foxy AL-300)**

Simultaneous measurements of PAO2 in the thoracic aorta and PbrO2 14 mm deep from brain surface were performed using uncoated 10 Hz fluorescence quenching of oxygen technology (Foxy-AL300, Ocean Optics, Dunedin, FL, USA).3 4 10 These PO2 probes are fibreoptic, aluminium-jacketed probes with an uncoated ruthenium complex at the probe tip allowing for ultrafast measurements at 10 Hz. The probes were calibrated in vitro according to the manufacturer’s instruction. The validity of the calibration was confirmed by conventional BGA.

**2.5 Hz white light photo-spectrometry and 20 Hz laser-Doppler flowmetry (O2C-device)**

SbrO2, (%) and CBF (AU) of the cerebral cortex at the capillary venous level were measured by combined 2.5 Hz white light spectroscopy and 20 Hz laser Doppler flowmetry (O2C-Device, LEA Medizintechnik GmbH, Giessen, Germany).11–13 Returning light is split into its spectral components by a charge-coupled device array and multiple white light wavelengths are detected simultaneously (500–630 nm, <30 mW). The spectrum is compared with universal reference values of deoxygenated and oxygenated haemoglobin spectra to determine SbrO2.14 15 A Doppler shift of the illuminated laser light (830 nm, <30 mW) caused by movements of erythrocytes is detected and analysed as CBF.

**1.0 Hz multi-wavelength spectrometry (Masimo SET)**

The Masimo SET-R-Device (Masimo SET-R, Masimo, Irvine, FL, USA) uses a new-generation multi-wavelength sensor. A special research version was provided by the manufacturer allowing for continuous non-invasive peripheral haemoglobin saturation (SpO2) measurements at 1.0 Hz.16

**Experimental protocol**

Ventilator settings were adjusted for baseline conditions defined as Vt 10–12 ml, PEEP 5 cm H2O, Ppeak <30 cm H2O, I/E 1:2, and RR 25–30 to maintain normocapnia (4.6–6 kPa PaCO2). Measurements were performed at FIO2 1.0 (baseline 1.0) and 0.3 (baseline 0.3) in a random fashion. During each measurement period, 1800–2400 single PO2 measurements, 3600–4800 single CBF measurements, and 180–240 single SpO2 measurements were recorded.

ALI was induced by repetitive bronchoalveolar lavage. The tracheal tube was clamped in inspiration and 30 ml kg⁻¹ of warmed Sterofundin solution (Braun) was instilled by gravity and afterwards immediately removed. This procedure was repeated until the PAO2/FIO2 ratio was <300 at a PEEP of 5 cm H2O for >60 min. Ventilator settings were adjusted as follows: Vt >20 ml kg⁻¹, PEEP 0 cm H2O (ZEEP), Ppeak >30 cm H2O, I/E 1:4, and RR 5 to provoke cyclic R/D and consecutive PO2 oscillations. Measurements during cyclic R/D were repeated at FIO2 1.0 (cyclic R/D 1.0) and 0.3 (cyclic R/D 0.3) in a random fashion. The experimental protocol including
induction of ALI and measurements at baseline conditions and cyclic R/D lasted about 4–6 h.

**Statistical methods**

Data are presented as mean (so). Comparisons were performed using the Mann–Whitney test. P-values below 0.05 were considered significant. Frequency domain analysis was performed using Matlab (Mathworks, Cambridge, MA, USA)3 and Igor Pro (Igor Pro 6.22a, WaveMetrics, Lake Oswego, OR, USA) for the calculation of waveform amplitudes, frequencies, phase shift as referenced to \( P_aO_2 \) oscillations (phasereference), and Fourier spectra. Linear models using the Bonferroni correction were fitted to test the influence of \( P_aO_2 \) oscillations and SAP variations on cerebral parameters (SPSS 18, SPSS Inc., Chicago, IL, USA).

**Results**

The experimental set-up was successful in all animals. The applied respiratory mechanics, haemodynamic variables, and blood gas analyses are summarized in Table 1.

**Baseline conditions**

During baseline, measurements of systemic (\( P_aO_2 \)), peripheral (\( S_pO_2 \)), and cerebral (\( P_bro2, S_brO_2 \)) oxygenation remained constant as indicated by small amplitudes (\( \Delta \)) (Table 2). Likewise, physiological SAP variation and CBF oscillations remained within normal limits (Table 2). All measured variables remained stable over time and were not influenced by the RR as illustrated in representative Figure 1.

**Cyclic R/D**

After induction of ALI [lavage 2 (3 times)] and during cyclic R/D at \( F_Io2 \) 1.0, respiratory-dependent oscillations in systemic oxygenation [mean \( P_{aO_2} \) oscillations 10.6 (8) kPa, phase\( P_{aO_2} \) – SAP \( -33 (72) \)] and circulation [mean SAP variation 20 (9) mm Hg, phase\( P_{aO_2} \) – SAP \( -33 (72) \)] was observed (Table 2). These oscillations were related to an RR of 5 bpm as confirmed by the Fourier transformation (peak at 0.08333 Hz \( \times 60 =4.999, P<0.05 \)).

Synchronized respiratory-dependent oscillations were detected in subcortical [mean \( P_{brO_2} \) oscillations 0.6 (0.4) kPa, phase\( P_{brO_2} \) – SAP \( 90 (39) \) ] and cortical [mean \( S_{brO_2} \) oscillations 4.1 (1.5)%, phase\( P_{brO_2} \) – SAP \( 182 (54) \) ] brain tissue as illustrated in representative Figure 2 (Table 2, \( P<0.05 \)). At \( F_Io2 \) 0.3, the mean \( P_{aO_2} \) oscillations decreased to 2.7 (3.5) kPa (\( P=0.0008, \) Fig. 3) and SAP oscillations remained unchanged (\( P=0.6235 \)). Contrariwise, the mean \( S_{brO_2} \) oscillations increased from 1.9 (1.7)% to 6.8 (3.9)% and the mean \( S_{brO_2} \) oscillations tended to increase from 4.1 (1.5)% to 8.5 (6.6)% at \( F_Io2 \) 0.3 (\( P=0.0524, \) Fig. 3). The phase shifts between

<table>
<thead>
<tr>
<th>( F_Io2 ) 1.0</th>
<th>( F_Io2 ) 0.3</th>
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<tbody>
<tr>
<td><strong>Baseline</strong></td>
<td><strong>Cyclic R/D</strong></td>
</tr>
<tr>
<td>MAP (mm Hg)</td>
<td>89 (20)</td>
</tr>
<tr>
<td>HR (beats min (^{-1}))</td>
<td>98 (14)</td>
</tr>
<tr>
<td>CI (litre min (^{-1}) m(^{-2}))</td>
<td>4.0 (1.0)</td>
</tr>
<tr>
<td>Temp ((^\circ)C)</td>
<td>37.0 (1.4)</td>
</tr>
<tr>
<td>RR (bpm)</td>
<td>28 (4)</td>
</tr>
<tr>
<td>( V_T ) (ml)</td>
<td>330 (46)</td>
</tr>
<tr>
<td>( V_E ) (litre min (^{-1}))</td>
<td>8.9 (1.7)</td>
</tr>
<tr>
<td>( P_{peak} ) (cm H(_2)O)</td>
<td>20.6 (5.3)</td>
</tr>
<tr>
<td>( P_{plat} ) (cm H(_2)O)</td>
<td>18.4 (4.1)</td>
</tr>
<tr>
<td>PEEP (cm H(_2)O)</td>
<td>4.7 (0.8)</td>
</tr>
<tr>
<td>ELWI (ml kg (^{-1}))</td>
<td>14.2 (3.3)</td>
</tr>
<tr>
<td>( I/E ) (ratio)</td>
<td>1.20 (0.6)</td>
</tr>
<tr>
<td>( P_{aco2} ), (kPa)</td>
<td>5.5 (0.7)</td>
</tr>
<tr>
<td>( S_{pO2} ), (%)</td>
<td>98.8 (1.6)</td>
</tr>
<tr>
<td>( P_{aO2} ), (kPa)</td>
<td>76.7 (10)</td>
</tr>
<tr>
<td>pH</td>
<td>7.46 (0.08)</td>
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<tr>
<td>Hb (g dl (^{-1}))</td>
<td>7.2 (0.7)</td>
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Table 2 Respiratory-dependent oscillations during cyclic R/D in macrocirculation (SAP, $P_aO_2$) and brain microcirculation ($P_brO_2$, $S_brO_2$, CBF) at $FIO_2$ 1.0 and 0.3. Data are presented as mean (SD). Comparisons between amplitudes ($\Delta$) at baseline and cyclic R/D were performed by the Mann–Whitney test. Amplitude $\Delta$, peak-to-peak amplitude; CBF, cerebral blood flow; cyclic R/D, cyclic recruitment and derecruitment; $FIO_2$, fraction of inspired oxygen; $P_aO_2$, arterial partial pressure of oxygen; $P_brO_2$, cerebral subcortical partial pressure of oxygen; N/A, not applicable; NS, non-significant; SAP, systolic arterial pressure; $S_brO_2$, cerebral cortical haemoglobin oxygen saturation; $SpO_2$, peripheral haemoglobin oxygen saturation.

<table>
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<tr>
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<th>(FIO_2) 1.0</th>
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<th>(FIO_2) 0.3</th>
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<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>Cyclic R/D</td>
<td>Baseline</td>
<td>Cyclic R/D</td>
</tr>
<tr>
<td>(P_aO_2) (kPa)</td>
<td>76.7 (10)</td>
<td>0.3 (0.1)</td>
<td>35.5 (14.5)</td>
<td>10.6 (8)</td>
</tr>
<tr>
<td>SAP (mm Hg)</td>
<td>117 (20)</td>
<td>2.7 (0.6)</td>
<td>101 (10)</td>
<td>20 (9)</td>
</tr>
<tr>
<td>(SpO_2) (%)</td>
<td>98.8 (1.6)</td>
<td>0.1 (0.3)</td>
<td>95.6 (9.3)</td>
<td>1.9 (1.7)</td>
</tr>
<tr>
<td>(P_brO_2) (kPa)</td>
<td>7.4 (2.2)</td>
<td>0.05 (0.04)</td>
<td>7.8 (4.1)</td>
<td>0.6 (0.4)</td>
</tr>
<tr>
<td>(S_brO_2) (%)</td>
<td>53.8 (16)</td>
<td>3 (1.4)</td>
<td>69.2 (14.4)</td>
<td>4.1 (1.5)</td>
</tr>
<tr>
<td>CBF (AU)</td>
<td>336 (144)</td>
<td>56 (49)</td>
<td>415 (171)</td>
<td>198 (176)</td>
</tr>
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</table>

Fig 1 Baseline measurements of systemic ($PaO_2$, AP) and cerebral parameters ($PbrO_2$, CBF) over time. No dependency on the rate of respiration could be observed; AP, arterial pressure; CBF, cerebral blood flow; $PaO_2$, arterial oxygen partial pressure; $PbrO_2$, cerebral subcortical partial pressure of oxygen.

Fig 2 Respiratory-dependent oscillations in systemic ($PaO_2$, AP) and cerebral ($PbrO_2$, CBF) oxygenation during cyclic R/D. AP, arterial pressure; CBF, cerebral blood flow; cyclic R/D, cyclic recruitment and derecruitment; $PaO_2$, arterial oxygen partial pressure; $PbrO_2$, cerebral subcortical partial pressure of oxygen.
cerebral measurement parameters, as referenced to phase reference $P_{aO2}$, are displayed in Figure 4. Linear models revealed that $P_{aO2}$ oscillations and SAP variations showed dependency on cerebral measurement parameters (Table 3).

**Discussion**

The present study investigated the influence of cyclic R/D on arterial ($P_{aO2}$), peripheral ($S_pO2$), cerebral subcortical ($P_{brO2}$), and cerebral cortical ($S_{brO2}$) oxygenation and on CBF at $F_{O2}$.
Table 3 Influence of the PAO2 oscillations and arterial pressure (AP) variation caused by cyclic R/D on PBRO2, SBR02, and CBF oscillations (P<0.05). CBF, cerebral blood flow; NS, non-significant; PAO2, arterial partial pressure of oxygen; PBRO2, cerebral subcortical partial pressure of oxygen; SAP, systolic arterial pressure; SBR02, cerebral cortical haemoglobin oxygen saturation

<table>
<thead>
<tr>
<th>PAO2 oscillations (mm Hg)</th>
<th>PBRO2 oscillations (mm Hg)</th>
<th>SBR02 oscillations (%)</th>
<th>CBF oscillations (AU)</th>
</tr>
</thead>
<tbody>
<tr>
<td>P&lt;0.001 (R²=0.383)</td>
<td>NS</td>
<td>P=0.03 (R²=0.152)</td>
<td></td>
</tr>
<tr>
<td>SAP variation (mm Hg)</td>
<td>P=0.001 (R²=0.267)</td>
<td>P=0.006 (R²=0.195)</td>
<td>P=0.0024 (R²=0.162)</td>
</tr>
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</table>

1.0 to 0.3, the mean amplitude of PAO2 oscillations decreased while the mean amplitude of SpO2 oscillations increased (Fig. 3). Past studies have shown that higher FIO2 (>0.6) causes atelectasis after 5–15 min and thereby can increase the shunt fraction.11 22. However, cyclic R/D remained mostly unchanged in the present study as repetitive measurements at FIO2 1.0 and 0.3 revealed reproducible values. In line with theoretical considerations, PAO2 oscillations should be monitored at higher blood oxygen content when a significant amount of dissolved oxygen is present. In contrast, oscillations of haemoglobin-bound oxygen (SpO2) ideally should be monitored at lower blood oxygen content (SpO2 <97%). As the monitoring of SpO2 oscillations can be performed non-invasively using fast peripheral SvO2 measurement, this approach might be promising for the detection of SpO2 oscillations in the clinical setting. Fast SpO2 measurement might serve as a surrogate parameter for the monitoring of cyclic R/D in patients at risk (e.g. obesity, pneumocapno-periodoneum, ALI/ARDS). Additionally, other fast devices based on photo-spectrometry (e.g. Hamamatsu NIRO–200) could also allow the detection of cyclic R/D attributed SO2 oscillations.16 23

Transmission of PAO2 oscillations to the brain
Cyclic R/D attributed oxygen oscillations occurred in subcortical and cortical brain tissue. These cerebral oxygen oscillations were accompanied by CBF oscillations. Phase shifts in cerebral macro- and microvasculature are regarded as cerebral autoregulatory mechanisms to counter-regulate alterations in CBF caused by SAP variations.24 25 Whereas the classical phase shift between systemic circulation and CBF is −40 to −80°, one former near-infrared spectroscopy study revealed a phase shift to the cerebral microvascular level of 80–90°.23 O2C-device parameters (SBR02, CBF) in the present study showed prolonged phases (182–355°). At this level of circulation, perfusion is slowed down to enable capillary diffusion of oxygen and energy substrates.26 During intact cerebral autoregulation, Pbr02 values should not change as CBF counteracts SAP variations.27 28 These considerations would suggest impairment of cerebral autoregulation during the present study as CBF regulation was not sufficient to maintain constant Pbr02.29 However, in contrast to brain oxygen monitoring technologies (e.g. Licox) where Pbr02 oscillations might not be detected because of the low temporal resolution, this study measured Pbr02 at an ultrafast (10 Hz) temporal resolution. The issue of assessing Pbr02 in view of cerebral autoregulation should be re-evaluated using fast oxygen-sensing technologies (e.g. 10 Hz) as of paramount clinical importance.

Clinical impact of cerebral PO2 oscillations
The impact of PAO2 and Sbr02 oscillations caused by cyclic R/D on brain integrity remains unknown. In theory, brain oxygen oscillations could affect steady-state microvascular oxygen gradients.20 These cyclic alterations of cerebral oxygenation might promote neuronal immunomodulation or, in the case
of altered oxygen levels, intermittent cerebral hypoxia. Recent studies investigating chronic obstructive pulmonary disease and sleep apnoea syndrome and high-altitude research suggest that cyclically altered arterial oxygenation might have detrimental effects on brain integrity. The underlying mechanism for these entities is attributable to an increase in reactive oxygen species with associated tissue damage, leading to apoptotic neuronal death. In contrast, intermittent cerebral hypoxia has been shown to be protective in some experimental settings. The effect of intermittent hyperoxia on the brain remains unknown. However, current knowledge is limited, and no conclusions can be made about effects of cyclic R/D on organs.

Limitations
The present study has a number of limitations. Experimental lavage models simulate surfactant depletion and associated impairment of oxygenation, diffusion, and perfusion of the lung. Using this model, alveolar surface tension increases and significant atelectasis is produced. This leads to cyclic R/D during injurious mechanical ventilation. However, the model applied in the present experimental study was rather extreme, and is not transferrable to clinical conditions. It remains unknown if cyclic R/D results in alterations in PaCO₂. In theory, PaCO₂ oscillations caused by cyclic R/D should be small in amplitude. However, cerebral CO₂ reactivity effects occur in a range of seconds to minutes and therefore might have biased the present results. Another problem of the present study is that cyclic R/D was not determined using more sophisticated techniques such as multiple inert gas elimination technique. Although results could be confirmed by repetitive measurements, it cannot be excluded that higher FiO₂ of 1.0 had an effect on cyclic R/D and thereby PaO₂ oscillation amplitude.

The relationship between systemic (PaO₂, oscillations, SAP variations) and cerebral oscillations (PbrO₂, SbrO₂, CBF) should be investigated under more physiological conditions in view of cerebrovascular autoregulation. It would be interesting to confirm the present results using alternative cerebral imaging techniques such as functional magnetic resonance imaging to monitor cerebral PaO₂ oscillations. Major technological confounders of the present study include accuracy, temporal synchronization, and porcine-specific alterations of the oxyhaemoglobin dissociation curve.

Conclusions
The present study demonstrates that cyclic R/D in an animal model of ALI induces respiratory-dependent systemic (PaO₂) and peripheral (SpO₂) oscillations. Fast photo-spectrometry may be a useful tool to monitor peripheral SpO₂ oscillations non-invasively. PaO₂ and SpO₂ oscillations were transmitted to the cerebral microcirculation and could be monitored in subcortical (PbrO₂) and cortical (SbrO₂) cerebral tissue, and were accompanied by CBF oscillations. Our findings suggest that oscillation monitoring depends on haemoglobin–oxygen binding characteristics and underlying measurement technique. High temporal resolution oxygen-sensing technologies are required to detect cyclic R/D-associated oxygen oscillations. The impact of the cerebral transmission of PaO₂ oscillations on the cerebral microcirculation remains unknown. This cyclic variation of systemic and cerebral oxygenation could play a major role in the crosstalk of acute lung and brain injury.

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Declaration of interest
None declared.

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