Clinical Use of Hypoxia
From Performance Enhancement in Endurance Athletes… and Team Sport Players … towards Therapeutic Benefits in Patients
Altitude/ Hypoxic Training
Altitude/Hypoxic Training

LHTH

1960-

LLTH

URSS ? 1950
2000 -

Altitude/Hypoxic Training

- LHTH
  - Natural/Terrestrial
  - Oxygen filtration

- LHTL
  - Nitrogen dilution

- LHTLH
  - Supplemental Oxygen
  - Oxygen filtration

- LLTH
  - IHE
  - IHT
  - IHIT


Altitude/ Hypoxic Training

- LHTH
  - Natural/ Terrestrial
  - Oxygen filtration

- LHTL
  - Nitrogen dilution

- LHTLH
  - Supplemental Oxygen
  - Oxygen filtration

- LLTH

- IHE
- CHT
- IHT
- RSH

(HH / NH)

**Altitude/ Hypoxic Training**

- **LHTH (HH)**
- **LHTL (HH / NH)**
- **LHTLH (HH / NH)**
- **LLTH (HH / NH)**

**Natural/Terrestrial (HH)**

- **Nitrogen dilution (NH)**

**Supplemental Oxygen (HH)**

- **Oxygen filtration (NH)**

**IHE**

**CHT**

**IHT**

**RSH**

**IHIT (HH / NH)**

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Panorama of all methods of altitude/hypoxic training in 2015

Altitude/ Hypoxic Training

LHTH (HH)

LHTL (HH / NH)

Natural/ Terrestrial (HH)

Nitrogen dilution (NH)

Suppl. Oxygen (HH)

LHTHL (HH)

Oxygen filtration (NH)

LHTLH (HH / NH)

LLTH (HH / NH)

IHE

CHT

IHT

RSH

RTH

IHIT

LHTH : Live High Train High; LHTL : Live High Train Low; LLTH : Live Low Train High


IHIT : Intermittent Hypoxia Interval-Training; LHTLH : Live High Train Low and High; LHTHL : Live High Train High and Low.

HH : Hypobaric Hypoxia ; NH : Normobaric Hypoxia.

Millet et al. 2015
Why?

Underlying mechanisms
Erythropoiesis vs. non-hematological factors

How?

$LHTH$ vs. $LHTL$ vs. $IHE/IHT$ (IHIT and LHTLH)
Altitude x duration / intensity

HH (terrestrial) vs NH (simulated)

for Who?

Endurance vs. “lactic” vs. intermittent sports

When?

Periodization in the yearly program
From endurance athletes...
LHTH: Live High Train High; LHTL: Live High Train Low; LLTH: Live Low Train High


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Millet et al. 2015
• Autonomic Tone
• Ventilation
• Blood Flow
• Tissue pH

• Glycolytic enzymes
• Angiogenic factors
• Oxidative stress defence
• pH Regulation

• ↓ Oxidative stress
• Wound Healing
• Sleep Regulation
• CNS
• Kidney
• Heart
• Skeletal Muscle
• Smooth Muscle
• Pancreas
• Lung
• Testis

• EPO
• Erythropoiesis

• \( \uparrow \text{Hb}_{\text{mass}} \)
• \( \uparrow \text{VO}_{2\text{max}} \)
• \( \uparrow \text{Performance} \)

Levine and Stray-Gundersen, 2006
% Change in Red Cell Mass

-0.5%
1.5%
2.2%
4.3% *
4.3% *

Levine and Stray-Gundersen, 2006
Owing to the flat shape of the oxyhemoglobin dissociation curve above 60 mmHg, changes in $P_aO_2$ may not have much effect on $S_aO_2$.

$P_aO_2$ values below 60 mmHg are reached from altitudes of about 2500 m (Anchisi et al., 2001)

Optimal altitude for LHTH are therefore slightly below this altitude (2200-2500 m) due to the combined effect of altitude- and exercise-induced desaturation (Woorons et al. 2007)
LHTH - Return to sea-level

1. a *positive* phase (2 to 4 days)
   - hemodilution
   - ventilatory adaptations

2. a *negative* phase (5-12/15 days) of progressive reestablishment of sea-level training volume and intensity.
   - altered energy cost
   - neuromuscular loss of adaptation

3. a third *positive* phase (after 15 to 21 days) characterized by a *plateau in fitness*.
   - increase in $O_2$ transport
   - delayed HVR benefits
   - increased economy

4. A *FOURTH* *negative* phase (30-35 days) ?
   (Bonetti and Hopkins 2009 ; Issurin 2007)
Why ?
Erythropoiesis
Increase in Hb and red blood cell mass

How ?
Altitude: > 1800 - 2200 – 2500 m
Duration: min 3-weeks. Up to 4 weeks

for Who ?
Endurance: 2-4 times a year
“lactic”: once during winter training

When ?
Intermittent: LMTM for general fitness
**Normobaric Hypoxia (NH) vs. Hypobaric Hypoxia (HH)**

- **Altitude/ Hypoxic Training**
  - **LHTH (HH)**
  - **LHTL (HH / NH)**
    - **Natural/ Terrestrial (HH)**
    - **Nitrogen dilution (NH)**
    - **Suppl. Oxygen (HH)**
  - **LLTH (HH / NH)**
  - **LHTHL (HH)**
  - **Oxygen filtration (NH)**
  - **LHTLH (HH / NH)**

**Schemes**
- **IHE**
- **CHT**
- **IHT**
- **RSH**
- **RTH**

**Abbreviations**
- **LHTH**: Live High Train High
- **LHTL**: Live High Train Low
- **LLTH**: Live Low Train High
- **IHE**: Intermittent Hypoxic Exposure
- **CHT**: Continuous Hypoxic Training
- **IHT**: Intermittent Hypoxic Training
- **RSH**: Repeated Sprint Training in Hypoxia
- **RTH**: Resistance Training in Hypoxia
- **IHIT**: Intermittent Hypoxia Interval-Training
- **LHTLH**: Live High Train Low and High
- **LHTHL**: Live High Train High and Low

**Nomenclature**
- **HH**: Hypobaric Hypoxia
- **NH**: Normobaric Hypoxia
Ventilatory responses
- $V_t$ & $V_E$ lower in HH
- Lower $P_{ET}O_2$ and $P_{ET}CO_2$ in HH
- Alveolar physiological dead space higher in HH


Fluids balance
- Higher diuresis in NH
- Larger decrease in plasma volume in NH
- Larger fluid retention in HH
- $[N_2]$ and $[O_2]$ influenced by BP in cerebrospinal fluid


Pre-acclimatization and AMS severity
- AMS higher in HH
- Pre-acclimatization in NH less effective than in HH

Fulco et al. 2013, Millet et al. 2013

Performance
LHTL in HH induce larger SL performance enhancement than in NH

Meta-analysis Bonetti & Hopkins 2009

NH vs. HH

Oxydative stress (OX)
- Markers of OX increased more in HH than NH

Faiss et al. 2013

Sleep
- Differences in sleep quality

Heinzer et al. 2013

HR
- Resting HR is higher in HH than NH

Di Pasquale et al. 2015

NO metabolism
- Exhaled NO lower in HH
- NOx decrease in HH but is stable in NH

Donnelly et al. 2011, Faiss et al. 2013
Maximal Exercise in NH vs. HH

Altitude/ Hypoxic Training

LHTH (HH)

LHTL (HH / NH)

Natural/ Terrestrial (HH)

Nitrogen dilution (NH)

Suppl. Oxygen (HH)

LHTHL (HH)

Oxygen filtration (NH)

LHTLH (HH / NH)

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IHE

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RTH

IHIT

LHTH: Live High Train High; LHTL: Live High Train Low; LLTH: Live Low Train High


IHIT: Intermittent Hypoxia Interval-Training; LHTHL: Live High Train Low and High; LHTHL: Live High Train High and Low.

HH: Hypobaric Hypoxia; NH: Normobaric Hypoxia.
F<sub>1</sub>O<sub>2</sub>: 20.93%
BP: 718.1 mmHg
P<sub>i</sub>O<sub>2</sub>: 140.5 mmHg
T° : 23.3 °C
485 m

F<sub>1</sub>O<sub>2</sub>: 20.93%
BP: 481.8 mmHg
P<sub>i</sub>O<sub>2</sub>: 90.9 mmHg
T° : 21.3 °C

F<sub>1</sub>O<sub>2</sub>: 13.6%
BP: 715.8 mmHg
P<sub>i</sub>O<sub>2</sub>: 91.0 mmHg
T° : 22.7 °C

NN
HH 3450m
NH 3450m

Same P<sub>i</sub>O<sub>2</sub>
Time Trial 250 kJ

- Ventilatory responses
- EMG
- SpO₂
- Cerebral Blood Flow
- Muscular NIRS
- Cerebral NIRS
- Power Output
- Heart Rate
- VAS leg and respi.
- Borg scale

Exposure duration

0h

26h
### Perception and Respiration

<table>
<thead>
<tr>
<th></th>
<th>NN</th>
<th>NH</th>
<th>HH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Final RPE [6-20]</td>
<td>18 ± 2</td>
<td>19 ± 1</td>
<td>19 ± 1</td>
</tr>
<tr>
<td>Final VAS legs [1-10]</td>
<td>8.3 ± 1.6</td>
<td>8.5 ± 2.4</td>
<td>8.2 ± 2.6</td>
</tr>
<tr>
<td>Final VAS breath [1-10]</td>
<td>8.7 ± 1.4</td>
<td>9.5 ± 1.2</td>
<td>9.3 ± 1.5</td>
</tr>
<tr>
<td>HR [bpm]</td>
<td>161 ± 8</td>
<td>163 ± 7</td>
<td>163 ± 7</td>
</tr>
<tr>
<td>$V_E$ [l/min]</td>
<td>115.1 ± 30.7</td>
<td>121.3 ± 25.7</td>
<td>120.1 ± 24.1</td>
</tr>
<tr>
<td>$V_T$ [l/min]</td>
<td>2.87 ± 0.32</td>
<td>2.97 ± 0.35</td>
<td>2.90 ± 0.40</td>
</tr>
<tr>
<td>$f$ [1/min]</td>
<td>40.0 ± 10.6</td>
<td>41.1 ± 8.8</td>
<td>42.6 ± 11.2</td>
</tr>
<tr>
<td>$P_{ET}O_2$ [mmHg]</td>
<td>101.5 ± 12.6</td>
<td>73.6 ± 16.1***</td>
<td>64.7 ± 4.0***</td>
</tr>
<tr>
<td>$P_{ET}CO_2$ [mmHg]</td>
<td>31.6 ± 3.7</td>
<td>25.9 ± 4.2***</td>
<td>27.4 ± 4.0***</td>
</tr>
<tr>
<td>$VO_2$ [l/min]</td>
<td>3.47 ± 0.67</td>
<td>3.09 ± 0.36***</td>
<td>2.87 ± 0.23*</td>
</tr>
<tr>
<td>$VCO_2$ [l/min]</td>
<td>3.31 ± 0.63</td>
<td>2.85 ± 0.40**</td>
<td>3.09 ± 0.41</td>
</tr>
<tr>
<td>$VE/VO_2$</td>
<td>32.1 ± 7.3</td>
<td>37.8 ± 5.6*</td>
<td>40.4 ± 7.0***</td>
</tr>
<tr>
<td>$VE/VCO_2$</td>
<td>33.1 ± 3.8</td>
<td>41.1 ± 6.4***</td>
<td>37.8 ± 6**</td>
</tr>
</tbody>
</table>
Pacing

Time [s] for 10 kJ period

HH
NH
NN
## Sleep assessment (PSG)

<table>
<thead>
<tr>
<th></th>
<th>NN</th>
<th>NH</th>
<th>HH</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AHI [1.h&lt;sup&gt;-1&lt;/sup&gt;]</strong></td>
<td>7.1 ± 1.2</td>
<td>35.9 ± 11.2*</td>
<td>38.0 ± 9.7*</td>
</tr>
<tr>
<td><strong>Microarousal index [1.h&lt;sup&gt;-1&lt;/sup&gt;]</strong></td>
<td>17.3 ± 1.8</td>
<td>26.2 ± 3.9*</td>
<td>24.6 ± 3.8*</td>
</tr>
<tr>
<td><strong>Lowest SpO&lt;sub&gt;2&lt;/sub&gt;[%]</strong></td>
<td>91.2 ± 2.8</td>
<td>74.7 ± 7.1***</td>
<td>72.6 ± 4.2***</td>
</tr>
<tr>
<td><strong>Sleep time [min]</strong></td>
<td>388 ± 13</td>
<td>317 ± 18**</td>
<td>351 ± 17***##</td>
</tr>
<tr>
<td><strong>SpO&lt;sub&gt;2&lt;/sub&gt; [%]</strong></td>
<td>96.5 ± 0.2</td>
<td>83.6 ± 0.5***</td>
<td>81.2 ± 0.9***#</td>
</tr>
<tr>
<td><strong>HR [bpm]</strong></td>
<td>48.1 ± 1.5</td>
<td>54.7 ± 1.6**</td>
<td>61.2 ± 2.7***##</td>
</tr>
<tr>
<td><strong>Hypopnea [n]</strong></td>
<td>6.7 ± 1.2</td>
<td>18.3 ± 4.4*</td>
<td>25.3 ± 5.2***##</td>
</tr>
</tbody>
</table>

*P<0.05; **P<0.01; ***P<0.001 for differences with NN

#P<0.05; ##P<0.01 for differences between NH and HH

Heinzer et al. In prep
LHTH : Live High Train High; LHTL : Live High Train Low; LLTH : Live Low Train High


IHIT : Intermittent Hypoxia Interval-Training; LHTLH : Live High Train Low and High; LHTHL : Live High Train High and Low.

HH : Hypobaric Hypoxia; NH : Normobaric Hypoxia.

Millet et al. 2015
LHTL - Increased $\text{VO}_2\text{max}$ / Improved performance

(Levine & Stray-Gundersen, 1997)
(Levine & Stray-Gundersen, 1997)
## Variability of responses

<table>
<thead>
<tr>
<th>Condition</th>
<th>Physiological Adaptations</th>
<th>Performance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiple 2-wk altitude (swimmers, &lt;10h·d⁻¹)</td>
<td>Hbₘass 0.9%</td>
<td>2K/VO₂max 1.2%</td>
</tr>
<tr>
<td>Repeated 3-wk LHTL (runners, 14h·d⁻¹)</td>
<td>4mM speed 0.9%</td>
<td>Comp/TT -0.4%</td>
</tr>
<tr>
<td>1st</td>
<td>2.8%</td>
<td>2.1%</td>
</tr>
<tr>
<td>2nd</td>
<td>2.7%</td>
<td>-1.4%</td>
</tr>
<tr>
<td>Extended 6-wk LHTL (runners, 14h·d⁻¹)</td>
<td>Hbₘass 4.0%</td>
<td>2K/VO₂max 4.3%</td>
</tr>
<tr>
<td>Combined LHTL+TH (runners, 14h·d⁻¹ +TH)</td>
<td>4mM speed 1.2%</td>
<td>Comp/TT -0.3%</td>
</tr>
<tr>
<td>3-wk TH (runners, TH 4·wk⁻¹)</td>
<td>Hbₘass 3.6%</td>
<td>2K/VO₂max 4.8%</td>
</tr>
<tr>
<td></td>
<td>4mM speed 2.8%</td>
<td>Comp/TT -1.1%</td>
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Garvican et al.
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HH: Hypobaric Hypoxia; NH: Normobaric Hypoxia.
18-days of LHTL in NH vs. HH
Cross-over study over 2 years

NH: Prémanon
1150 m
$F_iO_2$: 17.9 ± 0.2%
BP: 664.9 ± 2.9 mmHg
$P_iO_2 = 111.1 ± 1.1$

HH: Fiescheralp
2250m
$F_iO_2$: 20.93 ± 0.03%
BP: 579.7 ± 4.56 mmHg
$P_iO_2 = 111.5 ± 1.0$

Same $P_iO_2$
Sleep quality
Breathing Freq.

HH > NH

Night $S_pO_2$

Saugy et al. In prep
Hb\textsubscript{mass}

**HH**

**NH**

**CON**

Hauser et al. In prep
Performance

3000 m 2013

3000 m 2014

3000m 2013-2014

Saugy et al. In prep
to team sport players...
Altitude/Hypoxic Training

LHTH (HH)
- Natural/Terrestrial (HH)
- Oxygen filtration (NH)

LHTL (HH/NH)
- Nitrogen dilution (NH)
- Suppl. Oxygen (HH)

LLTH (HH/NH)
- IHE
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- RSH
- RTH

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## CHT - Continuous hypoxic training vs. CNT - Continuous normoxic training

<table>
<thead>
<tr>
<th>Author (year)</th>
<th>Design (number of training sessions, type, altitude, training content)</th>
<th>Groups</th>
<th>Statistically significant results (P&lt;0.05)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Roskamm et al. (1969)</td>
<td>Untrained, 24 over 4 wks, cycling, 2250 m (N=6) or 3450 m (N=6) (HH). 30-min aerobic training</td>
<td>CHT, N=12</td>
<td>+10-17% VO2max</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CNT, N=6</td>
<td>+6% VO2max</td>
</tr>
<tr>
<td>Emonson et al. (1997)</td>
<td>Untrained, 15 over 5 wks, cycling, 2500 m (HH). 45 min at 70% of VO2max</td>
<td>CHT, N=9</td>
<td>+12% VO2max</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CNT, N=9</td>
<td>+12% VO2max</td>
</tr>
<tr>
<td>Katayama et al. (1999)</td>
<td>Untrained, 10 over 2 wks, cycling, 4500 m (HH). 30 min at 70% of normoxic VO2max level</td>
<td>CHT, N=7</td>
<td>+7% VO2max</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CNT, N=7</td>
<td>+5% VO2max</td>
</tr>
<tr>
<td>Bailey et al. (2000)</td>
<td>Runners, 4 wks at ~2000 m (NH). Aerobic training, no details</td>
<td>CHT, N=18</td>
<td>+15% VO2max</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CNT, N=14</td>
<td>+10% VO2max</td>
</tr>
<tr>
<td>Geiser et al. (2001)</td>
<td>Untrained, 30 over 6 wks, cycling, 3850 m (NH). 30 min at 77%-85% of max heart rate</td>
<td>CHT, N=18</td>
<td>+11% VO2max, +17% 30-min TT mean PO</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CNT, N=15</td>
<td>+9% VO2max, +19% 30-min TT mean PO</td>
</tr>
<tr>
<td>Karlsen et al. (2002)</td>
<td>Cyclists, 9 over 3 wks, cycling, 3000 m (NH). 120 min aerobic training</td>
<td>CHT, N=8</td>
<td>NS changes in VO2max or 30-min TT</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CNT, N=8</td>
<td>NS changes in VO2max or 30-min TT</td>
</tr>
<tr>
<td>Hendriksen &amp; Meeuwsen (2003)</td>
<td>Triathletes, 10 over 10 days, cycling, 2500 m (HH). 105 min aerobic training</td>
<td>CHT, N=8</td>
<td>+5% PPO cycling Wingate</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CNT, N=8</td>
<td>NS increases</td>
</tr>
<tr>
<td>Ventura et al. (2003)</td>
<td>Cyclists, 18 over 6 wks, cycling, 3200 m (NH). 30 min aerobic training</td>
<td>CHT, N=7</td>
<td>NS changes in VO2max or 10-min TT</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CNT, N=5</td>
<td>NS changes in VO2max or 10-min TT</td>
</tr>
<tr>
<td>Dufour et al. (2006)</td>
<td>Runners, 12 over 6 wks, running, 3000 m (NH). 24-40 min &lt; VO2max</td>
<td>CHT, N=9</td>
<td>+5% VO2max, +35% Tlim at vVO2max</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CNT, N=9</td>
<td>NS changes</td>
</tr>
<tr>
<td>Hanlin et al. (2009)</td>
<td>Cyclists &amp; triathletes, 10 over 10 days, cycling, 3200-4400 m (NH). 90 min aerobic training followed by two 30-s Wingate tests</td>
<td>CHT, N=9</td>
<td>+3% PO cycling Wingate</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CNT, N=7</td>
<td>NS changes</td>
</tr>
<tr>
<td>Mao et al. (2011)</td>
<td>Active males, 25 over 5 wks, cycling, 2750 m (NH). 30 min aerobic training</td>
<td>CHT, N=12</td>
<td>+16% VO2max</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CNT, N=12</td>
<td>+10% VO2max</td>
</tr>
<tr>
<td>Holiss et al. (2014)</td>
<td>Runners, 16 over 8 weeks, running, 2150 m, (NH). 40 min &lt; VO2max</td>
<td>CHT, N=5</td>
<td>-3% submaximal VO2, -1% VO2max</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CNT, N=7</td>
<td>+2% submaximal VO2, +5% VO2max</td>
</tr>
<tr>
<td>Robach et al. (2014)</td>
<td>Active males, 20 over 6 weeks, cycling, 2500 m, (NH). 60 min aerobic training</td>
<td>CHT, N=9</td>
<td>+6% VO2max, +53% 20-min TT mean PO</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CNT, N=8</td>
<td>+9% VO2max, +50% 20-min TT mean PO</td>
</tr>
<tr>
<td>Author (year)</td>
<td>Subjects</td>
<td>Design (number of training sessions, type, altitude, training content)</td>
<td>Groups</td>
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<tr>
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<td>-------------------------------------------------------------------------------------------------------------------------------------</td>
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</tr>
<tr>
<td>Terrados et al. (1988)</td>
<td>Elite cyclists</td>
<td>12-20 over 3-4 wks, cycling, 2300 m (HH). Aerobic training and some intervals (15 s at 130% of aerobic peak power output)</td>
<td>HIT, N=4</td>
</tr>
<tr>
<td></td>
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<td>INT, N=4</td>
</tr>
<tr>
<td>Martino et al. (1995)</td>
<td>Elite swimmers</td>
<td>Swim sprints at 2800 m (HH) during 21 days at altitude. No details available</td>
<td>HIT, N=20</td>
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<td>INT, N=13</td>
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<tr>
<td>Truijens et al. (2003)</td>
<td>Swimmers</td>
<td>15 over 5 wks, swimming, 2500 m (NH), 12.5 min &gt; 100% VO2max (30 s or 60 s bouts)</td>
<td>HIT, N=8</td>
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<td></td>
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<td>INT, N=8</td>
</tr>
<tr>
<td>Morton &amp; Cable, (2005)</td>
<td>Team sport players</td>
<td>12 over 4 wks, cycling, 2750 m (NH). 10 x 1-min at 80% of 2-min PPO</td>
<td>HIT, N=8</td>
</tr>
<tr>
<td></td>
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<td>INT, N=8</td>
</tr>
<tr>
<td>Roels et al. (2005)</td>
<td>Cyclists &amp; triathletes</td>
<td>14 over 7 wks, cycling, 3000 m (NH). 6-8 x 2.3 min at 100% of aerobic PPO</td>
<td>HIT, N=11</td>
</tr>
<tr>
<td></td>
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<td>HIT, N=11</td>
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<td>INT, N=11</td>
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<tr>
<td>Dufour et al. (2006)</td>
<td>Runners</td>
<td>12 over 6 wks, running, 3000 m (NH), 24-40 min with intervals &lt; VO2max</td>
<td>HIT, N=9</td>
</tr>
<tr>
<td></td>
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<td>INT, N=9</td>
</tr>
<tr>
<td>Roels et al. (2007)</td>
<td>Cyclists &amp; triathletes</td>
<td>15 over 3 wks, cycling, 3000 m (NH), 9 x 60 min at 60% VO2max and 36 min with intervals of 2 min at 100% aerobic PPO (2 min bouts)</td>
<td>HIT, N=10</td>
</tr>
<tr>
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<td>INT, N=9</td>
</tr>
<tr>
<td>Lecoultre et al. (2010)</td>
<td>Cyclists</td>
<td>12 over 4 wks, cycling, 3000 m (NH). 4 x 12-18 min at 100-120% of aerobic PPO, 4 x 30-48 min &lt; VO2max and 4 x 100-min aerobic training.</td>
<td>HIT, N=7</td>
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<tr>
<td></td>
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<td>INT, N=7</td>
</tr>
<tr>
<td>Maninmanakorn et al.</td>
<td>Female team-sport players</td>
<td>15 over 5 wks, knee flexion and extension, ~4500 m (NH), 6 sets of low resistance knee extensions and flexions to failure with 30 s between sets</td>
<td>HIT, N=10</td>
</tr>
<tr>
<td>(2012)</td>
<td></td>
<td></td>
<td>INT, N=10</td>
</tr>
<tr>
<td>Hollins et al. (2013)</td>
<td>Active males</td>
<td>15 over 3 wks, leg-extension, 3000 m (NH), 10 x 60-70 s intense exercise with 20-30 s passive recovery. One leg IHT, the other leg INT.</td>
<td>HIT, N=9</td>
</tr>
<tr>
<td></td>
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<td>INT, N=9</td>
</tr>
<tr>
<td>Crabu et al. (2013)</td>
<td>Basketball players</td>
<td>9 over 3 weeks, running, 2500 m, (NH). 4-5 bouts of 4 min at 90% of vVO2max</td>
<td>HIT, N=6</td>
</tr>
<tr>
<td></td>
<td></td>
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<td>INT, N=6</td>
</tr>
</tbody>
</table>

IHT - Intermittent hypoxic training vs. INT – Intermittent normoxic training

Faiss et al. 2013
Repeated sprint training in hypoxia (RSH)

- 50 male cyclists
- Normobaric hypoxic chamber

Hypoxic group (n=20, 3000 m, \( F_{\text{O}_2} = 14.7\% \)) RSH
Normoxic group (n=20, 485 m, \( F_{\text{O}_2} = 20.9\% \)) RSN
Control group (n=10, no training)

- 4 weeks of cycling training
- 120 sprints in 8 sessions

Faiss et al. 2013
Results:

mean 10 s power of all sprints (W)

- + 6% Power output
- 38% more sprints

70% of best

Faiss et al. 2013
Results:
mean 10 s power of all sprints (W)

- + 7% Power output
- Not more sprints

Faiss et al. 2013
Muscle biopsies mRNA expression levels: significant modifications at muscular level after repeated sprint training in hypoxia (RSH)

Specific molecular adaptations: shift towards increased glycolytic activity
Hoppeler & Vogt. 2001; Dufour et al. 2006; He et al. 2011
Muscle oxygenation during the successive sprints -> variations in total hemoglobin $\Delta tHb$
# RSH – Repeated Sprint Training in Hypoxia vs. RSN – Repeated Sprint Training in Normoxia

<table>
<thead>
<tr>
<th>Author (year)</th>
<th>Subjects</th>
<th>Study design</th>
<th>Groups</th>
<th>Statistically significant results (p&lt;0.05)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Puype et al. (2013)</td>
<td>Moderately trained cyclists</td>
<td>18 over 6 wks, cycling, 3000 m (NH). 4-9 sprints of 30 s interspersed with 4.5 min recovery</td>
<td>RSH, N=10</td>
<td>+6% sprint PO, +6% VO(_{2\max}), +6% 10-min PO, +7% LT4</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>RSN, N=10</td>
<td>+5% sprint PO, +6% VO(_{2\max}), +6% 10-min PO, NS</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>CON, N=10</td>
<td>NS changes</td>
</tr>
<tr>
<td>Galvin et al. (2013)</td>
<td>Rugby players</td>
<td>12 over 4 wks, treadmill running, 3500 m (NH).</td>
<td>RSH, N=15</td>
<td>+33% Yo-Yo Intermittent Recovery Test performance</td>
</tr>
<tr>
<td></td>
<td></td>
<td>10 sprints of 6 s interspersed with 30 s recovery</td>
<td>RSN, N=15</td>
<td>+14% Yo-Yo Intermittent Recovery Test performance</td>
</tr>
<tr>
<td>Faiss et al. (2013)</td>
<td>Moderately trained cyclists</td>
<td>8 over 4 wks, cycling, 3000 m (NH). 3 x 5 all-out 10 s sprints interspersed with 20 s recovery</td>
<td>RSH, N=20</td>
<td>+6% sprint PO, +38% completed sprints in RSA test</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>RSN, N=20</td>
<td>+7% sprint PO, no change in completed sprints</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>CON, N=10</td>
<td>NS changes</td>
</tr>
<tr>
<td>Brocherie et al. (2014)</td>
<td>Football players</td>
<td>10 over 5 wks, running, 2900 m (NH). 5 x 4 all-out 5 s sprints interspersed with 45 s recovery</td>
<td>RSH, N=8</td>
<td>-4% first sprint time, -4% cumulated sprint time</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>RSN, N=8</td>
<td>-2% first sprint time, -2% cumulated sprint time</td>
</tr>
<tr>
<td>Faiss et al. (2014)</td>
<td>Competitive cross-country skiers</td>
<td>6 over 2 wks, double-poling, 3000 m (NH). 4 x 5 all-out 10 s sprints interspersed with 20 s recovery</td>
<td>RSH, N=9</td>
<td>+25% sprint PO, +57% completed sprints in RSA test</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>RSN, N=8</td>
<td>+21% sprint PO, no change in completed sprints</td>
</tr>
<tr>
<td>Gatterer et al. (2014)</td>
<td>Football players</td>
<td>7-8 over 5 wks, shuttle-runs, 3300 m (NH). 3 x 5 all-out 10 s sprints interspersed with 20 s recovery</td>
<td>RSH, N=5</td>
<td>+20% YO-YO Int. Rec. Test distance, -38% fatigue slope</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>RSN, N=5</td>
<td>+21% YO-YO Int. Rec. Test distance, +9% fatigue slope</td>
</tr>
</tbody>
</table>

### Additional benefits of hypoxia:
6 out of 6
LHTH : Live High Train High; LHTL : Live High Train Low; LLTH : Live Low Train High
IHIT : Intermittent Hypoxia Interval-Training; LHTLH : Live High Train Low and High; LHHTL : Live High Train High and Low.
HH : Hypobaric Hypoxia; NH : Normobaric Hypoxia.
≥14 h.day⁻¹ at simulated altitude of 2500-3000 m (FiO₂ = 15.1-14.5%)
≥14 h.day⁻¹ at simulated altitude of 2500-3000 m (FiO₂ =15.1-14.5%)

Optimizing aerobic and anaerobic fitness with ‘Live High-Train Low and High’ in team sports

Girard et al. 2013

Brocherie et al. 2015
14 days of LHTL(H) at ~2800-3000 m were sufficient to immediately increase $Hb_{mass}$ by ~3-4%.

Brocherie et al. 2015
A 2-fold superior RSA benefit for LHTLH compared to LHTL (cumulated sprint time: -3.6 versus -1.9%, respectively)

Maintained after 3 weeks
Relative mRNA expression of selected gene transcripts from baseline (Pre-) to the end of the intervention period (Post-1) and after 3 weeks (Post-2).

- **Oxygen signaling**
  - Hif-1α
  - VEGF
  - Mb

- **Oxygen carrier**
  - * indicates difference from Pre- (P<0.05)
  - # indicates difference from LLTL (P<0.05)

- **Mitochondrial metabolism**
  - COX4
  - PGC1α

- **Mitochondrial biogenesis**
  - TFAM

- **Contractile phenotype**
  - MHC-I
  - MHC-IIx

- **NOS pathways**
  - eNOS
  - nNOS

- Brocherie et al. In prep
Take-Home messages

1. Hypobaric hypoxia is different to normobaric hypoxia and is a more severe stimulus
   Aerobic performance more decreased - Different regulation.
   Altitude preparation for sea-level performance? Pros and cons of each

2. RSH is a novel hypoxic training method efficient for improving RSA
   Sport specific (muscle groups; posture; …)
   Work:Rest ratio; FT fibers recruitment.

3. Combination of methods (e.g. LHTLH) aiming to increase both Hbmass and RSA is promising in team sports
... and patients...
Reduced oxygen tension in tissue in obese patients (Ye 2009)

HIF-1α is increased in the adipose tissue of obese patients and its expression was reduced after surgery-induced weight loss (Semenza 2002)

Angiogenesis deficient in adipose tissue of obese mice: VEGF expression not increased (Ye 2004).

Obesity induces a chronic low-grade inflammatory state.

H induces gene expression in adipocytes and macrophages (Wood 2009)
## Compensatory adaptations to Hypoxic exposure or exercise

<table>
<thead>
<tr>
<th>Respiratory system</th>
<th>Cardiovascular system</th>
<th>Cellular and metabolic</th>
<th>Regulation of body weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperventilation</td>
<td>↑ basal and max HR</td>
<td>↑ HIF-1 and VEGF</td>
<td>↓ basal leptin levels</td>
</tr>
<tr>
<td>↑ lung diffusion capacity</td>
<td>↑ peripheral vasodilation</td>
<td>↑ Angiogenesis</td>
<td>↑ adrenergic system</td>
</tr>
<tr>
<td>↑CO₂ reserve in sleeping</td>
<td>↑ VO₂max</td>
<td>↑ diameter of arterioles</td>
<td>Basal noradrenaline remains high post-treatment</td>
</tr>
<tr>
<td>↓ Sleep desaturation</td>
<td>↓ Pro-inflammatory factors</td>
<td>↑ glycolytic enzymes &amp; mitochondria</td>
<td>↑ blood serotonin levels</td>
</tr>
<tr>
<td>↑ ventilatory response during exercise</td>
<td><strong>Cardiovascular protection</strong></td>
<td>↑ Hb–O₂ affinity</td>
<td>↓ Appetite</td>
</tr>
<tr>
<td><strong>Improves respiratory function</strong></td>
<td>↑ O₂, Fe and glucose conveyors</td>
<td>Improves insulin sensitivity</td>
<td>↑ body weight loss</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↑ glucose transporter GLUT-4</td>
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</tr>
</tbody>
</table>

*Urdampilleta (2012) Usefulness of combining intermittent hypoxia and physical exercise in the treatment of obesity. JPB*
Compensatory adaptations to Hypoxic exposure or exercise

<table>
<thead>
<tr>
<th>Brain</th>
<th>Cardiovascular system</th>
</tr>
</thead>
<tbody>
<tr>
<td>↑ vasoreactivity</td>
<td>↓ hypertension NO inactivation</td>
</tr>
<tr>
<td>↑ cerebral blood flow and oxygenation</td>
<td>↑ release vasodilators (NO/NOS pathway)</td>
</tr>
<tr>
<td>↓ desaturation</td>
<td>↑ circulating angiogenic factors</td>
</tr>
<tr>
<td><strong>Improves cerebral function</strong></td>
<td>↑ peripheral <strong>vasodilation</strong></td>
</tr>
<tr>
<td></td>
<td>↓ Arterial stiffness</td>
</tr>
<tr>
<td></td>
<td>↓ Pro-inflammatory factors</td>
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<tr>
<td></td>
<td>Oxidative stress modulation</td>
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<tr>
<td></td>
<td>↑ exercise-induced Hypoxemia – compensatory vasodilation</td>
</tr>
<tr>
<td></td>
<td><strong>Normalises blood pressure</strong></td>
</tr>
</tbody>
</table>
Thank you

Any Questions?
Few steps beyond..

La préparation physique.
D. Legallais & G. Millet
2007, Masson

S’entraîner en altitude
G. Millet & L. Schmitt
2011, deBoeck Univ

L’endurance.
Millet G. (ed), 2006
Edition EPS