YOGA, OXYGEN AND RESPIRATION

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MAIN HYPOTHESIS:

Whether YOGA can be used to modify or readjust important cardiovascular reflexes which are impaired in a large number of important diseases

• Respiration is one key to alter such reflexes
THE CARDIOVASCULAR AND RESPIRATORY SYSTEM ARE TIGHTLY CONNECTED

CONTROL OF THE HEART AND BLOOD VESSELS
heart rate
blood pressure...

CONTROL OF RESPIRATION
ventilation,
blood gas exchange

THE LINK IS THE AUTONOMIC NERVOUS SYSTEM
(sympathetic and parasympathetic)
However, some functions like the RESPIRATORY, are also under volitional control.
prolonged stress…. hypertension, heart failure, COPD, metabolic syndrome, diabetes

In the long term: increased cardiovascular risk

Reduced control of blood pressure
Low BAROreflex
= 
increases in BP

High CHEMOrflex

HIGH sympathetic

LOW parasympathetic
Increased control of blood pressure = high BAROreflex = Prevents increases in BP

Low stimulation of breathing = low CHEMOreflex

In the long term: Lowers BP, Relaxation, Red. Depression…

(yoga, physical training…)

High parasympathetic

Low sympathetic
INVERSE RELATIONSHIP BETWEEN BREATHING INTENSITY & EXERCISE CAPACITY

In heart failure

the more your breathing is stimulated during exercise

the LESS you can exercise!

Coats, BrHJ, 1994
in Heart failure:

It is NOT THE HEART that restricts exercise capacity, but rather:

1- the shorteness of breath due to the excessive stimulation of breathing (= unnecessary excessive breathing!)

2- the "DECONDITIONING" effect of the early shorteness of breath!

**Possible solutions:**

1) physical training of patients with CHF

2) train the reflexes
   (= reduce excessive stimulus to ventilate)
Baroreflex sensitivity (ms/mmHg)

In heart failure, slow breathing increases baroreflex sensitivity (BRS) and reduces sympathetic nerve traffic.

Bernardi et al, Circulation 2002

Gosoh et al, Circulation 2001
EFFECTS OF SLOW BREATHING ON HEART FAILURE

after 1 month training, unlike ctl group, improvement in exercise capacity all retained 1 month after the end of training

<table>
<thead>
<tr>
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<th>Baseline</th>
<th>Training</th>
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<tbody>
<tr>
<td><strong>Resting</strong></td>
<td></td>
<td></td>
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<tr>
<td>- Breaths/min</td>
<td>13.4±1.5</td>
<td>7.6±1.9 *</td>
</tr>
<tr>
<td>- SaO₂ %</td>
<td>92.5±0.3</td>
<td>93.2±0.4 *</td>
</tr>
<tr>
<td><strong>Exercise</strong></td>
<td></td>
<td></td>
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<tr>
<td>- Peak VO2 (ml/k/min)</td>
<td>13.9±0.8</td>
<td>15.9±0.8 *</td>
</tr>
<tr>
<td>- Peak Load (watts)</td>
<td>92±6</td>
<td>100±4 *</td>
</tr>
<tr>
<td>- AT (watts)</td>
<td>59.8±3.7</td>
<td>64.8±4.3 *</td>
</tr>
<tr>
<td>- Exercise time (sec)</td>
<td>422±22</td>
<td>615±18 *</td>
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Bernardi, Lancet 1998
SLOW-DEEP BREATHING INCREASES THE OXYGEN IN THE BLOOD

= BETTER MATCHING OF AIR AND BLOOD IN THE LUNG
= BETTER GAS EXCHANGE
= BETTER VENTILATION/PERFUSION MATCHING (reduced $V_d/V_t$ ratio)

lower stimulation of breathing and of sympathetic activity

SHALLOW-FAST BREATHING          SLOW-DEEP BREATHING

Bernardi et al, Lancet 1998
SLOW (deeper) BREATHING INCREASES THE OXYGEN IN THE BLOOD!

YOGA TRAINEES TEND TO NORMALLY USE SLOW (deeper) BREATHING

DOES YOGA-Like BREATHING GIVES ADVANTAGES WHEN THERE IS LITTLE OXYGEN = HIGH ALTITUDE?
Pyramid Laboratory, 5050m, Italian Ev-K2-CNR, Nepal, 1998
(12 yoga practitioners and 12 controls)
Everest Base Camp, 5200m, Tibet, Spring 2004
Italian Expedition to Everest and K2
after 2 weeks of acclimatisation at 5200m

Italian K2-Everest Expedition, May 2004

<table>
<thead>
<tr>
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<th>Summiters without Oxygen (N=5)</th>
<th>Others (N=6)</th>
<th>p</th>
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<tbody>
<tr>
<td>Vital Capacity (L)</td>
<td>5.2 ± 0.2</td>
<td>5.5 ± 0.1</td>
<td>NS</td>
</tr>
<tr>
<td>Max Volunt.Vent (L/min)</td>
<td>191.4 ± 15.9</td>
<td>183.0 ± 7.0</td>
<td>NS</td>
</tr>
<tr>
<td>Ventilation (L/min)</td>
<td>13.3 ± 0.8</td>
<td>19.2 ± 0.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Resp.Rate (br/min)</td>
<td>10.7 ± 1.9</td>
<td>20.2 ± 0.8</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>CO₂ (mmHg)</td>
<td>28.2 ± 0.6</td>
<td>24.2 ± 0.9</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>SaO₂ (%)</td>
<td>88.4 ± 1.9</td>
<td>87.9 ± 1.5</td>
<td>NS</td>
</tr>
<tr>
<td>Hypox Vent.R (L/min/%)</td>
<td>2.14 ± 0.51</td>
<td>5.09 ± 1.03</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Vent.reserve (%)</td>
<td>66.6±6.3</td>
<td>26.7±8.8</td>
<td>&lt;0.01</td>
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*Vent.efficiency:*

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<tbody>
<tr>
<td>SaO₂/Ventilation (%/L/min)</td>
<td>6.7 ± 0.4</td>
</tr>
<tr>
<td>Vd/Vt</td>
<td>0.09 ± 0.03</td>
</tr>
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</table>

Bernardi et al, Eur Resp J, 2006
• slow breathing proved very efficient at high altitude

• “efficiency” of breathing seems more important than “quantity”

• cardiovascular control (BRS) is preserved

• More efficient breathing reduces the stimulus to ventilate and thus improves breathing reserve (essential or even vital in extreme conditions)
Diabetes: worldwide increase in the last decade

Diabetic complications, rather than diabetes itself, account for the largest economic and social cost of its management (particularly in type 1)

Abnormalities in the autonomic nervous system are important factors predisposing to diabetic complications
1) **Large arteries:**

accelerates atherosclerosis, more than in the general population

Consequence: highly increased risk for

- hypertension
- stroke (both ischemic and hemorrhagic)
- coronary artery disease
- arterial diseases of the limbs

*early diagnosis:*

*by measures of arterial stiffness*

*(blood pressure profile, carotid imaging)*
DIABETIC COMPLICATIONS

2) **small arteries:**

main consequences:

Retina: diabetic retinopathy (leads to complete blindness)

kidney: renal insufficiency

lower limbs: ulcers

vessels directed to the nerves: neuropathy

(Peripheral, central, and autonomic nervous system)
3) *autonomic nervous system*:

- **gut**: diarrhea / constipation
- **bladder**: urinary dysfunction
- **reproductive s.**: impotence

**Blood pressure control**: blood pressure fall on standing (syncopes)

**perception**: loss of perception of cardiac pain or of hypoglycemia

*accelerates (or causes?) all previous complications*
AUTONOMIC NERVOUS SYSTEM AND DIABETES

INCREASED SYMPATHETIC TONE

REDUCED PARASYMPATHETIC TONE
AUTONOMIC DYSFUNCTION IN DIABETES:

⚠️ ALWAYS CONSIDERED ORGANIC
 (= dysautonomia, = structural damage of nerves, potentially irreversible)

⚠️ FUNCTIONAL HYPOTHESIS (ie potentially reversible)

NEVER TESTED
RESULTS:

ATTEMPTS TO TREAT ON THE BASIS OF STRUCTURAL DAMAGE FAILED

(eg treatments with aldose-reductase inhibitors)

TREATMENTS BASED ON THE UNDERLYING ASSUMPTION (though never declared) OF A FUNCTIONAL BASIS WERE SUCCESSFUL OR AT LEAST ENCOURAGING

Lyfestyle (physical exercise)
Exercise Training improves autonomic function (BRS) in Diabetes

Loimaala et al, 2003
Early autonomic dysfunction in type 1 diabetes: a reversible disorder?

Rosengård-Bärlund et al. Diabetologia, 2009
Early autonomic dysfunction in type 1 diabetes: a reversible disorder?

Rosengård-Bärlund et al. Diabetologia, 2009

A simple manoeuvre like slow breathing increases
Baroreflex sensitivity in short-duration Type 1 Diabetes

Healthy controls
T1DM
Early Heart transplanted subjects
DIFFERENT DEGREES OF AUTONOMIC INVOLVEMENT (CAN) REDUCE BUT DO NOT ABOLISH RESPIRATION-INDUCED BAROREFLEX CHANGE

Rosengård-Bärlund et al, Diabetologia, 2011
WHAT FUNCTIONAL FACTORS COULD “RESTRAIN” PARASYMPATHETIC / INCREASING SYMP.ACTIVITY?

some of them are well known:

- **Hyperglycaemia**
  
  *(Hoffmann, Int J Diab Compl 1999, Gordin, Diabetologia 2007)*

- **Insulin**
  
  *(Scherrer, Circulation 1997, Sartori JH 1999)*

- **Leptin**
  
  *(Paolisso, J Clin Endocr Metab 2000)*

  *(Tissue acidosis)*

- **Tissue hypoxia**
this hypothesis had never been tested until very recently, although it was demonstrated that:

1) the oxygen tension measured in the tissues is lower in diabetic subjects

2) funct. pulmonary abnormalities reduce oxygen diffusion

3) reduced oxygenation of arterial vessel cause loss of nerves in the long-term

4) reduced oxygenation induces a sustained increase sympathetic activity
about 15% of the Andean Population leaving ~ 4000m develop a maladaptation syndrome, called CHRONIC MOUNTAIN SICKNESS

abnormalities of the peripheral and autonomic nervous system, similar to diabetes, but reverse with descent to sea-level

Then, what would be the effect of oxygen in diabetic subjects?

If diabetic subjects are indeed more hypoxic than healthy subjects, then their response to $O_2$ could be even larger!

Conversely, a neural damage will show blunted response to oxygen in diabetic subjects.

Bernardi et al, Diabetologia 2011
BAREOREFLEX SENSITIVITY: much higher INCREASE in type 1 diabetes

Bernardi et al, Diabetologia 2011
both oxygen and slow breathing improve BRS in Type 1 Diabetes

Bernardi et al. Diabetologia 2011
BUT.. (SYSTOLIC) BLOOD PRESSURE INCREASED (in T1DM)

Type 1 diabetes

Healthy controls

Bernardi et al, Diabetologia 2011
slow breathing and arterial function
good or bad?

**oxygen** improves BRS but increases blood pressure
( oxygen $\rightarrow$ free radicals $\rightarrow$ endothelium dysfunction ?

*Budzinska et al J Physiol Pharmacol 2008* )

**slow breathing** improves BRS and oxygenation

*What would be the effect of slow breathing on blood pressure?*

still positive action?

or effect similar to oxygen ( = increase in free rad)?
SYSTOLIC BLOOD PRESSURE and OXYGEN
Slow breathing attenuates the increase in blood pressure

Spontaneous breathing

Slow breathing

Bernardi et al. Diabetologia 2011
slow breathing and arterial function

good or bad?

slow breathing effectively **counteracts the negative effects of oxygen** on arterial function

**why?**

- prevalent reduction in sympathetic activity/
  increased vagal (parasymp) activity?

- could vagal stimulation reduce the potentially negative effects of free radicals?  
  *(Tsutsumi Cardiovasc Res 2008)*

- the increased parasymp. activity, could it produce acute modulation of endothelial function (and suppress inflammation)?  
  *(Sabbah Heart failure Rev, 2011)*
“Vagus nerve stimulation in experimental heart failure”
(Sabbah et al, Heart failure Rev, 2011)

“A considerable body of pre-clinical investigations exists in support of the concept of electrical VNS as a therapeutic approach to treatment of chronic HF [heart failure].”

“VNS derives these potential clinical benefits from multiple mechanisms of action… These include restoration of baroreflex sensitivity, suppression of pro-inflammatory cytokines, normalization of nitric oxide signaling pathway …”

Vagus nerve stimulation device consisting of the signal generator (CardioFit stimulator), the right ventricular sensing lead and the CardioFit right Vagus nerve cuff stimulation lead
We found for the first time one intervention able to improve the parasympathetic activity in diabetic subjects:

1) Evidence against the idea that the autonomic nervous system is permanently damaged in diabetes.

2) This suggests that in type 1 diabetes there is a persisting “restraining” of the autonomic nervous system, likely due to lack of oxygen in the tissues, that can be corrected by slow breathing (or oxygen).

3) Unlike direct oxygen administration, slow breathing shows favourable effects also on the vasculature (no increase in blood pressure).

4) Relevant potential implications: positive effects on inflammation, endothelial function, free radicals, ageing?

5) Rationale for the use of pranayama in diabetes, in addition to many other diseases with autonomic imbalance.

6) Long-term effect to be verified.