Is Exercise Good for the Brain?

Prof Dr Romain MEEUSEN
Vrije Universiteit Brussel
Human Physiology - BLITS

Leçon Inaugurale Chaire Francqui 2008-2009

YES!

Or Not?

Contents
« Neurogenesis and Exercise »
« Central Fatigue »
« Thermoregulation – how hot is the Brain? »
« The Overtraining Syndrome: facts and fiction »
« Cryotherapy and Recovery from exercise »

Health benefits of exercise

<table>
<thead>
<tr>
<th>General</th>
<th>Brain</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Cardiovascular diseases</td>
<td>• Stroke</td>
</tr>
<tr>
<td>• Metabolic syndrome</td>
<td>• Depression</td>
</tr>
<tr>
<td>o Obesity</td>
<td>• Cognition</td>
</tr>
<tr>
<td>o Diabetes</td>
<td>• Alzheimers disease</td>
</tr>
<tr>
<td>o Hypertension</td>
<td>• Parkinsons disease</td>
</tr>
<tr>
<td>• COPD</td>
<td>• Spinal cord injury</td>
</tr>
<tr>
<td>• Osteoarthritis</td>
<td>• ...</td>
</tr>
<tr>
<td>• Osteoporosis</td>
<td></td>
</tr>
</tbody>
</table>

Structure CNS

| Cognitive Control | Hippocampus, Cortex |
| Executive Control | Prefrontal cortex |
| Emotional Control | Amygdala, Prefrontal cortex |
| Motivational Control | Reward, Wanting, ... |
| Motor Control | Striatum, Basal ganglia, Cerebellum, Spinal cord |
Exercise & Neurotransmission

Microdialysis studies showed that exercise increases neurotransmission (e.g. Meeusen et al 1995, 1996, 1997, 2001, 2003). Training has a 'sparing' effect potentially influencing receptors and their function.

Exercise & Neurotransmitters

Health Benefits of Exercise - neurobiology

- Cognition
- Alzheimers disease
- Parkinsons disease
- SCI
- ...

Is there proof for adaptive responses of the CNS due to exercise?

- Relative little is known about mechanisms underlying the influence of physical activity & exercise on the functioning of the CNS

Cognition declines with age

Meta analysis: effect exc training on cognition in elderly

Exercise has positive treatment effects in older patients with dementia & cognitive impairments.

Brain cells die – and do not get replaced

Neur

Heyn et al Arch Phys Med Rehabil 2004
Brain Derived Neurotrophic Factor (BDNF)

Is the most abundant neurotrophin in the brain

- growth factor within the brain
- It enhances the growth and maintenance of several neural systems
- Serves as a neurotransmitter modulator
- Participates in use-dependent plasticity mechanisms

Voluntary running (Van Praag et al Nature neurosci 1999)

Enhances the survival of 'newborn' neurons = cell proliferation
Or in neurogenesis (4 weeks old cells)
One day

Are neurotransmitters involved?

Human studies

- Does exercise increase BDNF in peripheral blood?
- Does a reuptake inhibitor facilitates this?

Reboxetine = Noradrenaline reuptake inhibitor
Citalopram = Serotonin reuptake inhibitor

BDNF expression correlates with the distance run/night

BDNF increases in peripheral blood due to exercise

To summarise

Exercise is used as a therapy for mental and neurodegenerative disorders:
- Neurotransmitters and other neuromodulators play an important role
- The interaction between the brain and the periphery relies on subtle 'crosstalk'
- These findings open new insights into the therapeutic effects of exercise
The Central Fatigue Hypothesis

During prolonged exercise athletes not only get fatigued because of a decrease in substrates, but there is also fatigue induced by brain mechanisms.

---

The Central Fatigue Hypothesis

Is based on the increase in brain Serotonin ([5-HT] during exercise.

Newsholme and colleagues (1987) assumed that during prolonged exercise increased brain serotonergic activity may augment:
- lethargy and loss of drive resulting in a reduction in motor unit recruitment,
- affecting physical and mental efficiency of athletes.

---

Central Fatigue: It’s All in the Brain?

Both peripheral and central regulatory mechanisms will be stressed
- Disturbance of Cerebral Homeostasis that eventually can lead to Central Fatigue
- Neurotransmitters are involved
- But although brain disturbances occur, fatigue mechanisms seem to need other stressors.

---

Thermoregulation - How hot is the Brain?

Ref Drug Performance
Wilson & Maughan ’92 Paroxetine
Shrader et al ’98 Paroxetine
Strachan et al ’04 Paroxetine (30°C)
Meeusen et al ’01 Fluoxetine =
Pannier et al ’95 Pizotifen =
Meeusen et al ’97 L-DOPA =
Meeusen et al ’97 Ritanserin =
Piacentini et al ’02 Venlafaxine =
Piacentini et al ’02 Reboxetine =
Piacentini et al ’04 Bupropion =
Watson et al ’05 Bupropion (30°C) =
Reuptake inhibition & Performance

---

Review Article
DOI: 10.1007/s12698-009-9060-5
Exercise time to exhaustion during cycling at 70% peak VO₂ in 40°C (HT), 20°C (NT), and 3°C (CT). Parkin et al 1999

How could high core temperature cause fatigue?
- Peripheral factors
- Change brain function?
- Change "motivation"?

Central Fatigue in the heat
- Which neurotransmitters are involved?
- Can performance in the heat be manipulated?
  ➔ studies with the TT protocol in the heat

Materials & Methods
- well trained cyclists
- age (yrs) = 23 ± 1.7
- weight (kg) = 73.5 ± 8.5
- height (cm) = 182 ± 5.8
- VO₂max = 73.5 ± 6.4 ml/kg/min
- Temp: 18°C or 30°C
- Double blind placebo contr.
- BUPROPION = DA/NA - RI
  ➔ 60 min à 55% Wattmax
  ➔ 30 min Time trial à 75% Wattmax

TT performance:
Bupropion = DA/NA reuptake inhibitor

Core Temperature
RPE
Subjects completed the time trial 3.4 min faster in the BUP trial, representing a 9% increase in performance over the placebo treatment.

Seven (of 9) subjects attained core temperatures equal to, or greater than, 40°C in the BUP trial. This difference occurred without any apparent change in the subjects’ perceived exertion or thermal sensation. ➔ Safety Brake ??

This could indicate that subjects were capable of pushing into a ‘danger zone’ close to critical core temperature without any negative feedback from the central nervous system ➔ Disinhibiting ‘Central control mechanisms’

Exc + BUP (rats) Temperature Microdialysis

Exc + BUP (rats) Neurotransmitters

Citalopram SSRI

Reboxetine NA-RI

Human experiments

DOPAMINERGIC MANIPULATION
Ritalin – methylphenidate (Humans)
Central Fatigue: It’s all in the Brain?

Limitations to neuromuscular performance:
- Motor command
- Multiple levels of the CNS
- Neurotransmitters
- Multiple levels of interaction
- Multiple control over homeostatic functions (e.g. executive cognitive function, learning, emotions, motivation, thermoregulation...)

Olympic Triathlon: Hero or nobody

Gold: 1:51'07''
Silver: 1:51'15''
Difference: 1'00''

Gold: 2:04'43''
Silver: 2:04'50''
Difference: 7'07''

The Overtraining Syndrome – Facts and Fiction

Acute exercise stimulus

\[ \text{Acute Fatigue (positive adaptation to training)} \]

\[ \text{Overreaching (positive adaptation if used correctly)} \]

\[ \text{FO} \leftrightarrow \text{NFO} \]

\[ \text{Overtraining Syndrome (maladaptation, decreased performance)} \]

ECSS Consensus Statement - 2006

<table>
<thead>
<tr>
<th>PROCESS</th>
<th>TRAINING (vertical)</th>
<th>INTENSIFIED TRAINING</th>
</tr>
</thead>
<tbody>
<tr>
<td>OUTCOME</td>
<td>ACUTE FATIGUE</td>
<td>FUNCTIONAL OR NON-FUNCTIONAL OVERREACHING</td>
</tr>
<tr>
<td>RECOVERY</td>
<td>Days</td>
<td>Days - weeks</td>
</tr>
<tr>
<td>PERFORMANCE</td>
<td>INCREASE</td>
<td>Temporary performance decrement (e.g. training camp)</td>
</tr>
</tbody>
</table>

Do we have tools to monitor?

- Persisting Underperformance
- Long recovery

Longitudinal monitoring

Medical
Psychological
Physiological
Performance

!!Exclusion Diagnosis!!

Search for Clear and simple markers

Profile of Mood State - POMS

- Questionnaire
- assesses the total mood disturbance experienced
- TENSION
- DEPRESSION
- ANGER
- VIGOR
- FATIGUE
- (Confusion)

Brain disturbance?

Central Nervous System
Chronic stress

Hormones are influenced by:
- Higher brain centres
- HPA dysregulation

'Deregulation'
Feedback or Feed forward?

Abnormalities in negative feedback:
How do we apply the KISS-principle??

Monitoring

Most athletes train more than once a day

Physiological disturbance:
- T-R disbalance
- ? Normal recovery

More than one exercise trigger
- Max test
- Different exercise
- Aerobic – anaerobic
- ...

2*VO$_{2\text{max}}$ Protocol

- B1 - B4 = Bloodsamples 1 - 4
- M1 + M2 = Meals

Measures et al 2004, 2009
OTS or NFO?

Nine athletes: ? Exclusion of OTS?
Clinical diagnosis: suspicious of OTS
- Different ‘triggering’ factors
- Medical screening
- Common features:
  - performance ↓
  - Mood disturbances
  - First test = POMS
- Double max test

Different ‘triggering’ factors

Medical screening

Common features:

Double max test

Meeusen et al 2004, 2009

Distinction between:

Non-functional Overreaching:
- Lower hormonal reaction in first test
- “Overshoot” in second test

Overtraining Syndrome:
- “Overshoot” in first test
- Suppression in second test

Meeusen et al 2004, 2009

Summary

« Neurogenesis and Exercise »
- Exercise is one of the most important ‘primers’ for neurogenesis

« Central Fatigue »
- Exists, but is linked to more than one neurotransmitter system
- Probably other ‘stressors’ are necessary to disturb this solid homeostatic mechanism

« Thermoregulation – how hot is the Brain? »
- The dopaminergic system has an important role in the ‘drive’ to continue during prolonged exercise in the heat

« The Overtraining Syndrome: facts and fiction »
- The hormonal disturbance due to NFO or OTS can be detected using a ‘double exercise protocol’

Is Exercise Good for the Brain?

Prof Dr Jacques Duchateau

Leçon Inaugurale Chaire Francqui 2008-2009

17/03/2009: 14:00h
- Exercise is one of the most important ‘primers’ for neurogenesis

05/03/2009: 18:00h
- Exists, but is linked to more than one neurotransmitter system
- Probably other ‘stressors’ are necessary to disturb this solid homeostatic mechanism

12/03/2009: 16:00h
- The dopaminergic system has an important role in the ‘drive’ to continue during prolonged exercise in the heat

24/03/2009: 10:00h
- The hormonal disturbance due to NFO or OTS can be detected using a ‘double exercise protocol’
• Location: downtown Brussels
• Date: 4–7 July 2012
• Organisers:
  ○ Vrije Universiteit Brussel (VUB)
  ○ Université Libre de Bruxelles (ULB)