Hibernating astronauts
Chances and Challenges

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Presenting discussions from the Topical Team

Hibernation and Torpor

TOPICAL TEAM HIBERNATING ASTRONAUTS

Team members

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Overview

Terminology (hibernation, torpor)
Types of Torpor
Natural Torpor
- hamster
- marmot
- bear

Efforts for artificial induction of torpor
Radioprotection and other benefits

Hibernating astronauts
Chances and Challenges

What do we associate with the term „Hibernation“ ?

Winter / Cold

Torpor – very low metabolism

Almost no drinking, no eating

Sleep (Winterschlaf)

Different signals

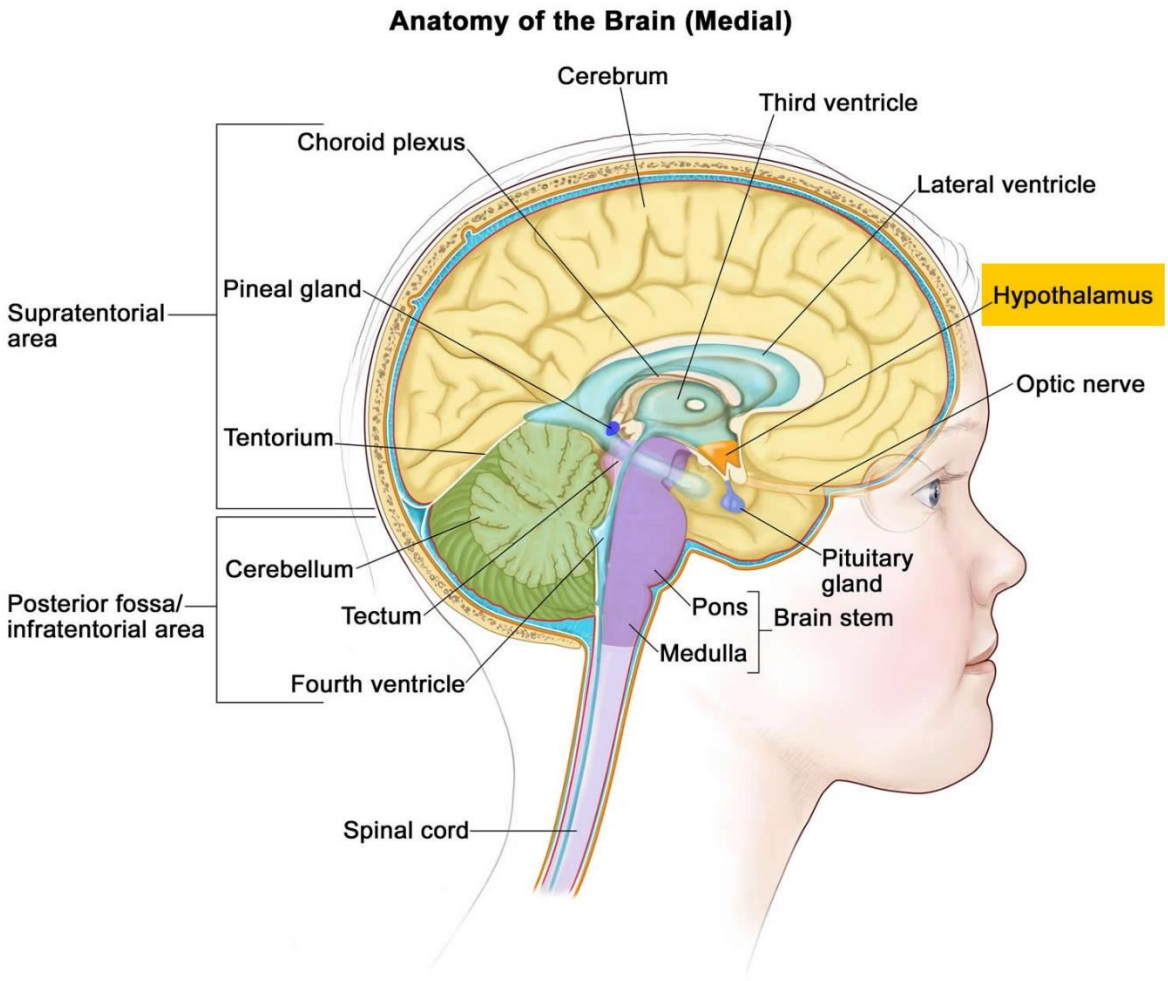
Seasonal	Circadian	Environmental
		
Hibernation Aestivation	Daily torpor	Torpor

Same Mechanism

Why can we assume that all these downregulations of metabolism follow the same scheme?

The most important anatomical structure in regulation of torpor is the hypothalamus

Hibernating astronauts
Chances and Challenges
The Hypothalamus



Regulates

Central regulator of the autonomous nerve system

involved in control of metabolism

Body temperature

Hunger and thirst

Sleep / Wake cycles

Controls the endocrine system (i.e. pituitary, hypophysis)

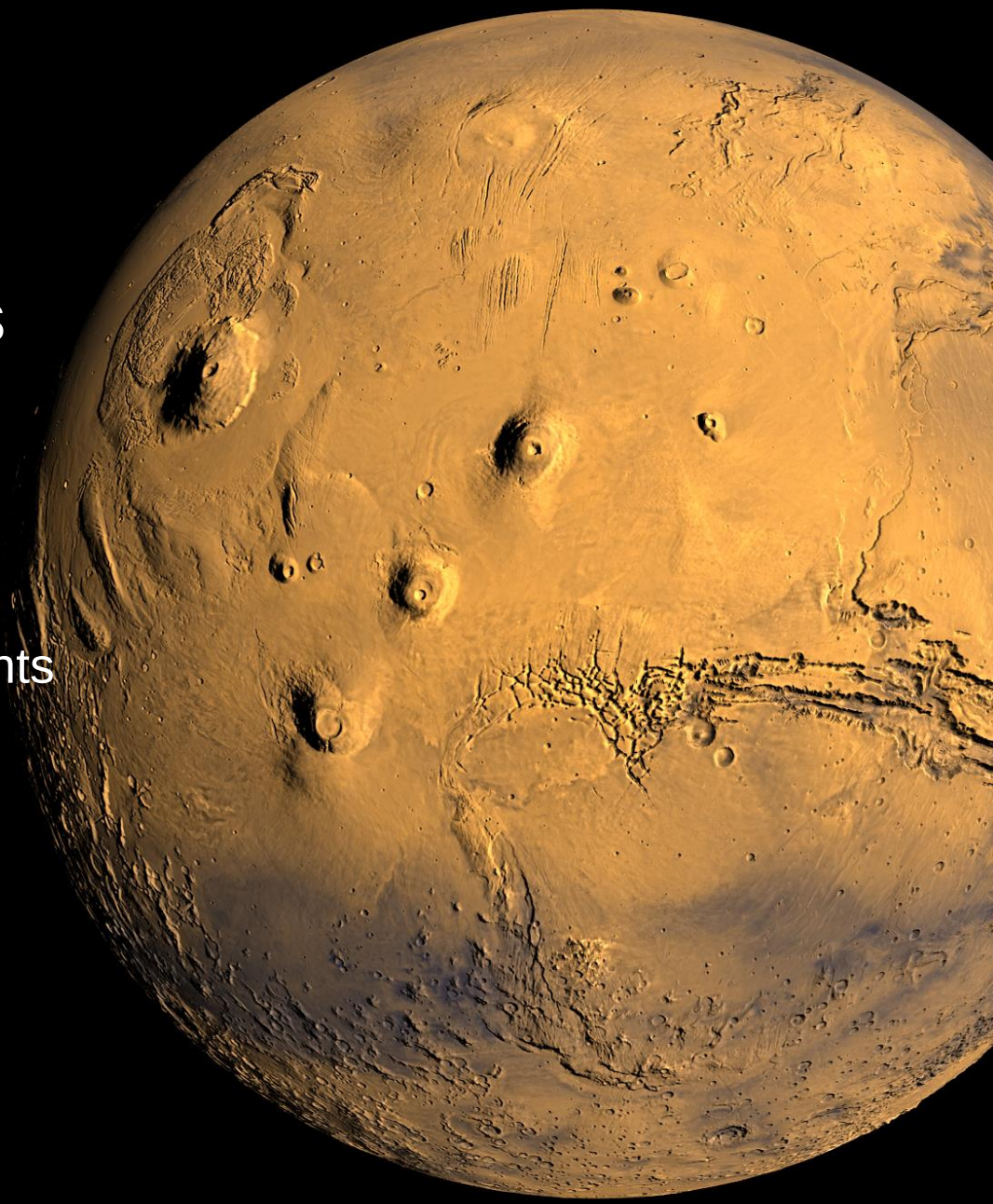
From: https://healthjade.com/what-does-the-hypothalamus-do/

Journey to Mars

Duration: ca. 9 months
3-4 months on Mars
9 months back home

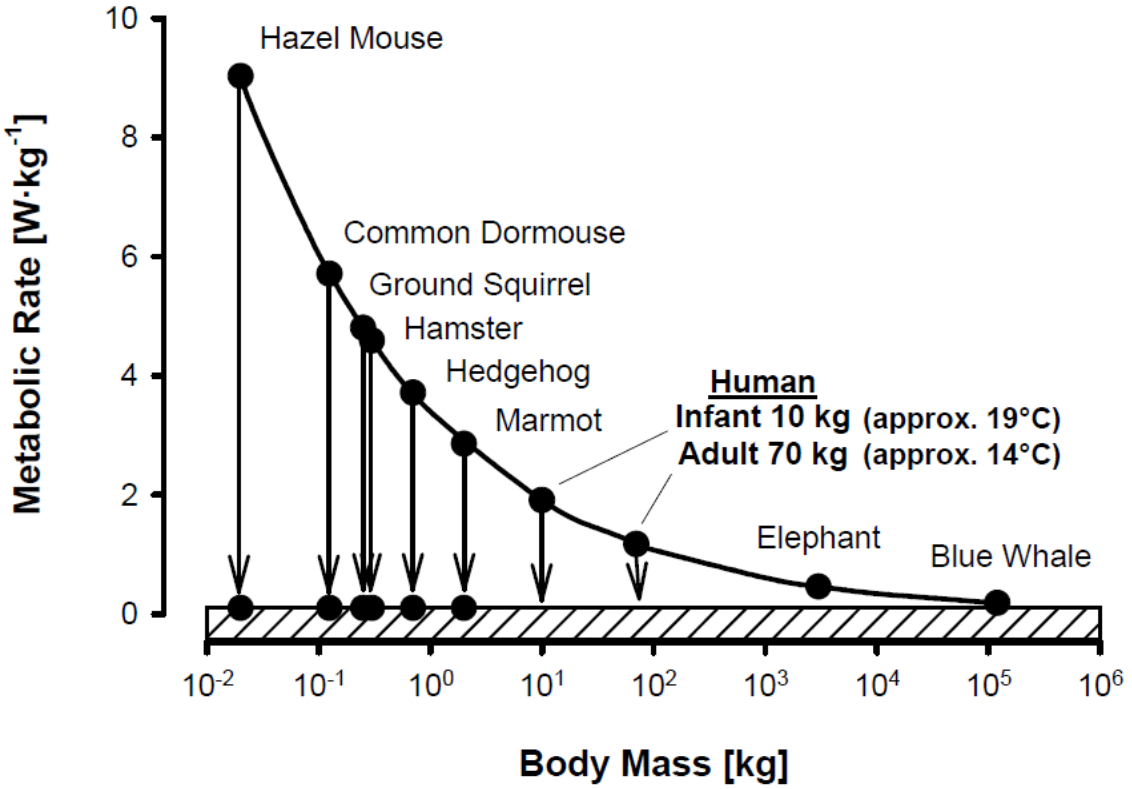
Requires amount of 70 shuttle flights
fuel
nutrition, drinking water
scientific instrumentation

Problems for astronauts:
mental
bone loss, muscle loss
radiation damage



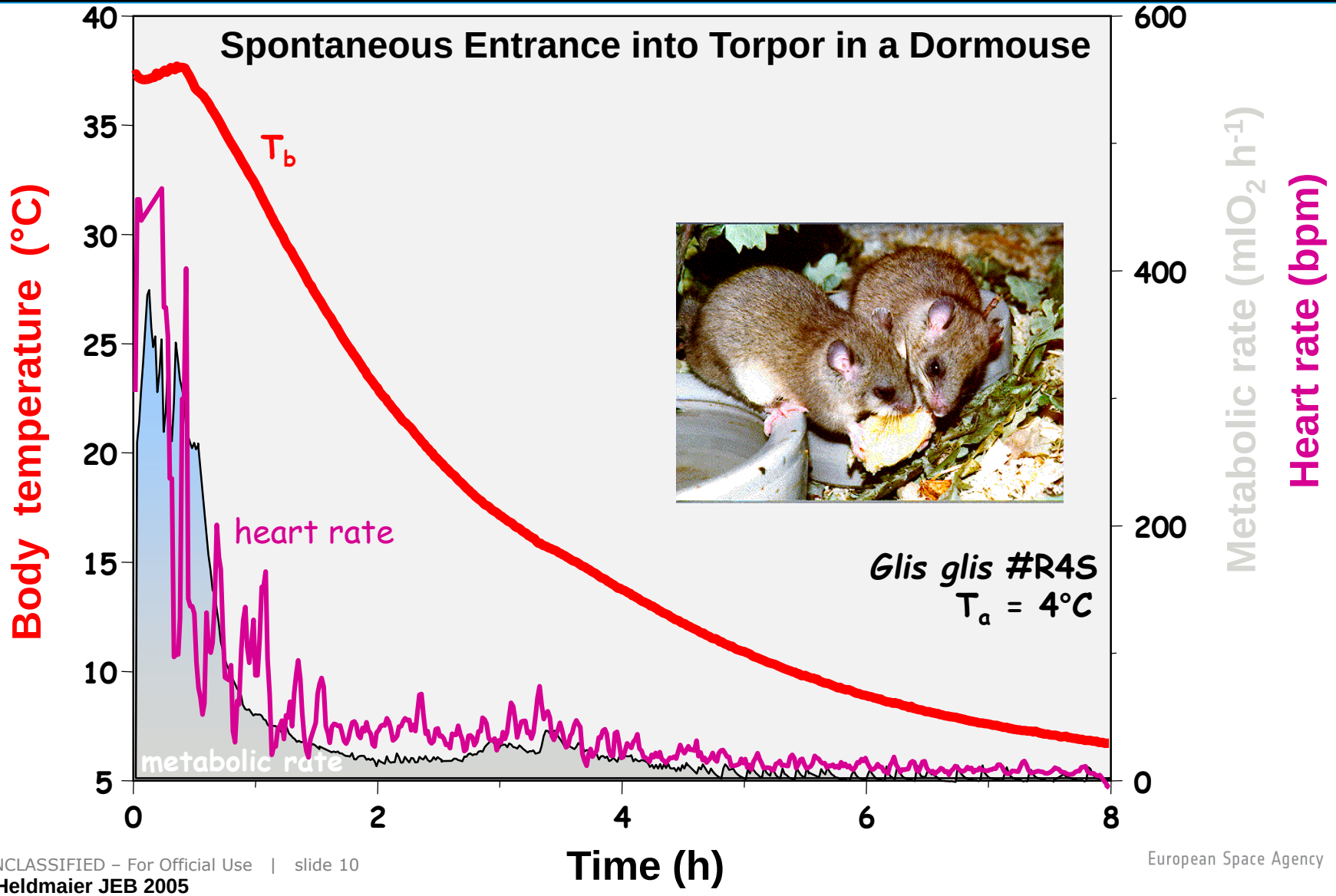
Hibernating astronauts
Chances and Challenges
How much energy can be saved?

What is the Theoretical „Hibernation Reserve“ of Human Beings?



Redrawn from Singer D: Phylogenese des Stoffwechsels der Säugetiere (Phylogeny of mammalian metabolism). AINS 2002; 37: 441-460; and Singer D: Warum 37 °C? (Why 37 °C?). Anaesthesist 2007; 56: 899-906

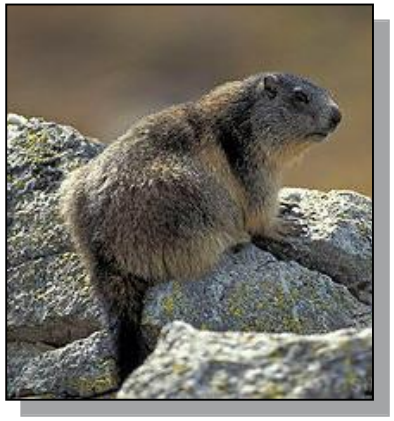
Seasonal topor animals



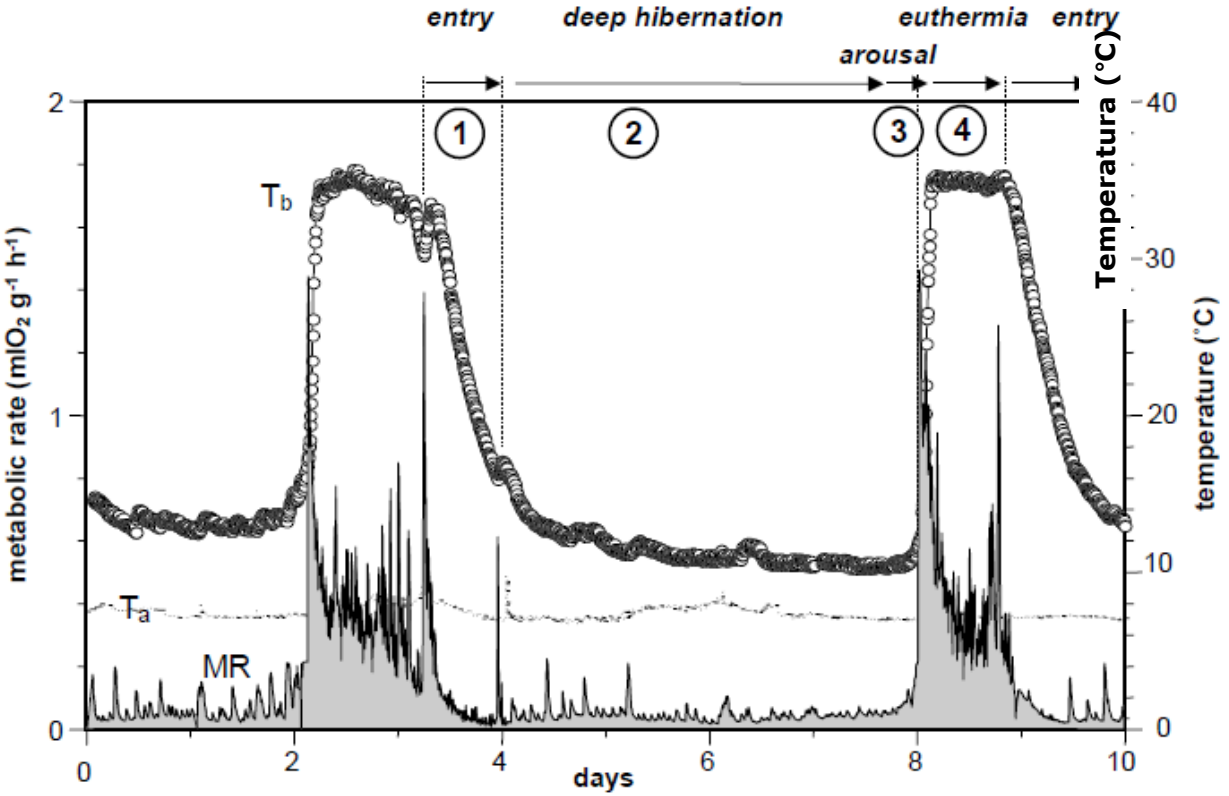
Elvert & Heldmaier JEB 2005

Seasonal topor animals

Metabolism decreases before temperature

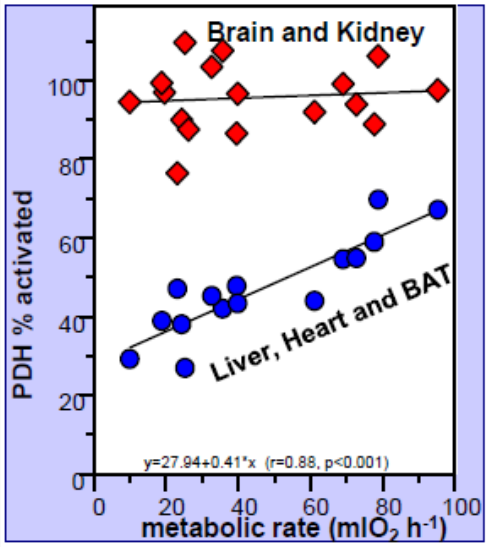


Marmota Marmota



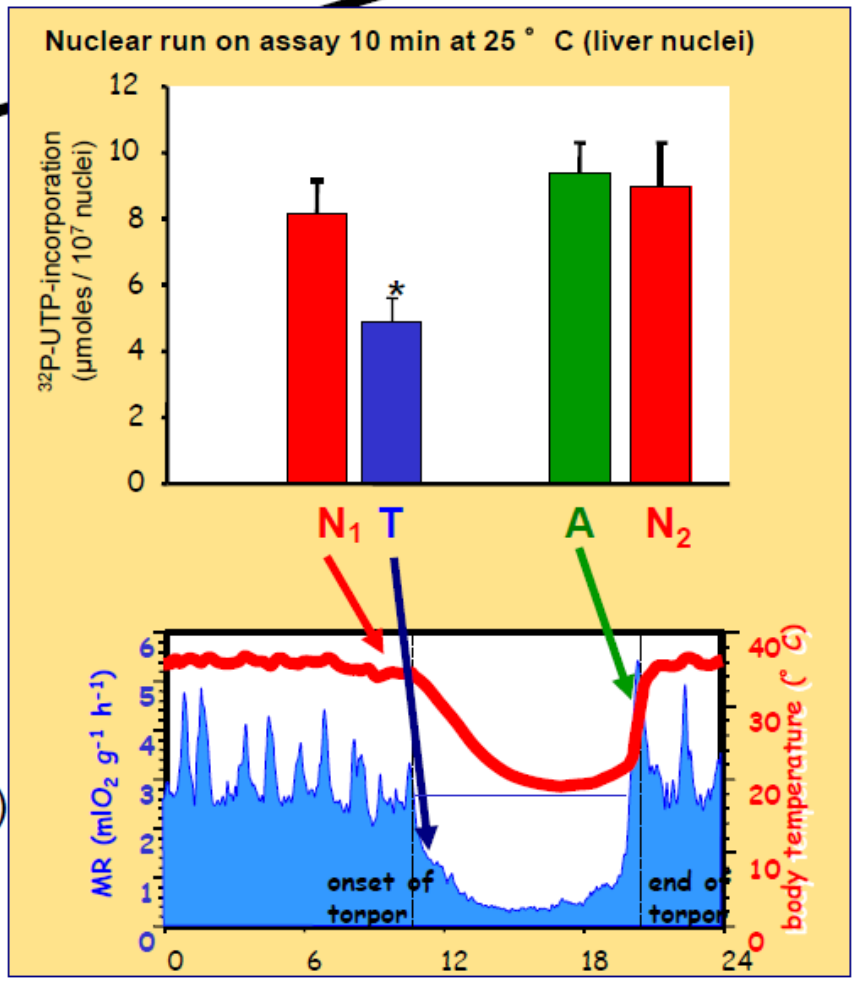
Heldmayer et al, Resp. Phys. & Neurobiology 141 (2004)

Rearrangement of Metabolic Pathways in Torpor



1. Inhibition of Glycolysis

- Fuel supply rerouted to lipid utilisation
- Slowing down metabolic rate
- Enhancement of gluconeogenesis
- Accumulation of ketone bodies



2. Inhibition Protein Metabolism

- Inhibition of transcription
- Inhibition of translation
- Inhibition of protein degradation
- No cell growth (proliferation, differentiation)

Differences between Low T_b and High T_b Hibernation

	Low T_b Hibernation	High T_b Hibernation
Torpor bout duration	multiday	continuous
Body temperature	< 20 °C	>30°C
Energy savings	95 %	75%
Active behaviour	zero	zero / low
Duration of arousal	2-4 hours	instantaneous
Work for arousal	very high	negligible
Blood pressure	very low	normal
Periph. vascular resistance	high	normal

Strategies for human torpor

Low T_b benefits:

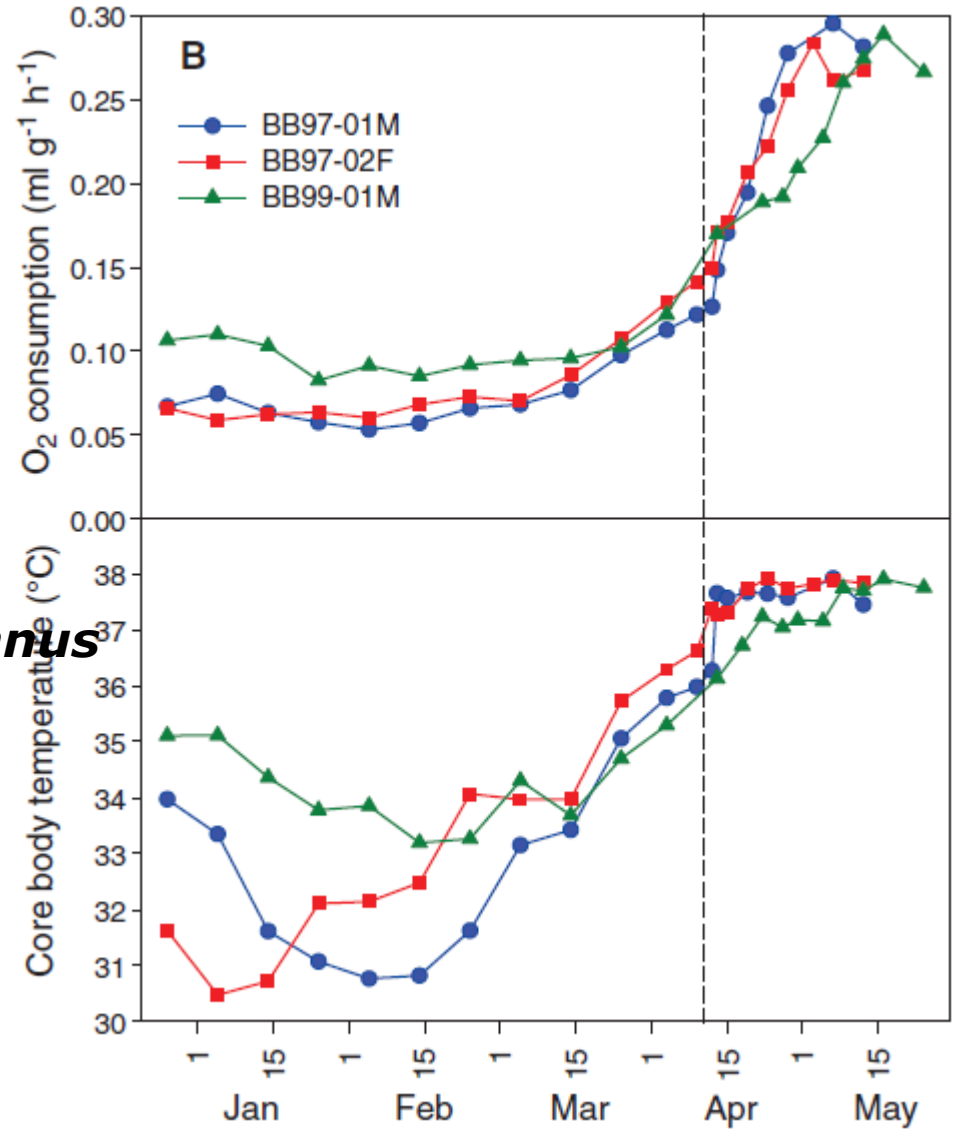
- greater energy savings
- exploit depressing effect of low temperature
- eliminate consciousness/dreaming (< 28°C)

High T_b benefits:

- avoid cardiac fibrillation (> 28°C)
- reduces passive ion leaks
- avoid expensive arousals
- avoid CNS complications

Hibernation in Black Bears: Independence of Metabolic Suppression from Body Temperature

Ursus americanus



active RMR
0.276 ml O_2 g^{-1} h^{-1}

torpid RMR
0.069 ml O_2 g^{-1} h^{-1}

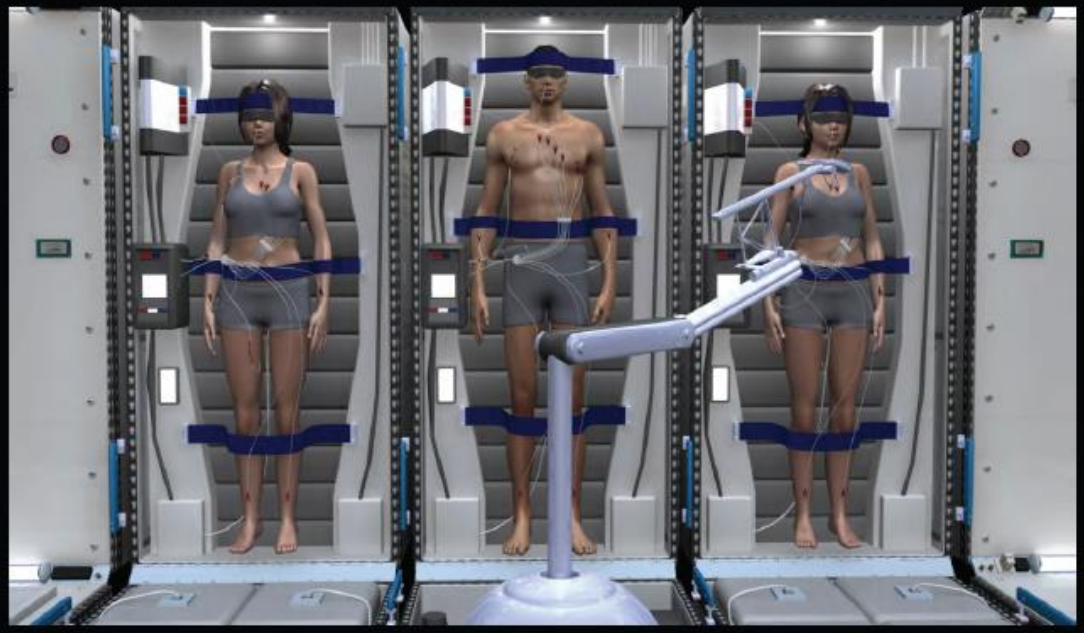
75.4 % reduction of energy expenses in hibernation*

**Temperature effect predicts 35 % reduction of energy expenses (0.179 ml g^{-1} h^{-1})*

Toien O, Blake J, Edgar DM, Grahn DA, Barnes BM, *Science* Vol 331 (2011)

CREW ACCOMMODATIONS

- Crew nutrition provided through automated administration of TPN with active monitoring and feedback
- Body thermal control maintained with redundant cooling (intranasal) and warming (conduction/convection) systems



SpaceWorks

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NIAC

Intestinal consequences of parenteral nutrition (TPN) (animal models)

Hibernation

↓ enterocyte proliferation, ↑ mucosal atrophy	↓ proliferation, ↑ atrophy
↓ intestinal barrier function (↑ gut permeability)	↓ barrier function
↓ intraepithelial lymphocytes, LP Tregs	↑ IELs, Tregs
↑ pro-inflammatory cytokines (TNF-α, IFN-γ)	transient ↑ during arousal
↓ anti-inflammatory cytokines (IL-10)	↑ IL-10
↑ TLR-4 expression (LPS receptor)	↓ TLR4, ↑ TLR5
↓ secretory IgA	↑ IgA
↑ enterocyte apoptosis	↓ apoptosis
↓ p-Akt signaling	↑ Akt
↓ tight junction proteins	↑ tight junction protein (occludin)
● change In gut microbiota	● change in gut microbiota

Efforts to induce artificial torpor

Using GABA agonists locally within the brain

14 Male Sprague-Dawley rats (300-350g)

Three days before being injected with **Muscimol**, animals were exposed to environmental conditions that are known to facilitate the entrance into torpor/hibernation:

- **Ta 15°C**
- **High-fat diet**
- **Continuous darkness**

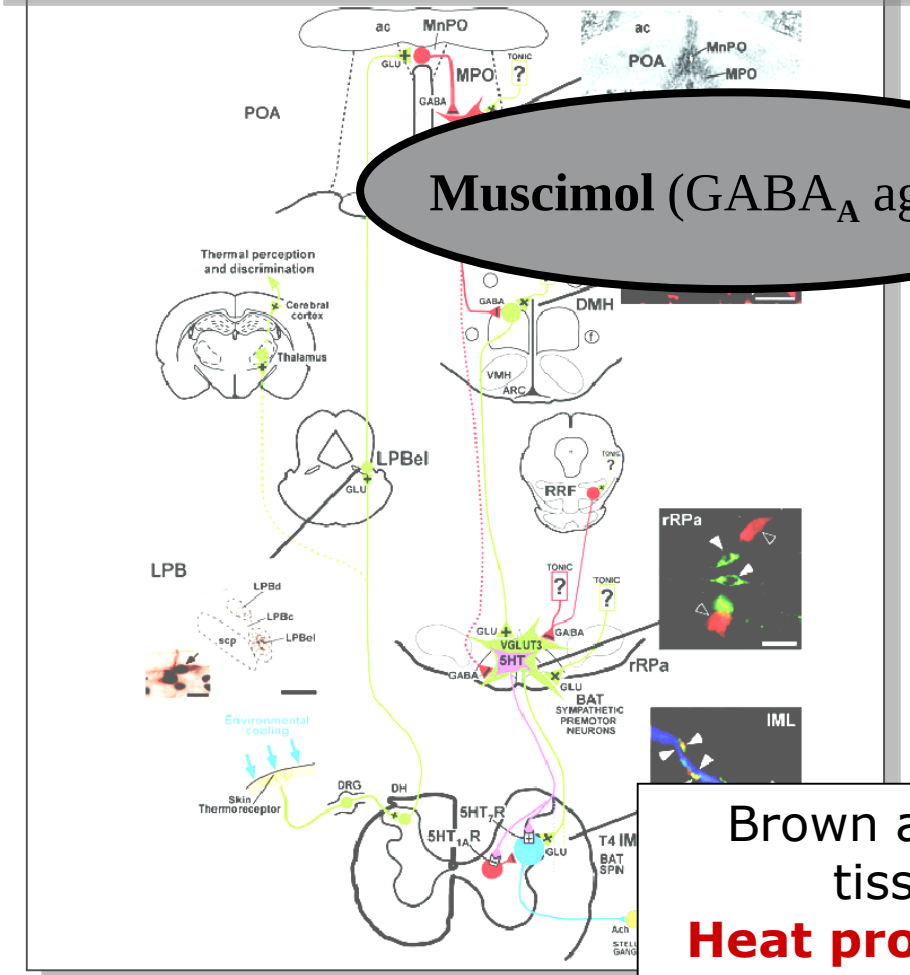
Exp Physiol 93.7 pp 773–797

Experimental Physiology – *Review Article*

Central control of thermogenesis in mammals

Shaun F. Morrison, Kazuhiro Nakamura and Christopher J. Madden

Neurological Sciences Institute, Oregon Health & Science University, Beaverton, OR 97006, USA



Preoptic area
warm sensors

Muscimol ($GABA_A$ agonist)

Raphe pallidus

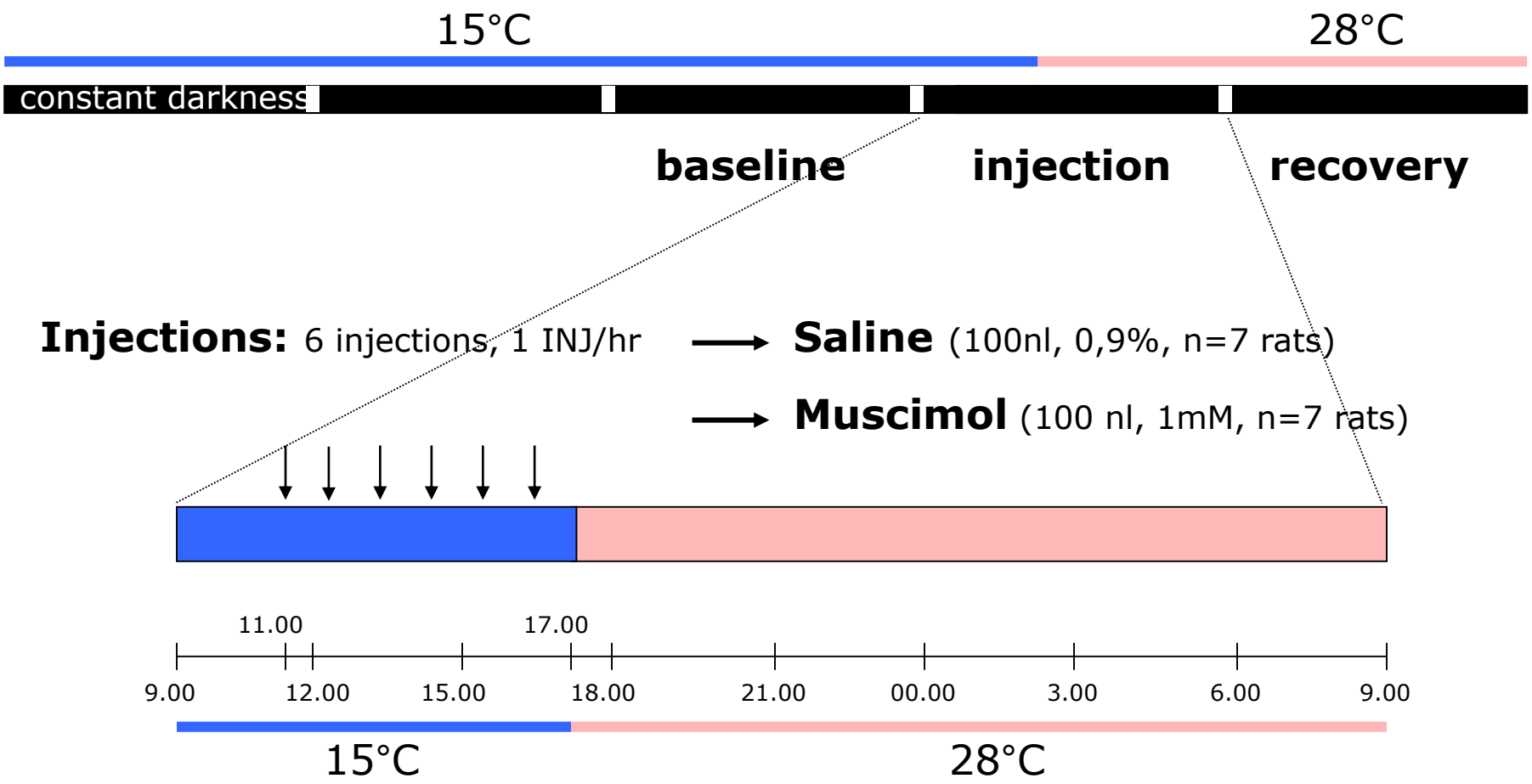
Sympathetic motor neurons

Brown adipose tissue
Heat production

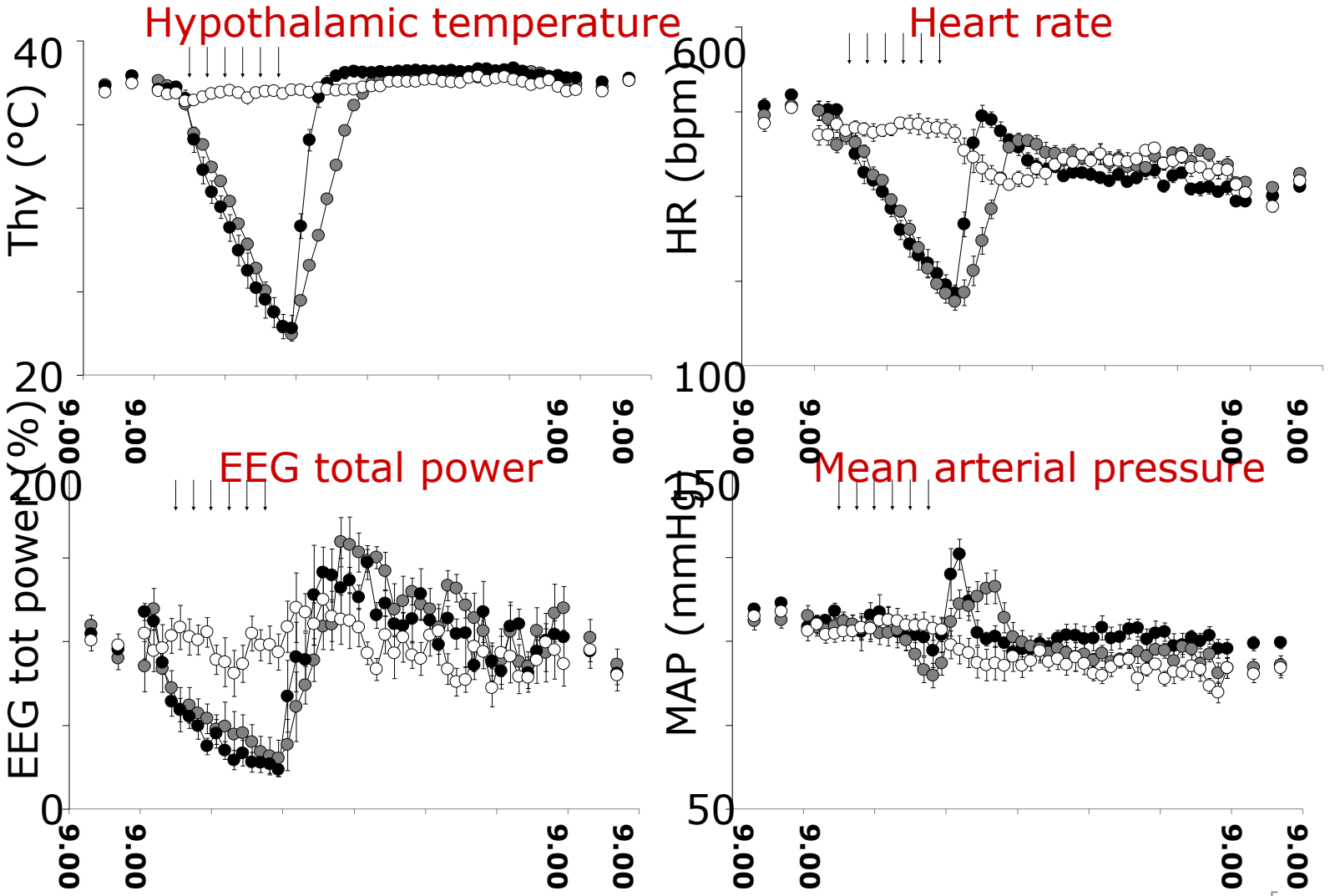
Cutaneous blood vessels
Vasoconstriction

Heart
Tachicardia

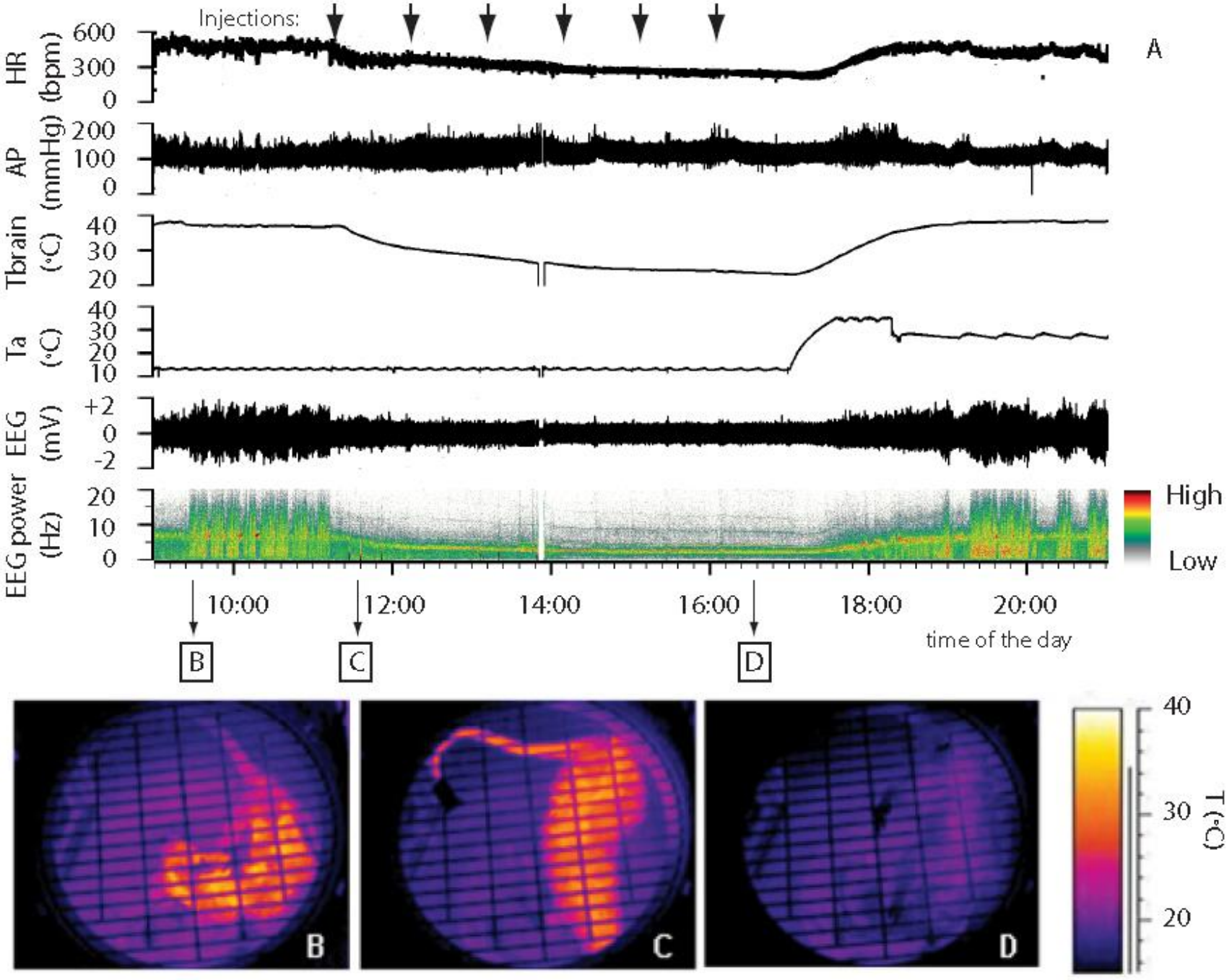
„artificial torpor“ in rats



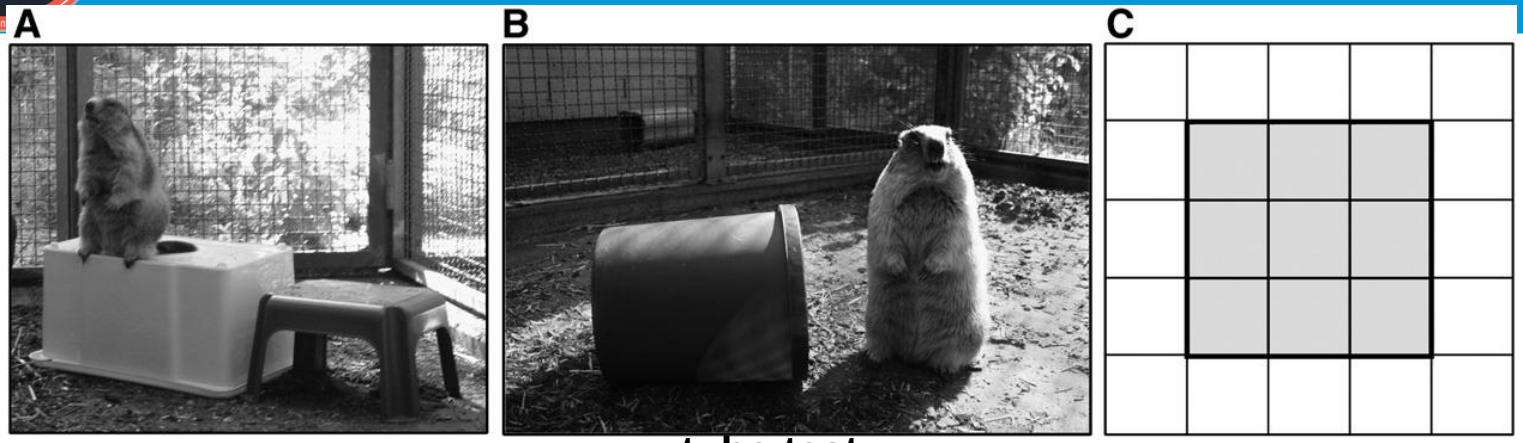
Injection of muscimol into the Raphe pallidus



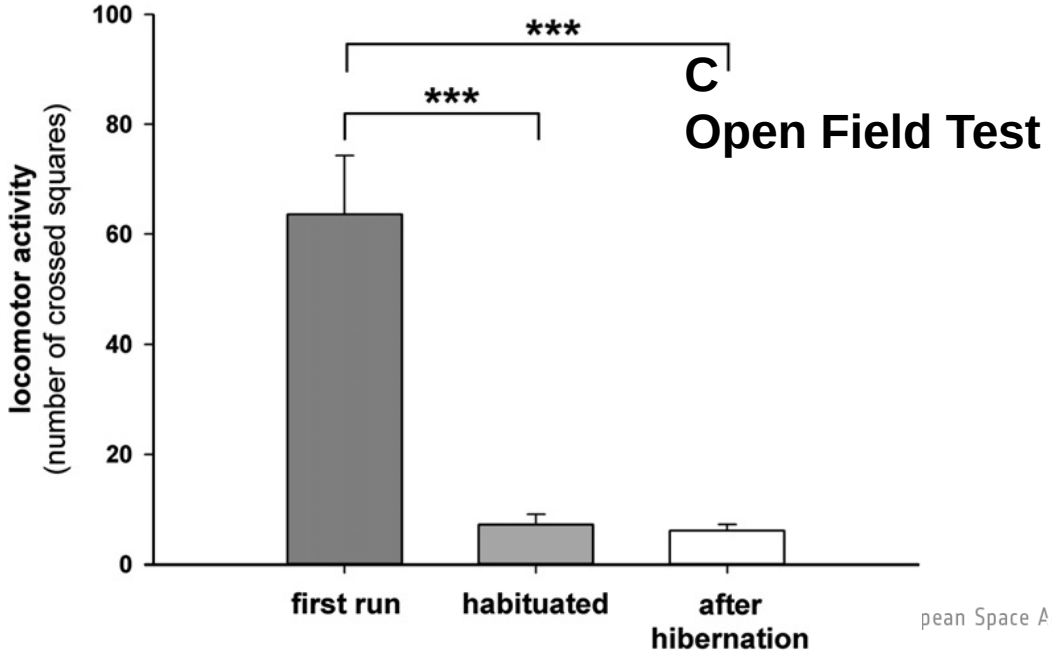
Matteo Cerri, Bologna


Injections:
HR (bpm)
600
300
0
A
AP (mmHg)
200
100
0
Tbrain (°C)
40
30
20
Ta (°C)
40
30
20
10
EEG (mV)
+2
0
-2
EEG power (Hz)
20
10
0
High
Low
10:00
12:00
14:00
16:00
18:00
20:00
time of the day
B
C
D
B
C
D
40
30
20
T (°C)

Preservation of memory during hibernation (marmots)



tube test
(passing tube 10 times)



Keep Cool: Memory is Maintained during Hibernation

Clemens et al. Physiol. Behav. 2009

Torpor would be game changer !

- no psychostress
- no bone and muscle degradation
- brain: loss of synaptic contacts but repaired during arousal
- Increased resistance against irradiation damage
- less payload: smaller life support systems, less nutrition, less waste

Benefits for Life on Earth

- Facilitate extended surgery and intensive care;
- Facilitate organ transplantation;

- high benefits in the treatment of perinatal asphyxia and ischemic stroke
- Increased resistance against radiation damage
- Increase the resistance to haemorrhagic shock
- Suppress immune/inflammatory responses

Thank you for your Attention