

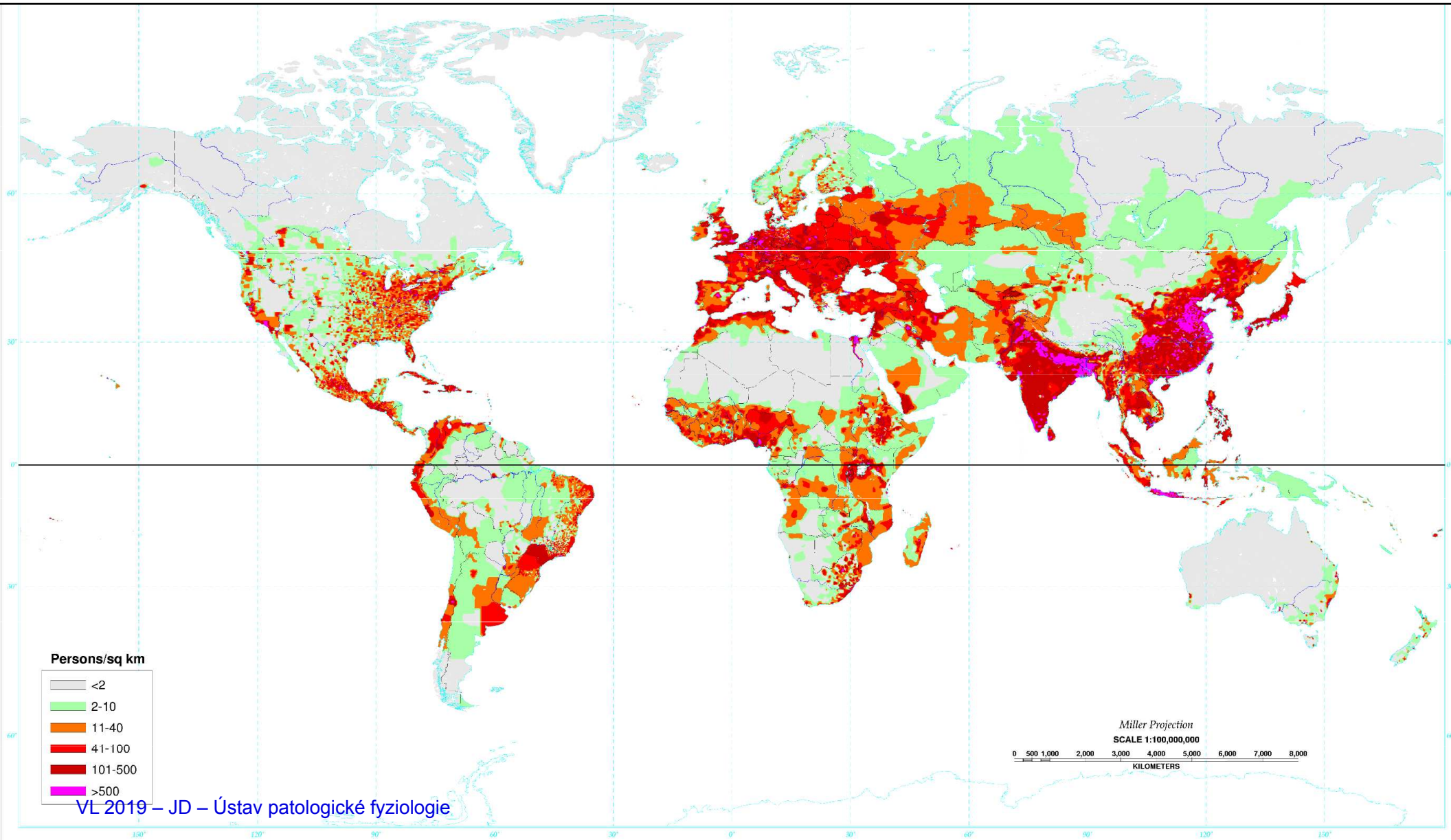
**MUNI**  
**MED**

# **Homeostasis, adaptation, stress.**

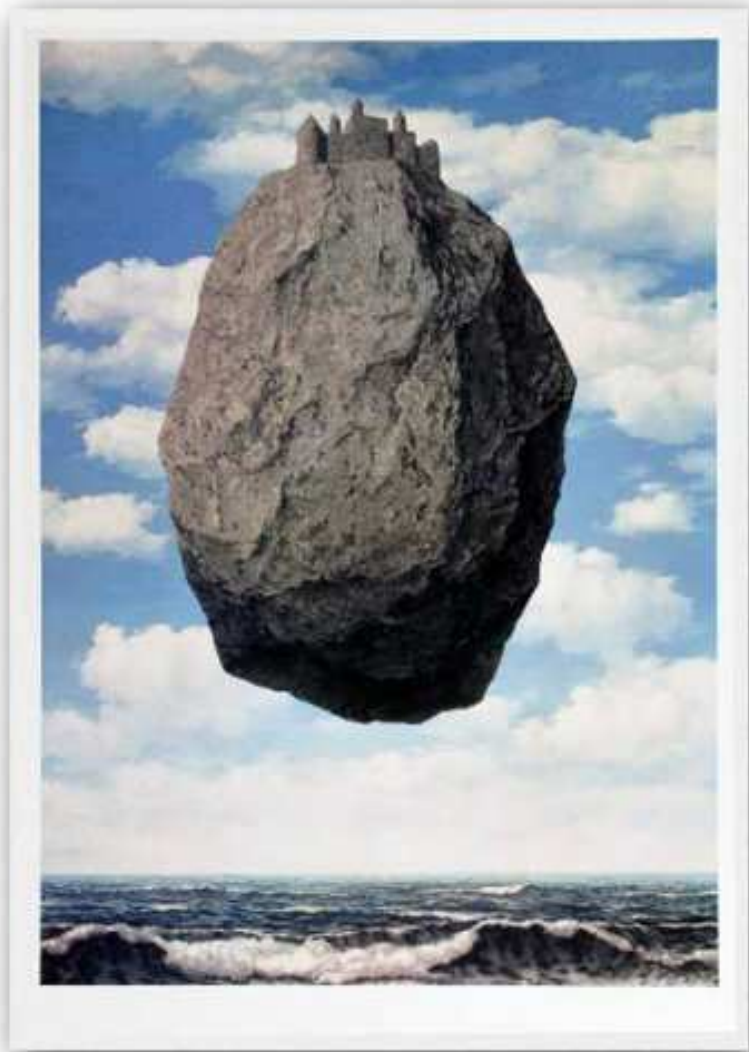
## **Endocrine organs I**

Julie Dobrovolná

Department of Pathological Physiology MED MUNI



VL 2019 – JD – Ústav patologickej fyziologie







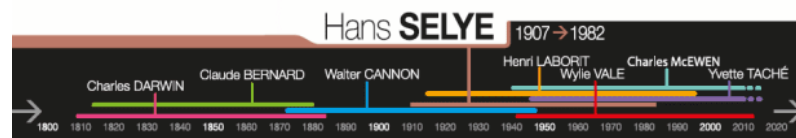
To be totally without  
stress is to be dead.

Hans Selye

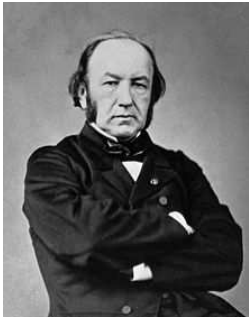
 quote fancy

## Stress and environment

# So what is stress?



# Evolution of the term „stres“



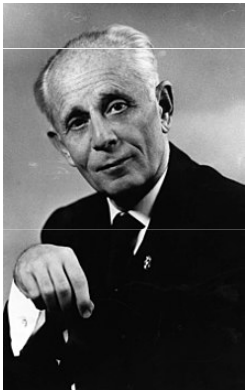
## Claude Bernard (1813-1878)

- *Leçons sur les phénomènes de la vie communs aux animaux et aux végétaux*
- Vnitřní prostředí je udržováno jako stálé



## Walter Cannon (1871-1945)

- *The Wisdom of the Body*
- Homeostáza, stres, autonomní (sympatický) nervový systém



## Hans Selye (1907-1982)

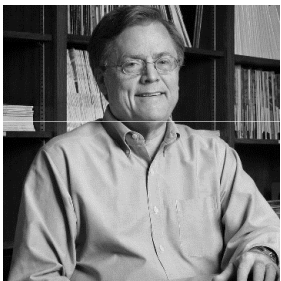
- *The Physiology and Pathology of Stress; a Treatise Based on the Concepts of the General-Adaptation-Syndrome and the Diseases of Adaptation*
- Hypotalamo-hypofyzárně nadledvinková osa (HPA)

# Evoluce termínu „stres“



## Robert Sapolsky

*Stress, the Aging Brain, and the Mechanisms of Neuron Death*  
*Why Zebras Don't Get Ulcers: an Updated guide to Stress, Stress-Related Diseases, and Coping*  
Úloha limbického systému (hippocampus) v regulaci HPA



## Bruce McEwen & Theresa E. Seaman

- *The End of Stress as We Know It*
- Allostáza, homeodynamika



## Gordon Lithgow a další

- Hormeze, endokrinní regulace délky života u much, hlístů a myší



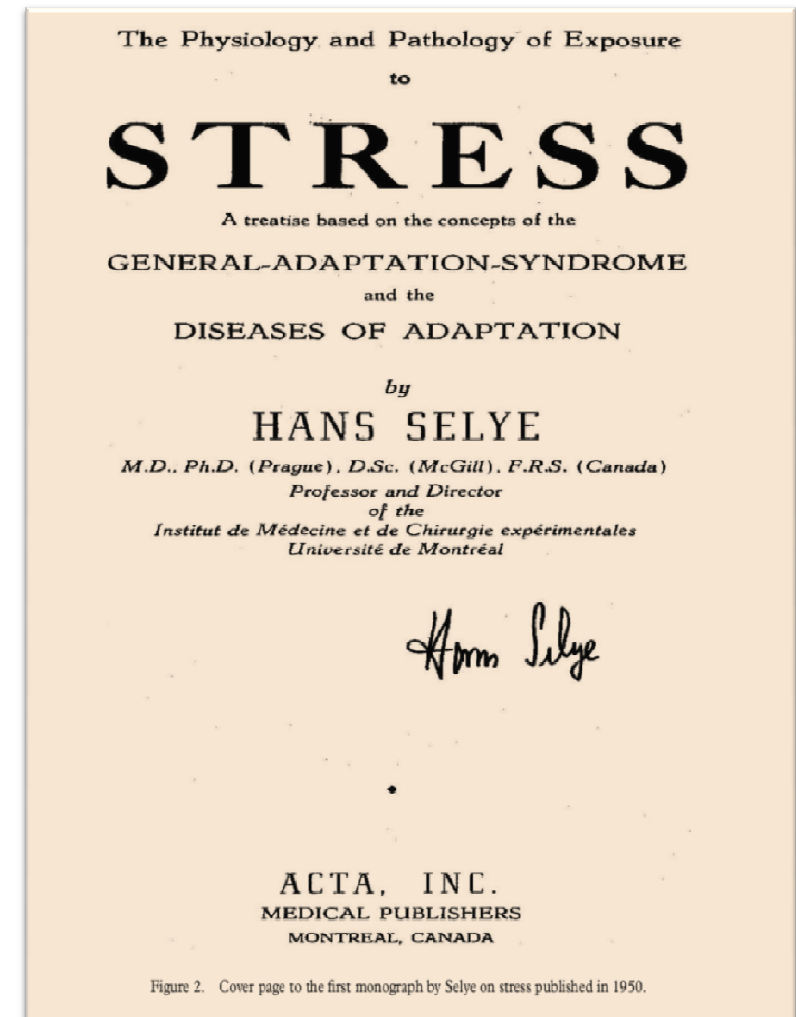
# So what is stress?



# Definition?

**The Stress of Life, Hans Selye, 1956:**

*„... the non-specific response of the body to any demand made upon it, whether it is caused by, or results in, pleasant, or unpleasant conditions“*

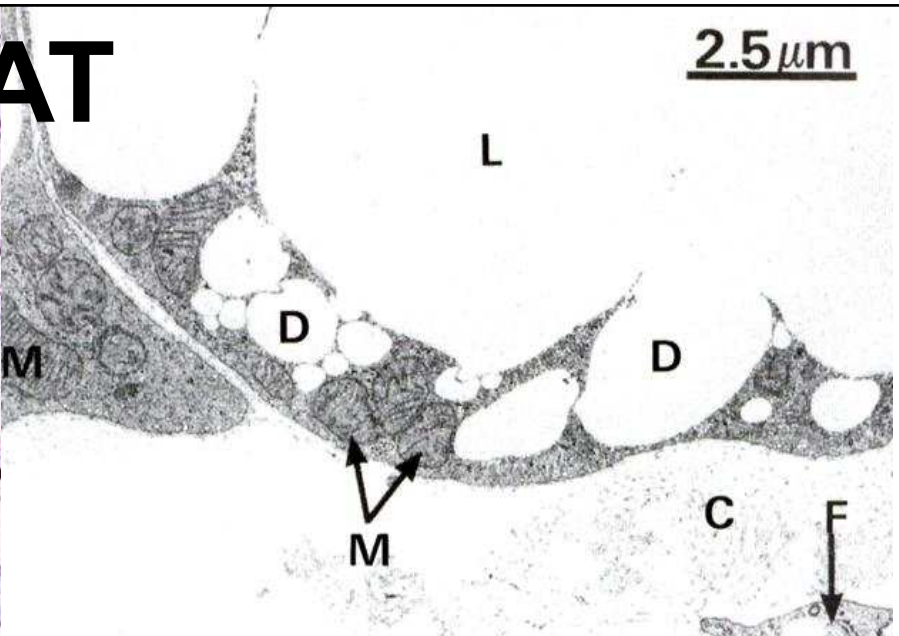
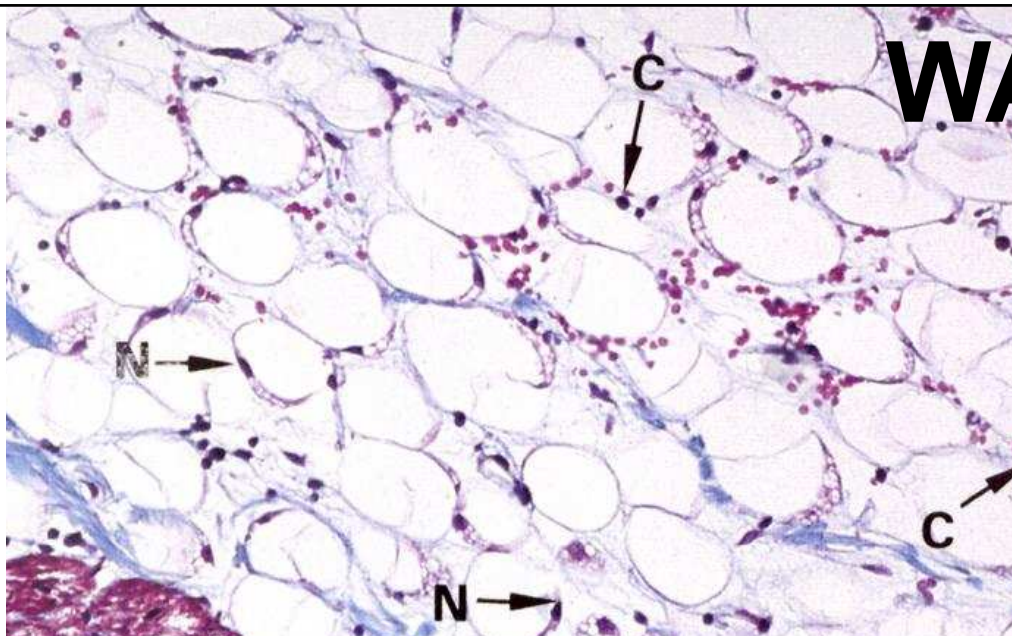


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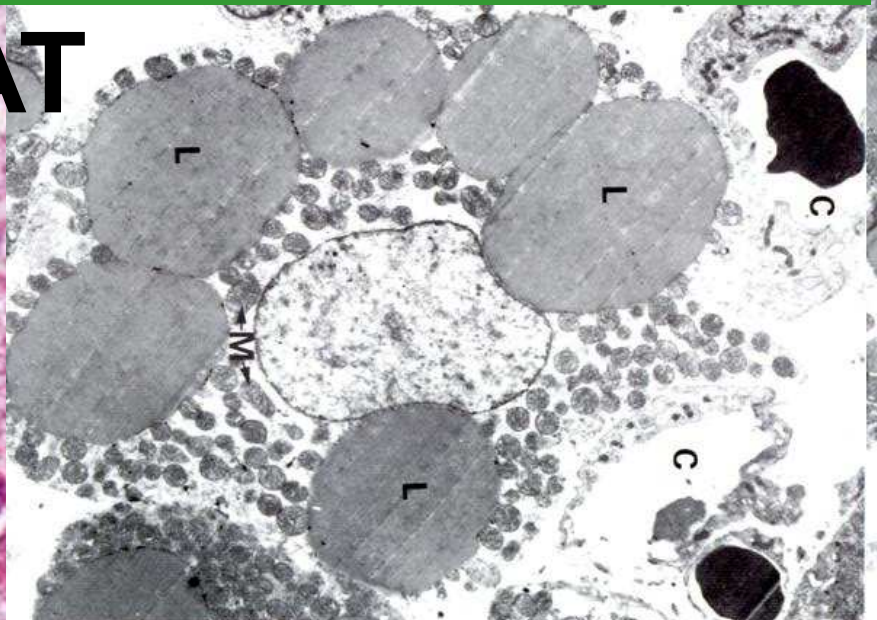
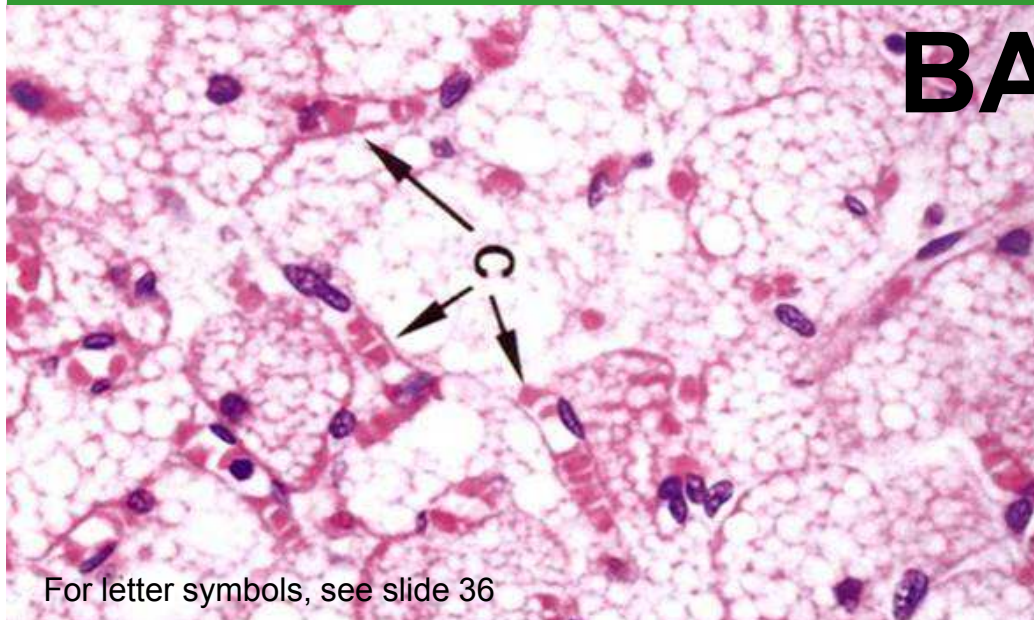
Stress and control of adaptation

# **The role of the adipose tissue**

# WAT



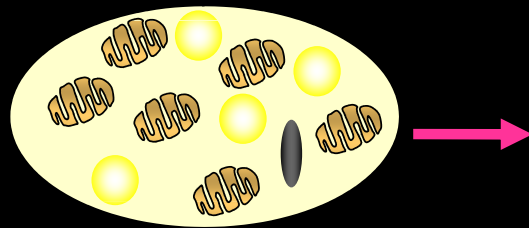
# BAT



For letter symbols, see slide 36

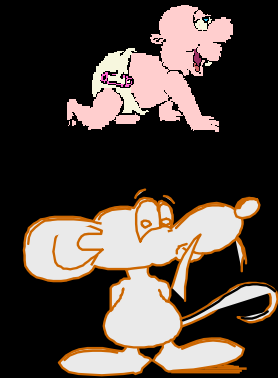
# White and brown adipocytes

## Brown adipocyte

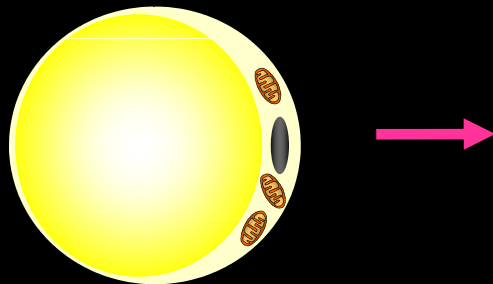


Multilocular  
Storage and mobilization of lipids (++)  
Mitochondria (+++)  
Beta oxidation (+++)  
Respiratory chain (+++)  
UCP1 (+++)

PGC-1 $\alpha$  (+++)



## White adipocyte



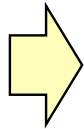
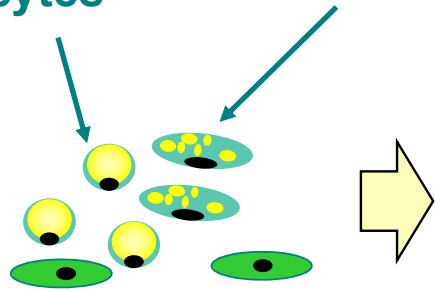
Unilocular ( $\rightarrow$  200 $\mu$ m)  
Storage and mobilization of lipids(+++)  
Mitochondria (+)  
Beta oxidation (+)  
Respiratory chain (+)  
UCP1 (0)

PGC-1 $\alpha$  (+)

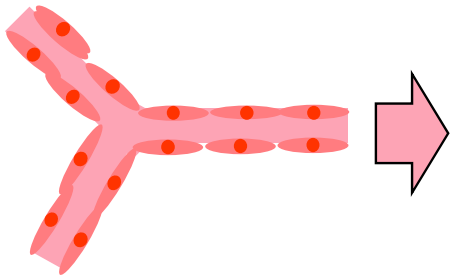


# Adipose tissue – there is more than just pure differentiation

Mature adipocytes      Preadipocytes



Hypertrophy and hyperplasia

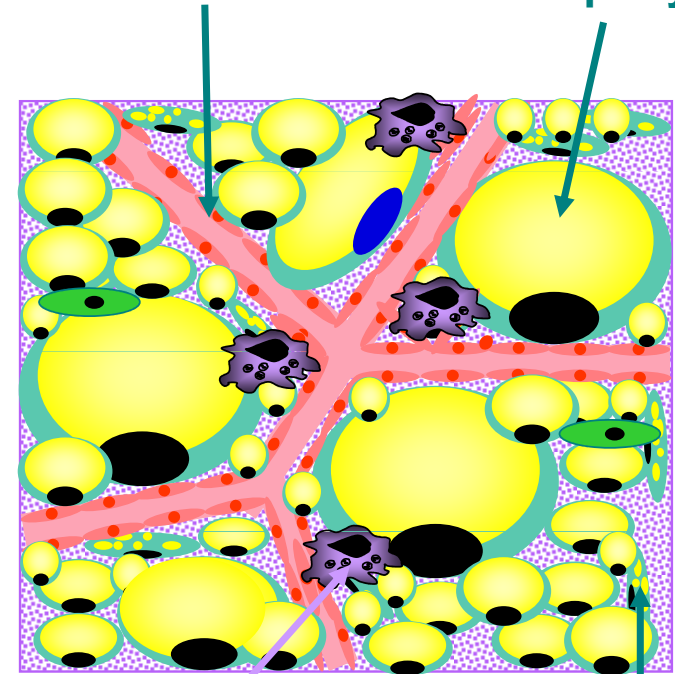


Angiogenesis



Inflammation

Endothelia      Mature adipocytes

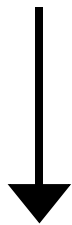
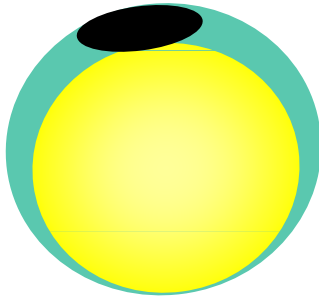


Macrophages

Preadipocytes

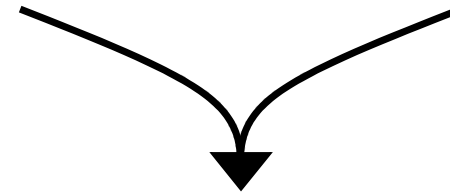
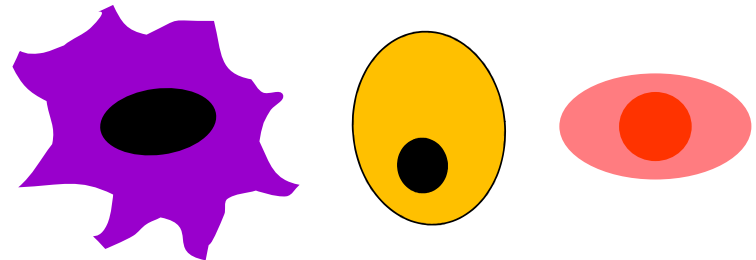
# Cellular origin of secreted molecules

**Adipocytes → Adipokines**



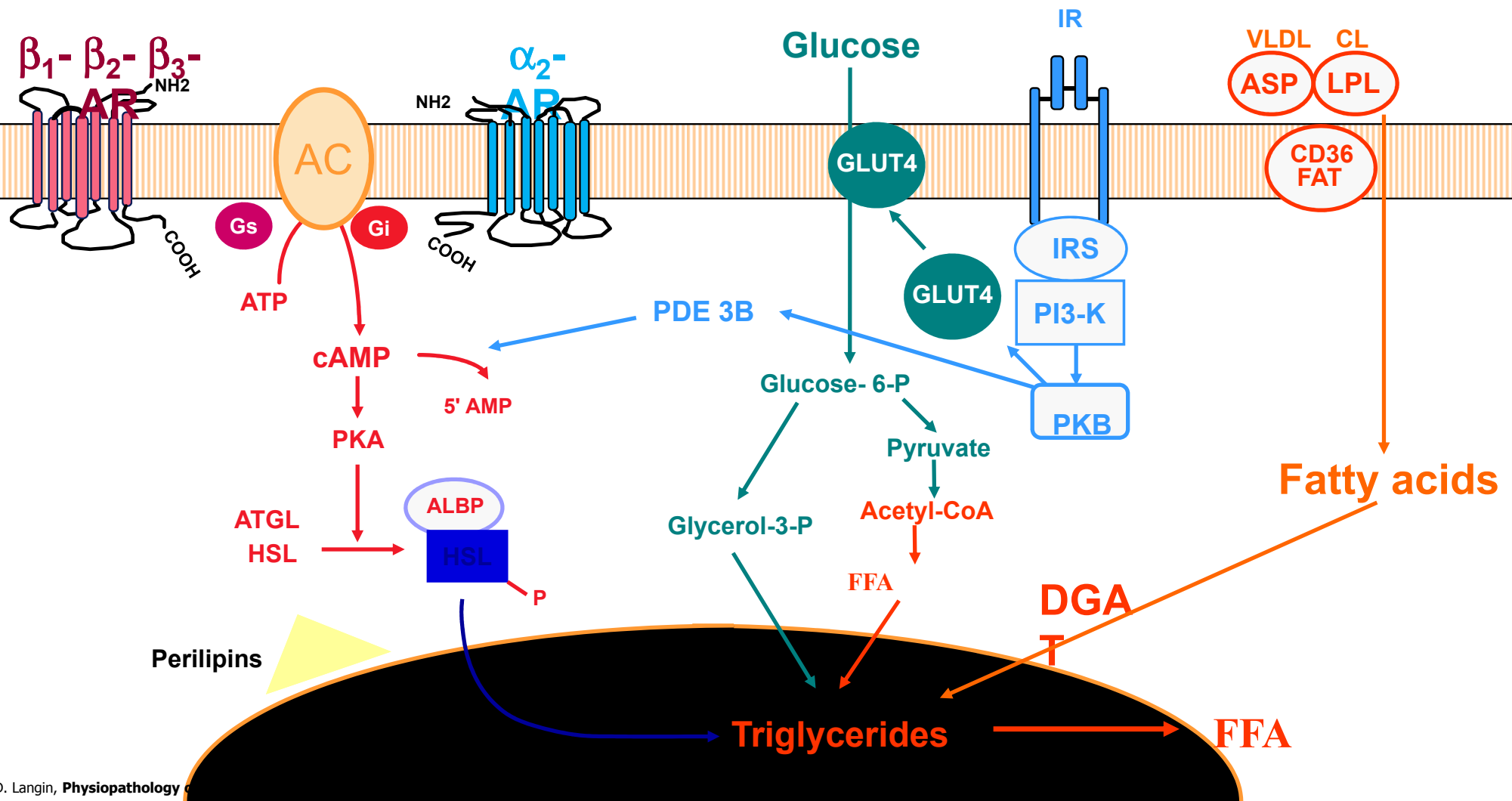
**Leptin**  
**Adiponektin**  
**Serum amyloid**  
**Retinol binding protein 4 (RBP4)**  
**Apelin**

**Stromal vascular fraction cells  
→ cytokines & chemokines**



**Monocyte chemoattractant protein 1 (MCP-1)**  
**Macrophage inflammatory protein (MIP)**  
**Tumor necrosis  $\alpha$  (TNF $\alpha$ )**  
**Interleukins 1 $\beta$ , 6, 8, 10, ....**  
**Chemokines**  
**Resistin**

# Adipocytes and nerves



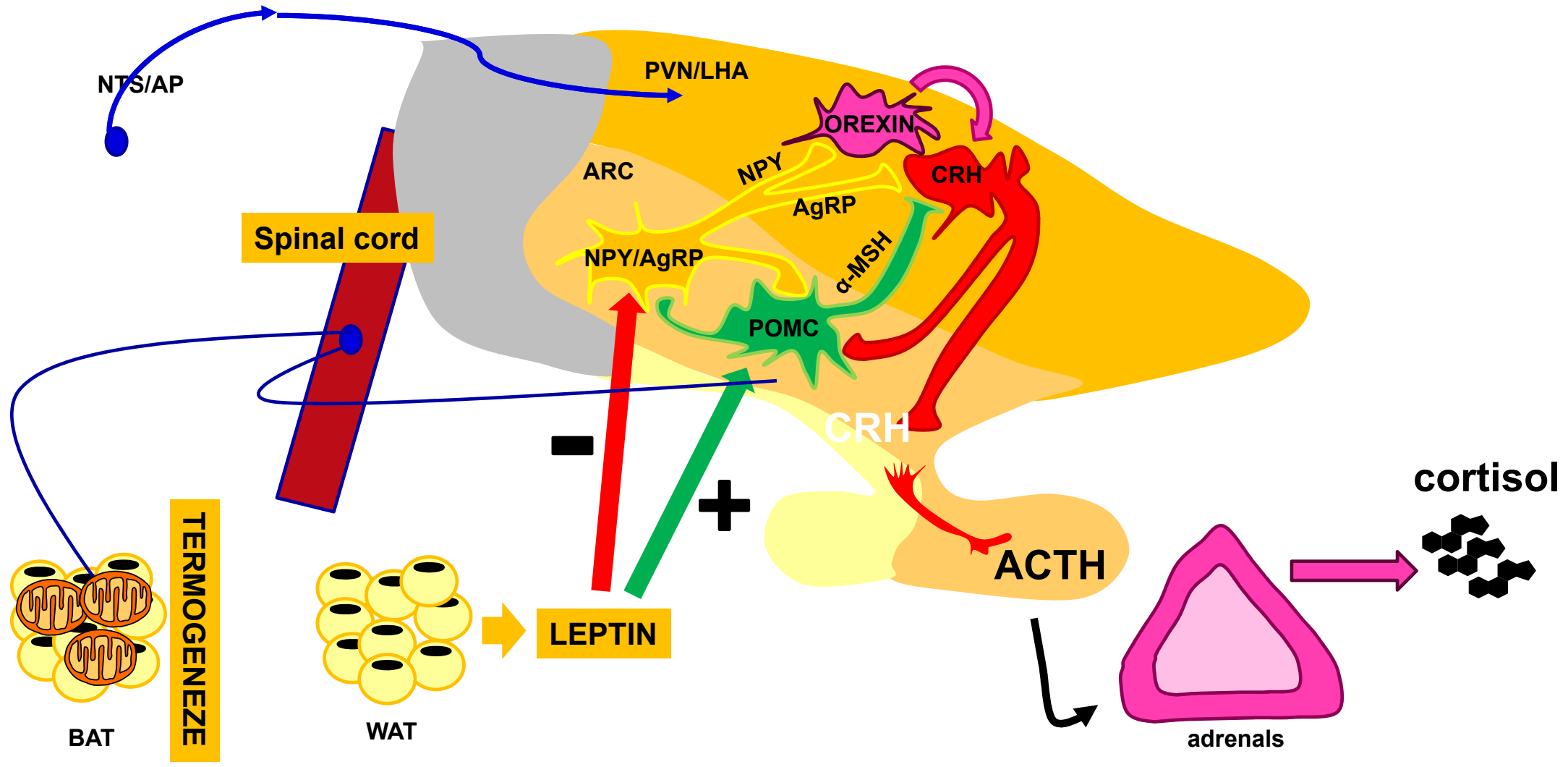


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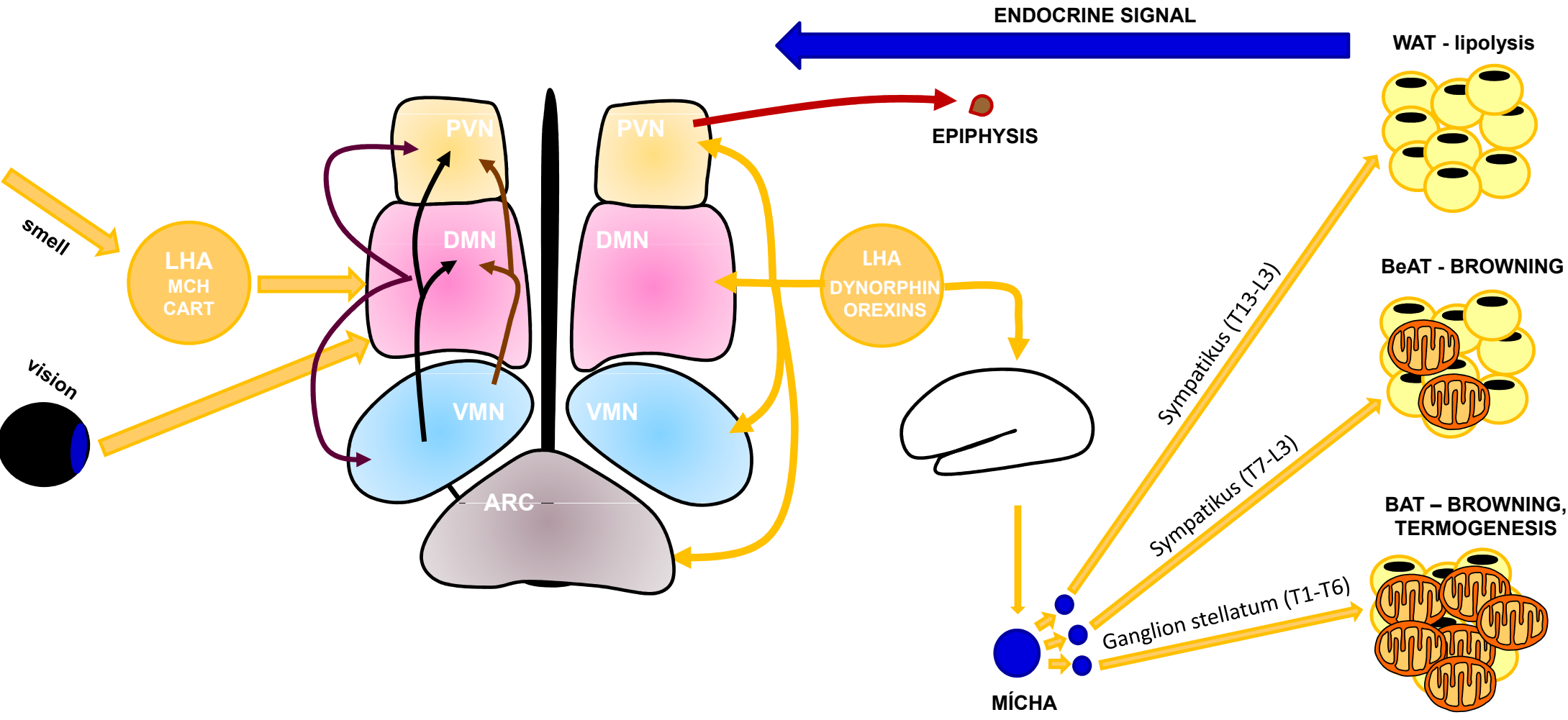
Stress and metabolic control

# **Brain vs. adipose tissue**

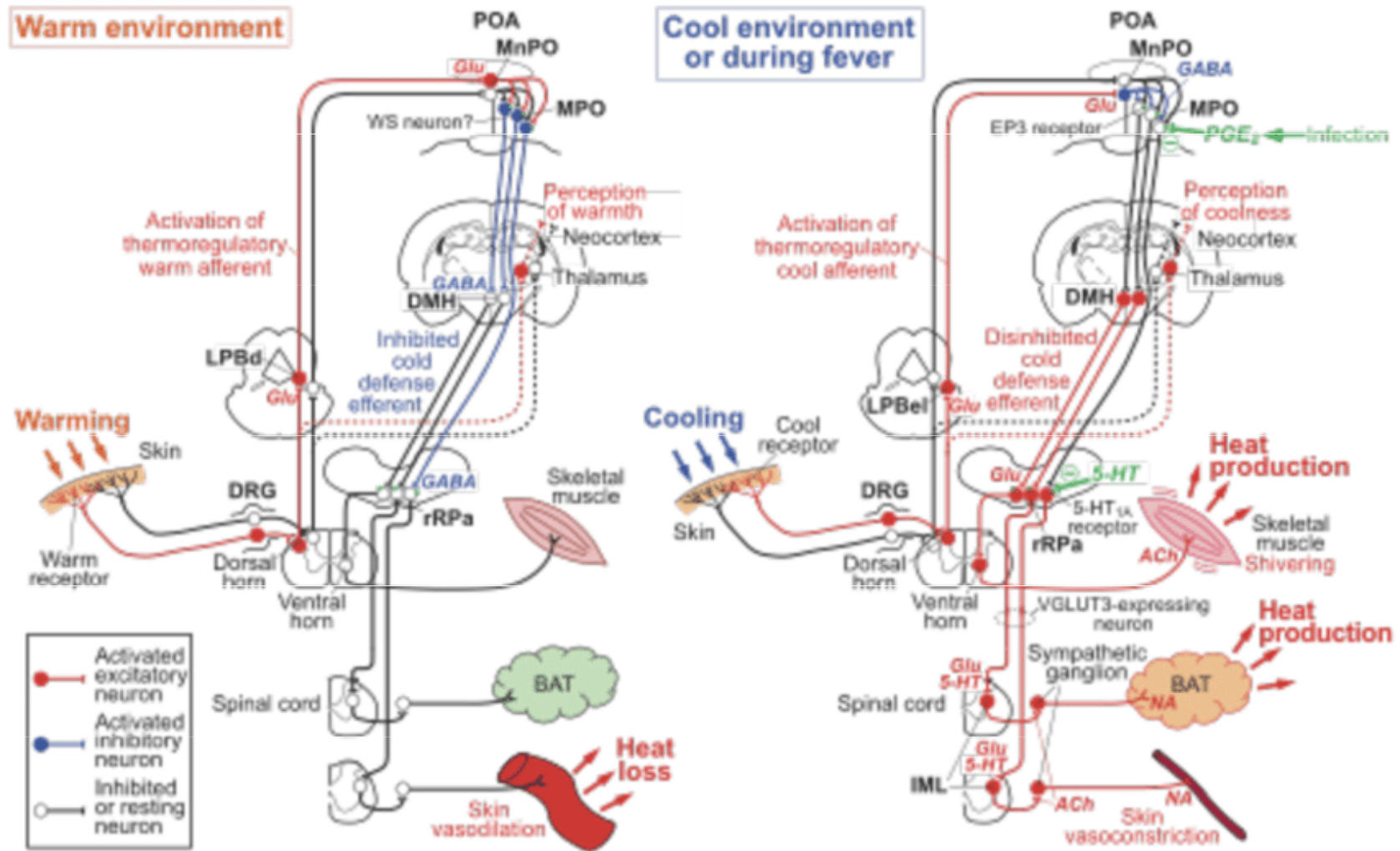
# Brain-adipose tissue axis I



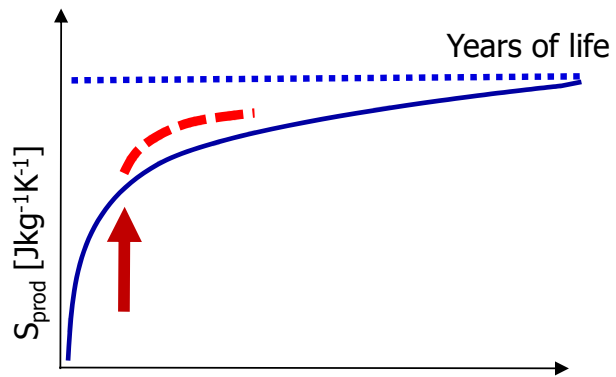
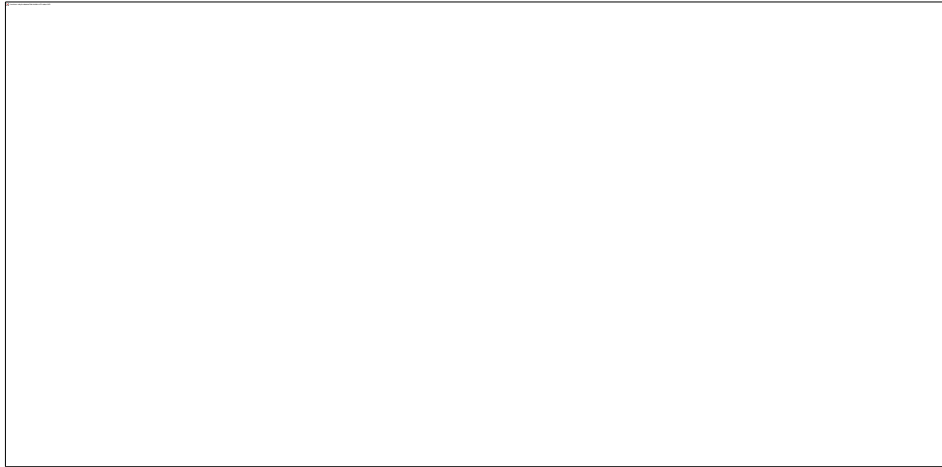
# Brain-adipose tissue axis II



# Can stress be calculated? Can temperature be calculated?



# Really?



Stress and metabolic control

## **What it all means?**

Impaired social environment?

Impaired social context?

Isolated „social animals“?

Loneliness?

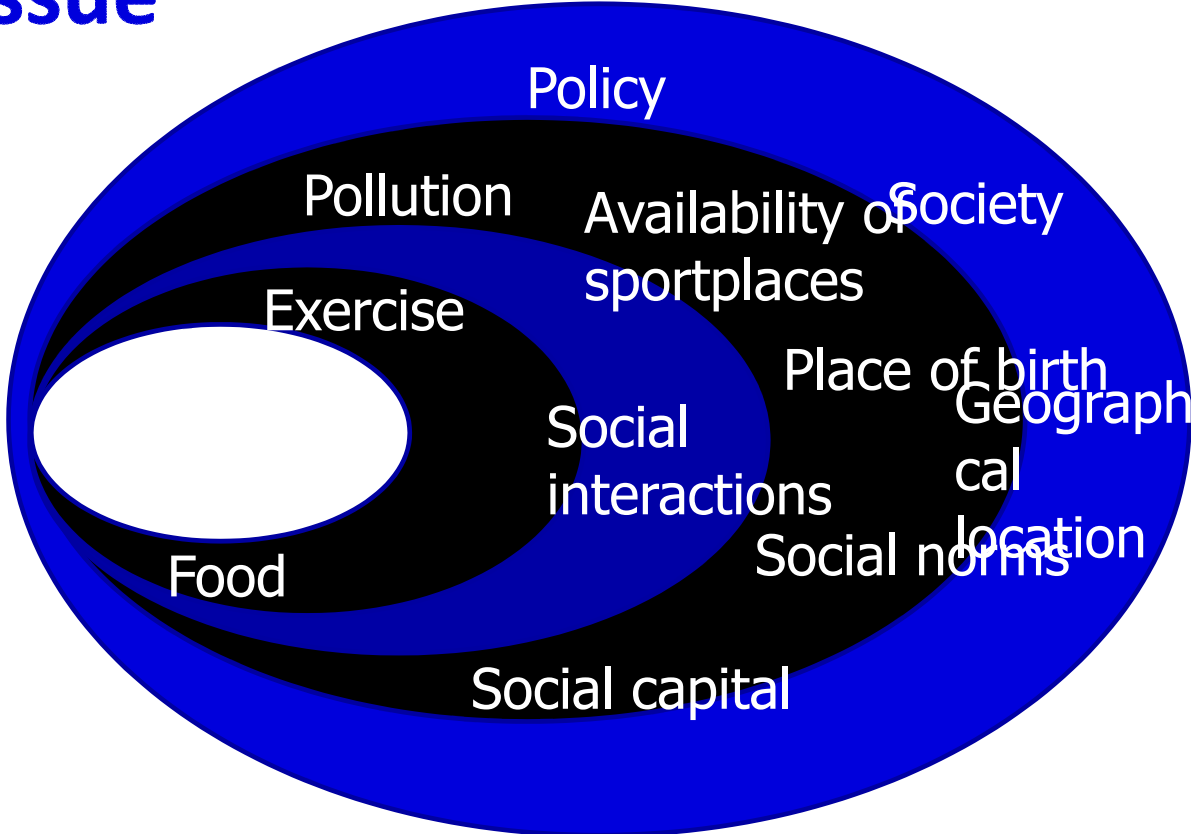
Perceived discrimination?

Prenatal modelling?

Absence of contact with the „real“ environment?

...

# Changing the paradigm of understanding of adipose tissue



Is it more practical to attempt to change the human or the environment?

# Adipose tissue and change of paradigm?

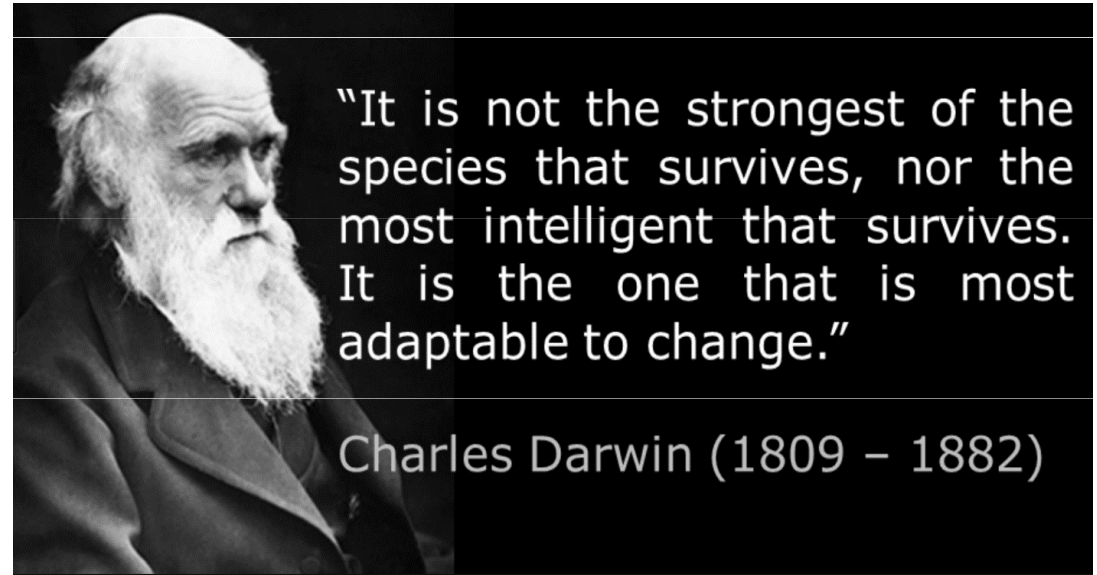
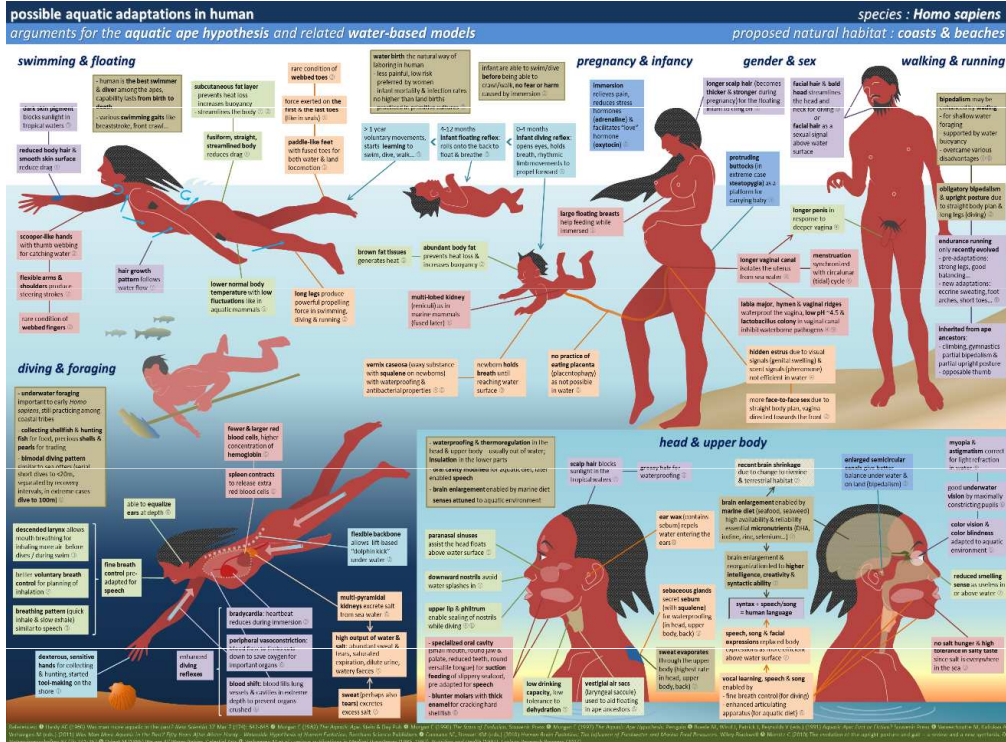
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*„Obesity is not simply about bodyweight or body image. It is about human vulnerability arising from excess body fat, the origins of which lie in multiple determinants ranging from molecular genetics to market forces.“*

Ralston J, Brinsden H, Buse K, Candeias V, Caterson I, Hassell T, Kumanyika S, Nece P, Nishtar S, Patton I, Proietto J, Salas XR, Reddy S, Ryan D, Sharma AM, Swinburn B, Wilding J, Woodward E. Time for a new **obesity** narrative. **Lancet**. 2018 Oct 20;392(10156):1384-1386.



# How do we adapt?

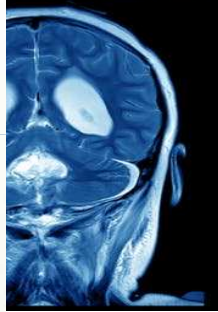


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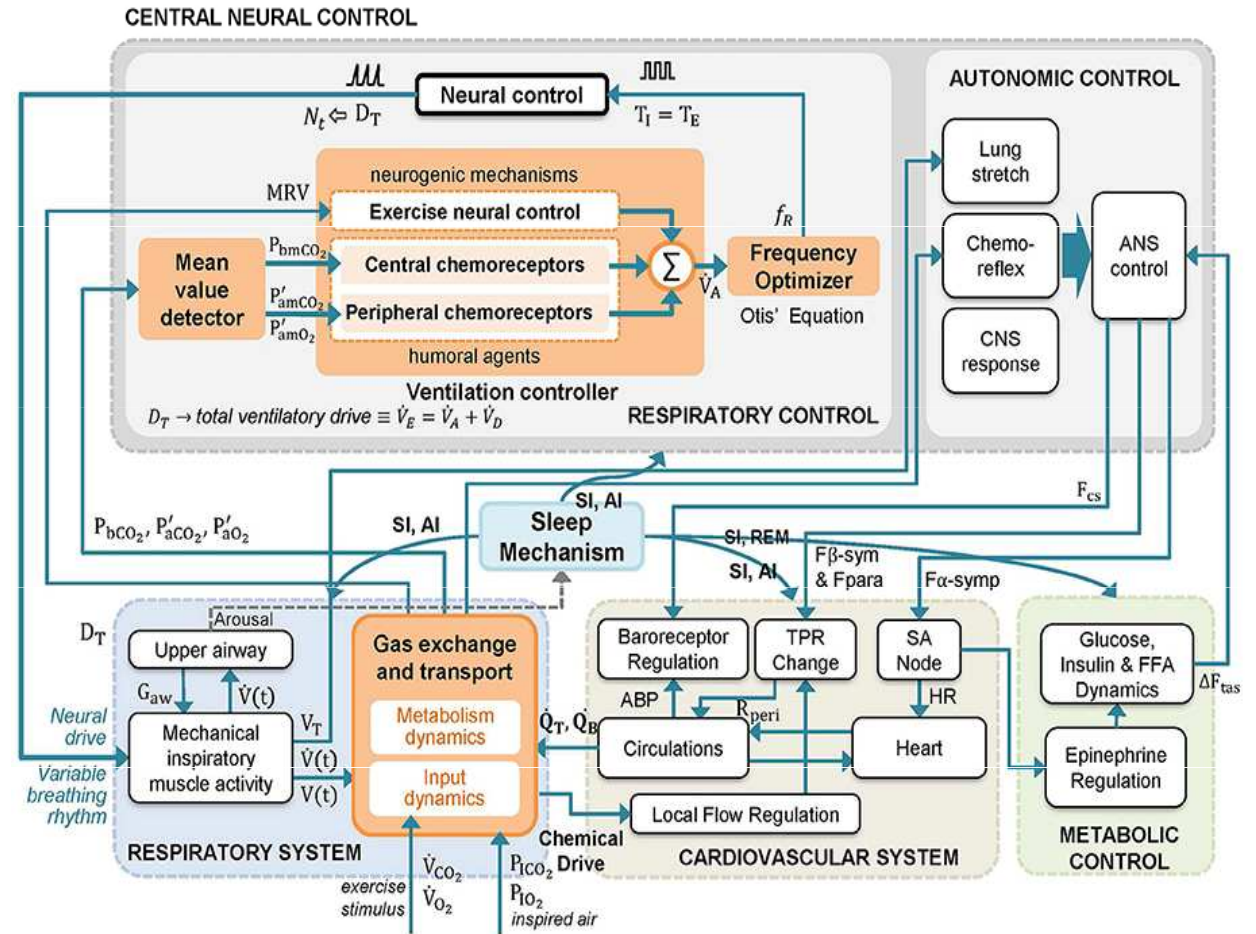
Let's get back to adaptation!



Marine diet



# Breathable air?



## Breathable air

Most of the adaptation during the first 2 weeks to 2 months after arrival to the high altitude area, but in permanently living populations the changes occur prenatally already  
Most of the changes go unnoticed  
Typical morphology of populations living in the high altitude – the barrel chest  
Different mechanism of adaptation (decreased or increased hemoglobin levels, etc.)  
Higher hydration  
Different distinct populations: Tibetans, Andians, Ethiopians.



# Breathable air: record



# :Shelter: cold and heat - records

Very dry air: 120+ °C (248+ °F)  
 short-term, 70+ °C (158+ °F) long-term  
 (with access to water with lower temperature)

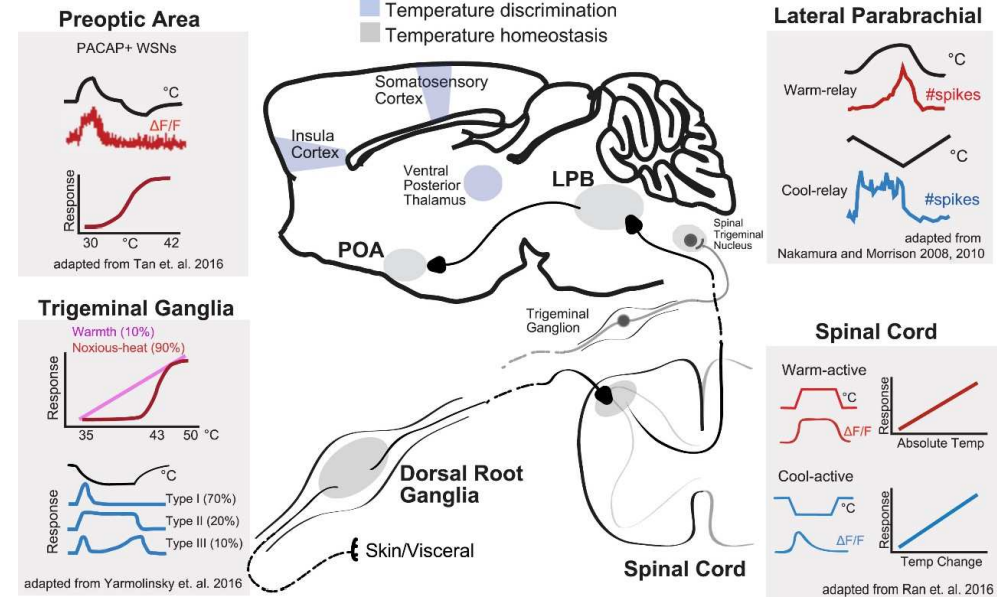
Tropical air: 60+ °C (140 °F) short-term,  
 47 °C (117 °F) long-term

Saturated air: 48 °C (118 °F)

short-term, 35 °C (95 °F) long-term

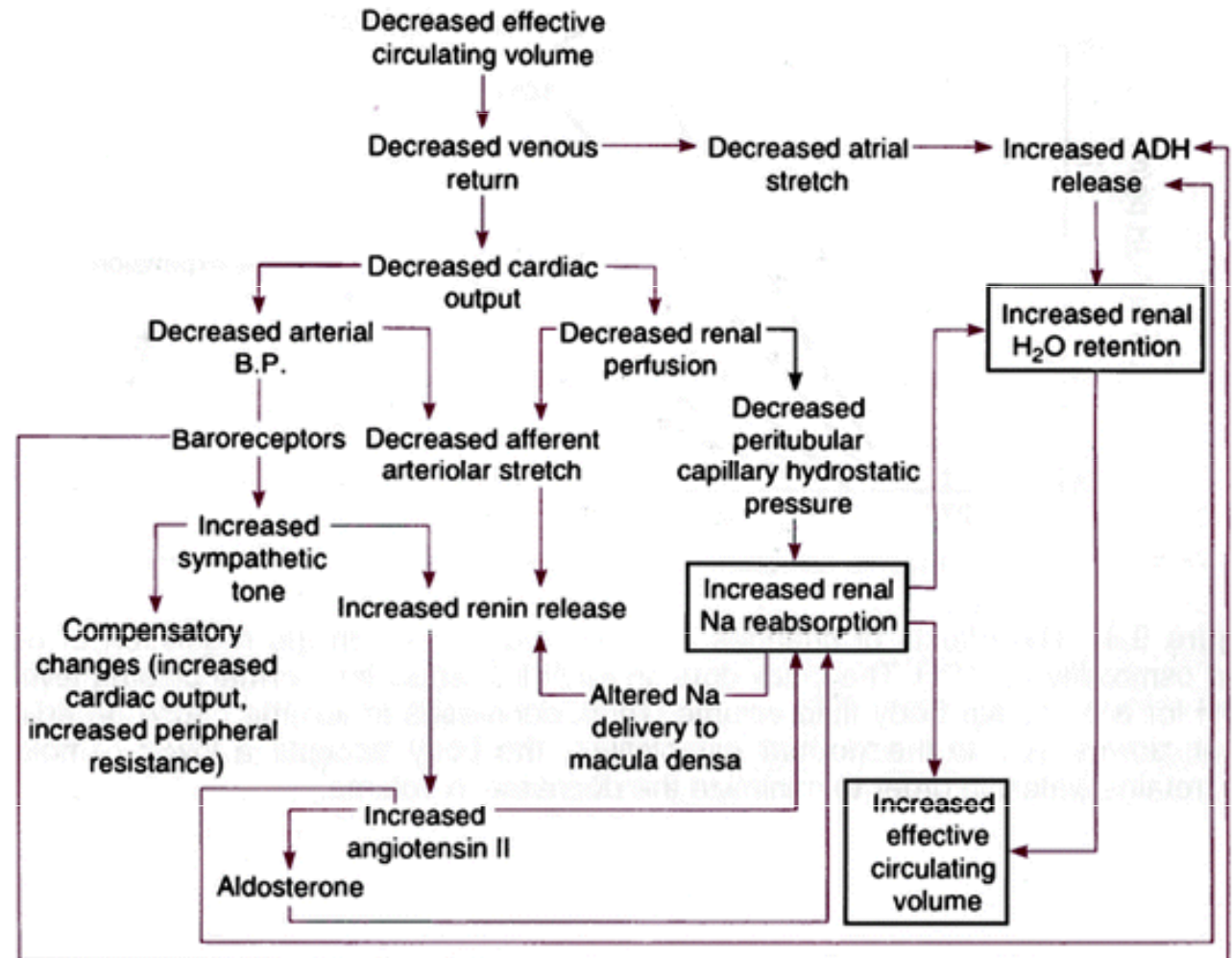
Water: 46° C (115 °F) short-term

and 41°C (106 °F) long-term



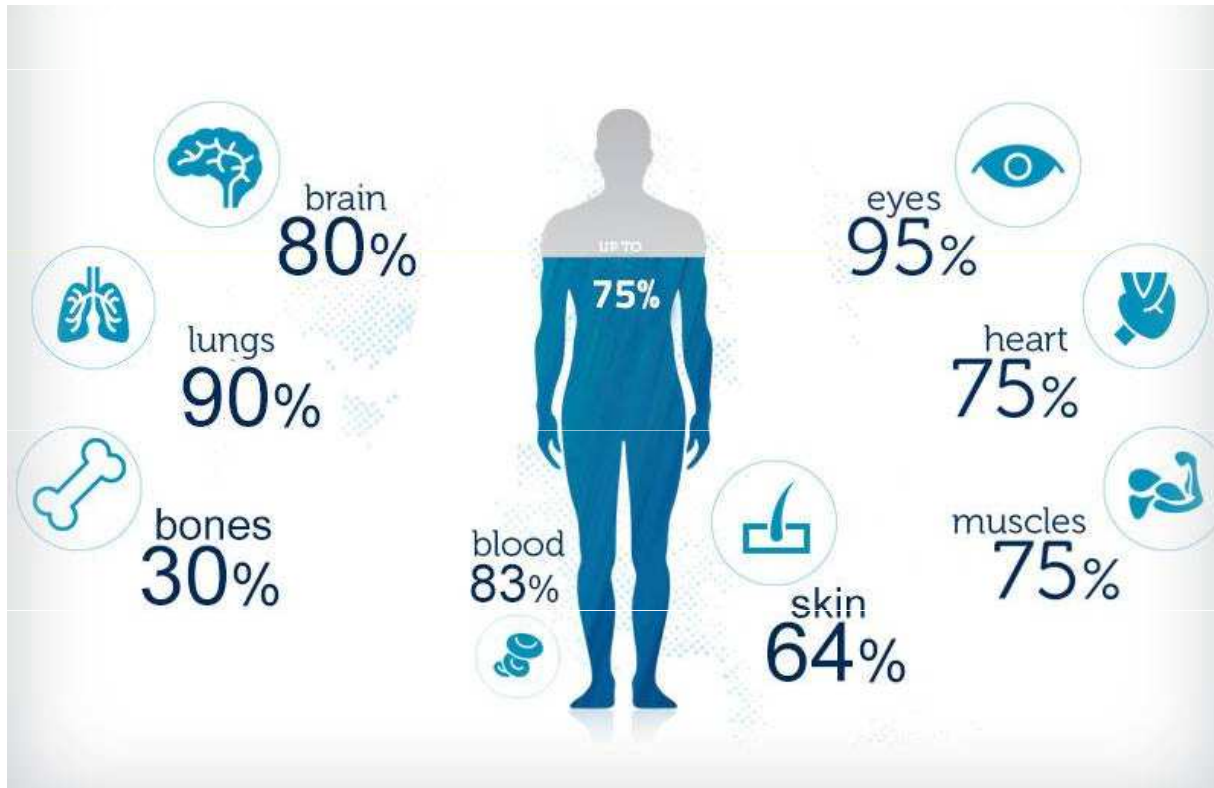
**Regulation of Body Temperature by the Nervous System**  
 Chan LekTan<sup>1</sup>Zachary A.Knight<sup>1234</sup>

# Water?

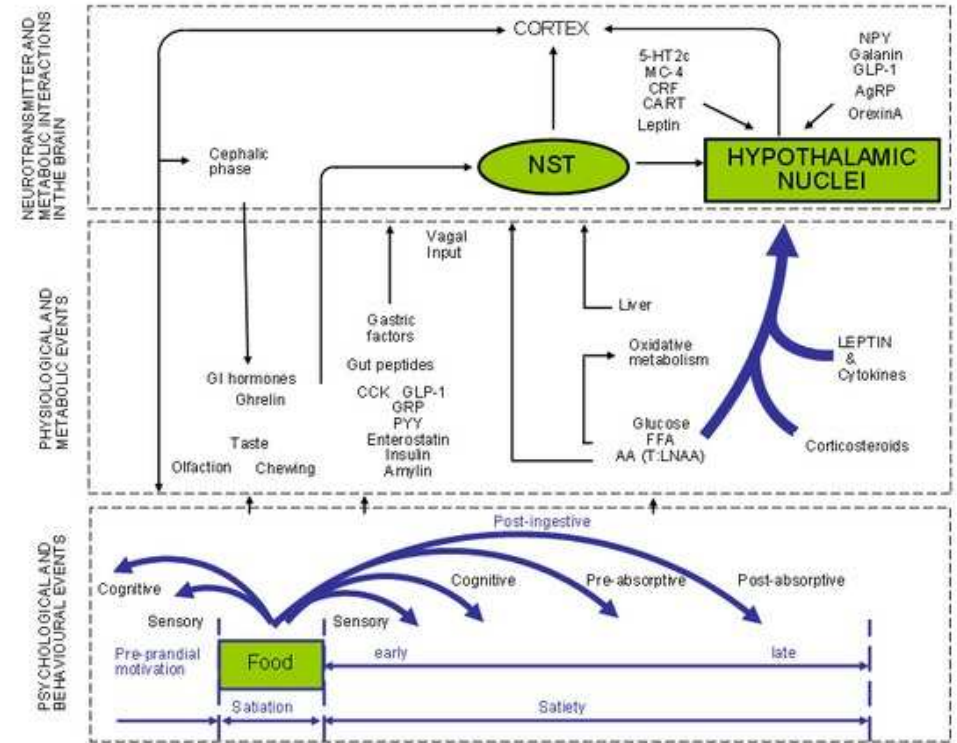




# Water: physiological demands: record



# Food intake?



# Food: physiological demands, record?



**74 vs. 382 days?**

# Stress and the surrounding environment

What do we know?

# Human wellbeing vs stress

*Epictetus: "If you wish your house to be well managed, imitate the Spartan Lysurgus. For as he did not fence his city with walls, but fortified the inhabitants by virtue and preserved the city always free; so do you not cast around (your house) a large court and raise high towers, but strengthen the dwellers by goodwill and fidelity and friendship, and then nothing harmful will enter it, not even if the whole band of wickedness shall array itself against it. Also, that city is well fortified which has a wall of men instead of brick."*

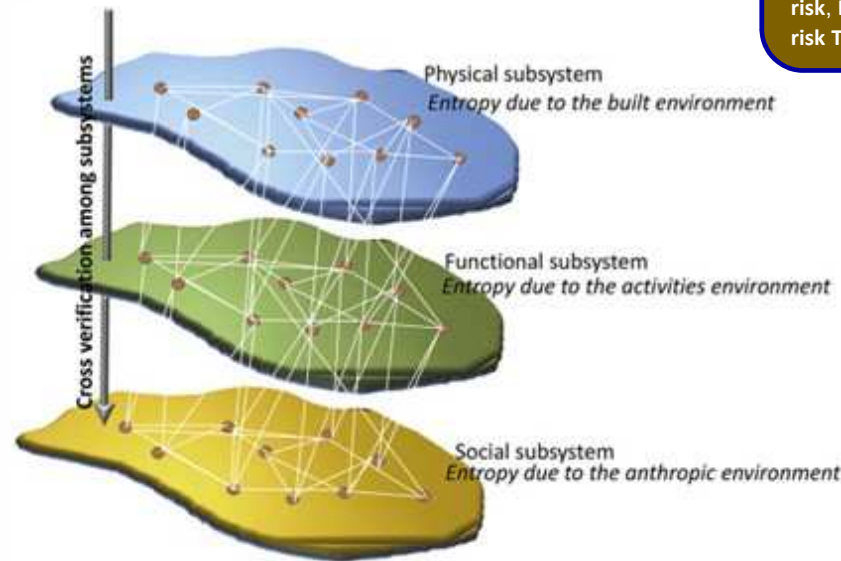
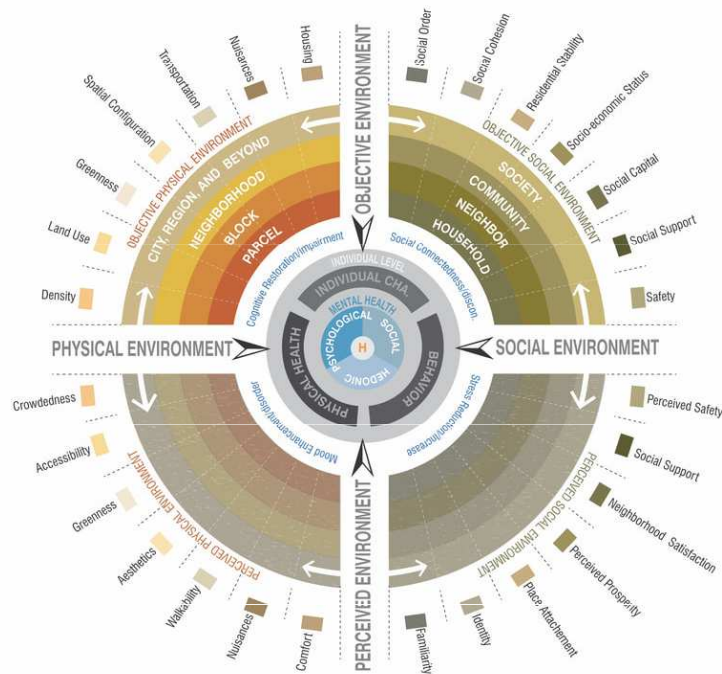
*There is increasing acknowledgement that design of urban spaces can contribute to the health and well-being of residents. Development of green spaces, design of parks and appropriate proximate infrastructure may promote increased physical activity leading to improved health outcomes within populations (Honold et al., 2015, Nordh et al., 2011, [Nordh et al., 2009](#), Nordh and Østby, 2013).*



# The WHO Expert Committee on Environmental Health in Urban Development

*"The **health of a city's people** is strongly determined by physical, social, economic, political and cultural factors in the urban environment, including the processes of social aggregation, migration, modernisation and industrialisation, and the circumstances of urban living..... [T]he impact of urban processes on health is not just the sum of the effects of the various factors taken individually, since they interact synergistically with each other." (WHO, 1991, pag.11)*

# So, what constitutes human wellbeing?



Percentage of Energy-efficient buildings Density of disused buildings, Roads conditions Traffic intensity, Quality of the Local Transport Network Percentage of soft mobility lanes, Density of areas subjected to flooding risk, Density of areas subjected to seismic risk, Density of areas subjected to hydrogeological risk Territorial utilization for agriculture

Population density Presence of Tertiary activities Status of the housing stock, Waste production Building obsolescence Bigger emission sources Building quality Clime characteristics, Density of Illegal buildings Density of Sport and recreational structures Crowding index

Noise pollution  
 Electromagnetic pollution  
 Unemployment rate  
 Multi-ethnic composition of residential population  
 Safety and care of elder population

Urban form and mental wellbeing: scoping a theoretical framework for action  
 Amir Hajrasouli(1), Vicente del Rio(1), James Francis (1) and Jessica Edmondson(2) The Journal of Urban Design and Mental Health

The Stress of Life, Hans Selye, 1956:

*„... the non-specific response of the body to any demand made upon it, whether it is caused by, or results in, pleasant, or unpleasant conditions“*

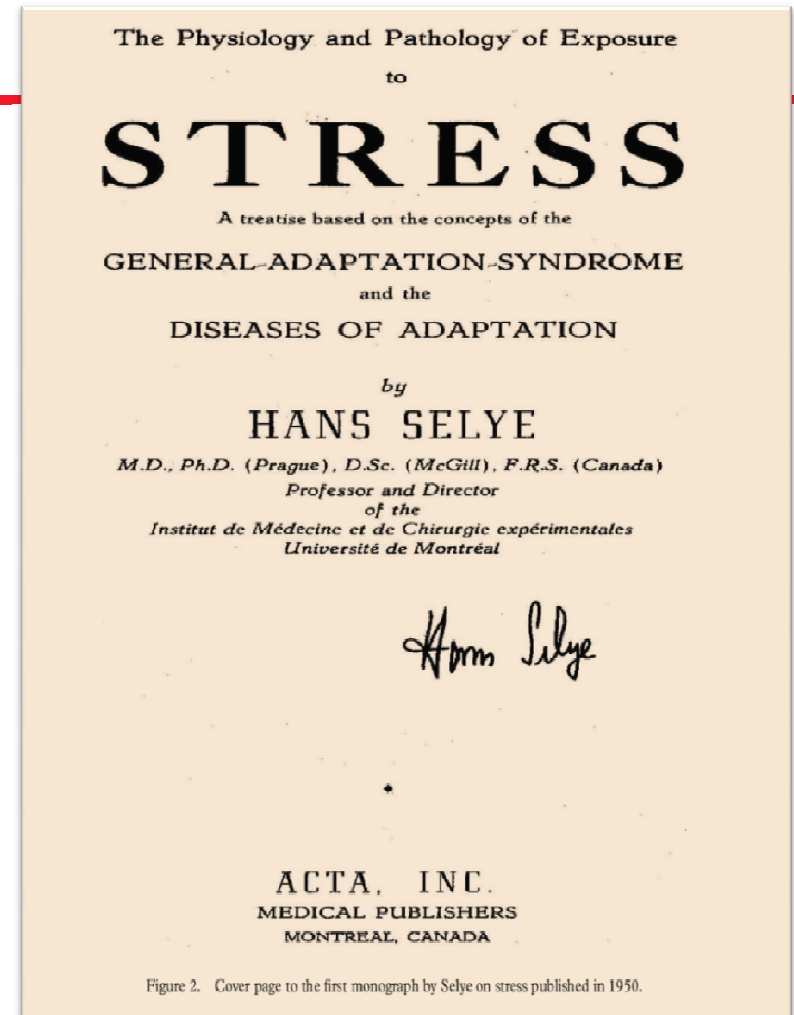
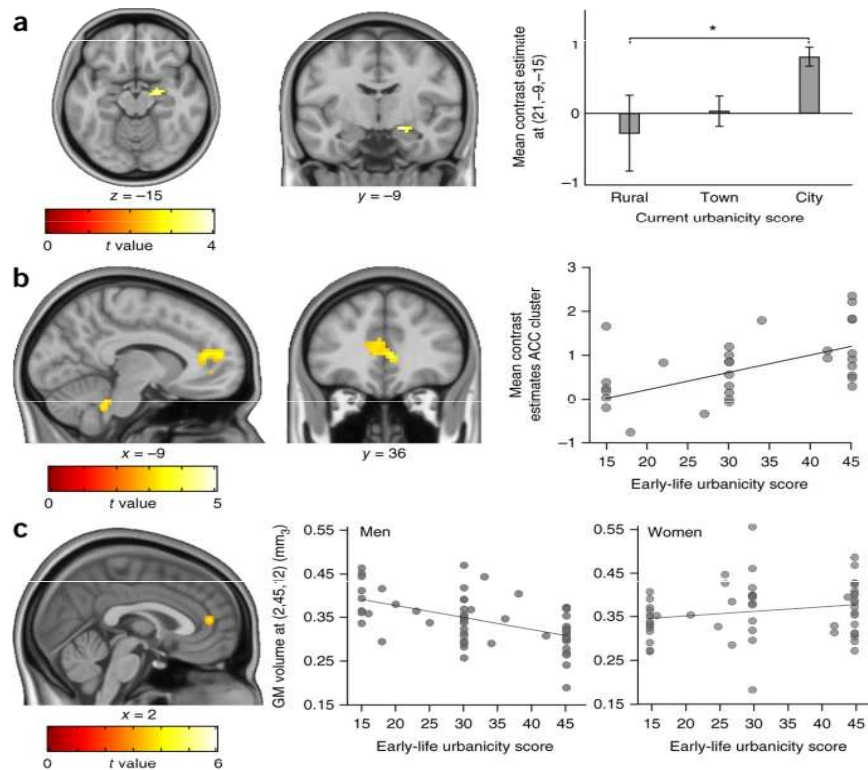


Figure 2. Cover page to the first monograph by Selye on stress published in 1950.



# So what is the problem?



How does extent of a given land cover type in a citizens' view affect her or his level of emotional arousal, while controlling for walk speed, direction, and distance to automobile roads, and how do changes in direction (turns) explain additional variation in physiological parameters when the other variables are accounted for?

# So what is urban stress in terms of human health?



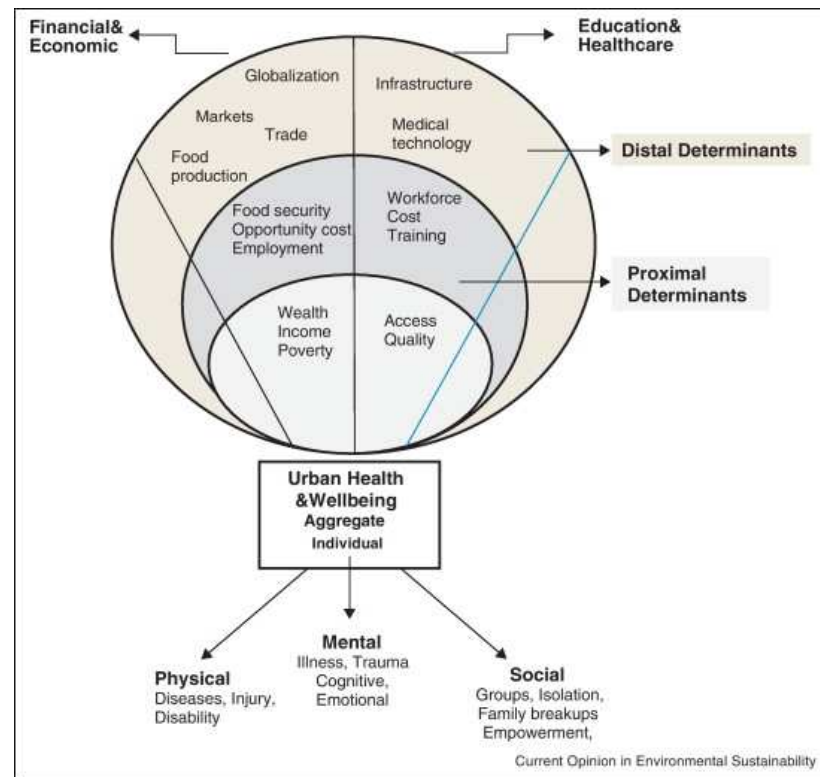
A state of bodily or mental tension developed through city living, or the physical, chemical, or emotional factors that give rise to that tension.

**Urban health: an example of a "health in all policies" approach in the context of SDGs implementation** [Oriana Ramirez-Rubio](#), [Carolyn Daher](#), [Gonzalo Fanjul](#), [Mireia Gascon](#), [Natalie Mueller](#), [Leire Pajin](#), [Antoni Plasencia](#), [David Rojas-Rueda](#), [Meelan Thondoo](#) & [Mark J. Nieuwenhuijsen](#) *Globalization and Health* volume 15, Article number: 87 (2019)

# So what are the determinants of urban health?

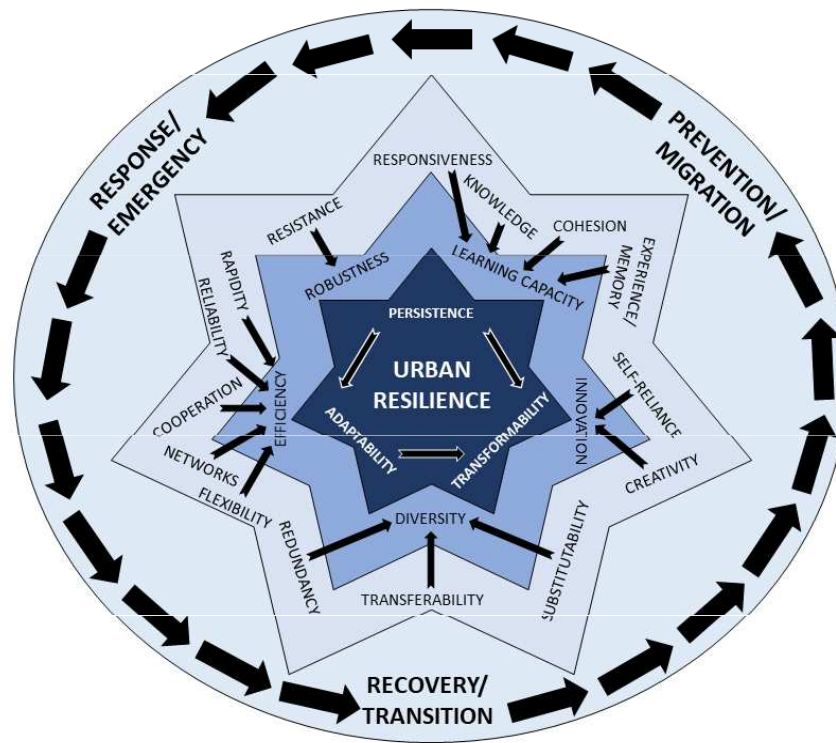


J. Boydell et al. *Br. J. Psychiatry* **182**, 45–49; 2003



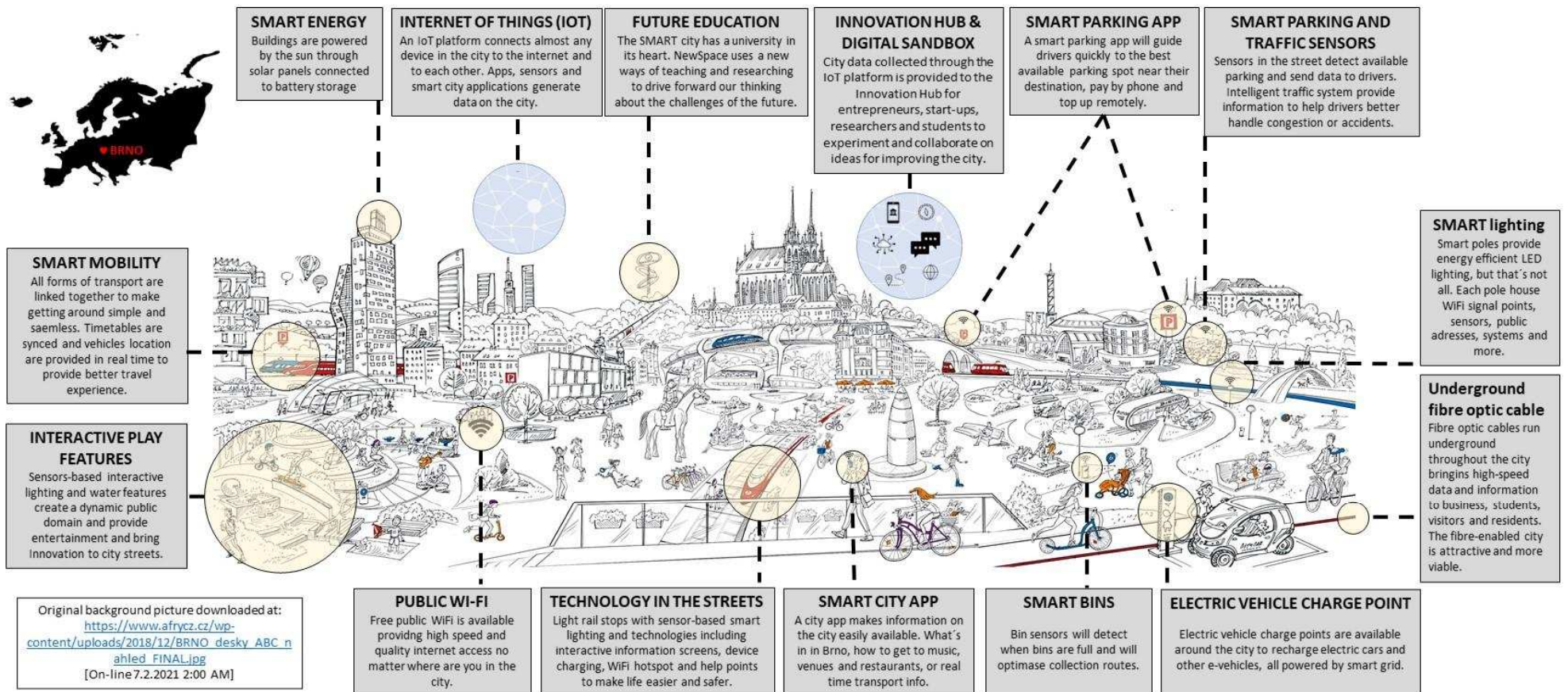
Health and wellbeing in the changing urban environment: complex challenges, scientific responses, and the way forward Xuemei Bai Indira Nath Anthony Capon Nordin Hasan Dov Jaron, *Current Opinion in Environmental Sustainability* Volume 4, Issue 4, October 2012, Pages 465-472

# Why is it important?



„Urban resilience has conventionally been defined as the "measurable ability of any urban system, with its inhabitants, to maintain continuity through all shocks and stresses, while positively adapting and transforming towards sustainability".<sup>[1]</sup> Therefore, a resilient city is one that assesses, plans and acts to prepare for and respond to hazards - natural and human-made, sudden and slow-onset, expected and unexpected. Resilient Cities are better positioned to protect and enhance people's lives, secure development gains, foster an investible environment, and drive positive change.<sup>[1]</sup> Academic discussion of urban resilience has focused primarily on three distinct threats; climate change, natural disasters, and terrorism.“ – Wikipedia as of 2021

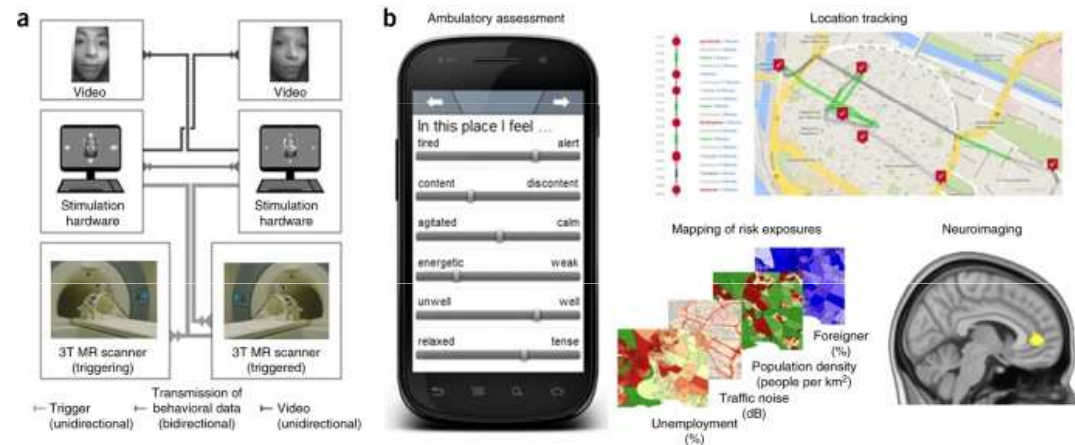
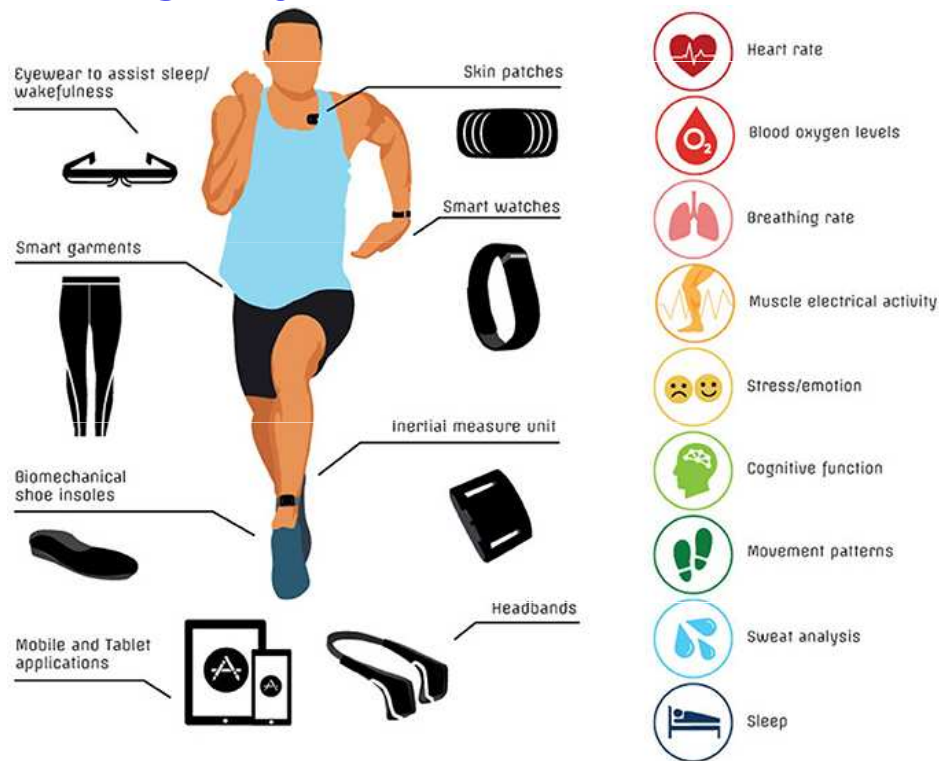
# Smart cities – where we want-could be



# So what can physiology offer to urbanism?

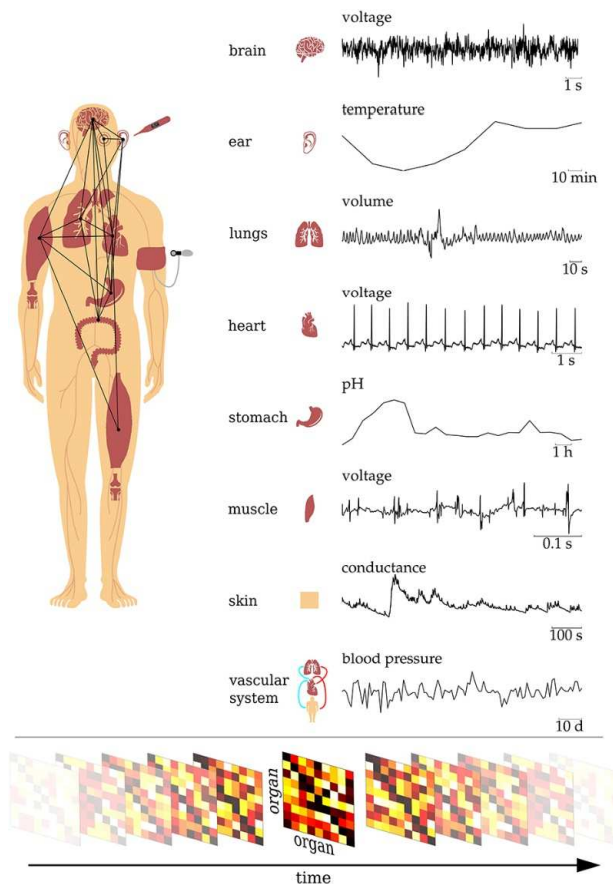
- Deep understanding of pathogenic processes behind common illnesses
- Deep insight into methodology of measurement of various urban-stress-related variables
- Explanations of pathways between exposure and final health outcome, instead of plain association of exposure with disease
- Looking at the city as a platform capable of managing ENVIRONMENTAL DATA (pollution levels, water and waste management), SECURITY (health of buildings, bridges and dams or emergency situations), TRANSPORTATION (lighting on roads, real-time traffic, reduction of travel times and refueling), QUALITY OF LIFE (health, accessibility, sport and leisure) and BUILDINGS (energy consumption and user comfort), should enable major short-term improvements in health of citizens.

# And, how do we measure stress in real world?



[A Critical Review of Consumer Wearables, Mobile Applications, and Equipment for Providing Biofeedback, Monitoring Stress, and Sleep in Physically Active Populations.](#) **Peake JM**, Kerr G, Sullivan JP. *Front Physiol.* 2018 Jun 28;9:743. doi: 10.3389/fphys.2018.00743.

# Humans as sensors

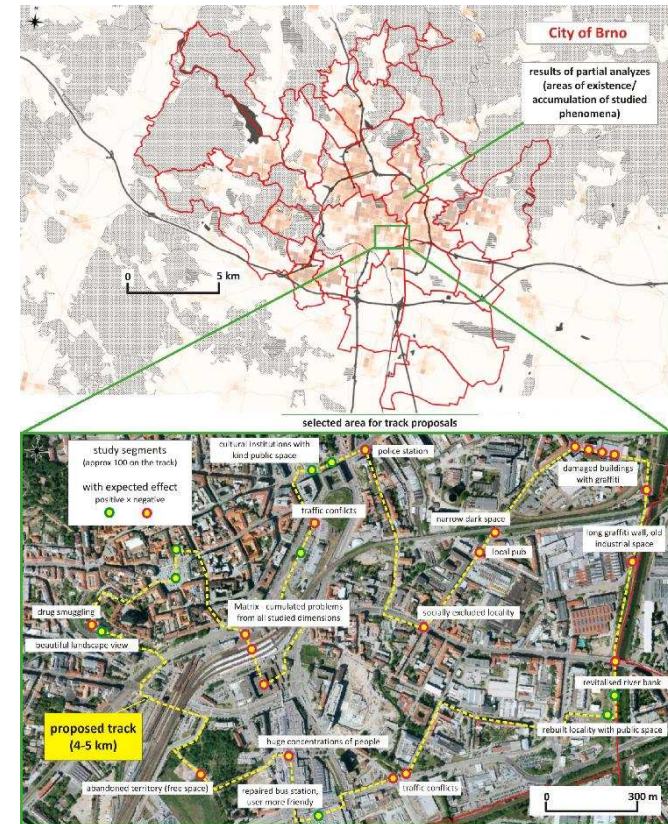
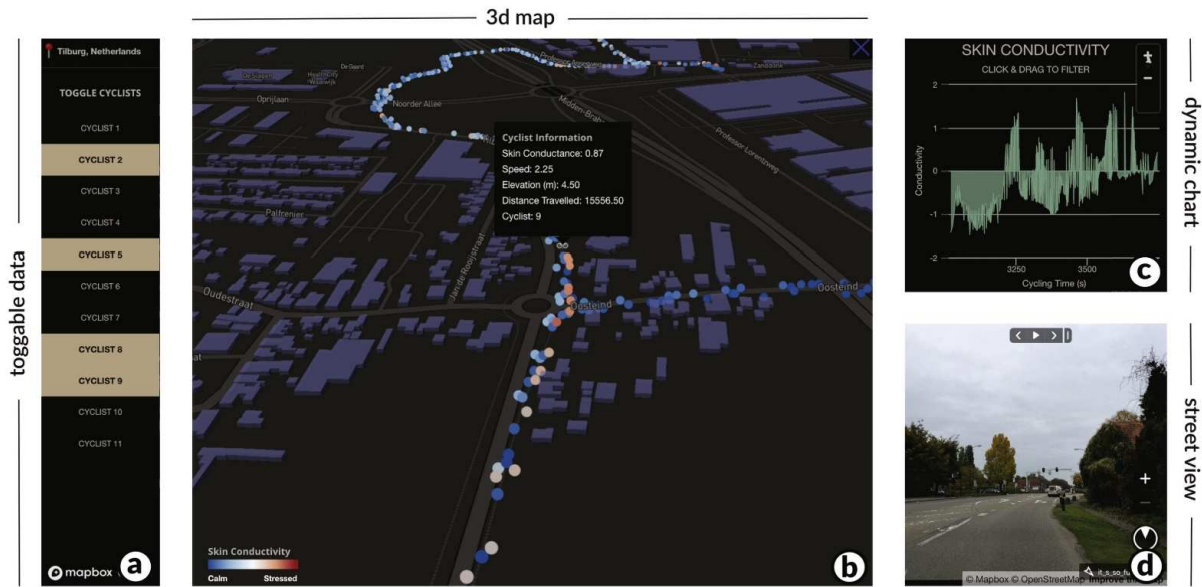


- We often do not know exactly the systems' equations of motion;
- We lack knowledge as to how to merge/combine these equations (e.g., due to the issue of time-scale matching);
- We may have insufficient knowledge about relevant structural connections;
- We may not have direct access to interactions between systems (e.g., via probing).

[The Human Organism as an Integrated Interaction Network: Recent Conceptual and Methodological Challenges.](#)  
**Lehnertz K**, Bröhl T, Rings T. *Front Physiol.* 2020 Dec 21;11:598694. doi: 10.3389/fphys.2020.598694. eCollection 2020.



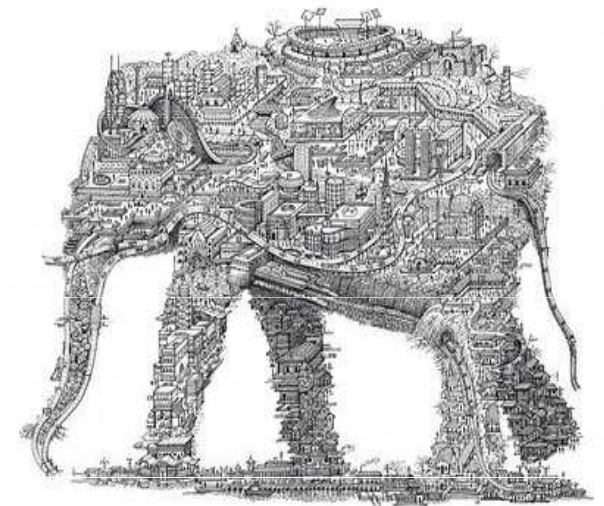
# Collective sensing



Space-time analytics of human physiology for urban planning  
 Garrett C. Millara,\*, Ondrej Mitasb, Wilco Boodeb, Lisette Hoekeb, Joost de Kruijfb,  
 Anna Petrasovaa, Helena Mitasova, Computers, Environment and Urban Systems 85 (2021) 101554

# What is the point? Change of paradigm?

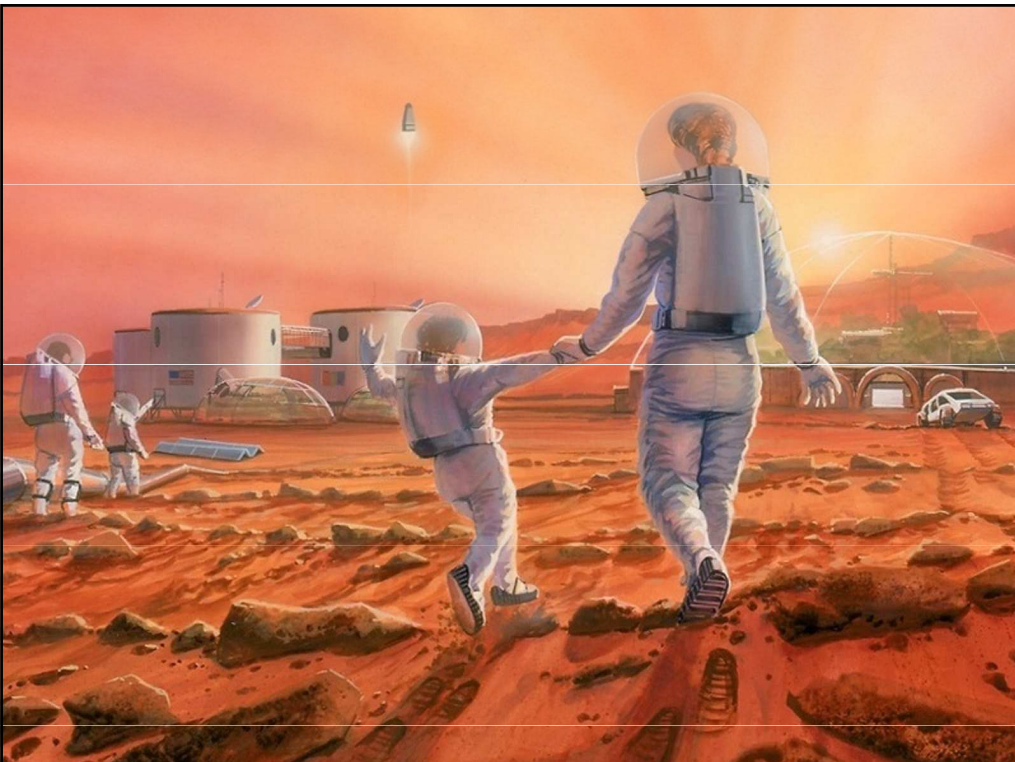
Formal structures of cities are often inspired by a combination of human geometry and cosmological patterns in both Eastern and Western civilizations, from early representations in mandalas to the Vitruvian Man. Cities have also been understood **as a living system**, a macroscopic organism, linked through its collective consciousness, communicative structure and relationship to natural resources and cycles. Like the human body or other natural organisms, the city is comprised of multiple parts, organs, cells and functions, each autonomously working with its own requirements. However, we need to learn much more about the interconnectedness to understand better the processes.





***“It is our attitude toward events, not events themselves, which we can control. Nothing is by its own nature calamitous -- even death is terrible only if we fear it.”***

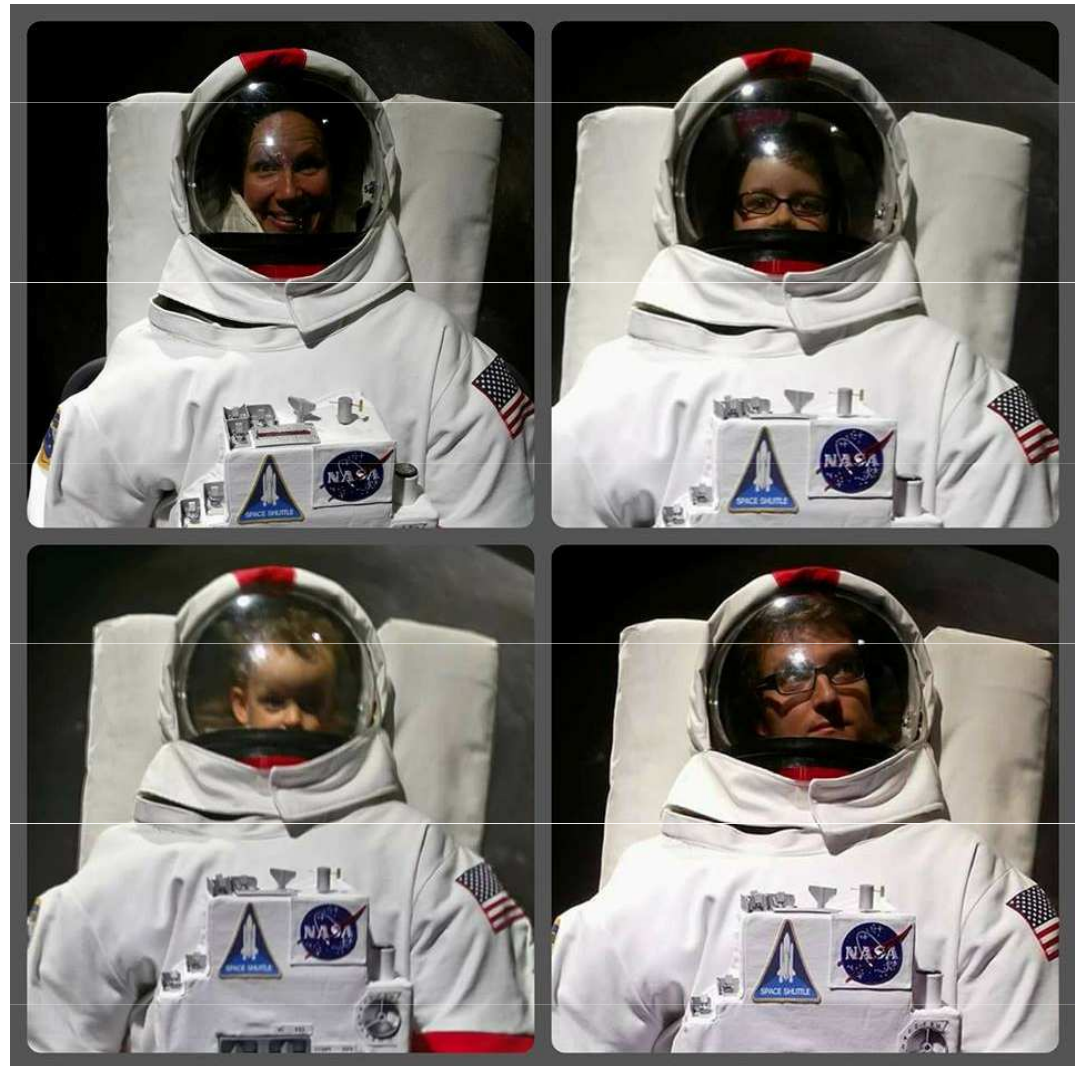
***— Epictetus***



MARS  
MAX RYMER

# Budeme u toho?

– Ano!



**MASARYKOVA  
UNIVERZITA**