Brain-immune axis in fatigue

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Disclosure
This certifies that I, ADD NAME HERE, have no financial relationship that is relevant to the subject matter of this presentation.
Brain-immune communication in fatigue

- Sickness behavior
- Immune activity in the brain
- Changes in peripheral immunity
The immune system affects physiology

- Inflammatory overload on tissues
- Metabolism: CD8+ T cells induce cachexia by adipose-tissue remodeling. 
  

- Immune system senses physiological changes and tissue damage.

Fatigue is induced by the brain

Immune interoception
Immune interoception

Immune Conditioning

- Cyclosporine: Immune-suppressive drug
- Saccharine: Immune suppression

Metalnikov and chorin; Ader and Cohen; Manfred Schedlowski
The TRAP* model
Guenthner et al, Neuron 2013

Tamoxifen + Neuronal activity

Cre-dependent expression (e.g. fluorescent marker, DREADD)

DSS

DSS-induced colitis
Eleveated activity in the brain during inflammation
Elevated activity in the Insular cortex
What does it mean?
Immune-related information is stored in the insular cortex

How specific?
Zymosan-induced peritonitis

DIO-Gq/sham-mCherry

Peritonitis

TM

CNO

sacrifice

3w

0h

48h

3w

-24h

Monocytes

MHCI\textsuperscript{+} MQ

TLR2\textsuperscript{+} MQ

MHCI\textsubscript{II} on MQ (MFI)

Koren et al; bioRxiv 2020.12.03.409813
Brain-immune communication

Pseudorabies virus (PRV)

Oren Kobiler
TAU
Brain-immune communication

Pseudorabies virus (PRV)

Oren Kobiler

TAU

AAV1
Immune-related information is stored in the brain as a mnemonic representation.

Immune-related information can mean many things.

The brain can initiate immune reactions—psychosomatics.

Anatomical connectivity supports the functional potential.

Immune interoception?
Fatigue and interoception in humans

Only patients with fatigue:
- Decreased interoceptive accuracy
- Decreased gray matter volume
- Increased functional connectivity in core interoceptive regions, the insula, and the anterior cingulate cortex.
- Each of these alterations was positively associated with fatigue.

Gonzalez Campo, 2020 26(14): 1845–1853

In sports, cognitive fatigue and physical fatigue depend on:
- Interoceptive mechanisms
- Motivation: the dopaminergic mesocorticolimbic and the locus coeruleus-noradrenaline pathways are also vital.

The brain constantly regulates peripheral immunity

Motivation

Activation of the reward system boosts innate and adaptive immunity

Tamar L Ben-Shaanan1,2, Maya Schiller1,2, Hilla Azulay-Debby1,2, Tania Dubash1, Elina Stanovnik1, Ben Korin1,2, Maya Schiller1,2, Nathaniel I. Green2, Tsali Admon2, Faded Hakim2,3, Shai S. Shen-Orr4,5,6,7 & Asya Rots2,7,8

Modulation of anti-tumor immunity by the brain's reward system

Tamar L Ben-Shaanan1,2, Maya Schiller1,2, Hilla Azulay-Debby1,2, Ben Korin1,2, Nadia Bashuk1,2,3, Tamar Korin1,2,3, Maria Knoll1,2,3, Juan Shaky2,4, Michael A. Rahal2,4, Faded Hakim2,3 & Asya Rots2,7,8

Short-term sleep deprivation in mice induces B cell migration to the brain compartment

Asya Rots2,7, Wendy W. Pang3, Ingrid Ibarra4, Damien Cols3, Patricia Bonavion1, Ben Korin2, H. Craig Heller4, Irving L. Weissman5,6 & Luis de Lecea1,3

Sleep disruption impairs hematopoietic stem cell transplantation in mice

Asya Rots2,7, Wendy W. Pang3, Ingrid Ibarra4, Damien Cols3, Patricia Bonavion1, Ben Korin2, H. Craig Heller4, Irving L. Weissman5,6 & Luis de Lecea1,3
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