NIH Blueprint for Neuroscience Research

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Beyond the Symptom: The Biology of Fatigue
September 27 – 28, 2021

Using LPS to model fatigue

Julie LASSELIN, PhD

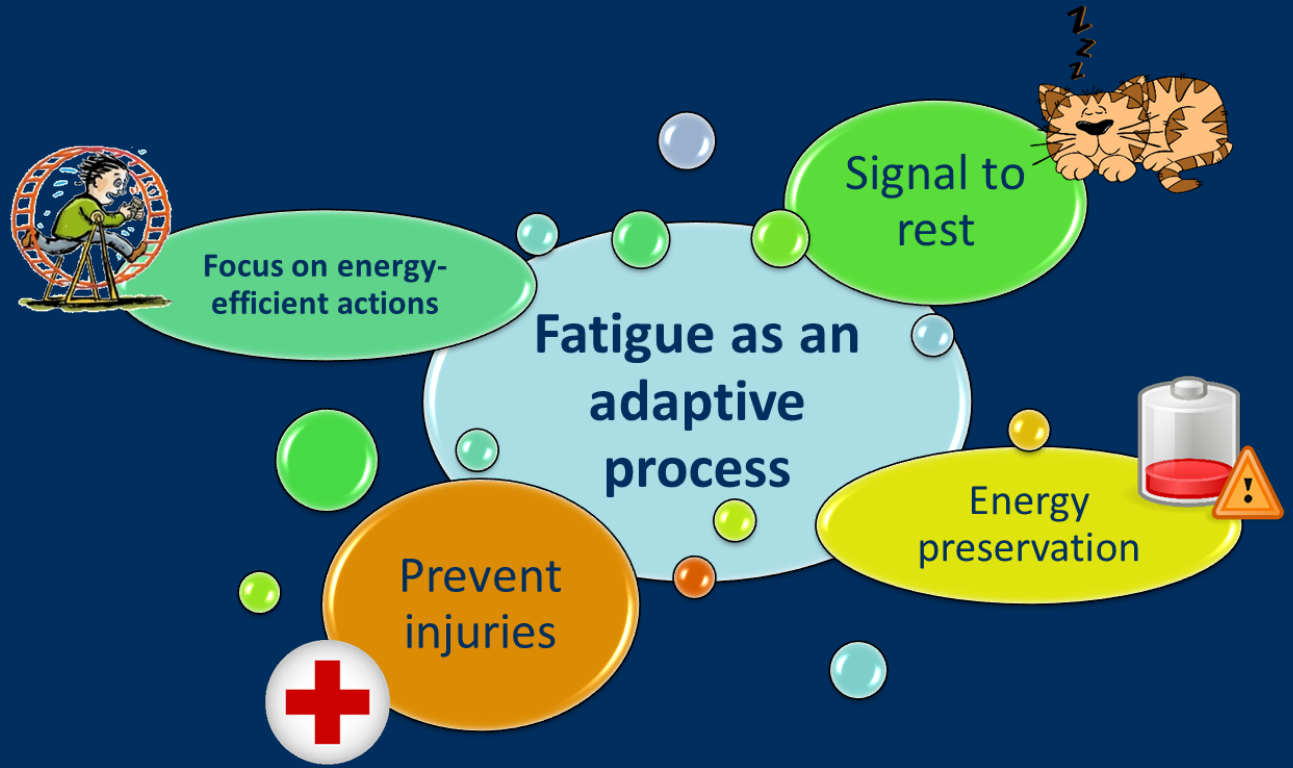
Stockholm University and
Karolinska Institutet
Stockholm, Sweden

Disclaimer and Disclosures

Disclaimer
This certifies that the views expressed in this presentation are those of the author and do not reflect the official policy of the NIH.

Disclosure
This certifies that I, JULIE LASSELIN, have no financial relationship that is relevant to the subject matter of this presentation.

Physiological, inflammation-related fatigue



Induced by e.g. exercise but also inflammation

Inflammation-related fatigue: patients AND healthy individuals (infection)

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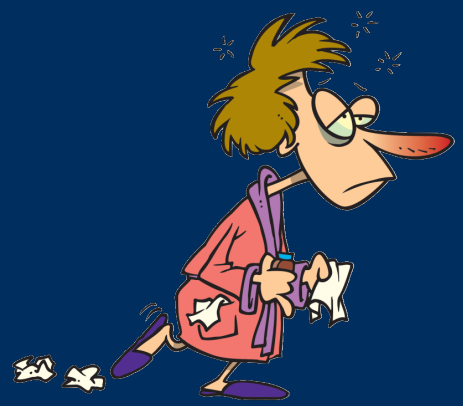
Sickness behavior during acute inflammation (infection)



Fatigue

Changes in gait

Motivational reorganization

Decreased motivation to e.g. play

Increased motivation to e.g. sleep

Social withdrawal

Anxiety

Reduced appetite

Cognitive alterations

Hyperalgesia

Negative mood

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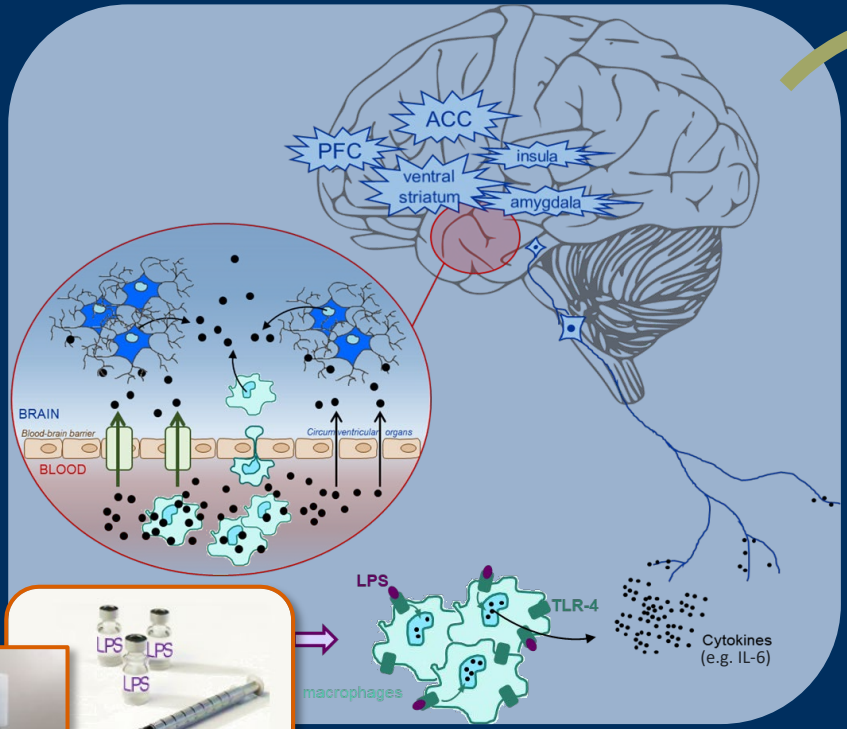
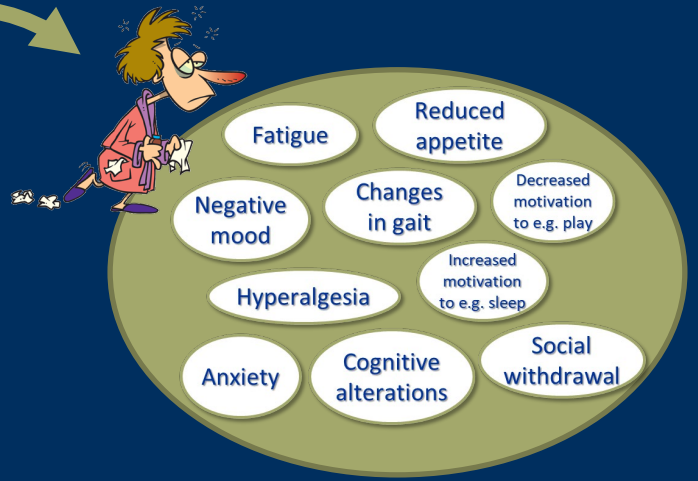
LPS model and sickness behavior





LPS (lipopolysaccharide)
= bacterial **endotoxin**

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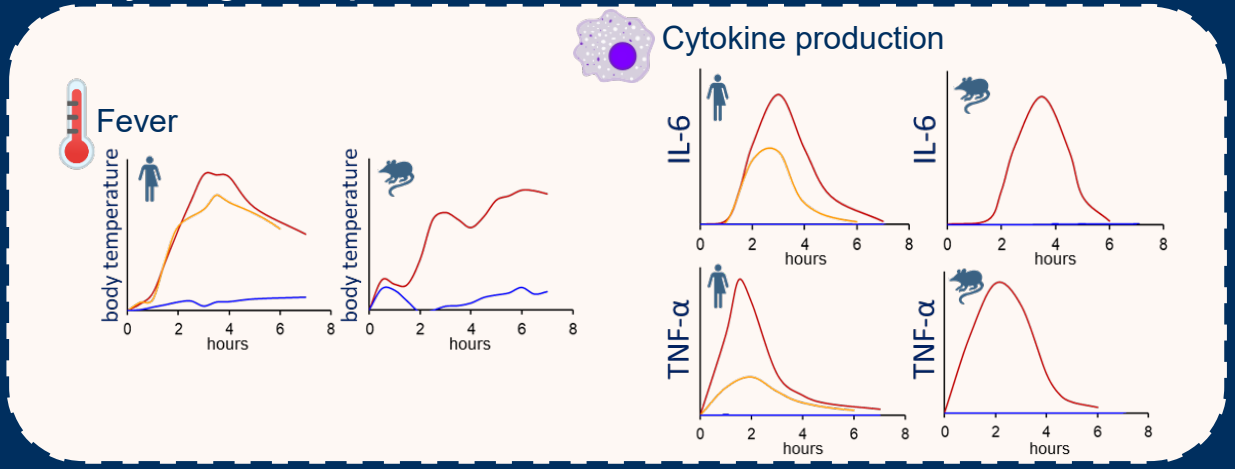
LPS model: transient, dose-dependent, translational

Physiological response



Lasselin et al., 2020, Neurosc Biobeh Rev

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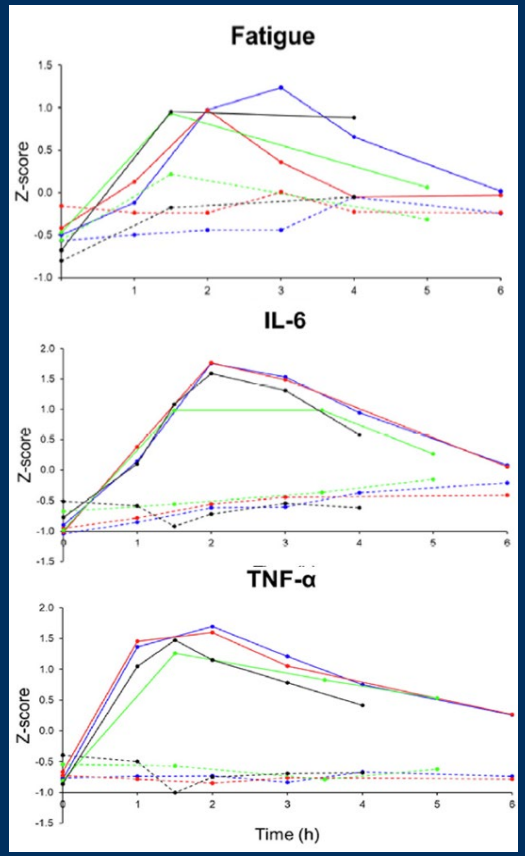
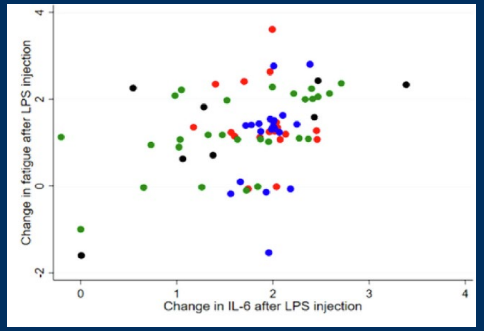
Subjective fatigue after LPS

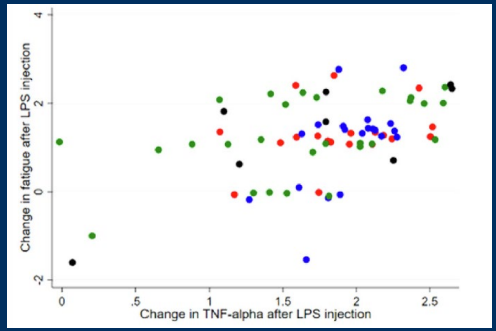


ΔFatigue- ΔIL6



β(SE)=0. 592(0.178), p=.001

ΔFatigue- ΔTNF-a



β(SE)=0. 785(0.173), p < .001

Study S1 (between-subject)
Study S2 (crossover)
Study E1 (between-subject)
Study E2 (crossover)

Lasselin/Karshikoff et al., 2020, Brain, Behavior and Immunity

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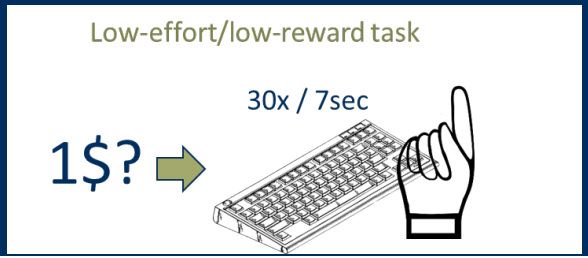
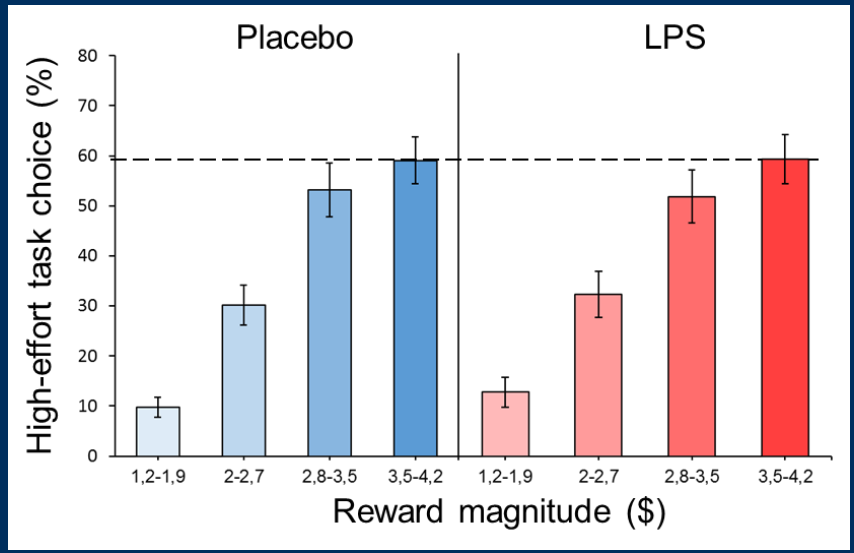
Effort/reward allocation after LPS

EEfRT (Effort Expenditure for Rewards Task, Treadway et al. 2009):



WILLINGNESS TO EXPEND MORE EFFORT DEPENDING ON REWARD MAGNITUDE



Lasselin et al., 2017, Neuropsychopharmacology

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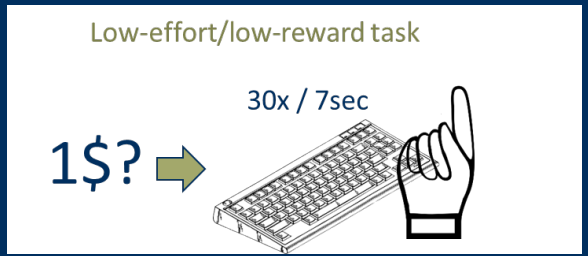
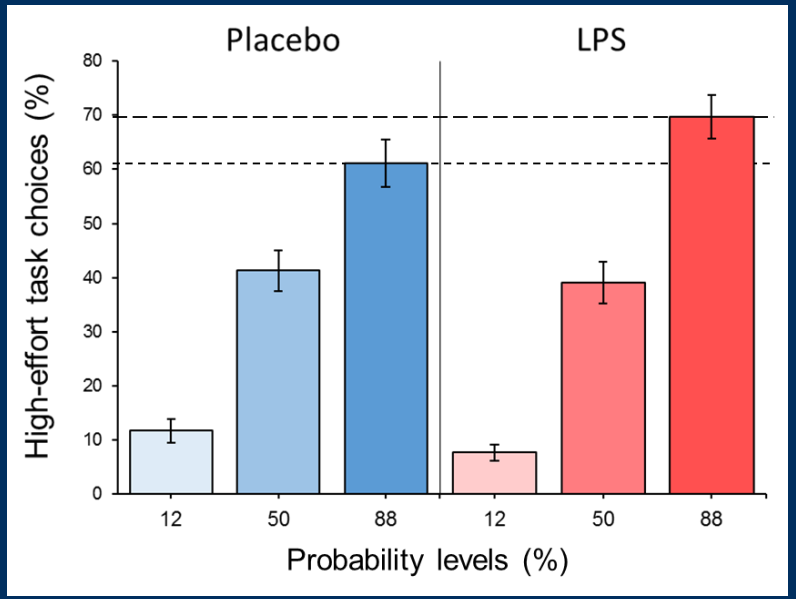


WILLINGNESS TO EXPEND MORE EFFORT DEPENDING ON PROBABILITY TO GET REWARD



Competition between need to rest and need for comfort?

Lasselin et al., 2017, Neuropsychopharmacology

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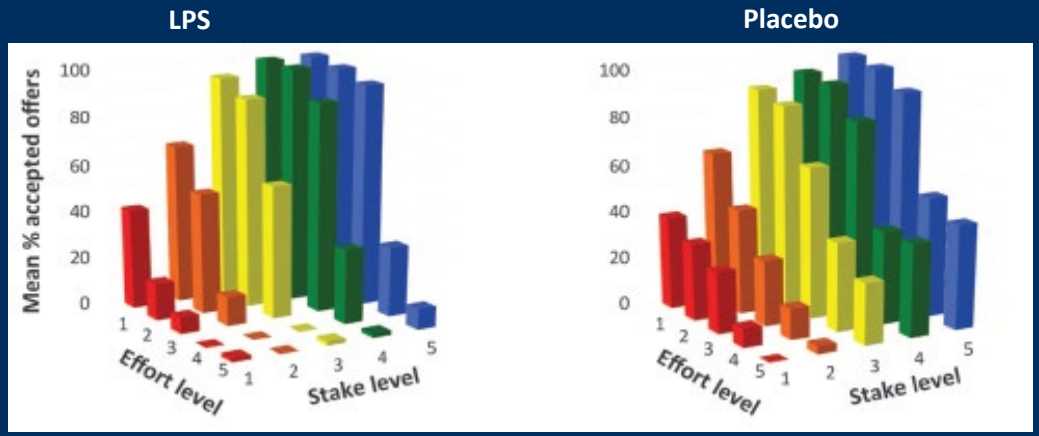
Effort/reward allocation after LPS



Draper et al., 2017, Neuropsychopharmacology

Higher reward → more effort
Similar in LPS and Placebo condition
(similar liking)

Higher effort needed → less effort
Stronger in LPS condition
(reduced wanting)

BUT! Participants had to choose between making an effort to get a reward or do nothing (i.e. rest)

→ motivational drive to rest was stronger than to get a monetary reward
IN THIS CONTEXT

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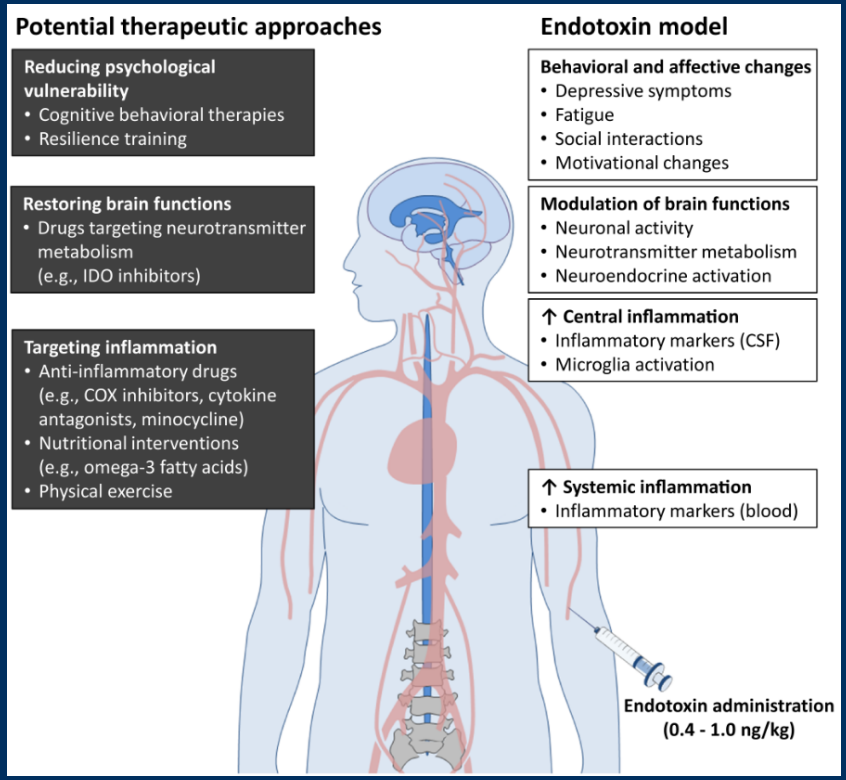
LPS model and inflammation-related fatigue

- Understanding physiological inflammation-related fatigue (dimensions, effect of context and type of rewards) and how it compares or differs to clinical fatigue
- Findings can be translated between animals and humans
- What make people more *vulnerable* or more *resilient* to develop inflammation-related fatigue
- Test therapies targeting the vulnerability factors



Lasselin, et al. Mol Psychiatry 2020

Thank you

Vetenskapsrådet

Alexander von Humboldt
Stiftung/Foundation

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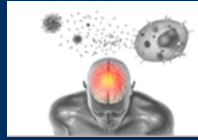
THE SWEDISH FOUNDATION FOR HUMANITIES AND SOCIAL SCIENCES



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und Verhaltensimmunbiologie

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