

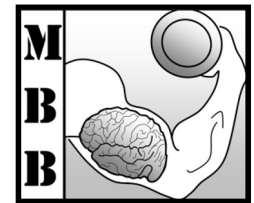
Inserm



UNIVERSITÉ
PIERRE & MARIE CURIE
LA SCIENCE À PARIS



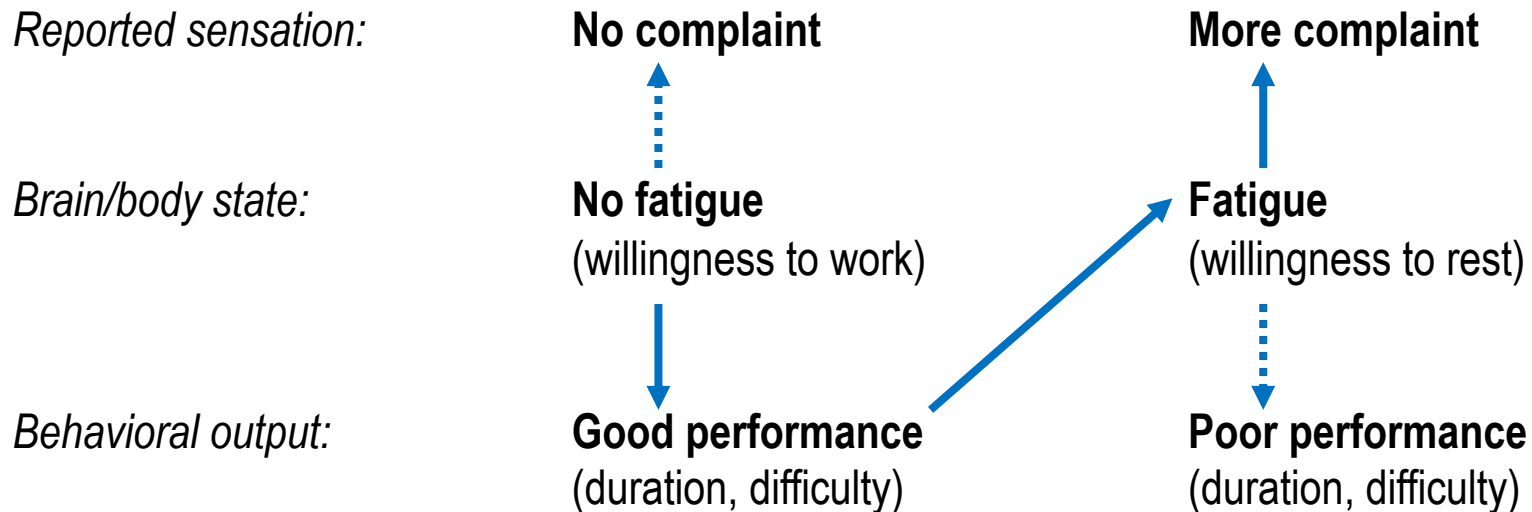
Origines et conséquences de la fatigue cognitive



What is cognitive fatigue?

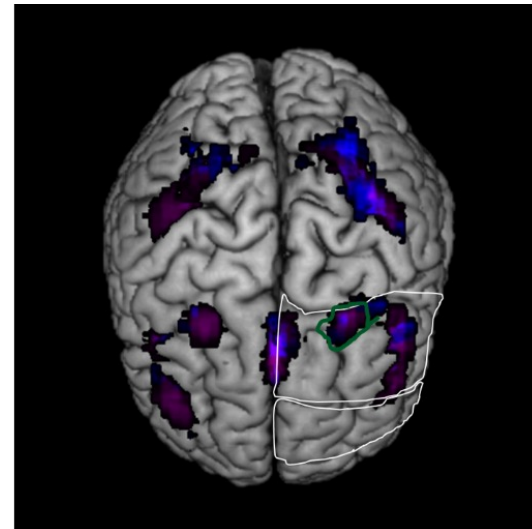
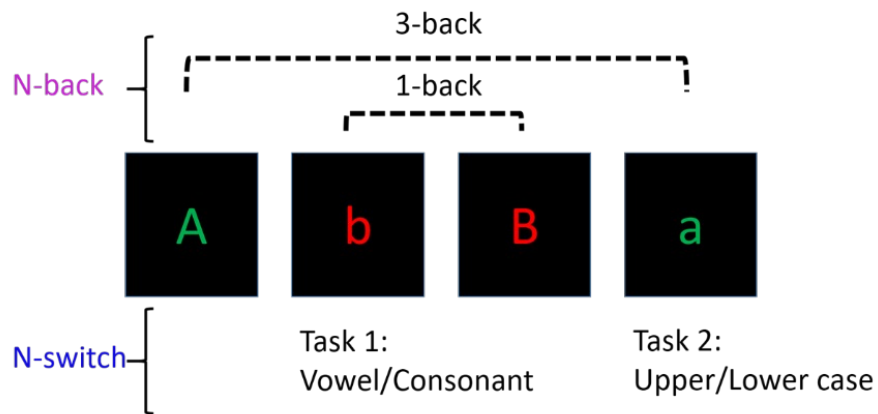
An **acute neurophysiological state** induced by cognitive work, characterized by

- A negative subjective experience (fatigue sensation)
- A willingness to stop working and start resting

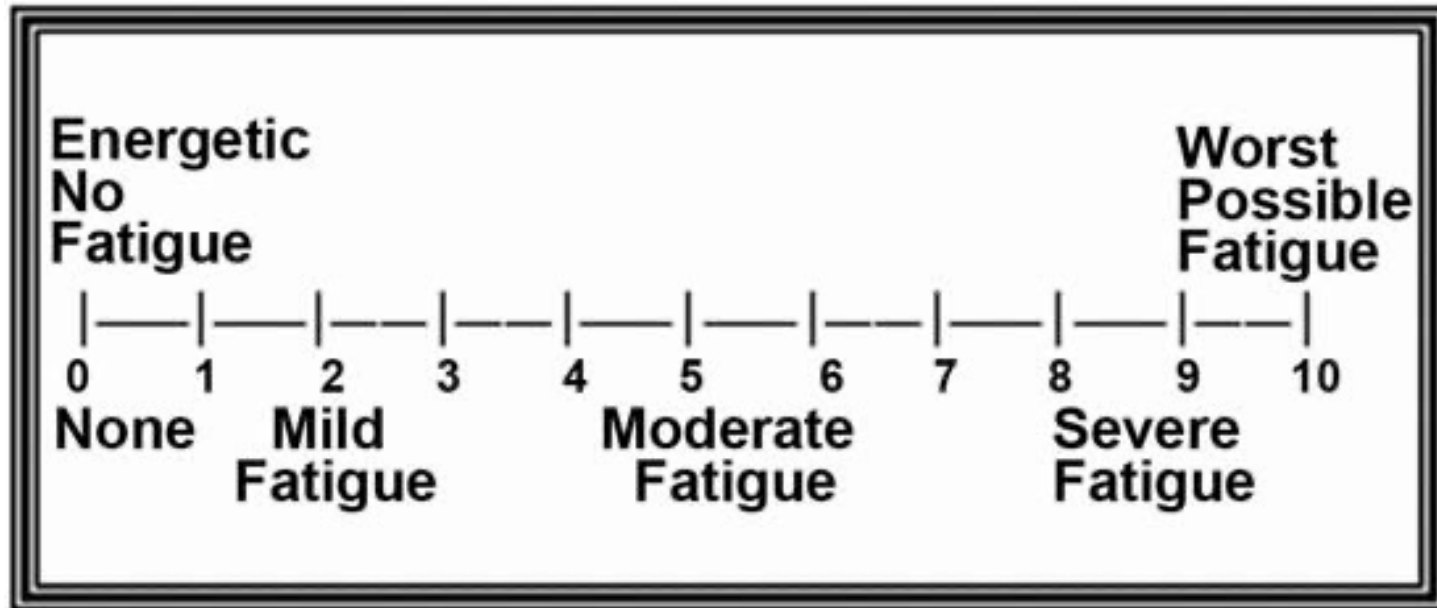


How to induce cognitive fatigue? by requesting cognitive control

- Cognitive control is opposed to automatic routines (context-response mapping)
- Examples:
 - Overcoming physical pain (endurance effort / cold water)
 - Inhibiting detrimental impulses / socially unacceptable behaviors
 - Performing cognitive control tasks (Stroop, N-back, task switching ...)

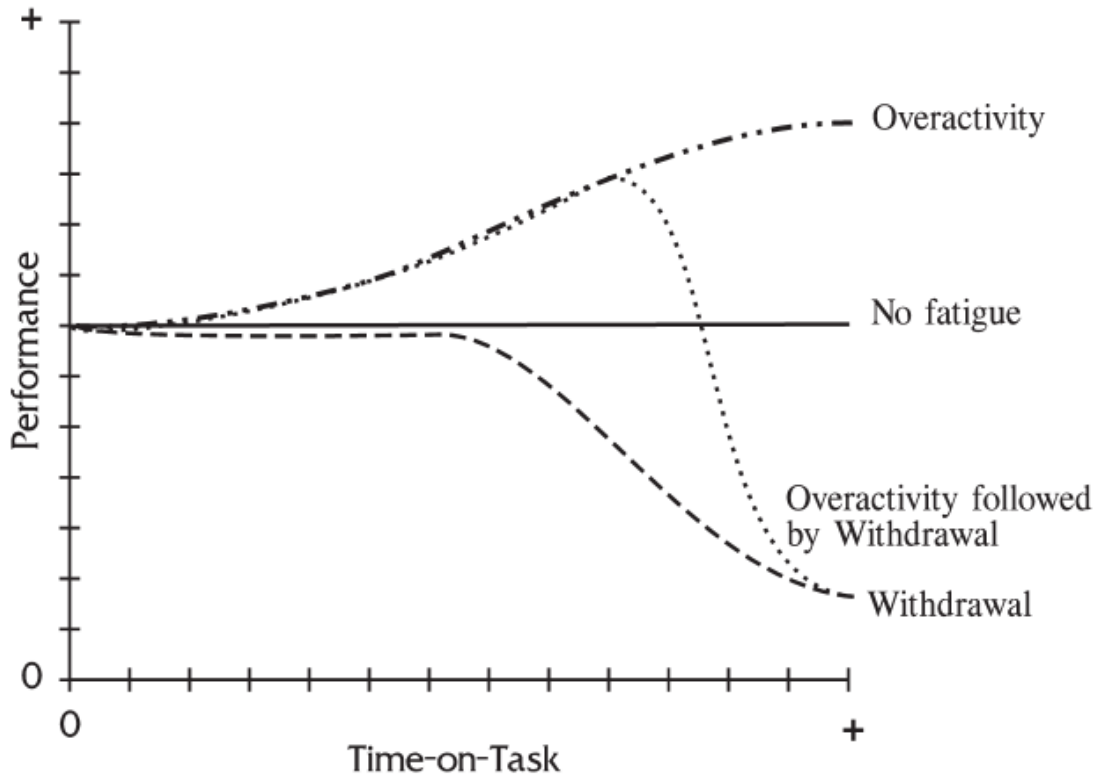


How to measure fatigue? ... with self reports



- Mental fatigue documented with fatigue scales in a variety of
 - neurological conditions (stroke, multiple sclerosis, degenerative diseases ...)
 - psychiatric conditions (depression, chronic fatigue syndrome, burnout ? ...)
- But: depends on introspection (subjective sensation and not neurophysiological state)
 - + not super specific (confound with apathy) + desirability bias

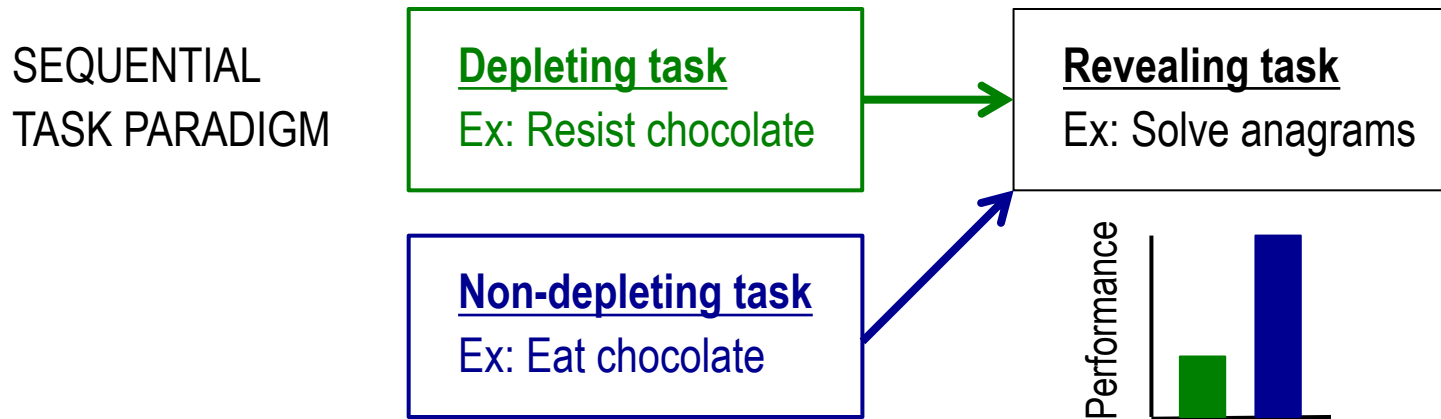
How to measure fatigue? ... with performance along time on task



- Every pattern has been observed:
- Increase (due to learning), no change (even if fatigue, because of motivation)
- decrease possibly due to fatigue but confounded with boredom / frustration

How to measure fatigue? ... with interference between tasks

- **Suggestions of ego depletion theory** (Baumeister et al., *Curr Dir Psychol* 2007)
 - Self-control capacity is **common** to a variety of tasks (including choice)
 - Self-control capacity relies on a **limited** resource (possibly glucose)
 - Self-control capacity is **depleted** by its utilization (over seconds to minutes)



- **Criticisms of ego depletion theory**
 - Empirical: **replication failures** + **susceptibility to beliefs / incentives**
 - Theoretical: **unclear resource** + **not adaptive** + **not specific**

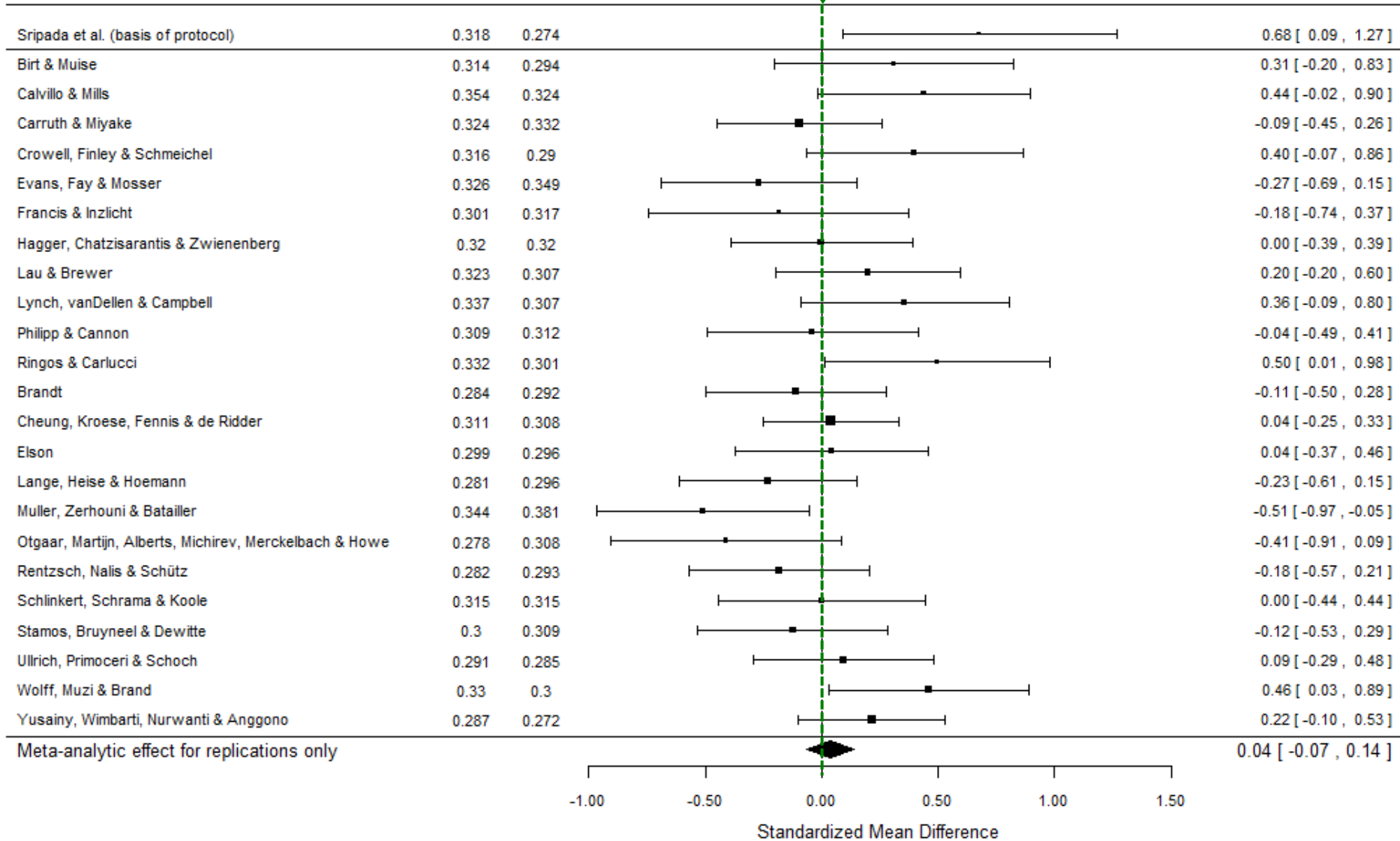
(Job et al. *Psychol Sci* 2010; Molden et al. *Psychol Sci* 2012)

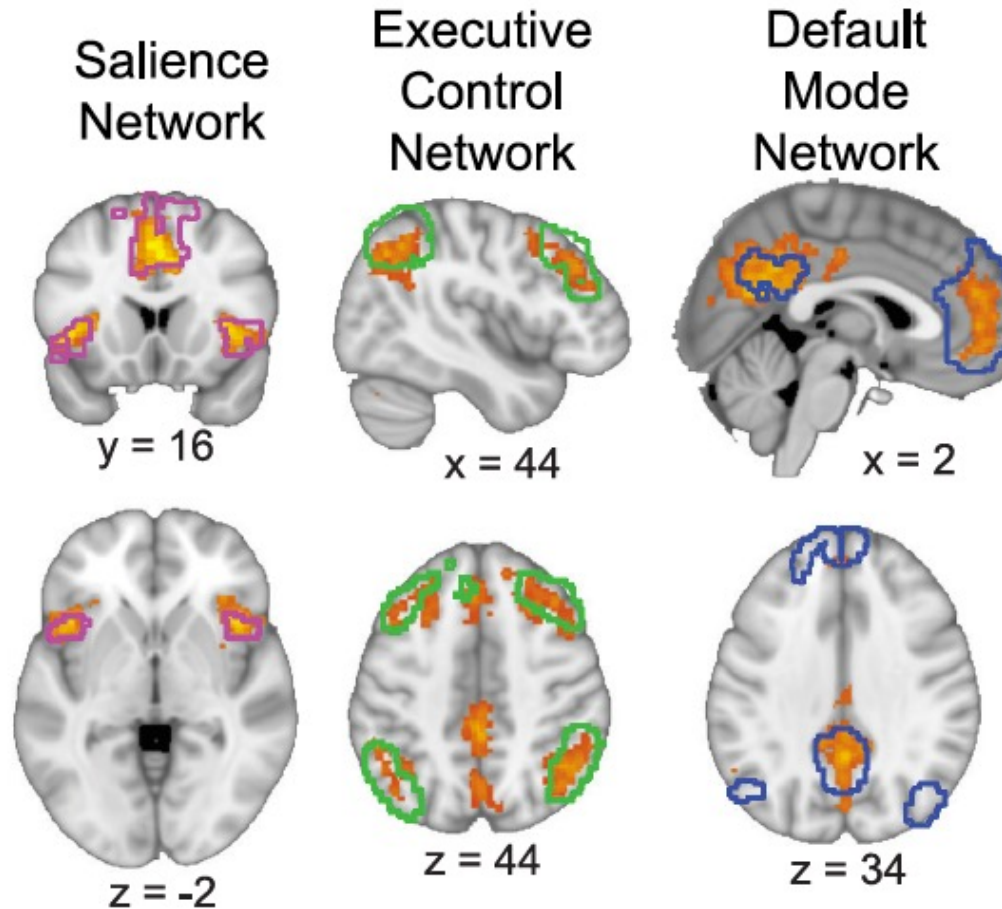
Multilab pre-registered (failed) replication

Hagger et al. 2015

Perspectives on Psychological Science

Null effect within confidence interval



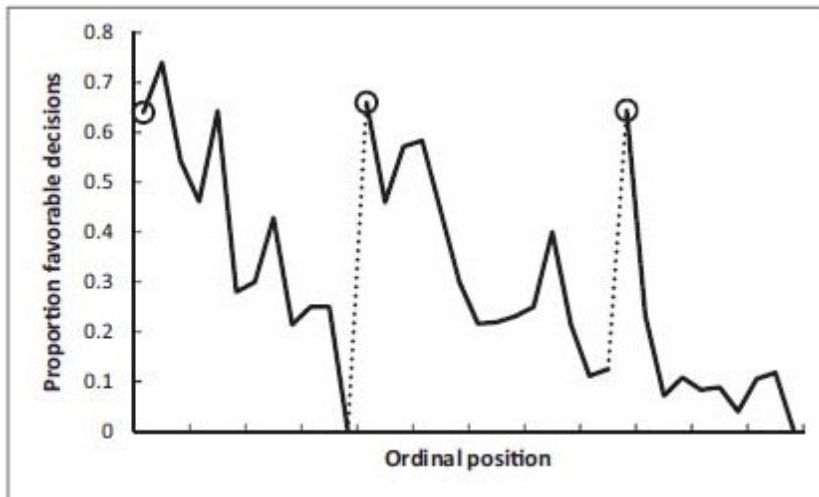
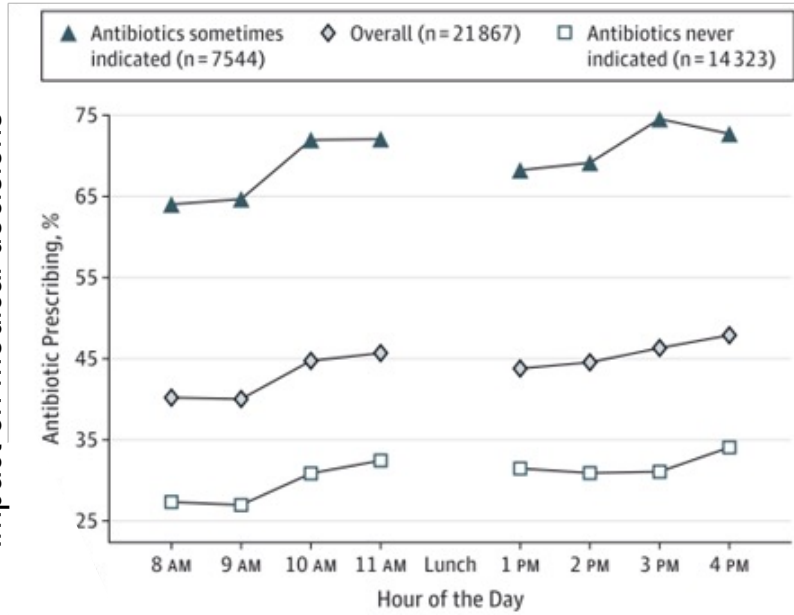


- Cognitive control corresponds to a specific neural network, (whose activity should change with fatigue)

How to measure fatigue? ... with economic choice

one day of work

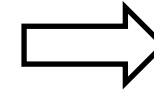
Impact on medical decisions



Impact on judiciary decisions



- Can daylong cognitive work affect LPFC activity?
- make choices more impulsive?



Figner et al. Nat Neurosci 2010
Essex et al. J Neurosci 2012

The concept of cognitive fatigue (as opposed to ego depletion)

1) **Biological substrate** is not blood glucose but the lateral PFC

- Isolate difference in cognitive control between tasks / check with fMRI



2) **Time scale** is not seconds or minutes but from hours to weeks

- Compare beginning and end of a workday / of a week-long work program



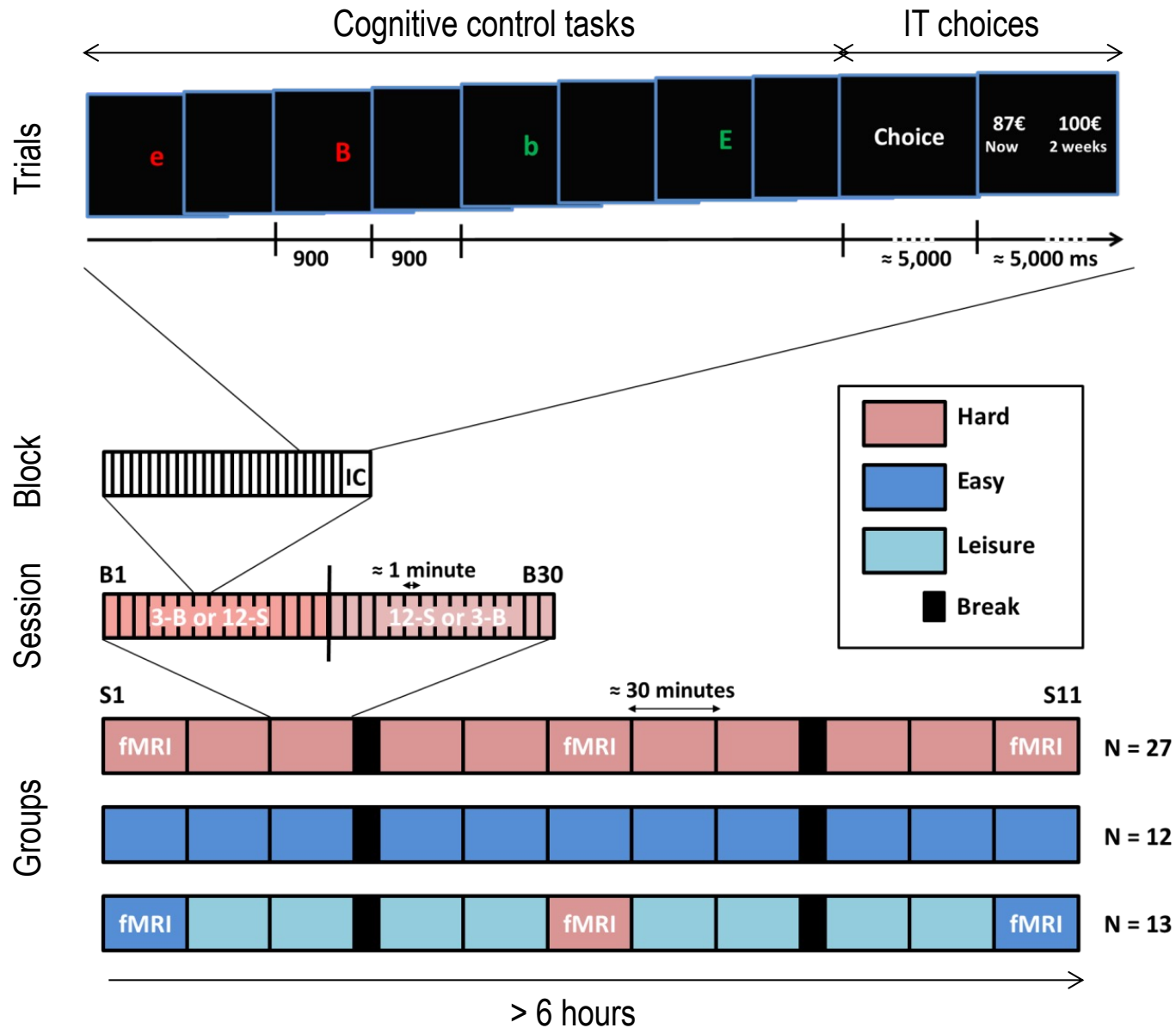
3) **Underlying mechanism** is not resource depletion but cost/benefit adaptation

- Test effects on economic choice, not task performance

10€	11€
now	tomorrow

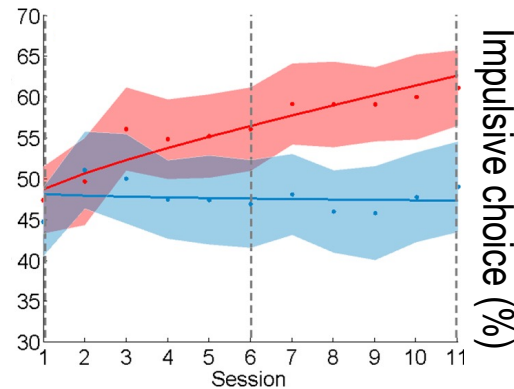
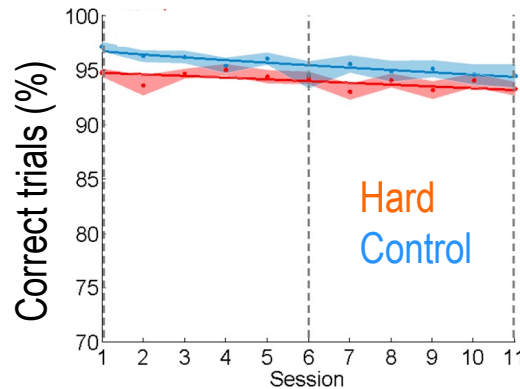
How to induce and reveal cognitive fatigue

Blain et al. PNAS 2016

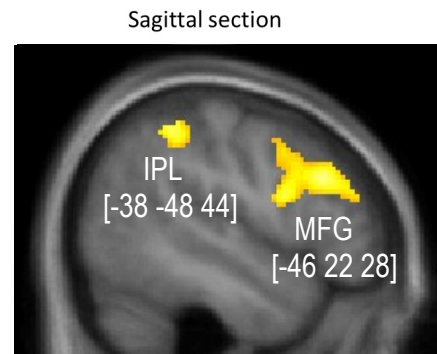
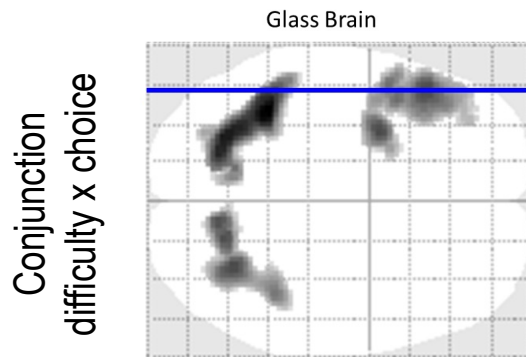


Behavioral and neural effects of cognitive fatigue

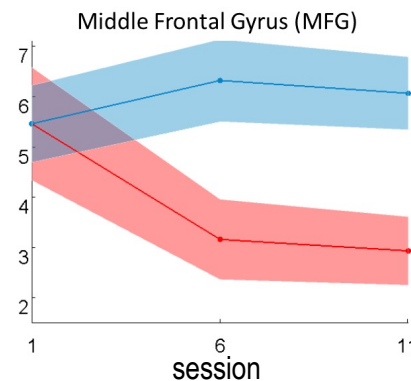
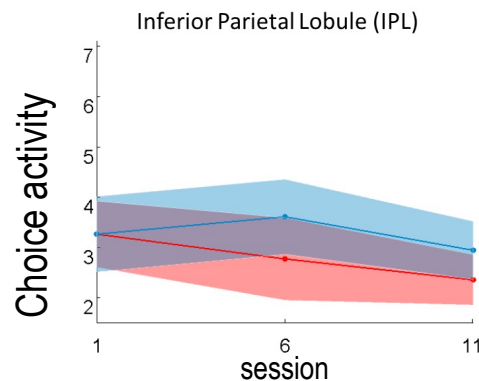
Blain et al. PNAS 2016



➤ Cognitive fatigue:
- increases choice impulsivity
(but no effect on performance)



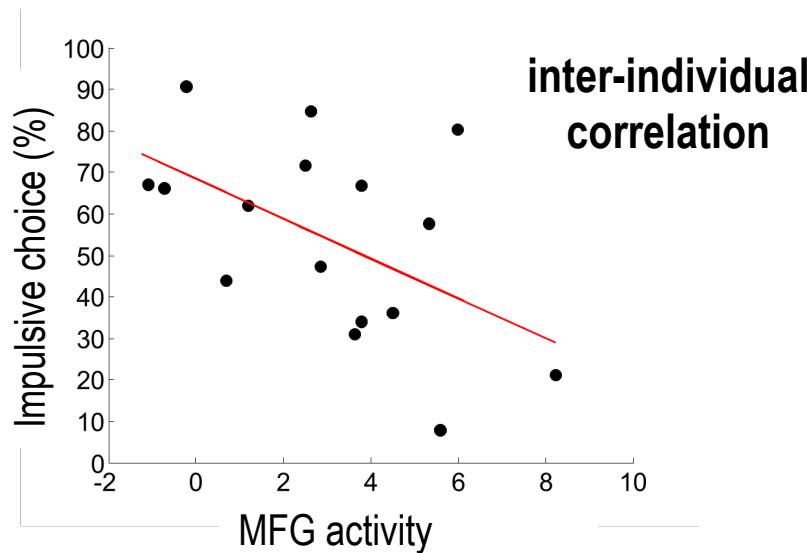
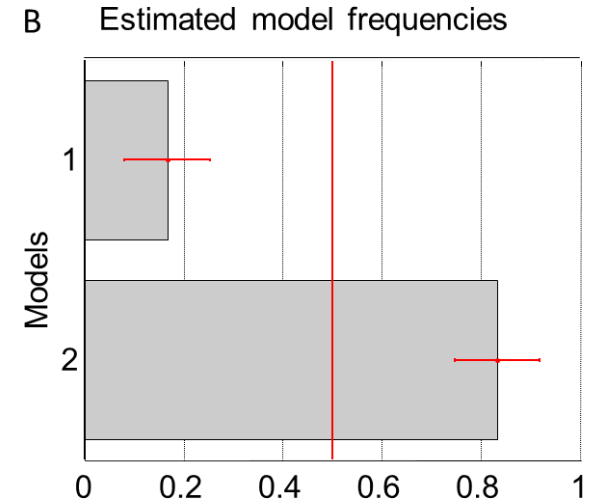
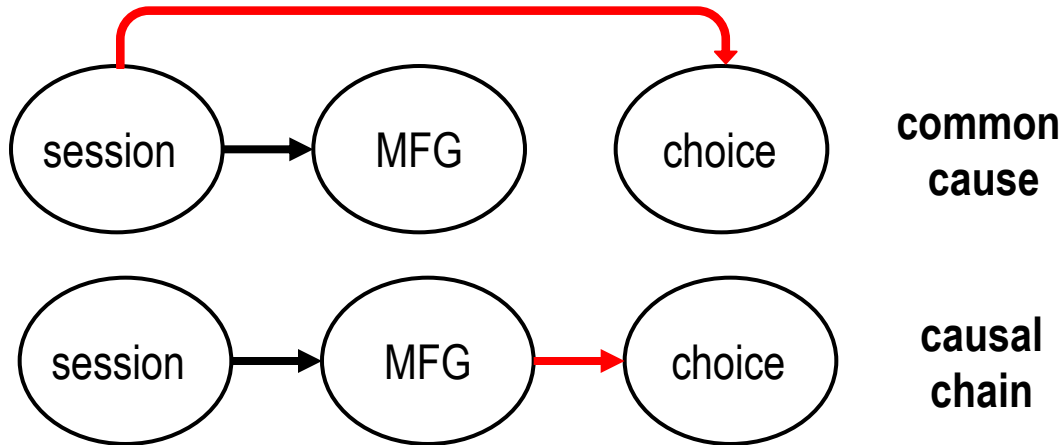
NB: subjects trained
so as to start with
95% correct response
50% impulsive choice



➤ Cognitive fatigue:
- reduces IPFC activity
(but not any other brain region)

Brain-behavior correlation (mediation analysis)

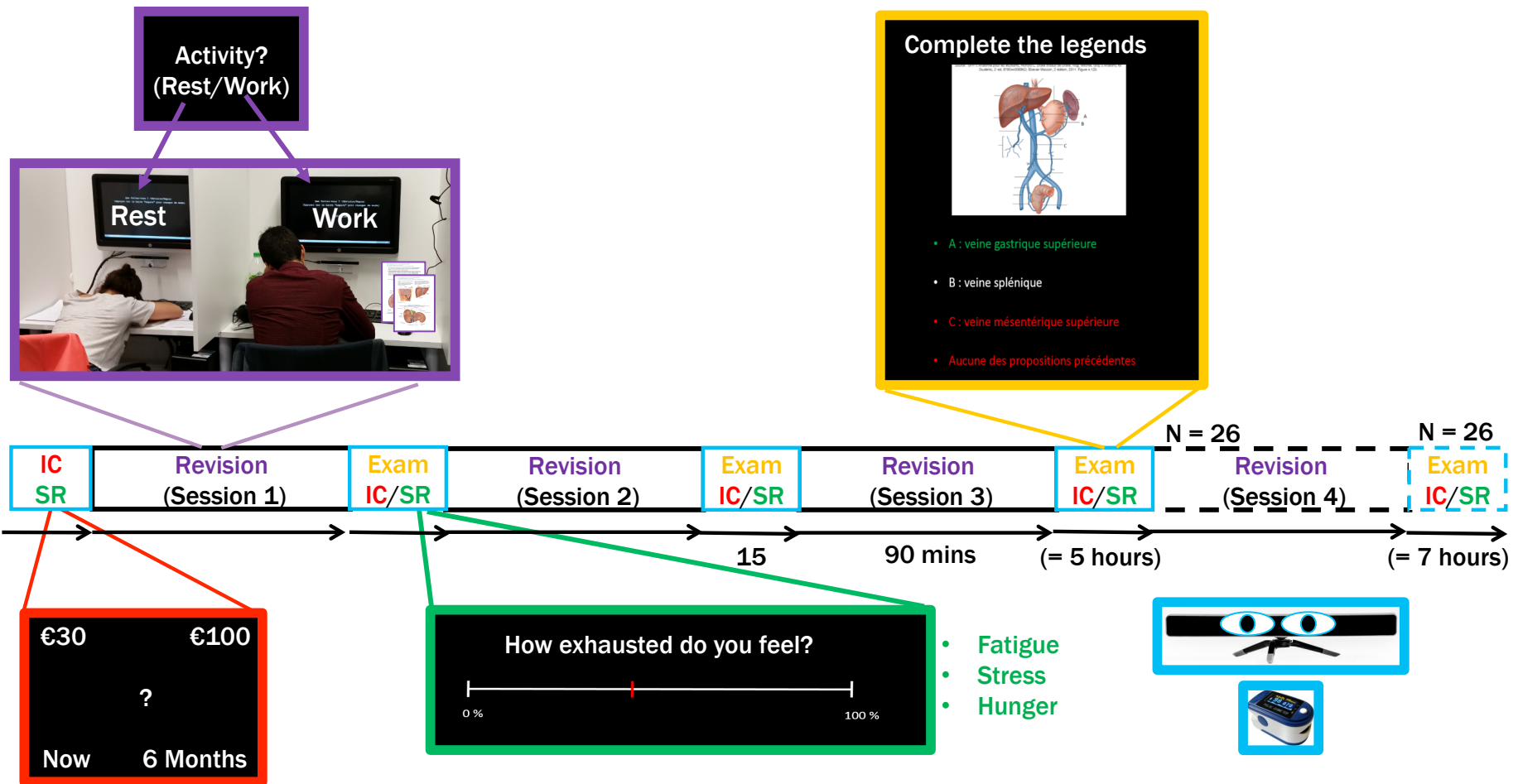
Blain et al. PNAS 2016



➤ IPFC activity mediates the effect of cognitive fatigue on choice impulsivity

A more ecological paradigm (at PRISME)

Naik et al. in prep

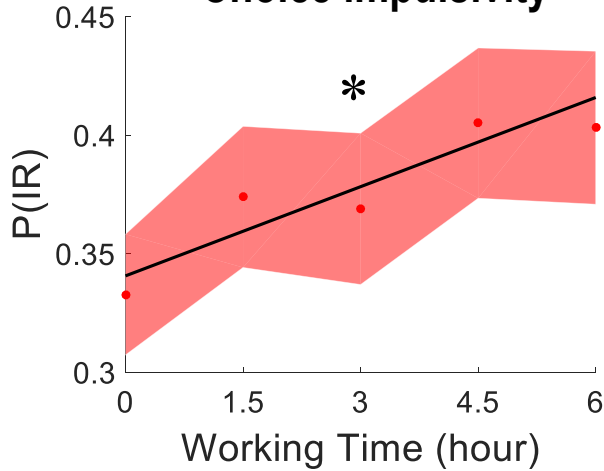


- Exam revisions instead of cognitive control tasks
- Breaks allowed

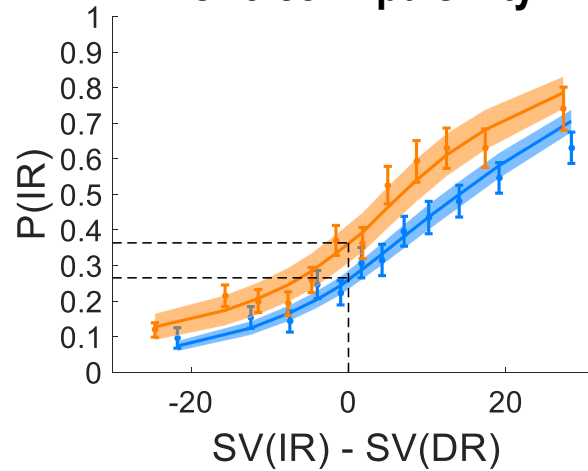
Revisions & impulsivity: computational analysis

Naik et al. in prep

Choice impulsivity



Choice impulsivity

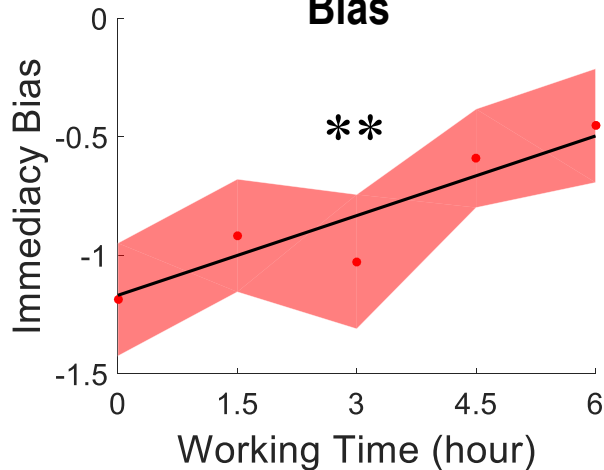


Discounting function

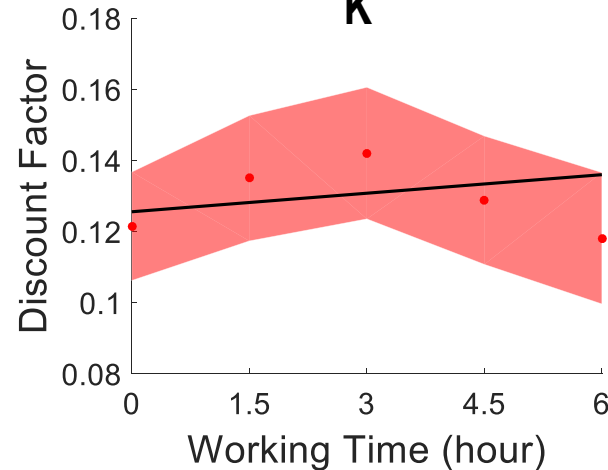
$$V_d = R \cdot \exp(-k \cdot D)$$

$$V_i = R$$

Bias



K



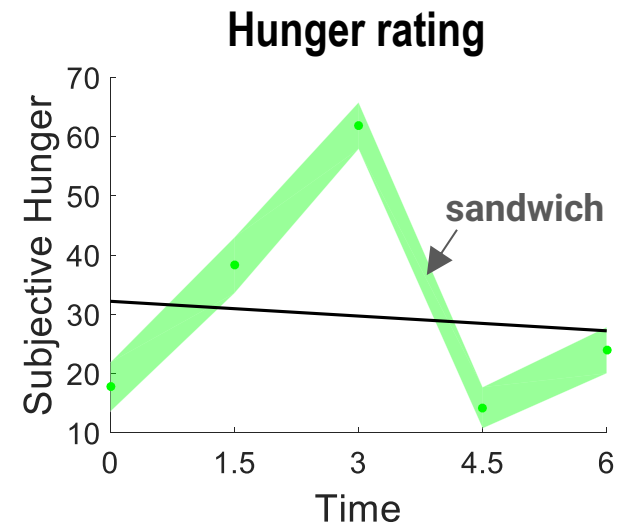
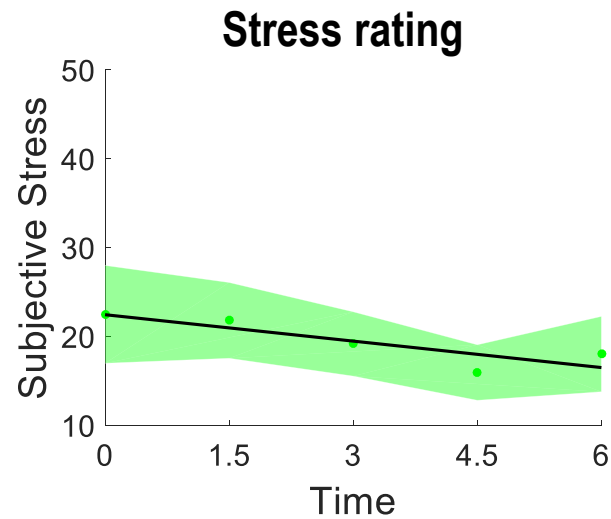
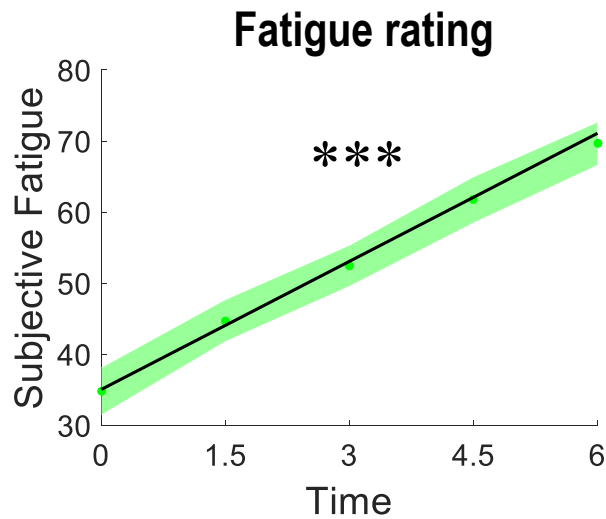
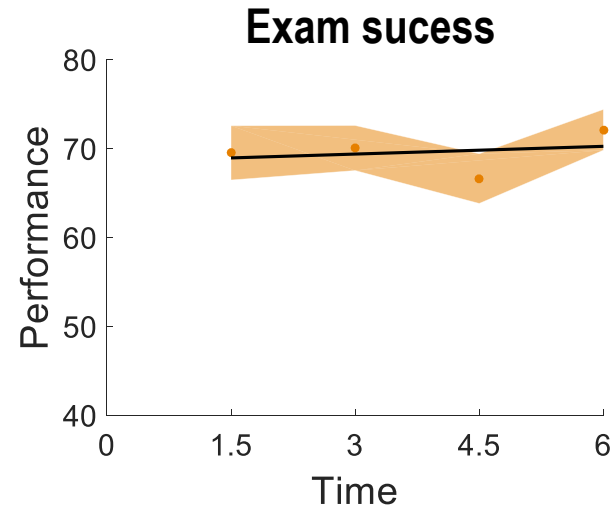
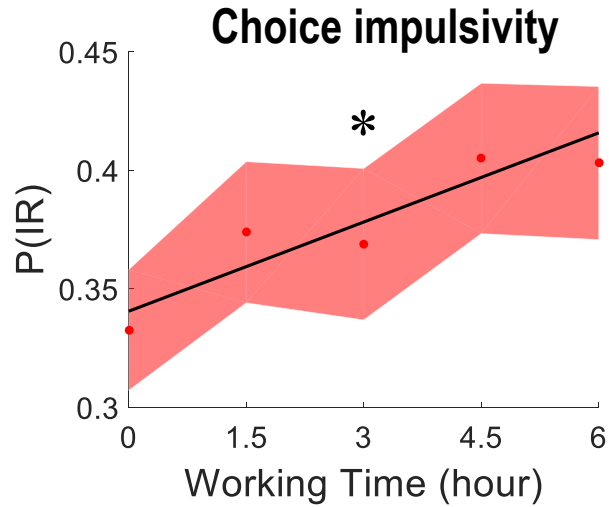
Choice rule

$$P_i = 1 / (1 + \exp(-\beta \cdot (V_i - V_d + \text{bias})))$$

➤ More cognitive fatigue
= higher immediacy bias

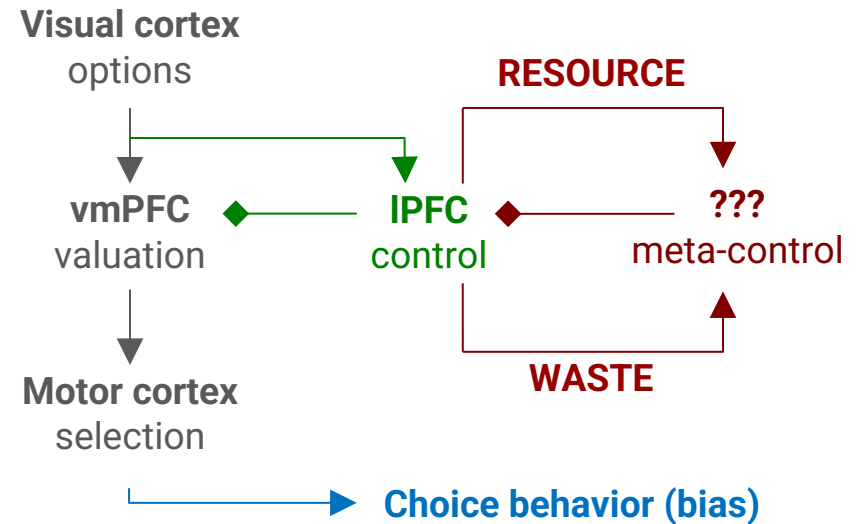
Revisions & impulsivity: link with subjective fatigue

Naik et al. in prep

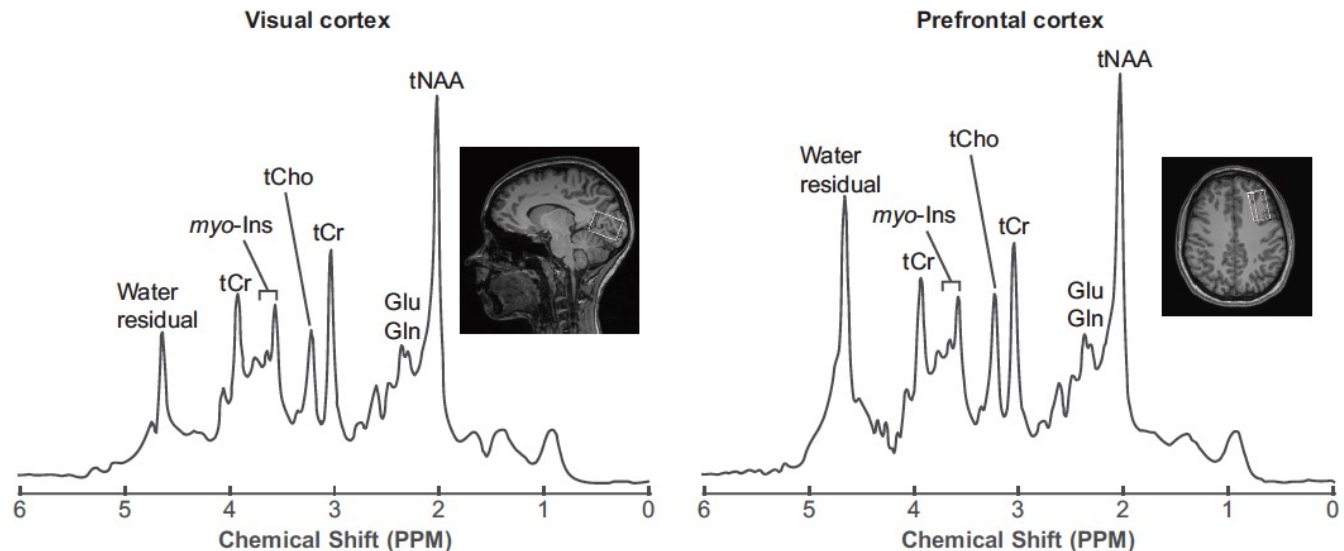


Question: why exerting control would increase its cost?

- Because of functional adaption?
(Kurzban et al. 2013; Inzlicht et al. 2014)
- Or biological alteration?
(Baumeister et al., 2017; Holroyd, 2016)
= energy depletion? waste accumulation?
- Or both?

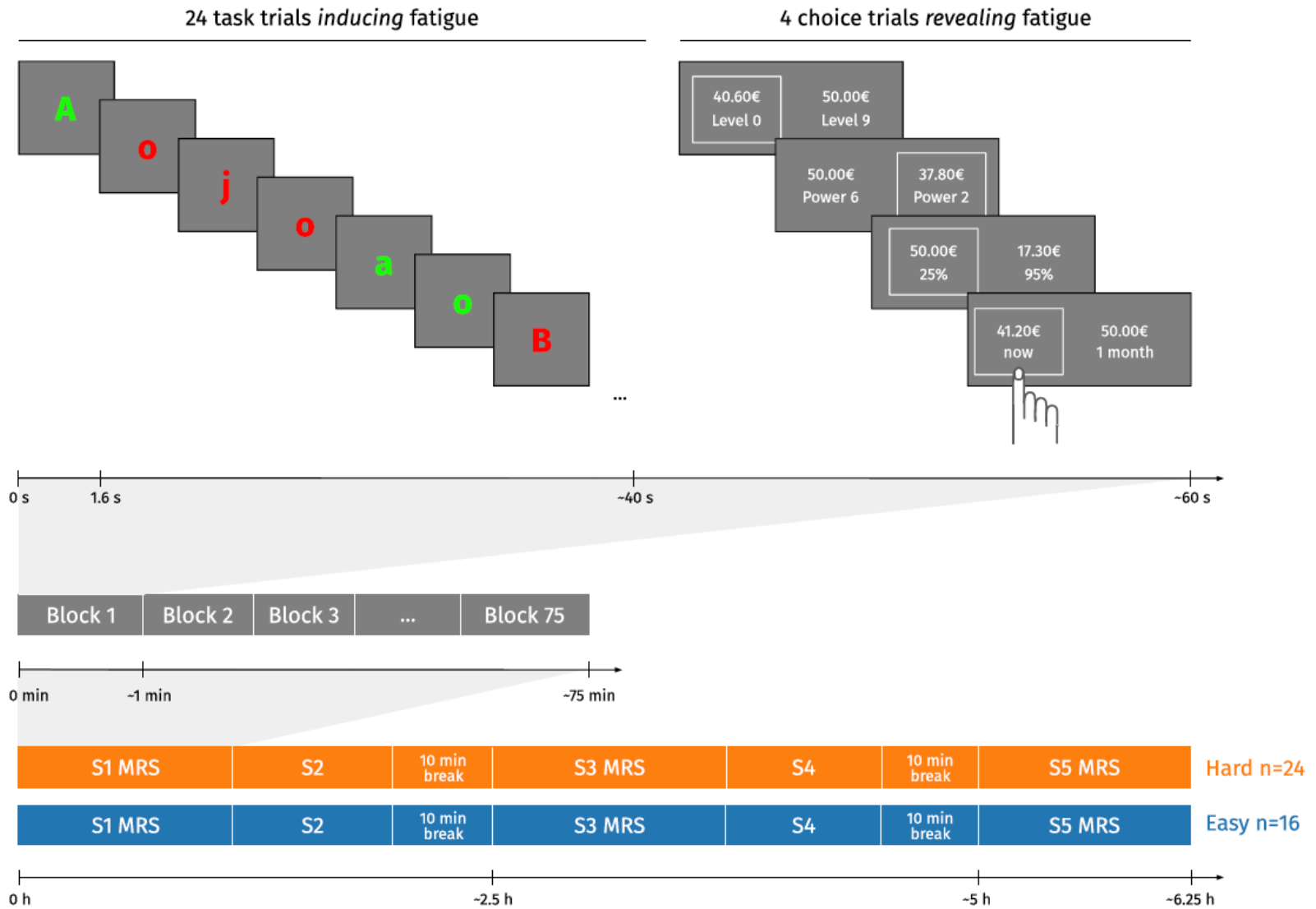


Spectroscopy experiments



How to induce and reveal cognitive fatigue

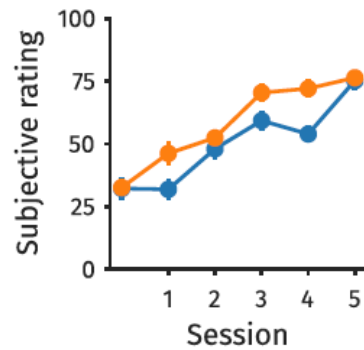
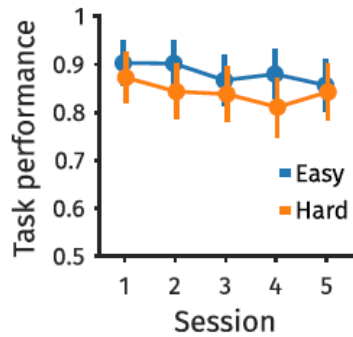
Wiehler et al. *Cur Biol* 2022



➤ Same behavioral tasks, now looking for neuro-metabolic markers of cognitive fatigue

Computational decomposition of choice behavior

Wiehler et al. *Cur Biol* 2022

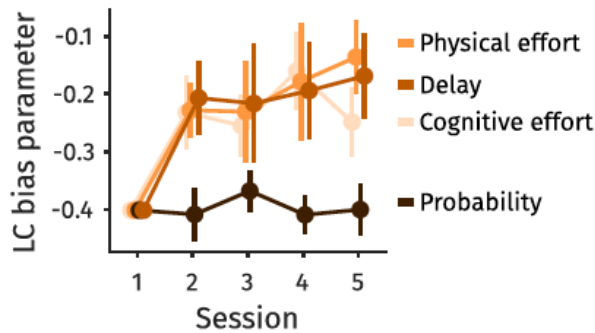
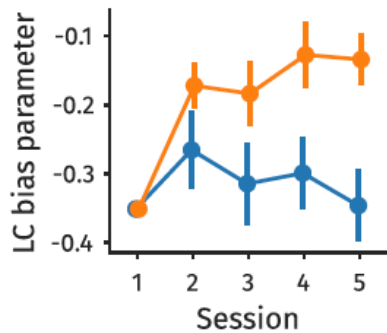


Discounting function

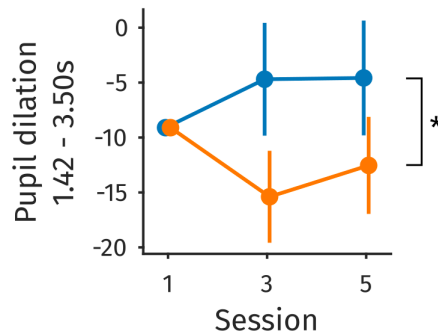
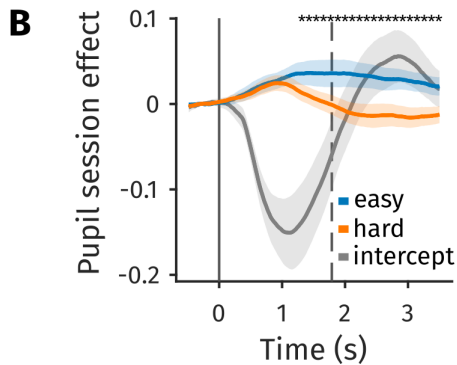
$$V = R \cdot \exp(-k \cdot D)$$

Choice rule

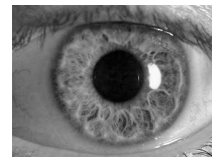
$$P_i = 1 / (1 + \exp(-\beta \cdot (V_i - V_d + \text{bias})))$$



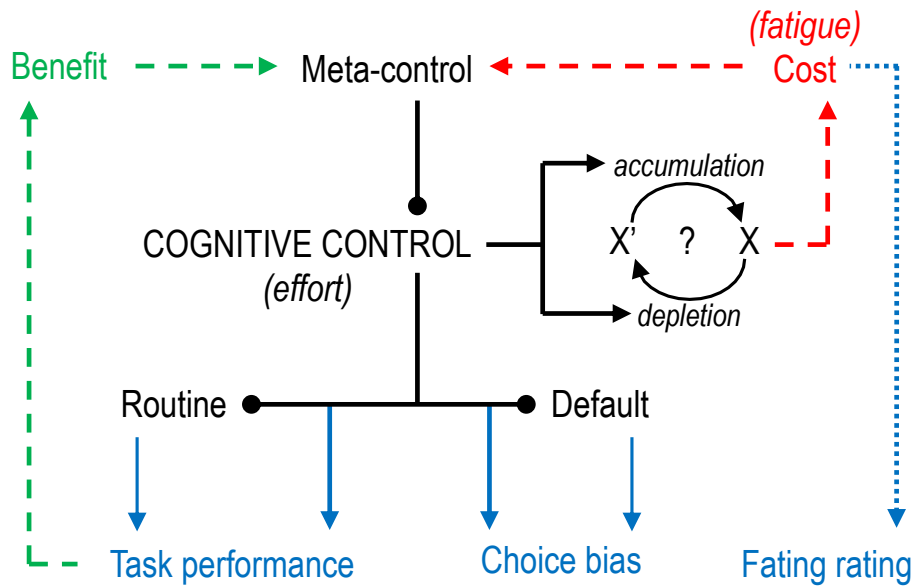
➤ 0-cost bias parameter (no wait, no effort) = better marker of fatigue than introspection or performance



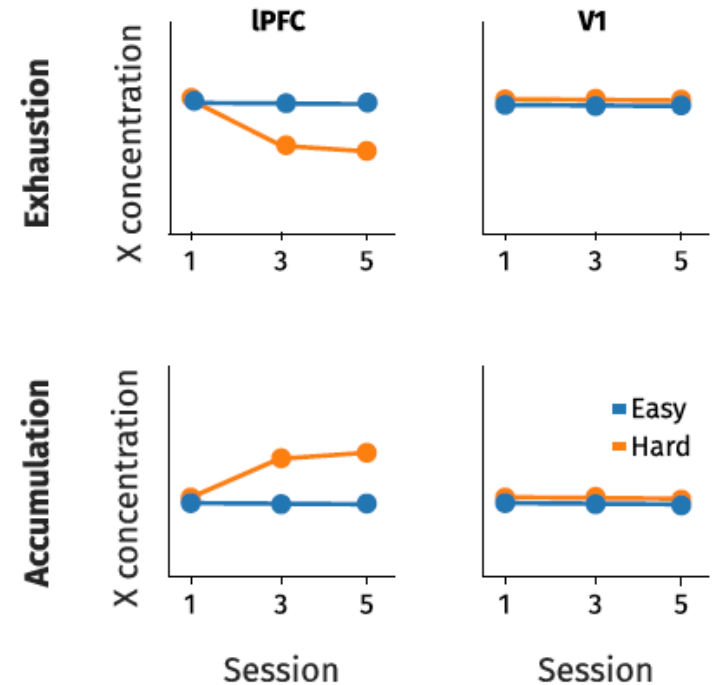
Pupil size



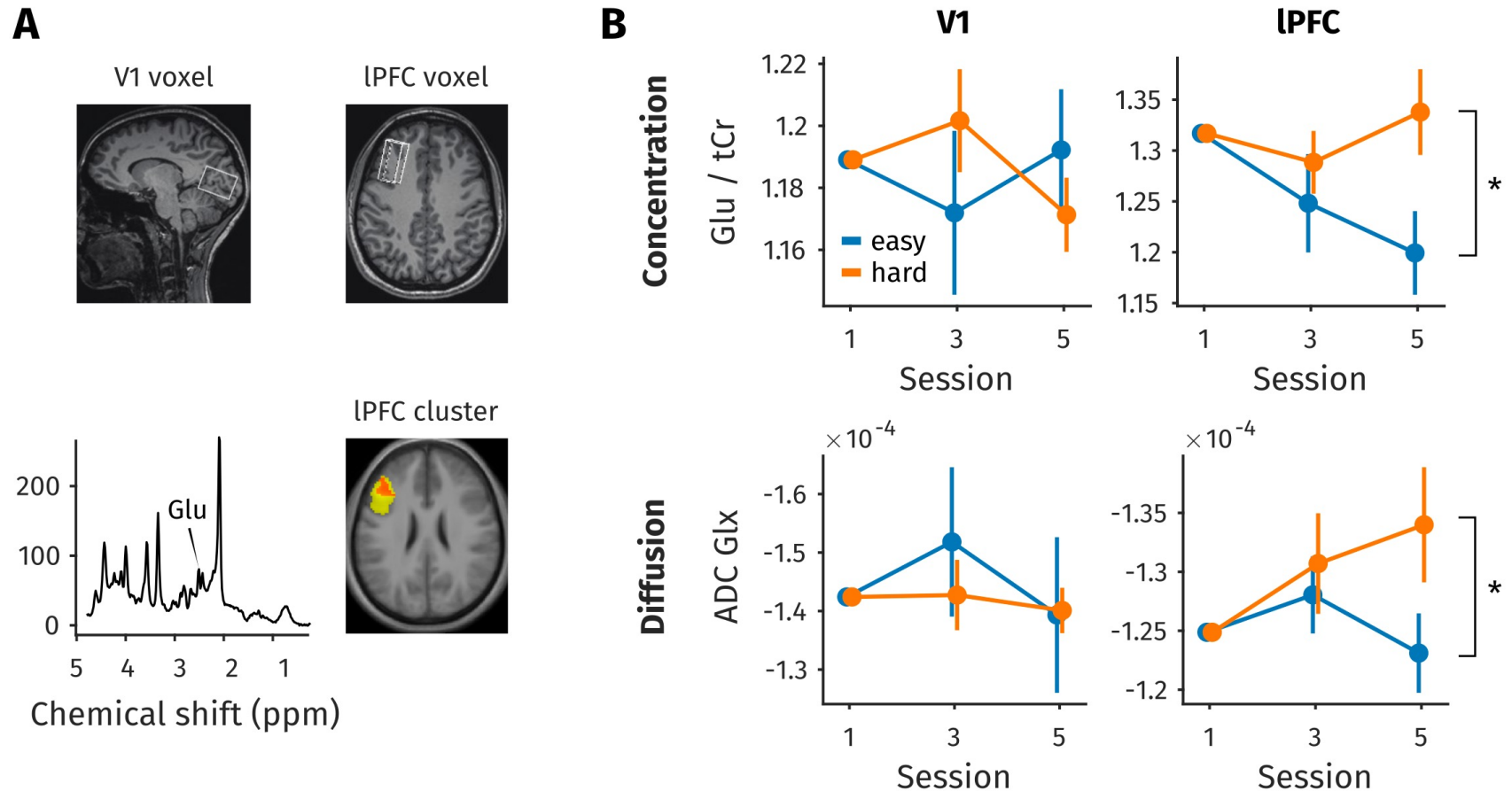
➤ Reduced pupil dilation = less control over choices



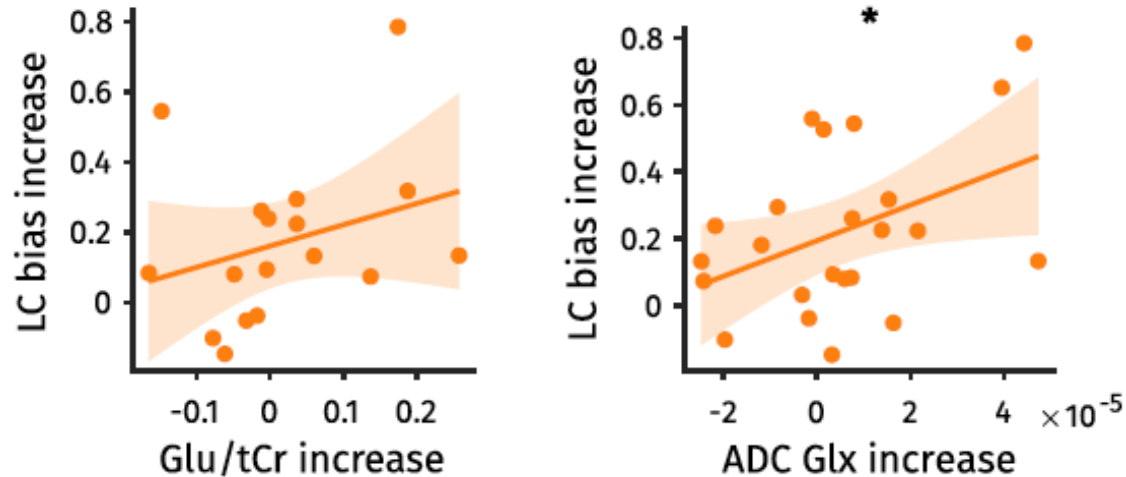
MR spectroscopy



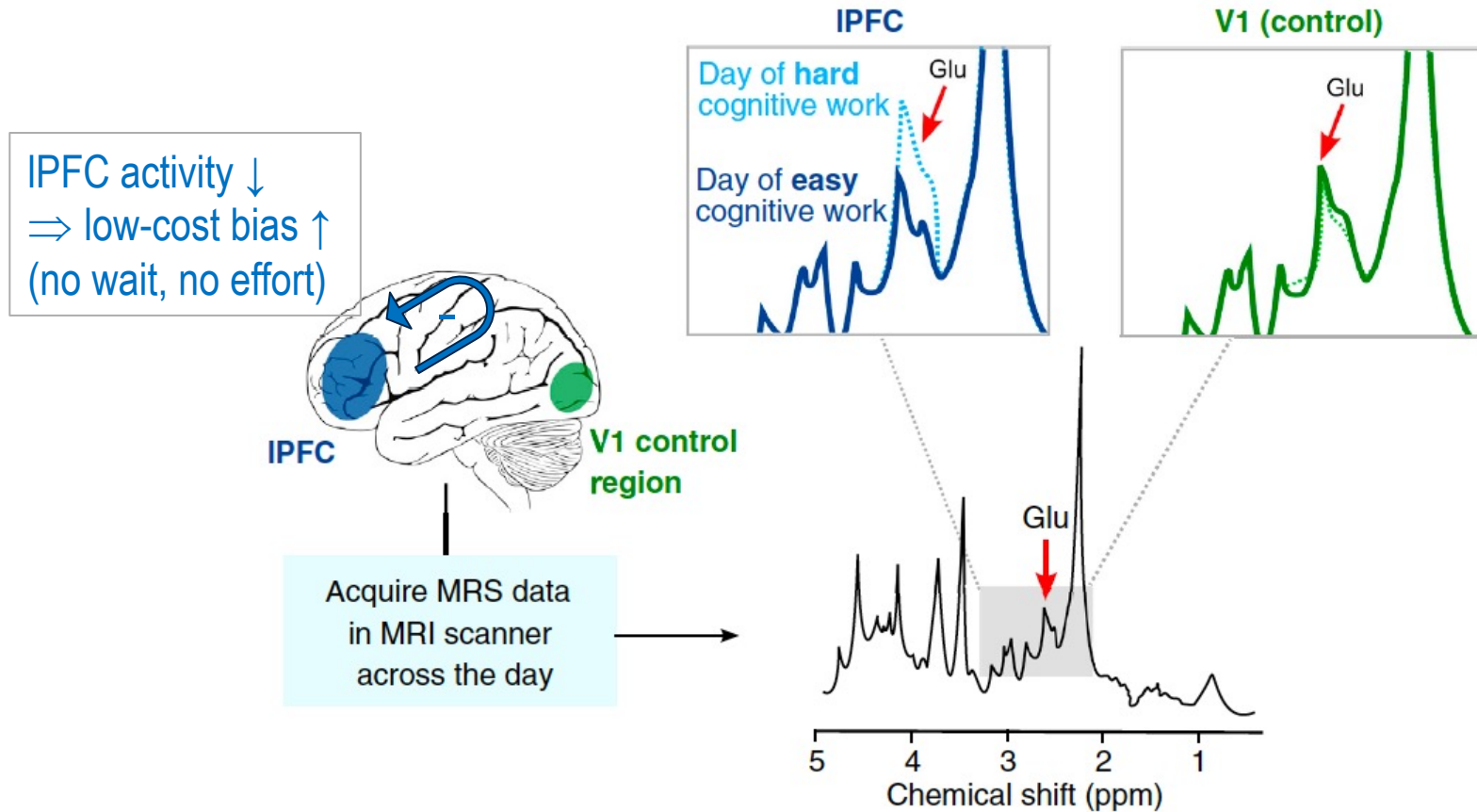
- Whether the exhaustion theory or the accumulation theory is correct, we expect a three-way interaction between group, region and session



- Three-way interaction (group x region x session)
- Glutamate accumulation in the synapse (or exhaustion in the cell) as a candidate explanation for cognitive fatigue



- Correlation between neuro-metabolic and behavioral signatures of cognitive fatigue
- At the end of the day:
participants with more glutamate accumulation in their LPFC synapses
=> show more pronounced shift toward low-cost options in their decisions



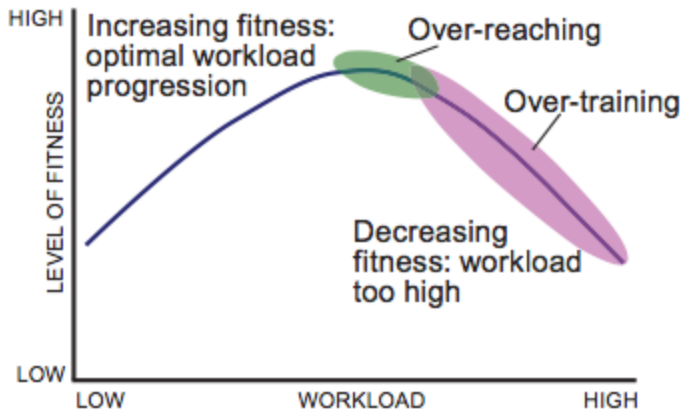
Applications to clinical conditions?

- Let's examine burnout syndrome in endurance athletes

The overtraining syndrome: a mysterious form of burnout in sport



SYMPTOMS OF OVERTRAINING SYNDROME		
<i>Performance Issues</i>	<i>Physiological Symptoms</i>	<i>Psychological Symptoms</i>
<ul style="list-style-type: none">• Early Fatigue• Increased Heart Rate w/less Effort• Decreased Strength, Endurance, Speed and Coordination• Decreased Aerobic Capacity• Delayed Recovery	<ul style="list-style-type: none">• Persistent Fatigue• On-going Muscle Soreness• Loss of Appetite• Excessive Weight Loss• Excessive Loss of Body Fat• Irregular Menses• Increased Resting Heart Rate• Chronic Muscle Soreness• Increase in Overuse Injuries• Difficulty Sleeping• Frequent Colds or Infections	<ul style="list-style-type: none">• Irritation or Anger• Depression• Difficulty in Concentration• Increased Sensitivity to Emotional Stress• Loss of Competitive Drive• Loss of Enthusiasm



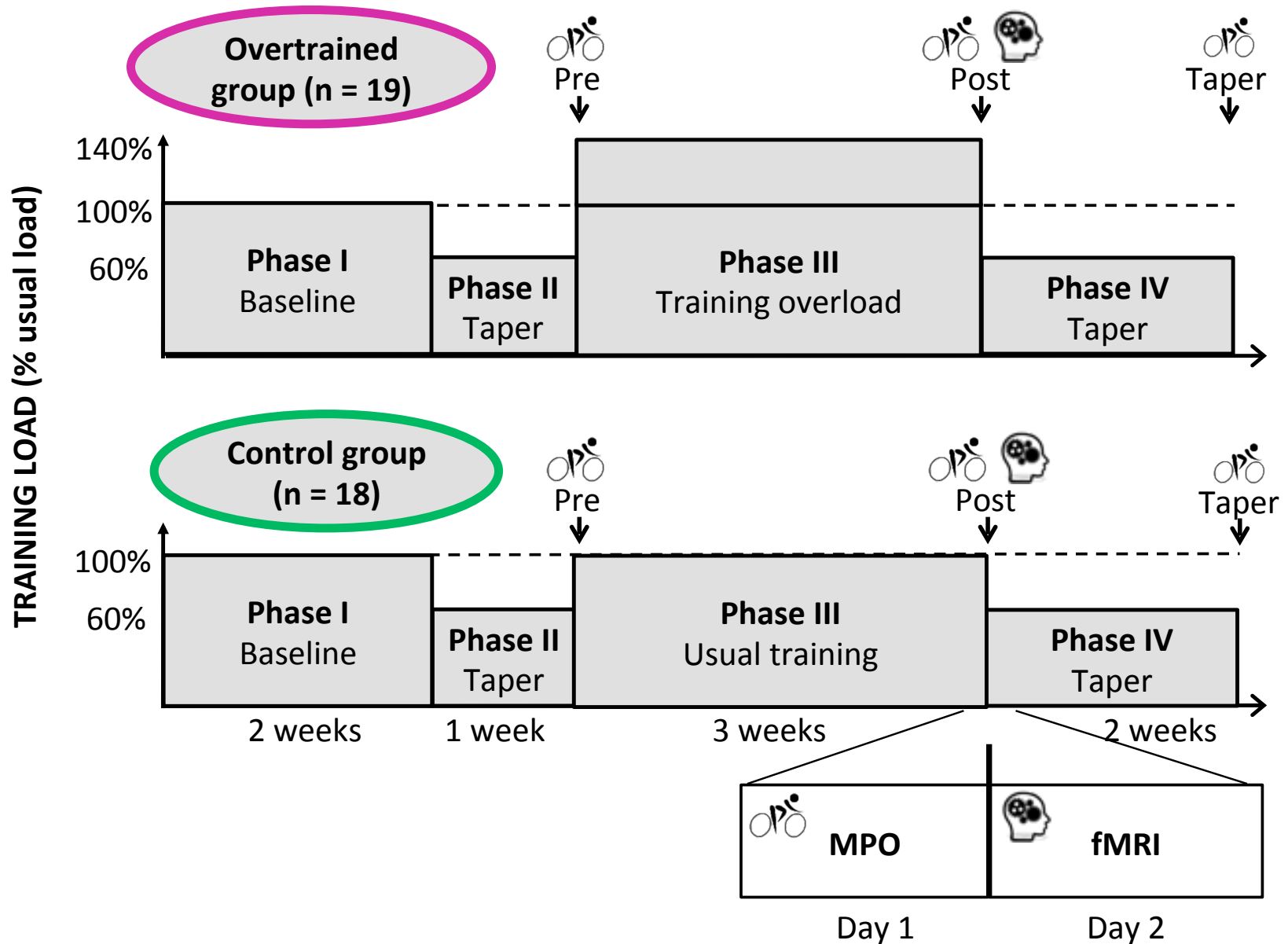
- **Training overload** might result in:
- decrease in performance
 - mental and physical fatigue
 - without other overtraining symptoms

Going on with training despite aversive signals (pain, fatigue) might require cognitive control

- Could overtraining represent another form of cognitive fatigue?
- Let's look at neural and behavioral signatures (LPFC activity) and (choice impulsivity)

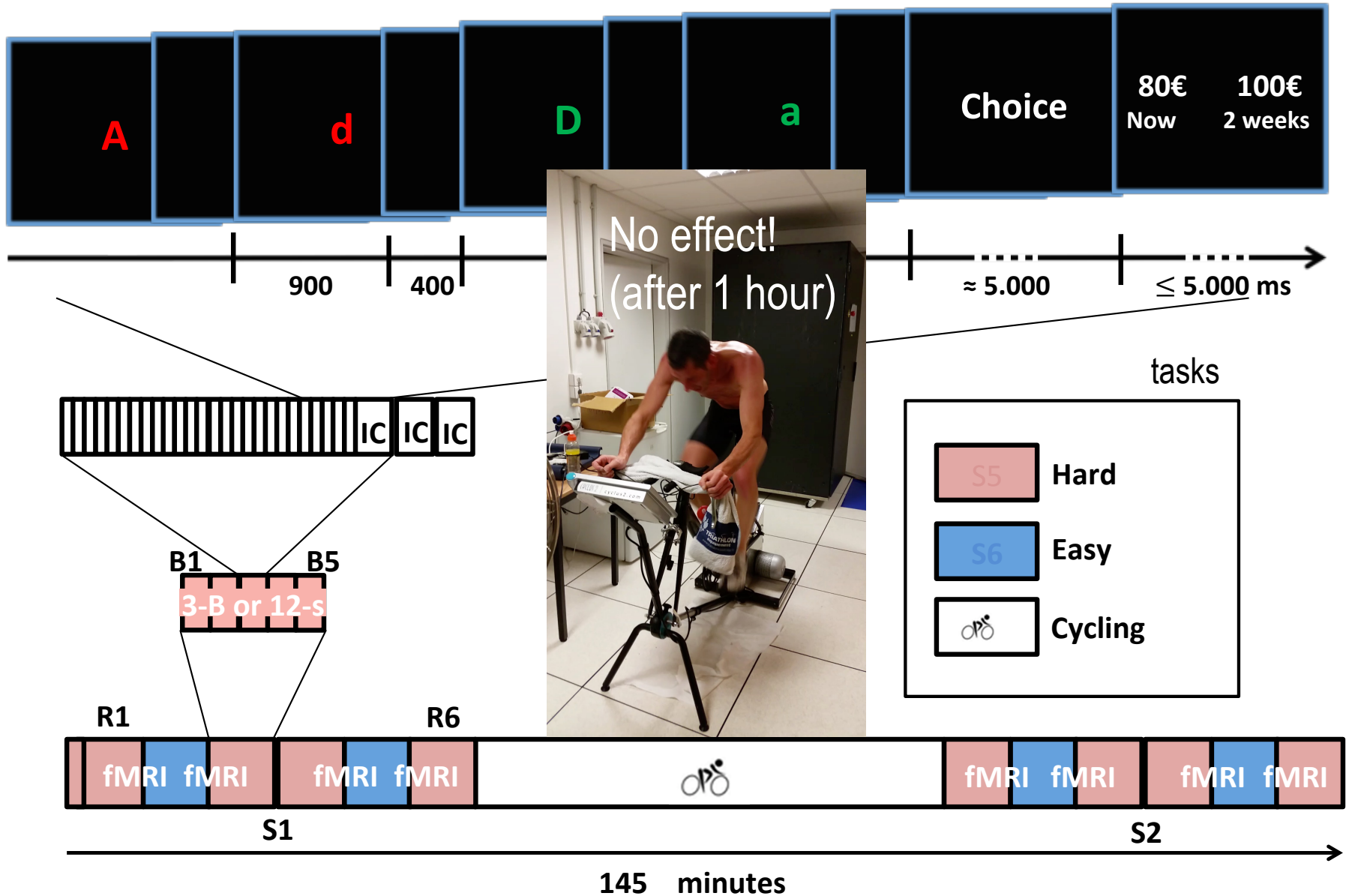
General training procedure (at Insep)

Blain et al. *Cur Biol* 2019



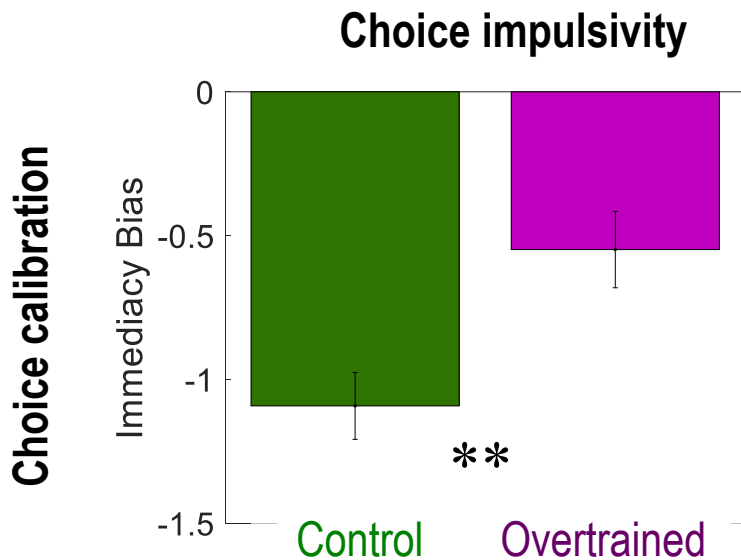
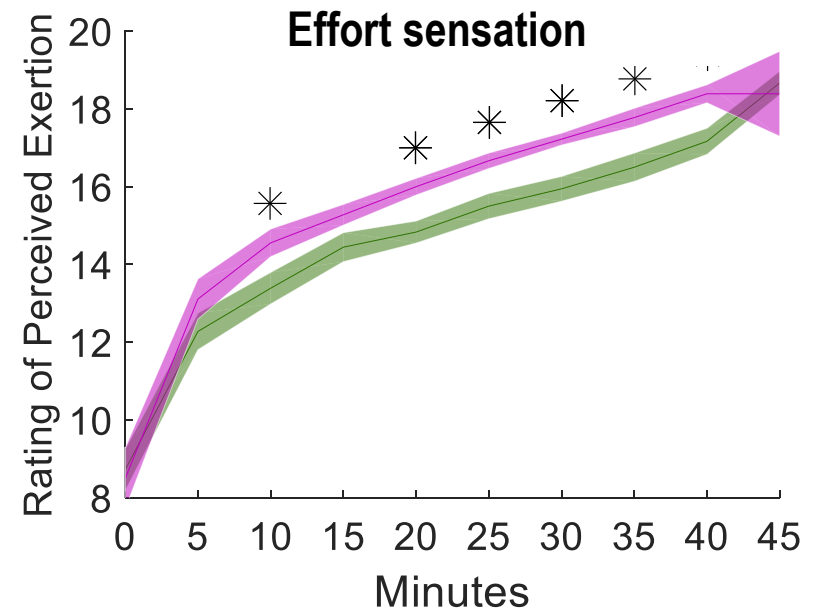
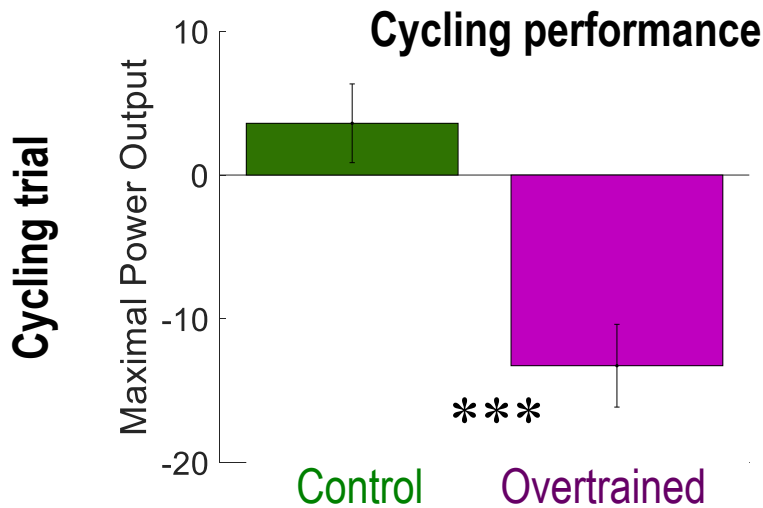
Post-training fMRI experiment

Blain et al. *Cur Biol* 2019



Checking the effects of training overload

Blain et al. *Cur Biol* 2019



Discounting function

$$V_d = R \cdot \exp(-k \cdot D)$$

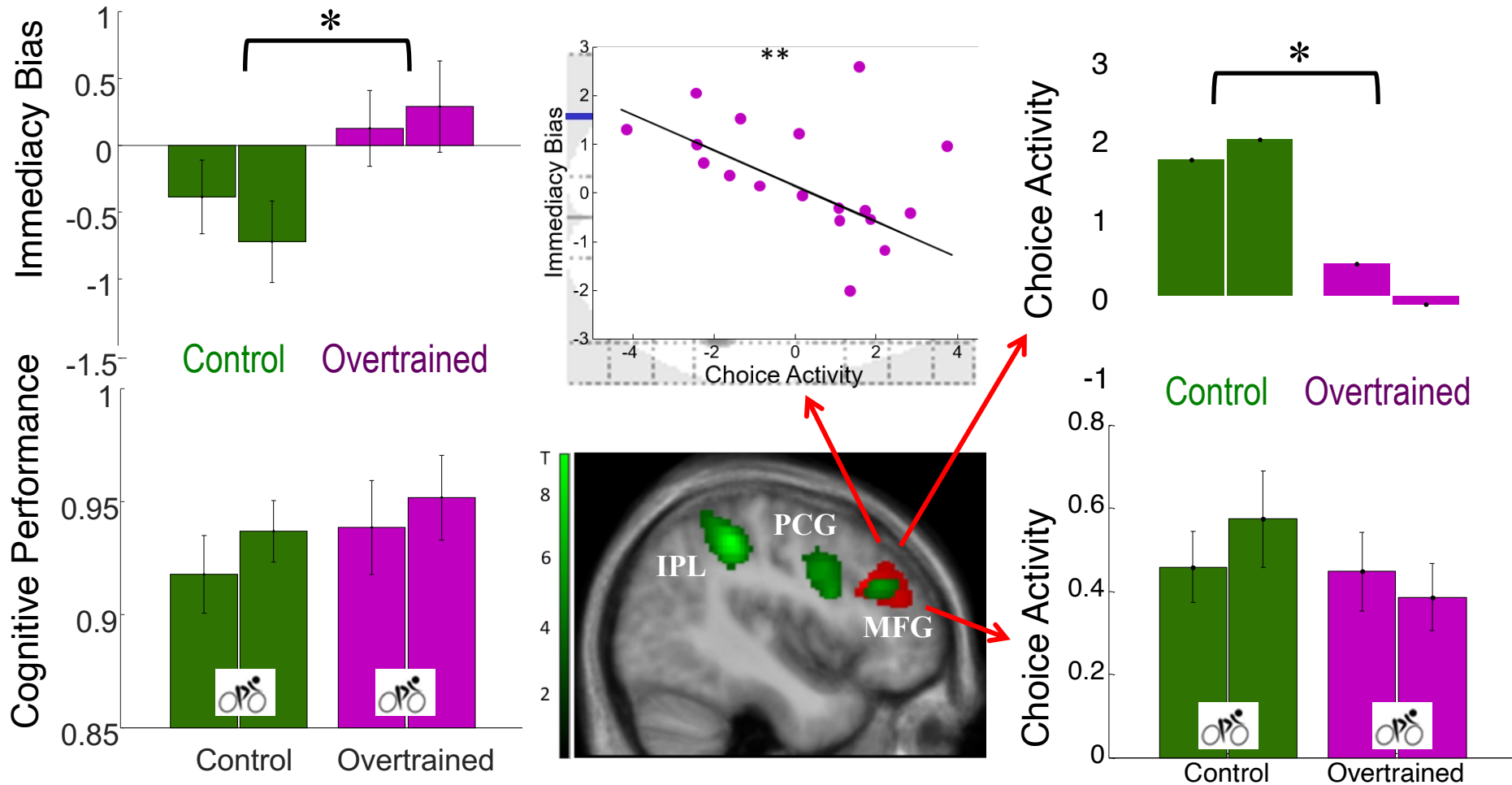
Choice rule

$$P_i = 1 / (1 + \exp(-\beta(V_i - V_d + \text{bias})))$$

➤ Training overload
= more immediacy bias

Impact of training overload on economic choice

Blain et al. *Cur Biol* 2019



➤ Training overload enhances choice impulsivity (but no effect on performance)

➤ Training overload reduces IPFC activity (but only during choice)

Conclusions

Origines de la fatigue cognitive

- La fatigue cognitive est due à l'exercice intense et prolongé de contrôle cognitif ...
- ... ce qui produit des changements neuro-métaboliques
(comme l'accumulation de glutamate dans les synapses du cortex préfrontal latéral)

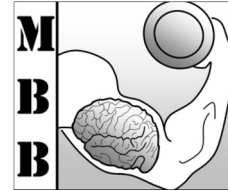
Conséquences de la fatigue cognitive

- La fatigue cognitive se traduit par une difficulté à mobiliser le contrôle cognitif pendant la prise de décision ...
- ... ce qui se manifeste par un changement de préférences lors de choix
(en faveur des options qui n'impliquent ni d'attendre ni de faire un effort)

Thanks to the MBB team

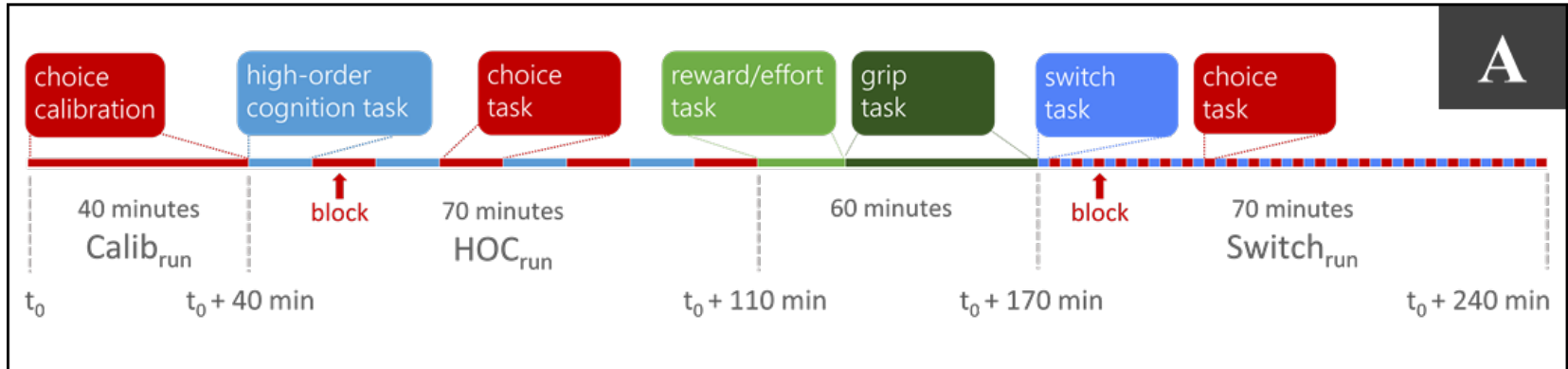
<https://sites.google.com/site/motivationbrainbehavior>

Paris Brain Institute
Fondation pour la Recherche Médicale
European Research Council



Fatigability in neuropsychological assessment

Facque et al. Cortex 2022



B

choice task

switch task

50.00€ 1 year	?	32.00€ 3 days
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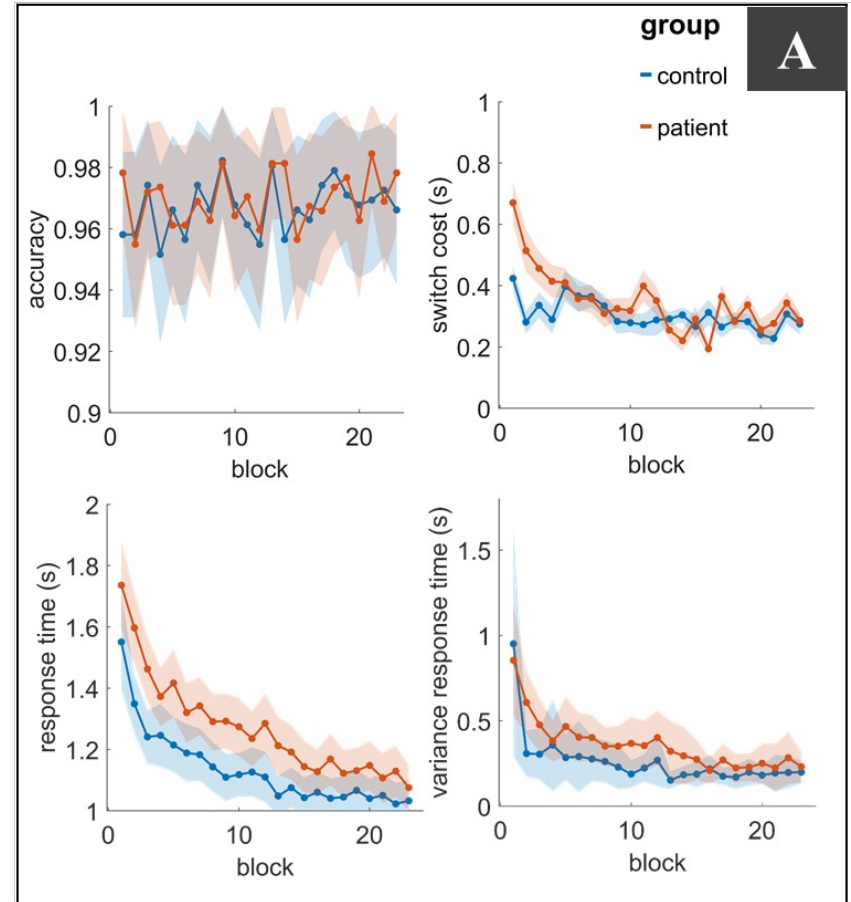
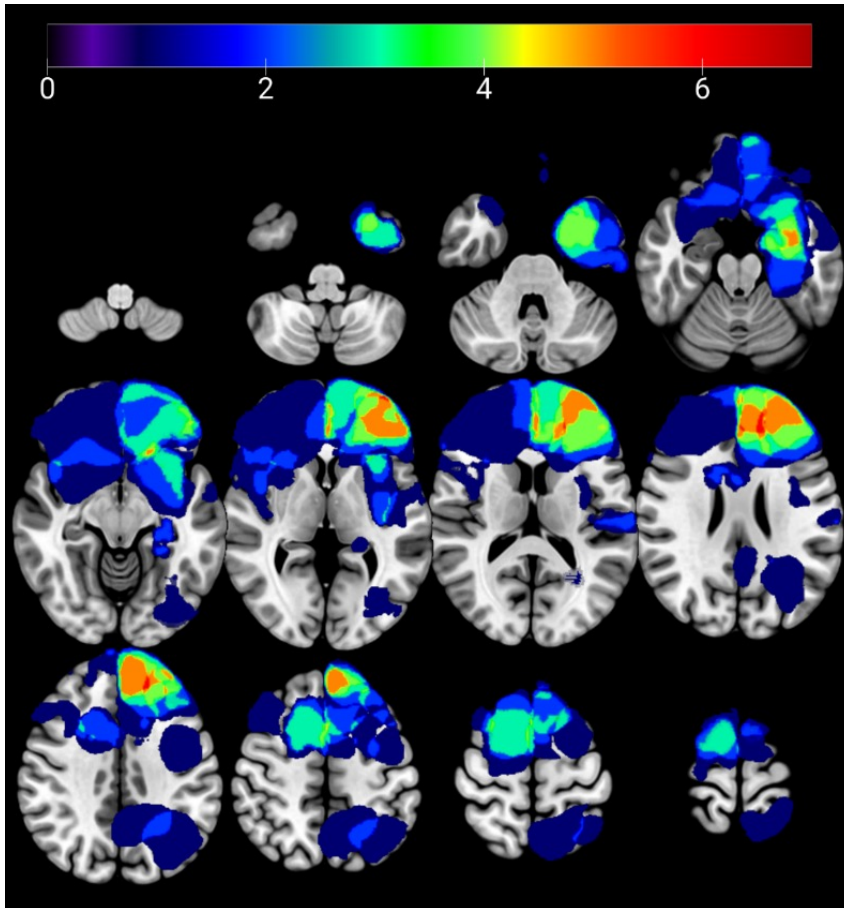
50.00€ 1 week	?	17.80€ now
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Lower case ex: « b » Upper case ex: « A » Vowel ex: « A » Consonant ex: « b »

Lower case ex: « b » Upper case ex: « A » Vowel ex: « A » Consonant ex: « b »

a

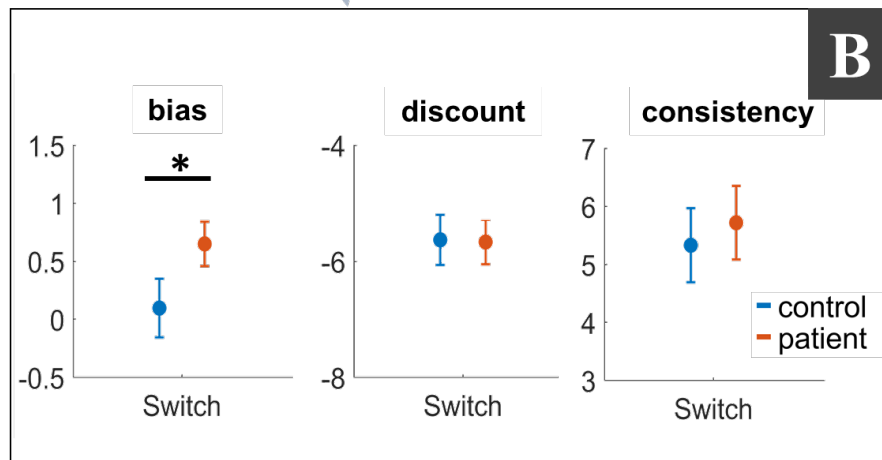
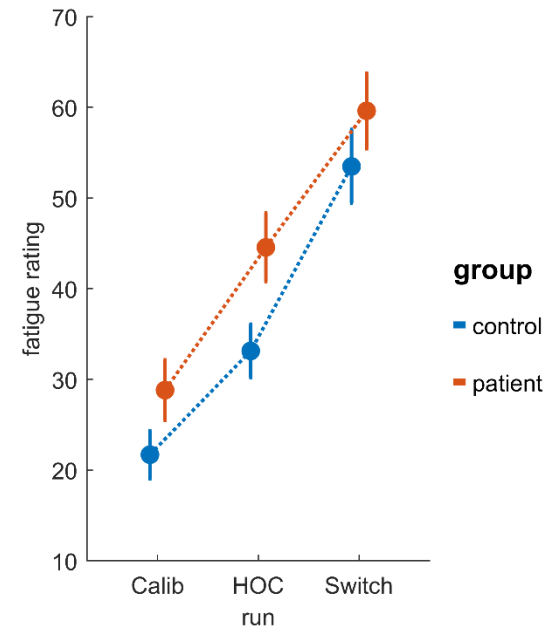
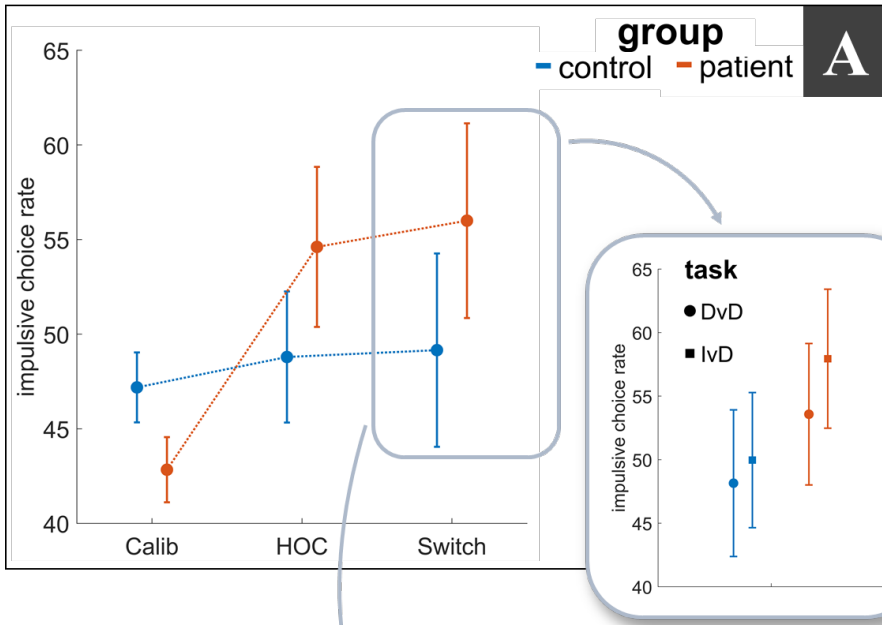
d



- Patients (n=29) with either intact or resected glioma compared to matched healthy controls (n=27)
- No interaction between group and time-on-task in cognitive control performance

Markers of cognitive fatigue

Facque et al. Cortex 2022



- Immediacy bias is a good marker of cognitive fatigue induced by cognitive control tasks
- No link with glioma-related brain regions, as if removing routines forces patients to use cognitive control, which induces fatigue