Why don't you try harder? Computational approach to motivation deficits

Mathias Pessiglione

Motivation, Brain and Behavior (MBB) team

Brain & Spinal chord Institute (ICM)

Hôpital de la Pitié-Salpêtrière, Paris, France

A case of motivation deficit

The issue with motivation deficits

- ✓ Frequent in most neurological and psychiatric conditions (e.g., apathy in Parkinson's disease)
- ✓ Poorly assessed by questionnaires (e.g., Starkstein's scale)

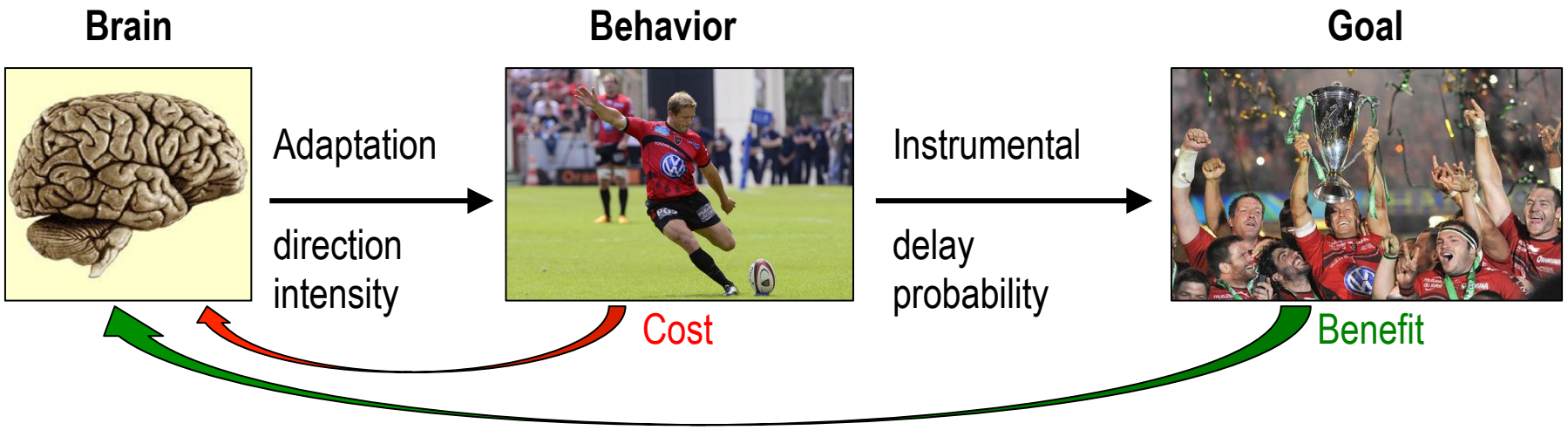
1. Are you interested in learning new things?	not at all	slightly	some	a lot
2. Does anything interest you?	not at all	slightly	some	a lot
3. Are you concerned about your condition?	not at all	slightly	some	a lot
4. Do you put much efffort into things?	not at all	slightly	some	a lot
5. Are you always looking for something to do?	not at all	slightly	some	a lot
6. Do you have plans and goals for the future?	not at all	slightly	some	a lot
7. Do you have motivation?	not at all	slightly	some	a lot
8. Do you have the energy for daily activities?	not at all	slightly	some	a lot
9. Does someone have to tell you what to do each day?	not at all	slightly	some	a lot
10. Are you indifferent to things?	not at all	slightly	some	a lot
11. Are you unconcerned with many things?	not at all	slightly	some	a lot
12. Do you need a push to get started on things?	not at all	slightly	some	a lot
13. Are you neither happy nor sad, just in between?	not at all	slightly	some	a lot
14. Would you consider yourself apathetic?	not at all	slightly	some	a lot

- ➢ Quick and simple but:
  - depends on quality of insight
  - no link with underlying neural mechanisms

- ➢ **<u>Use a computational approach</u>**

- Decompose motivation into variables and processes formalized in a mathematical model
- Fit the model on the behavior observed in objective tests to obtain computational phenotypes

Empirical definition of motivation



Motivation is a concept used by an observer to understand the behavior of an agent

In the framework of goal-directed behavior:

- Motivation as a process = adapts direction and intensity of the behavior
- Motivation as a content = the goal (an anticipated world state)
- Motivation as a quantity = the cost that the agent is willing to accept (corresponds to goal value)

Empirical assessment of motivation

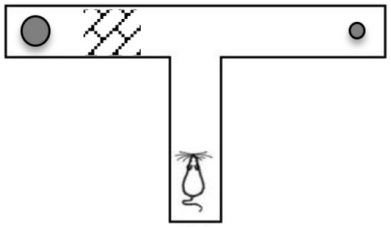
(effort discounting)

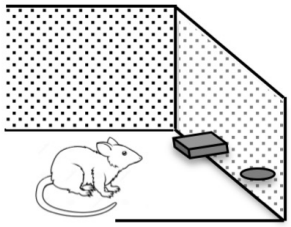
Binary choice task

(incentive motivation)

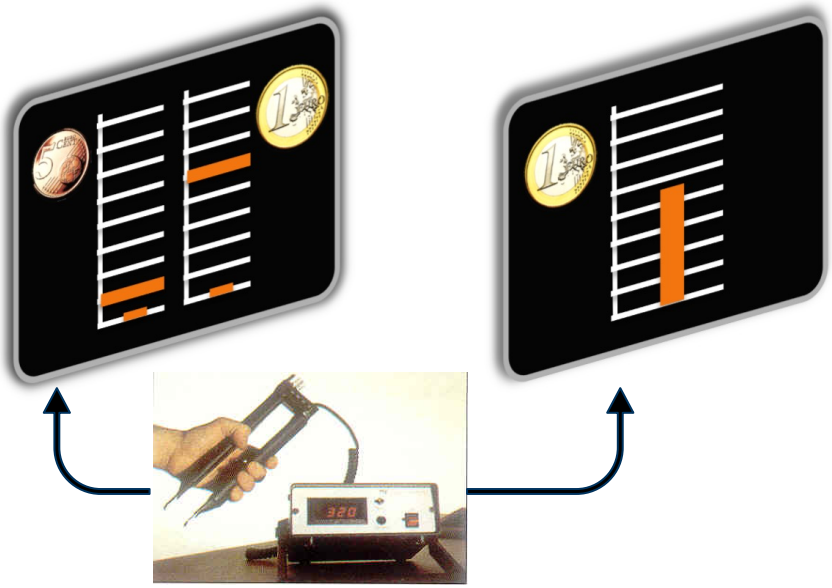
Free operant task

ANIMALS





HUMANS



Motivation (for a given reward)

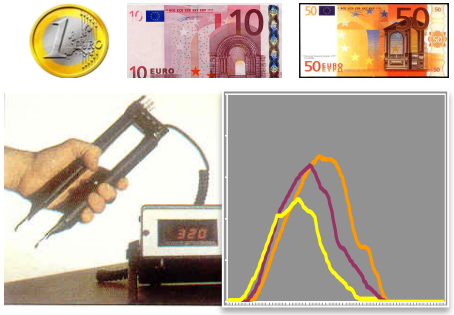
= the amount of effort

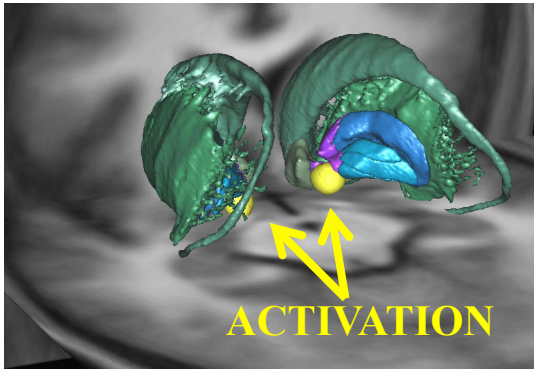
that the subject is willing to exert

Combining neuroimaging and patient studies

➢ Neuroimaging studies

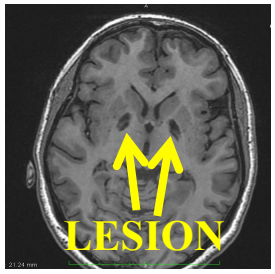
Implication of ventral striato-pallidum in subliminal motivation (Pessiglione et al. Science 2007)
of both mental and physical effort (Schmidt et al. Plos Biol 2012)

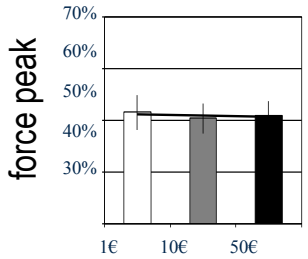




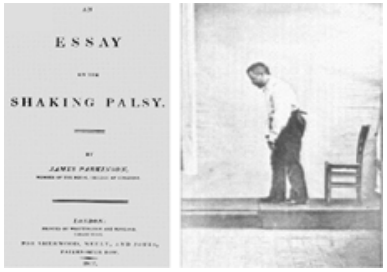
➢ Clinical studies

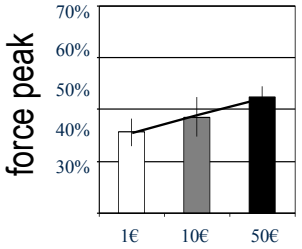
Motivation deficit (apathy) induced by bilateral striato-pallidal lesions (Schmidt et al. Brain 2008)
or striatal dopamine depletion (Le Bouc et al., J Neurosci 2016)





Auto-activation deficit



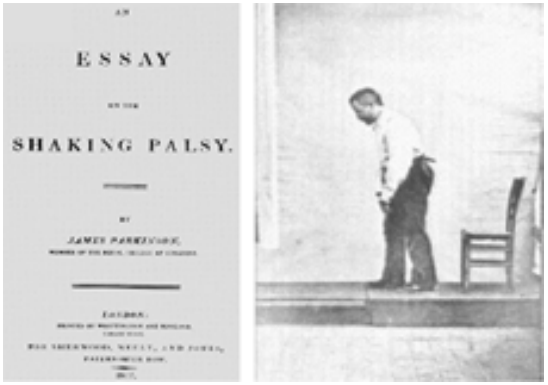


Parkinson's disease

Outline

How the brain adjusts the intensity of effort production

The issue of apathy in Parkinson's disease



Symptoms include both motor deficit (e.g. akinesia) and motivational deficit (e.g. apathy)

- **How can we explain a reduction of behavior?**
  - dysfunction of motor control
  - under-estimation of goal value
  - over-estimation of action cost

Control Parkinson

PD is primarily characterized by dopamine depletion, and treated with dopamine enhancers

- **What is the role of dopamine in these deficits?**

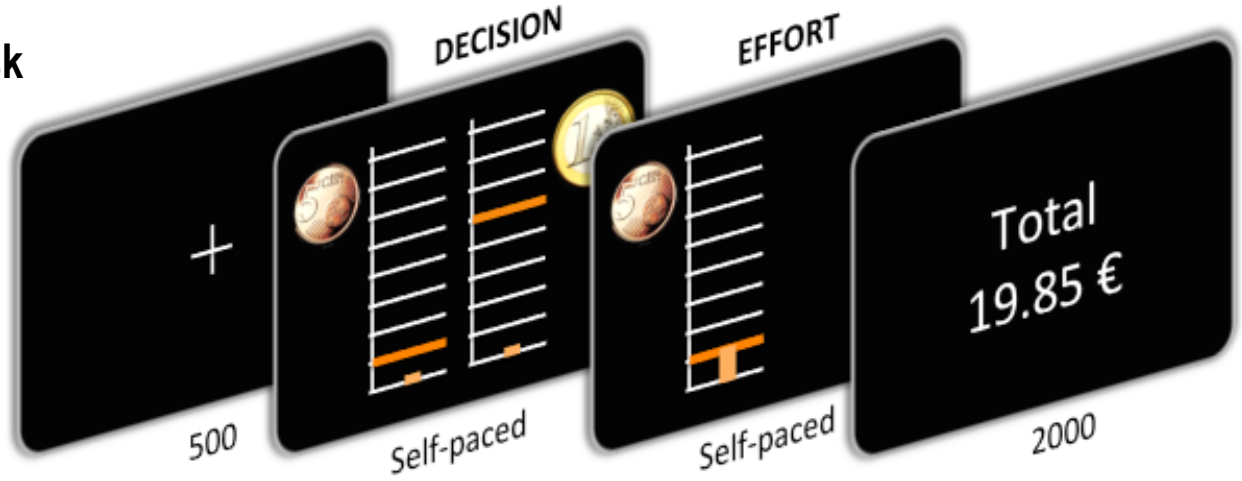
(would dopamine impact motor control, goal value, action cost, or any combination ?)

Two tasks implementing cost/benefit trade-off

Le Bouc et al. J Neurosci 2016

Effort-based choice task
(binary options)

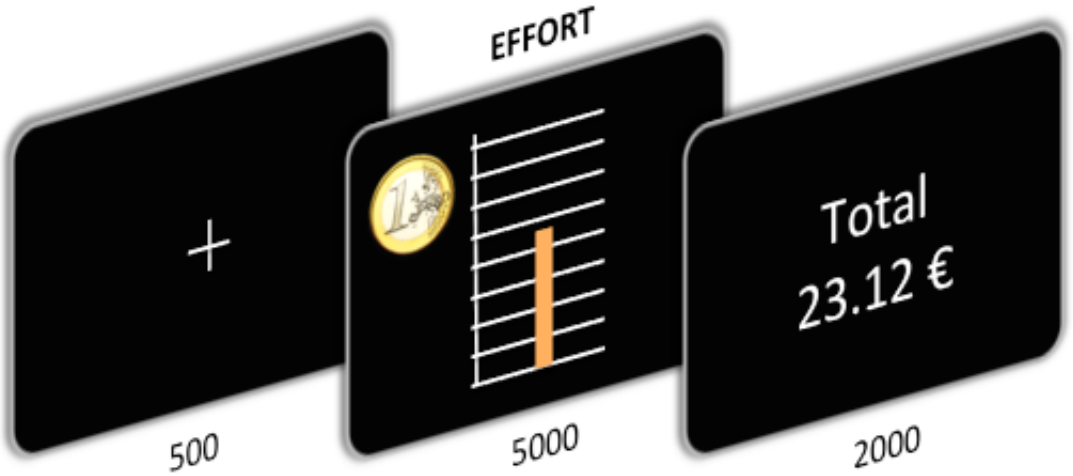
Payoff
= chosen option



- Force level is normalized to individual maximal force
- Payoff is proportional to peak force

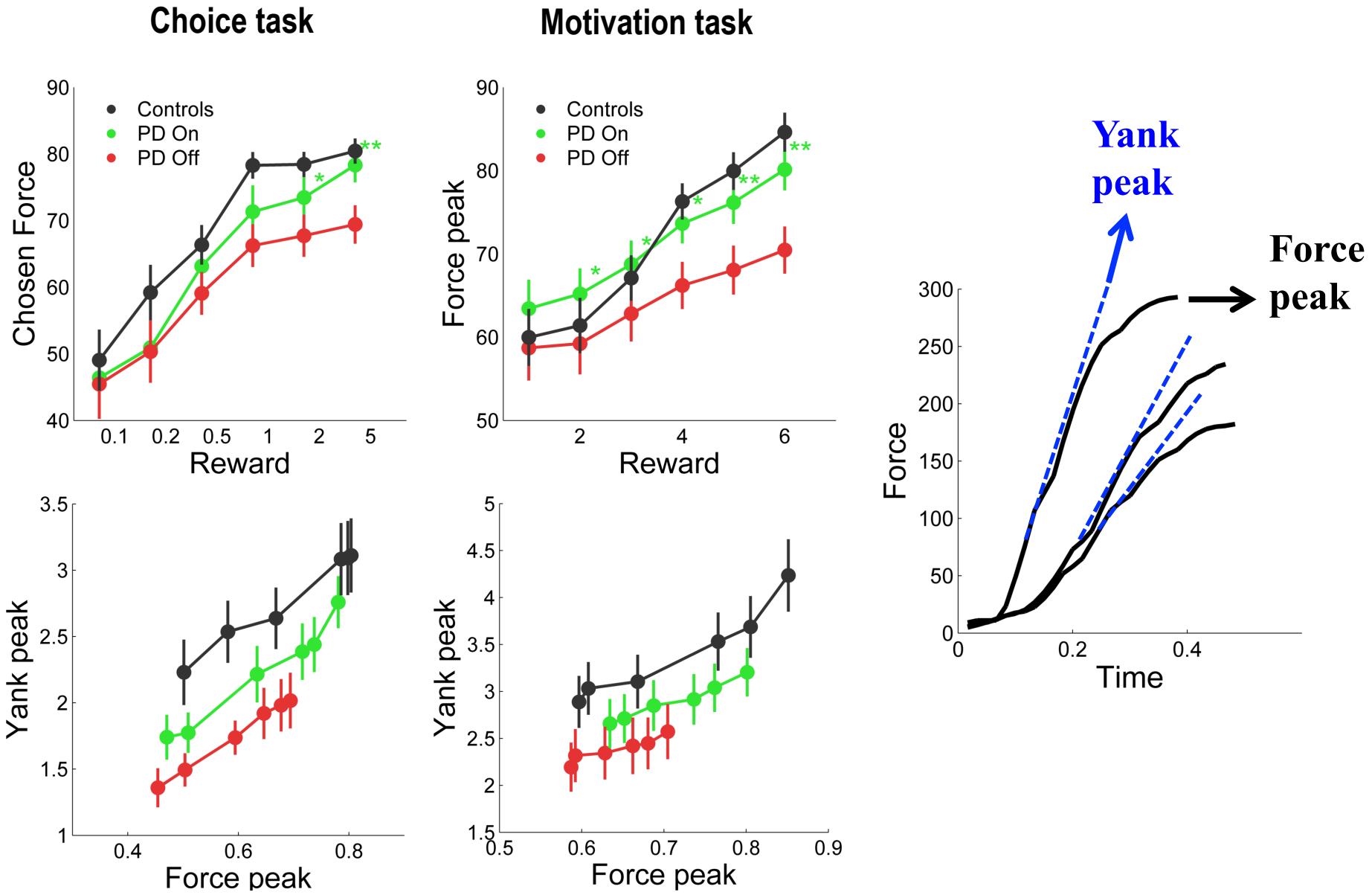
Incentive motification task
(continuous options)

Payoff
= reward * force



Reading the role of dopamine in force profile

Le Bouc et al. J Neurosci 2016



Merging economic decision and motor control

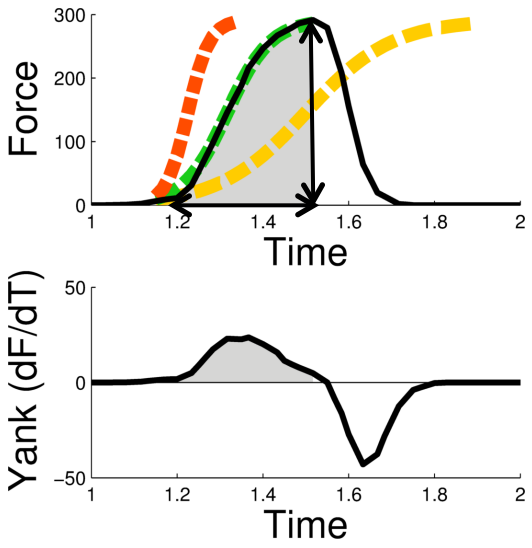
Le Bouc et al. J Neurosci 2016

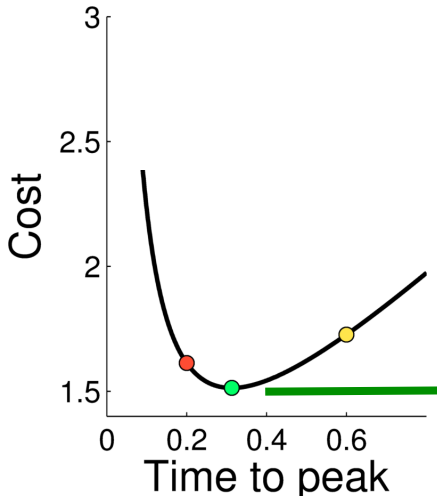
Discounted value: $dV_F = B_F - C_F$

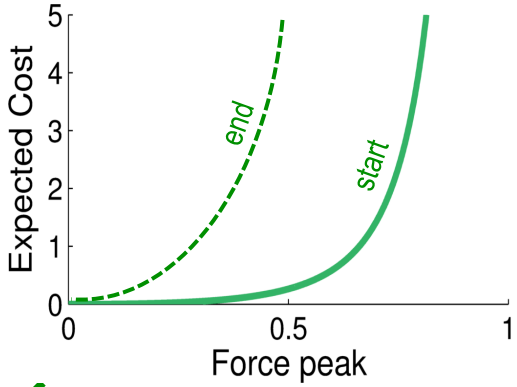
Cost: $C_F = k_c J(1 + k_f N)$

$$J_{F,T} = \min_u \int_0^T u_t^2 dt$$

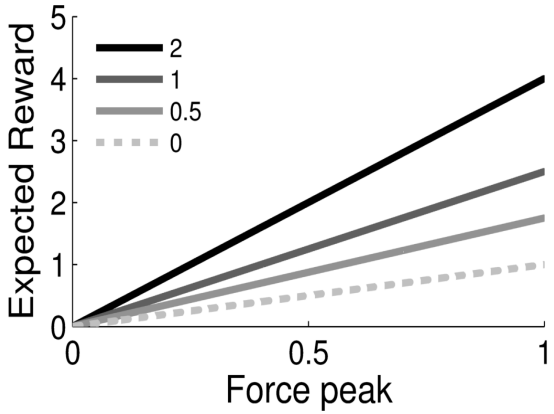
$$\dot{f}_t = \tau(F_{max} - f_t)u_t - \tau f_t$$

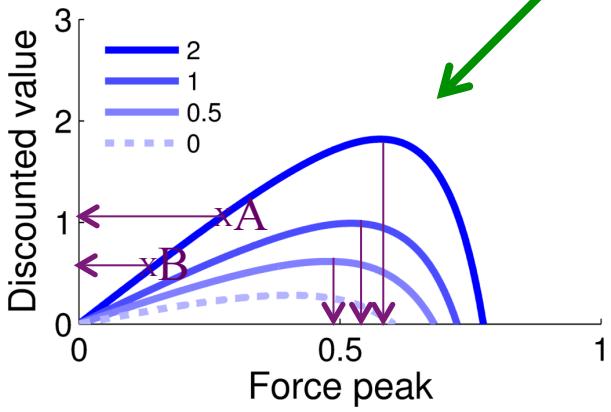






Benefit: $B_F = k_r RF + k_0 F$





Predicted force:

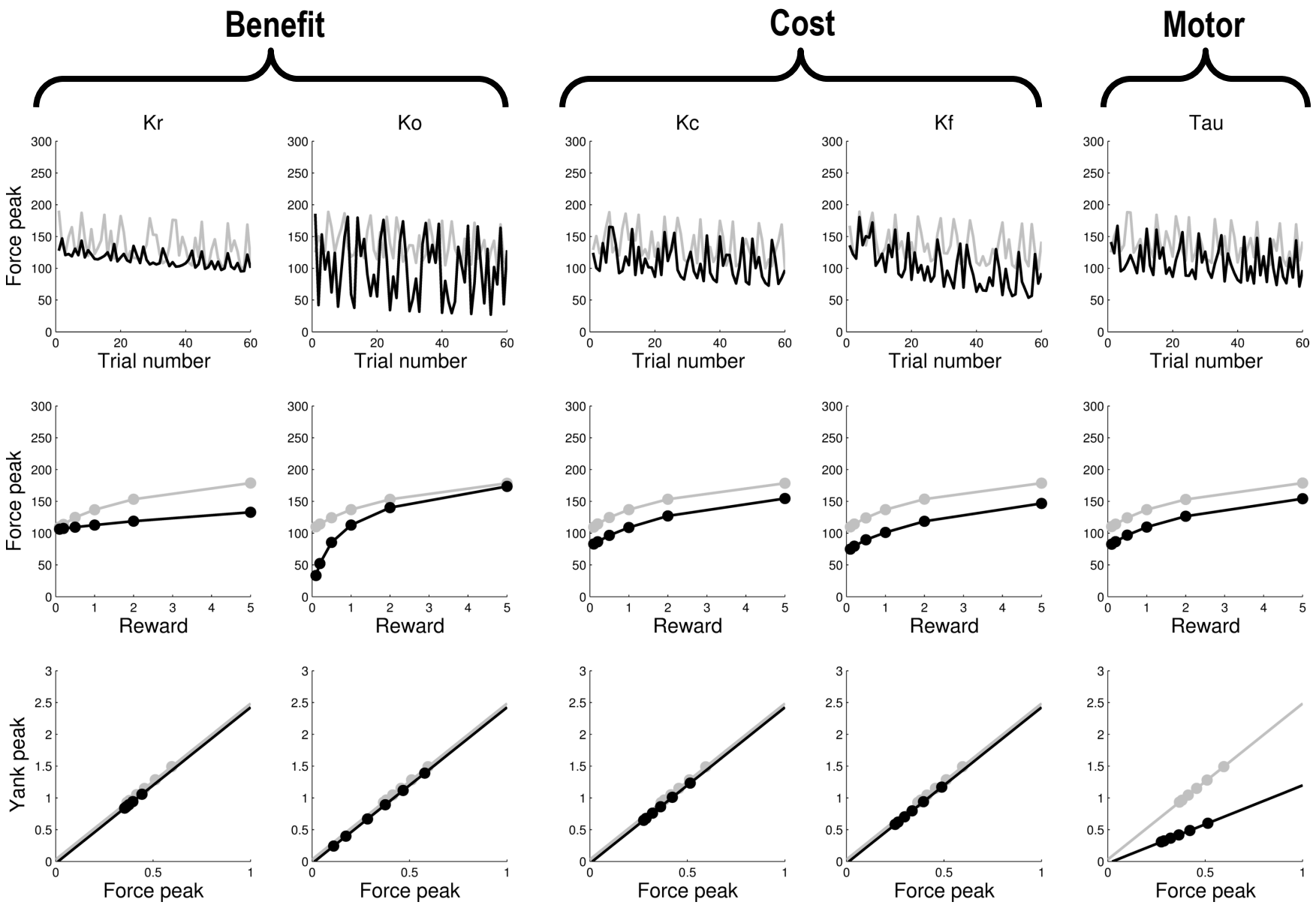
$$F^\star = \underset{\mathrm{F}}{\operatorname{argmax}}\, dV$$

Predicted choice:

$$P_B = \frac{1}{1 + e^{\frac{(Vd_A - Vd_B)}{\beta}}}$$

Simulating the effects of free parameters

Le Bouc et al. J Neurosci 2016

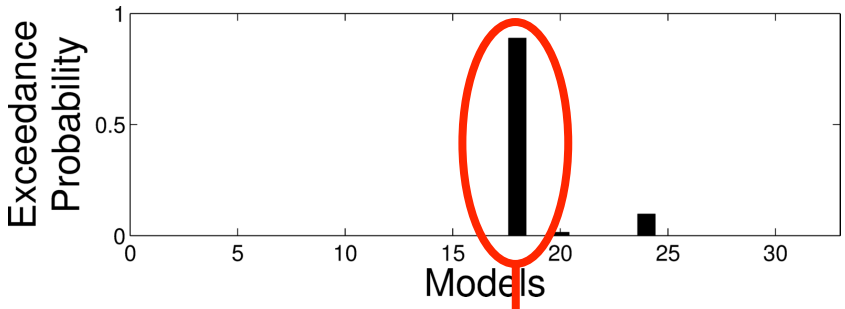


Dissociation of dopamine functions

Le Bouc et al. J Neurosci 2016

Bayesian model selection

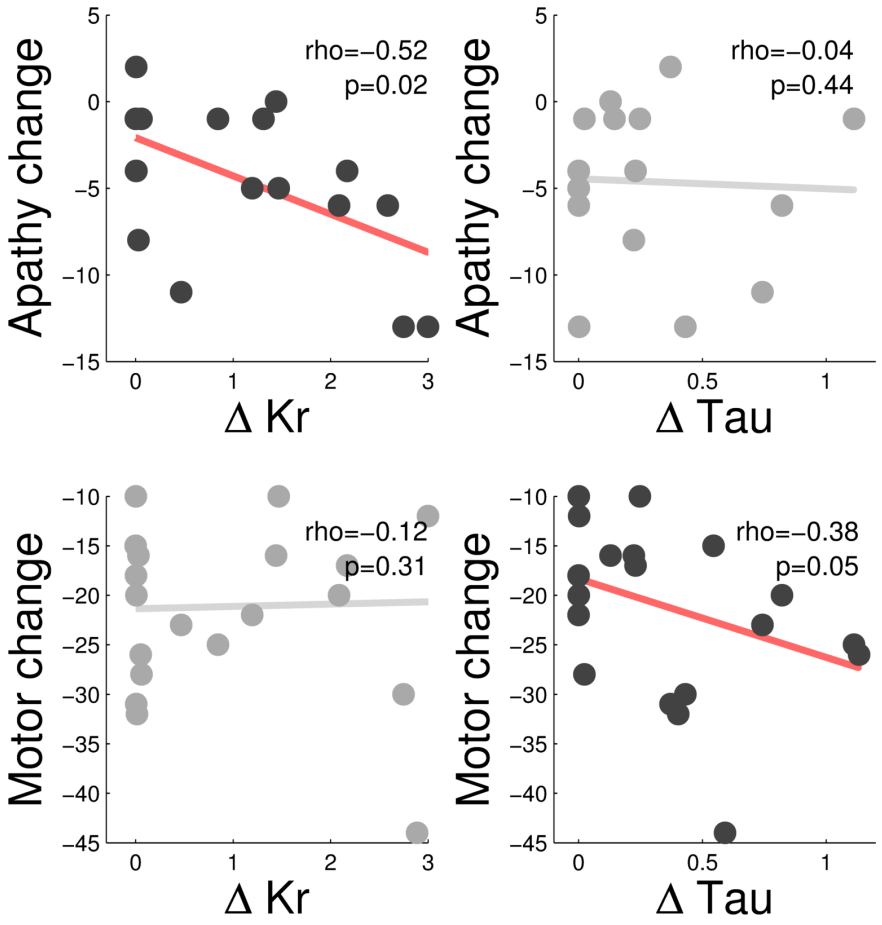
(fitted on choice, force and yank data)



Winning model:
L-dopa selectively modulates
- Kr (= reward sensitivity)
- Tau (= motor time constant)

(but not cost or fatigue sensitivity)

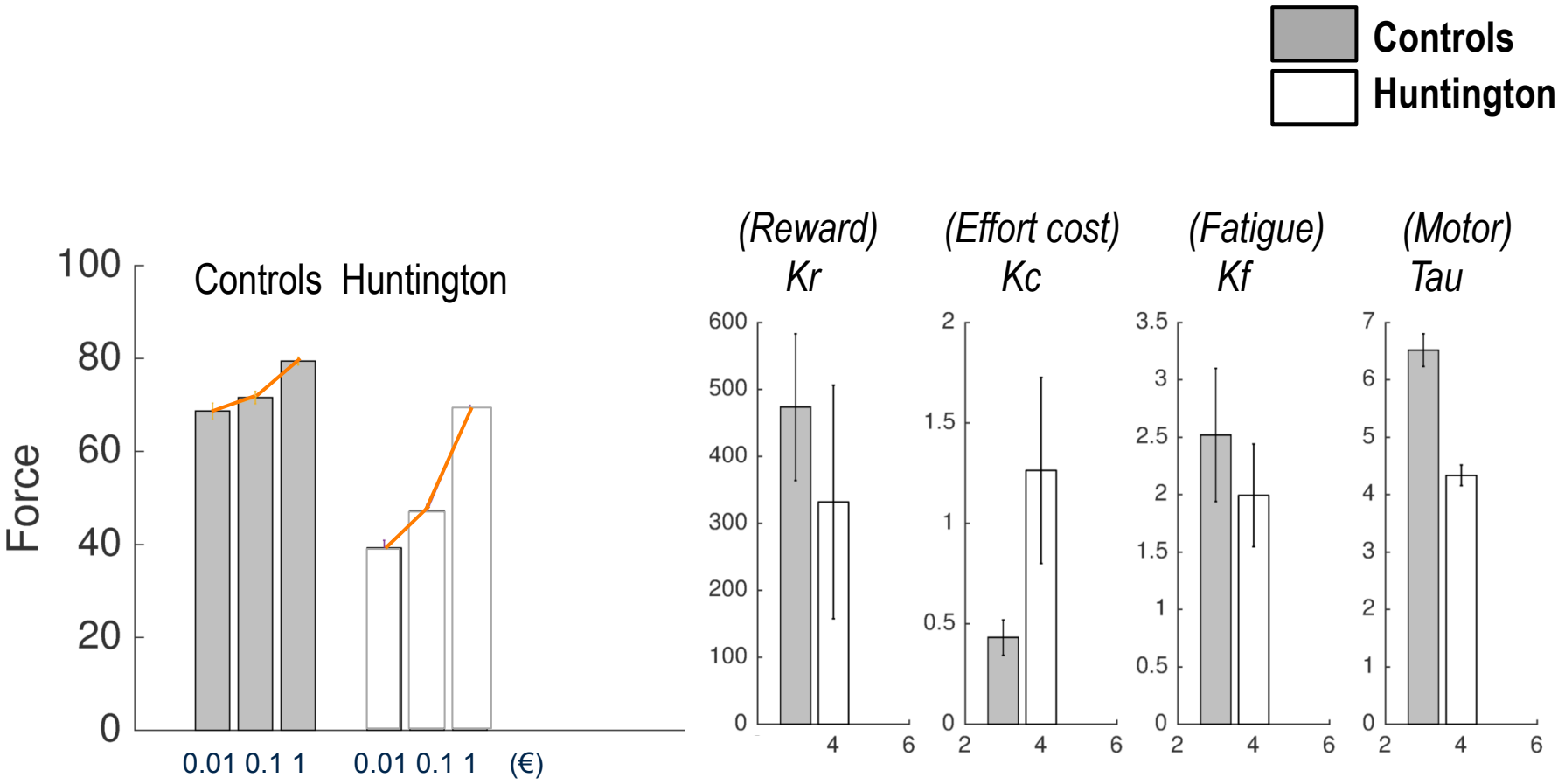
Clinico-computational correlation



➢ **2 independent effects (Kr and Tau) of dopamine enhancers (through separate pathways ?)**

Computational phenotyping of Huntington's disease

Le Bouc et al. in prep



- **3 computational features associated with HD: ↓Kr, ↑Kc and ↓Tau**
- **Separate neural underpinnings?**

Linking model parameters to local atrophy

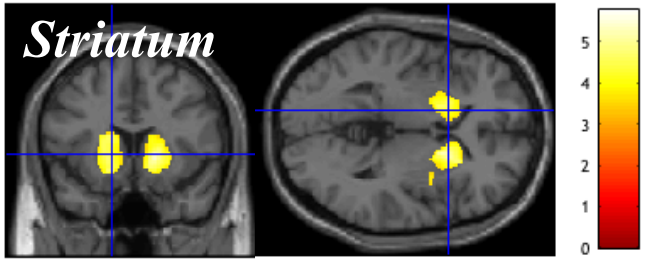
Le Bouc et al. in prep

Clinical scales

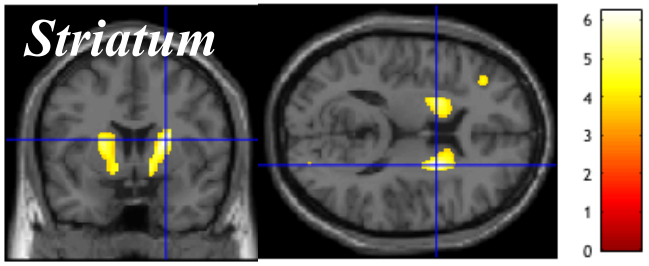
Model parameters

Motor symptoms

UHDRS

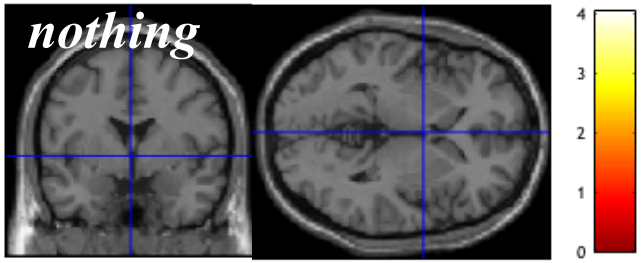


Tau

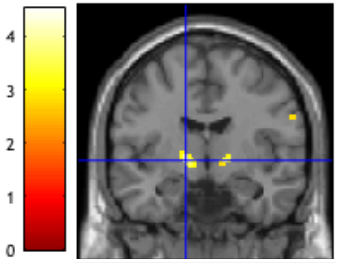


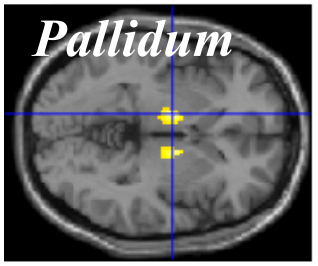
Motivation deficit

Starkstein

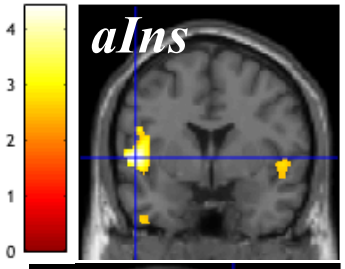


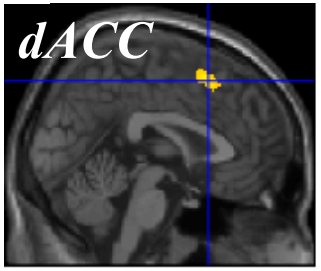
↓Kr





↑Kc

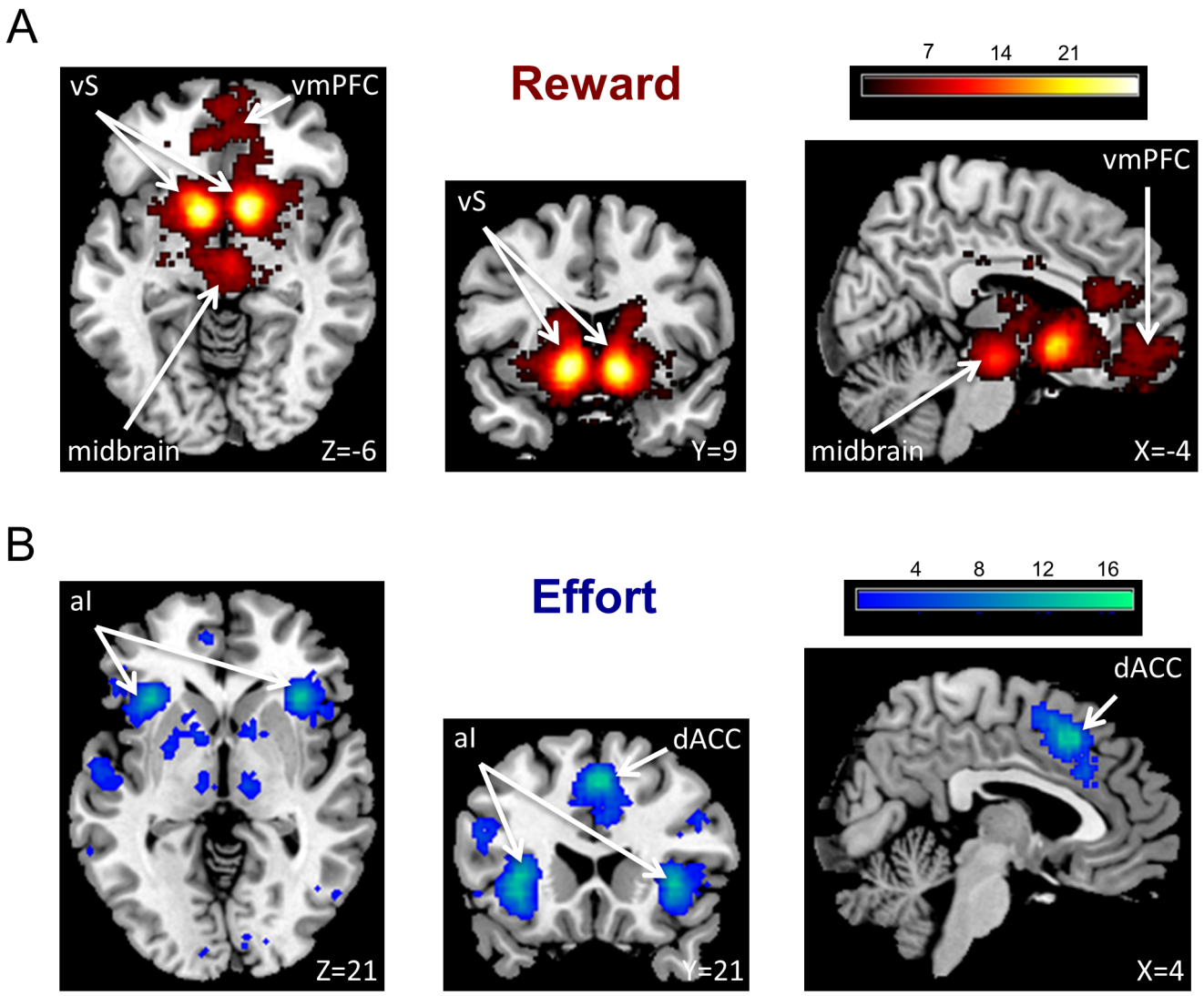




- Atrophy in DS => ↓Tau
- Atrophy in VS/VP => ↓Kr
- Atrophy in aIns/dACC => ↑Kc

Meta-analysis of fMRI studies

Pessiglione et al. Brain, in press



Outline

How the brain adjusts the intensity of effort production

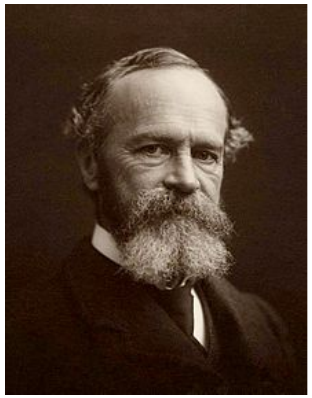
- Normative model (integrating motor control into economic decision theory)
- Dissociated implication of - ventral striato-pallidal complex in incentive motivation
  - anterior insula and cingulate cortex in effort cost
- Dopamine adjusts both sensitivity to incentives and motor activation rate

How the brain allocates effort production over time

The issue of continuous cost/benefit trade-off

- What if the effort allocation problem unfolds over time?
- How do we know when to have a break?
- Is there an opponent system signaling effort cost and limiting performance?

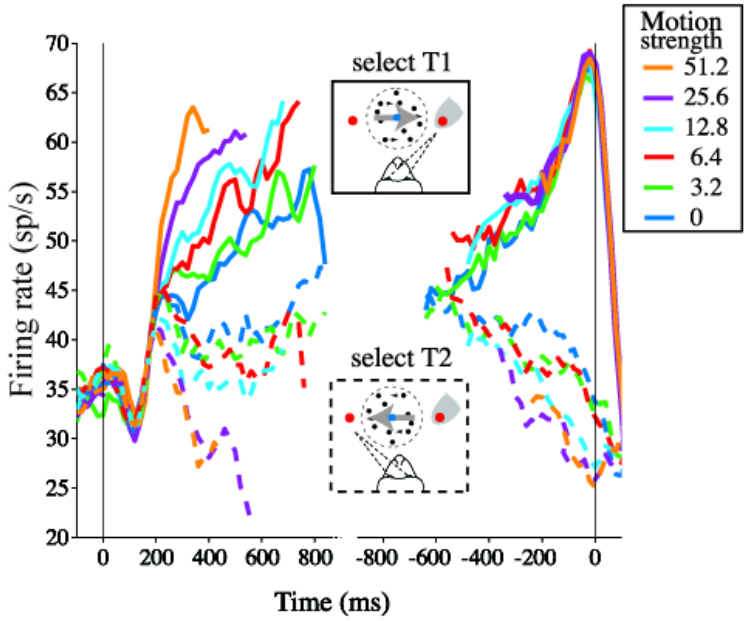
An accumulation model for effort allocation

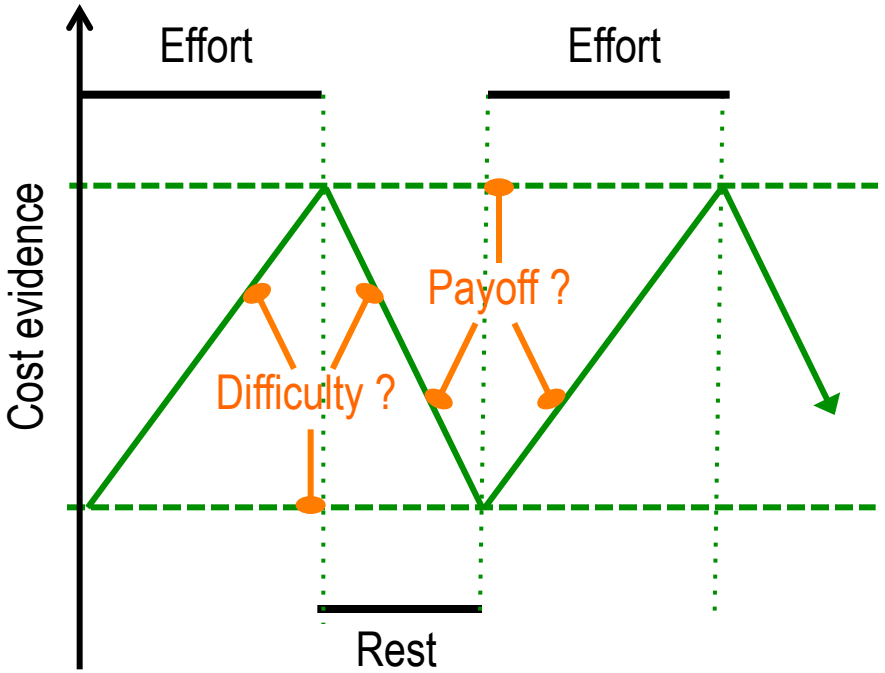


William James (1905):

'Ordinarily, we stop when we meet the first effective layer, so to call it, of fatigue. (…) But if an unusual necessity forces us to press onward, a surprising thing can happen. The fatigue gets worse up to a critical point, when gradually or suddenly it passes away (…). We have evidently tapped a level of new energy'

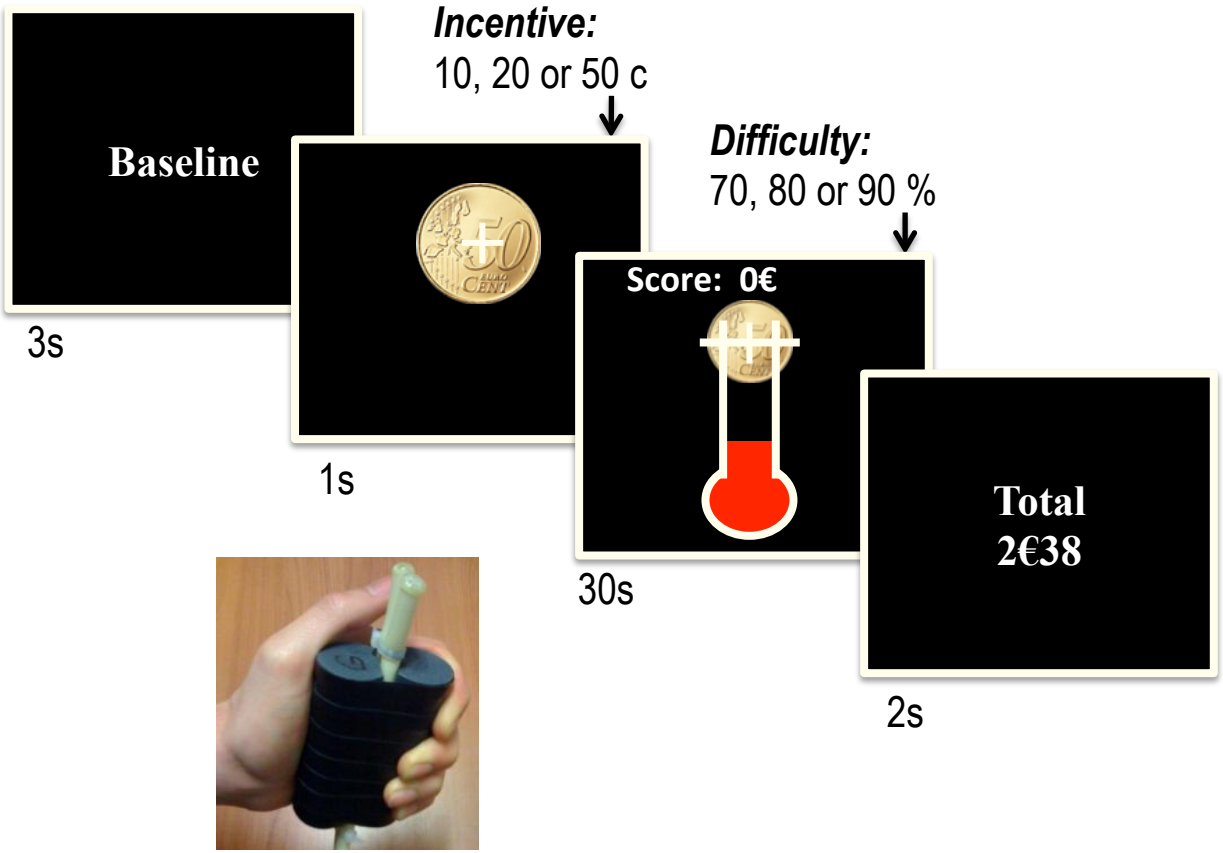
Perceptual evidence (Shadlen & colleagues)





The effort allocation task

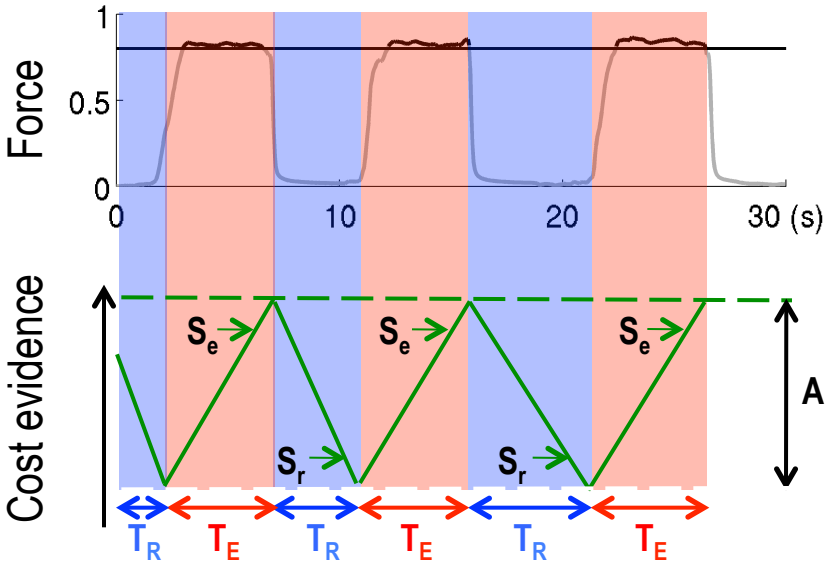
Meyniel et al. PNAS 2013

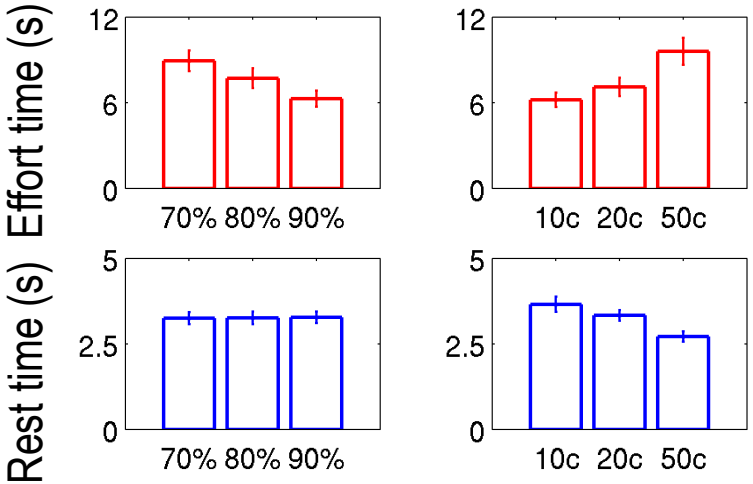


- Force level is normalized to individual maximal force
- Payoff is proportional to the cumulative effort duration
- Participants believe they play for real money

Different factors impact effort and rest durations

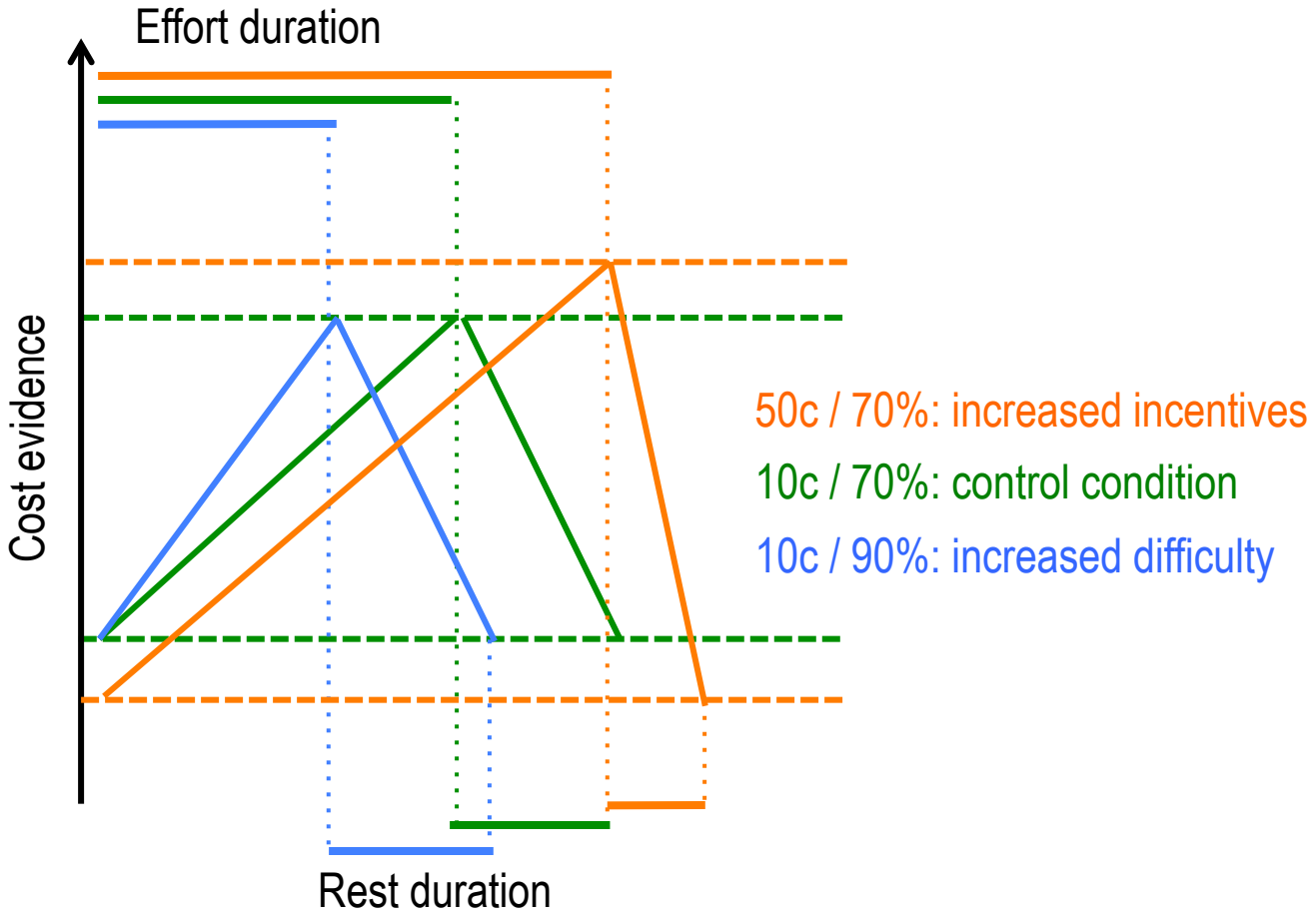
Meyniel et al. PNAS 2013





Summary of incentive and difficulty effects

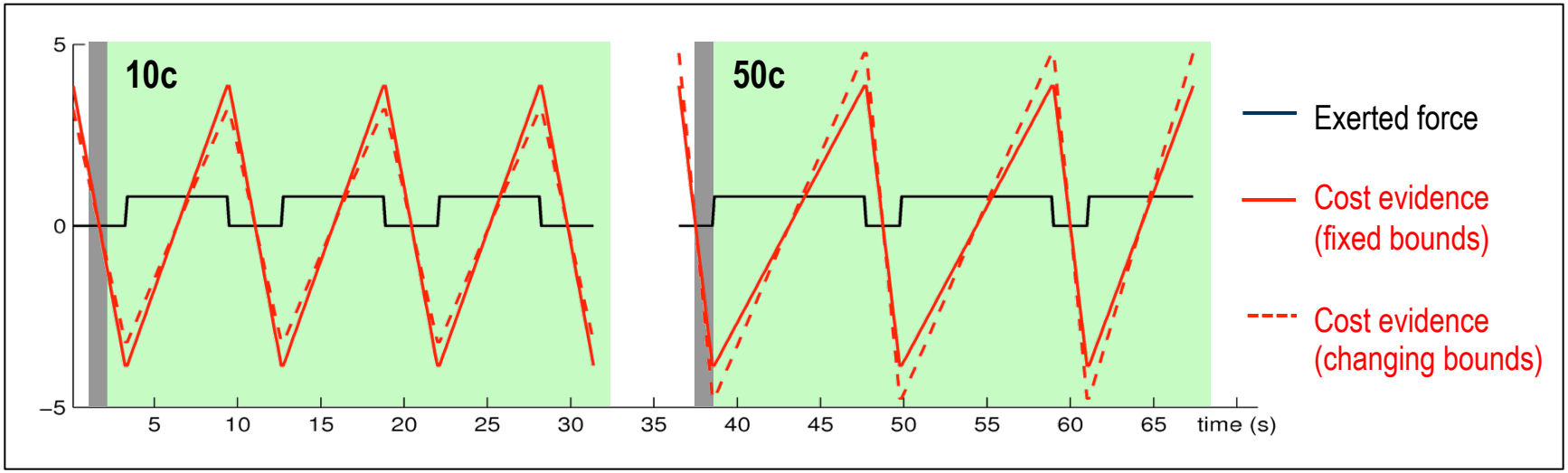
Meyniel et al. PNAS 2013



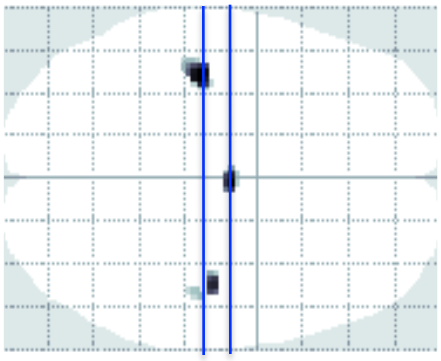
The cost evidence signal viewed through fMRI

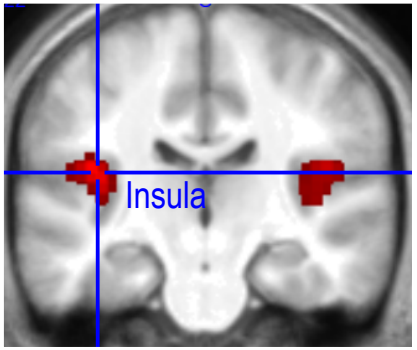
Meyniel et al. PNAS 2013

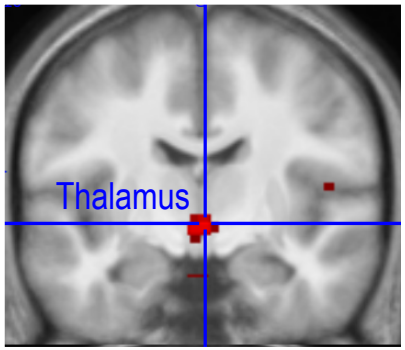
Modeled cost evidence accumulation signal



Localization of cost evidence accumulation signal (best fit with changing bounds)



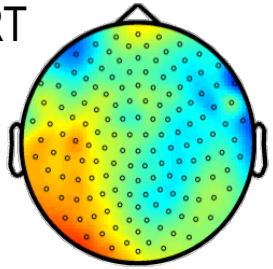


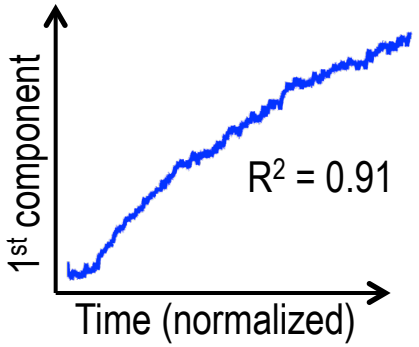


The cost evidence signal viewed through MEG

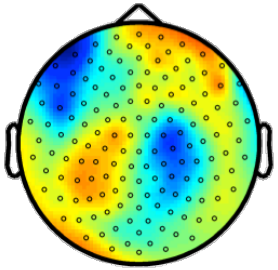
Meyniel et al. PNAS 2013

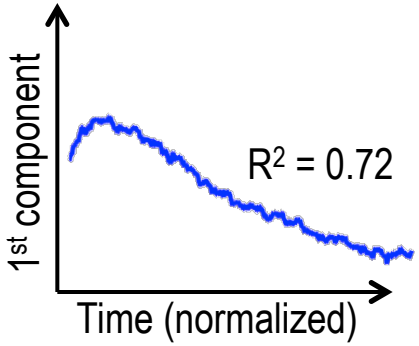
PCA / EFFORT
xp = 0.90



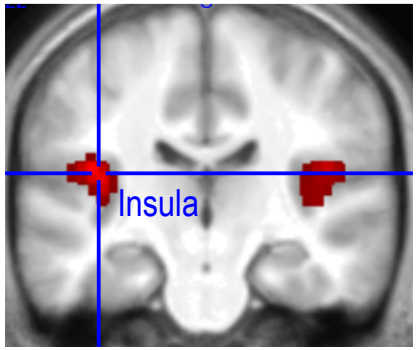


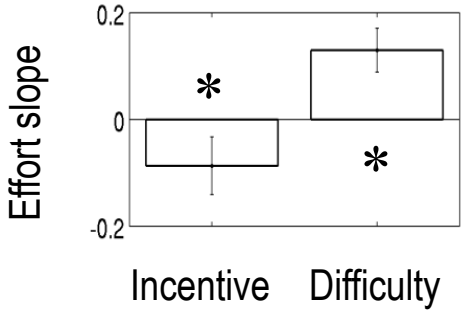
PCA / REST
xp = 0.94

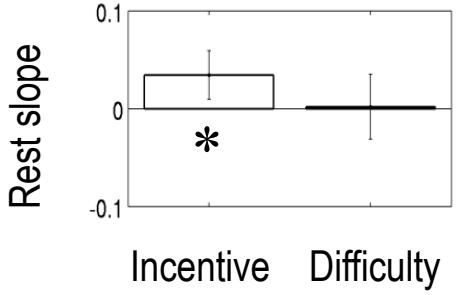


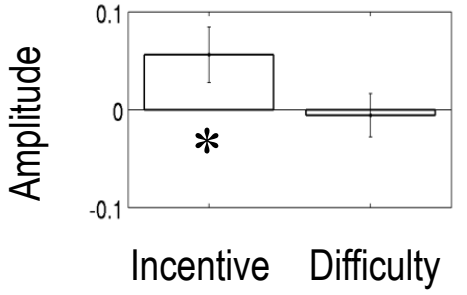


SOURCE
RECONSTRUCTION





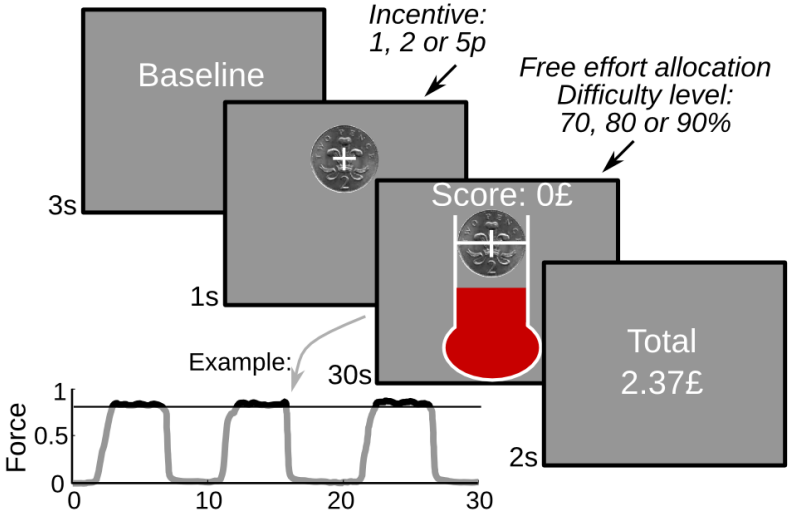




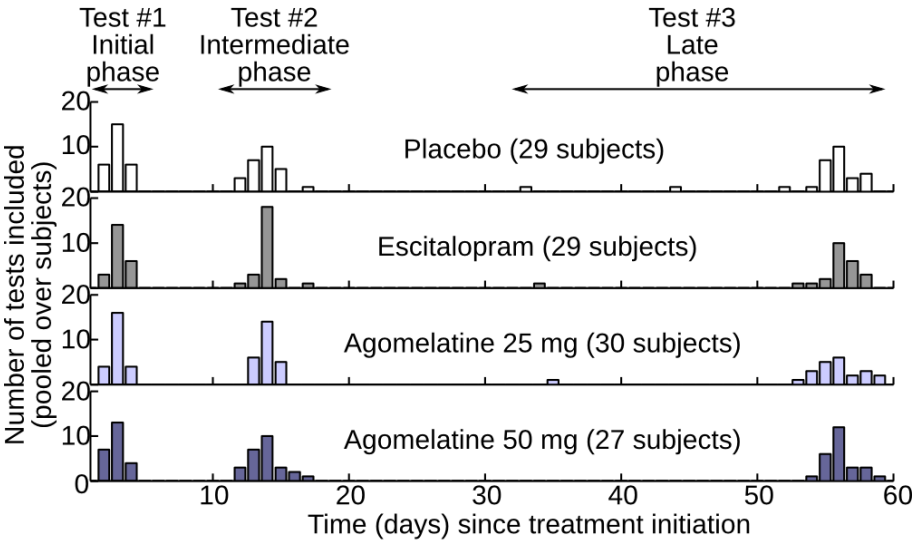
Effects of anti-depressant drugs on effort allocation

Meyniel et al. eLife 2016

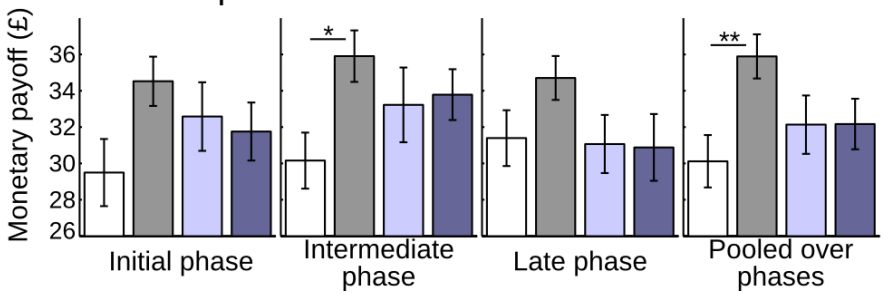
A: Effort Allocation Task



B: Treatments and testing schedule



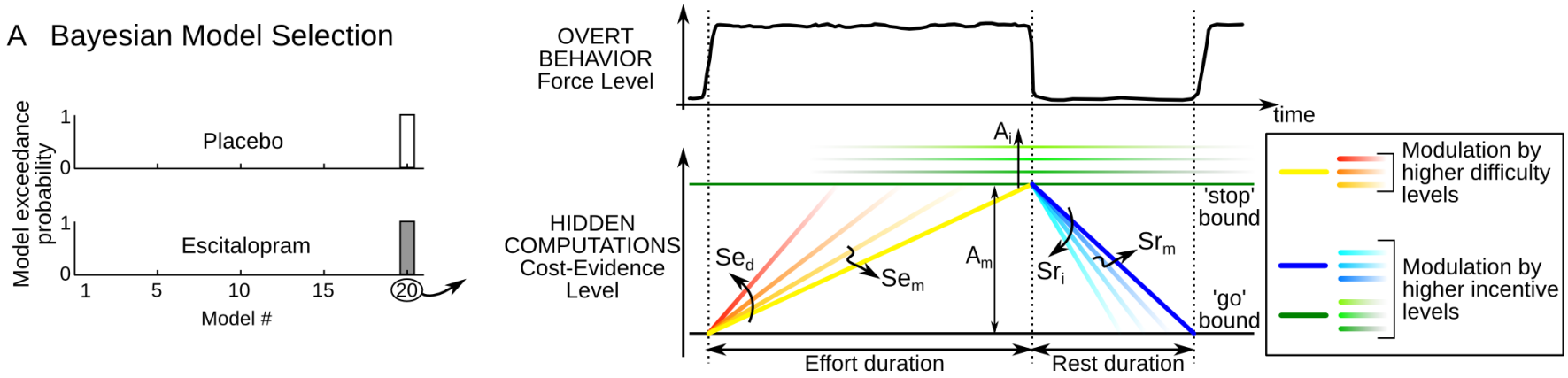
C: Behavioral performance

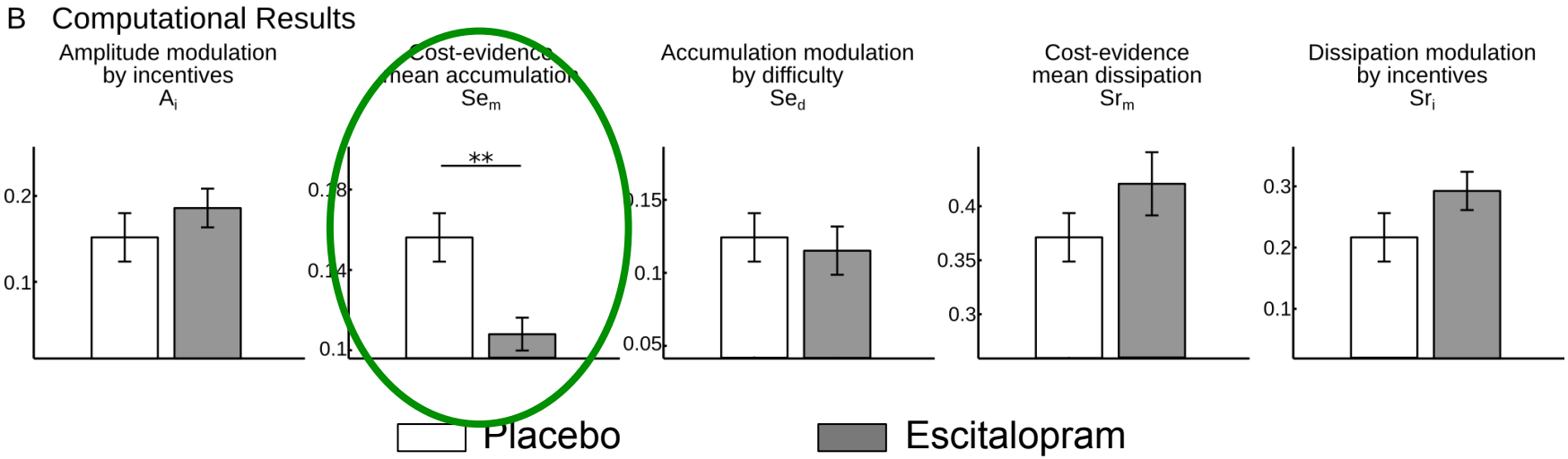


➢ Only SSRI have an effect (improved performance)

SSRI effect specific to effort cost accumulation

Meyniel et al. eLife 2016





➢ SSRI enhance the slope of cost evidence accumulation

Outline

How the brain adjusts the intensity of effort production

- Normative model (integrating motor control into economic decision theory)
- Dissociated implication of - ventral striato-pallidal complex in incentive motivation
  - anterior insula and cingulate cortex in effort cost
- Dopamine adjusts both sensitivity to incentives and motor activation rate

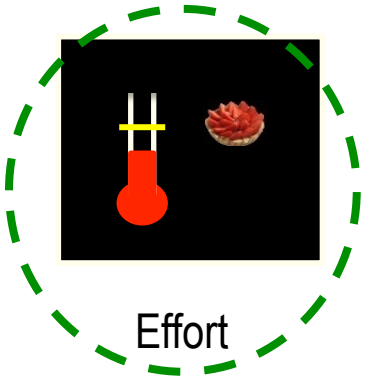
How the brain allocates effort production over time

- Descriptive model (accumulation-to-bound model applied to cost monitoring)
- Posterior insula represents the decision variable (cost evidence)
- Serotonin prolongs effort by lowering the rate of cost evidence accumulation

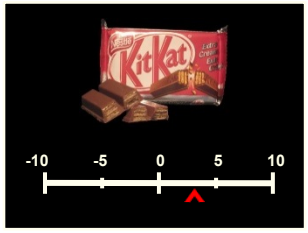
⇒ **Better treat** **- reduced reward sensitivity with psychostimulants (DA)**
- enhanced effort cost sensitivity with antidepressants (5HT)

A test battery for motivation disorders

Behavioral tests

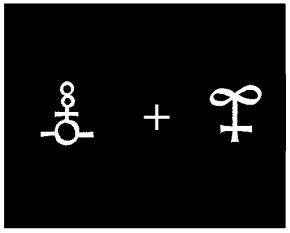


Effort



Rating

Choice



Learning

Model parameters

Sensitivity to reward, punishment, effort, delay, etc.

= cardinal dimensions of psychiatric conditions (links to apathy, impulsivity etc.)

= possibly susceptible to different treatments (DA for reward, 5HT for effort …)

➢ **Computational phenotyping**

- Behavioral tests at bedside => computational parameters
- Computational fingerprint => disease evolution and treatment effects

Thanks to the MBB team

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

Schlumberger foundation research grant
City of Paris emergence grant
ERC starting grant
ICM young investigator grant

Raphaël Le Bouc

Florent Meyniel