Computational Models for Precision Psychiatry

PEAC Lab
Website: fpetzschner.com/lab
Mail: frederike_petzschner@brown.edu
X: @rikepetzschner

BROWN

The Goal: Precision Psychiatry

The goal is
to provide the **right treatments**
to the **right patients**
at the **right time.**

The goal is Precision Psychiatry, what are the hurdles?

- **Lack of mechanistic understanding**

  → Heterogeneity

- **Lack of predictors**

  → Trial and error treatment

- **Lack of effective treatments**

***Petzschner**, Science, 2024*

The goal is Precision Psychiatry, what are the hurdles?

- **Lack of mechanistic understanding**
  - → Heterogeneity
- **Lack of predictors**
  - → Trial and error treatment
- **Lack of effective treatments**


nature

MENTAL HEALTH

U.S. Mental Health Chief: Psychiatry Must Get Serious about Mathematics

New NIMH chief Joshua Gordon says he will focus on quick wins, brain circuits and mathematical rigor

By Alison Abbott, Nature magazine on October 28, 2016

***Petzschner**, Science, 2024; **Redish & Gordon**, MIT Press, 2018; **Gordon, Dzirasa, Petzschner**, Cell (in press) , 2024*

1. Disease insights

Mechanistic Models

2. Predictive validity

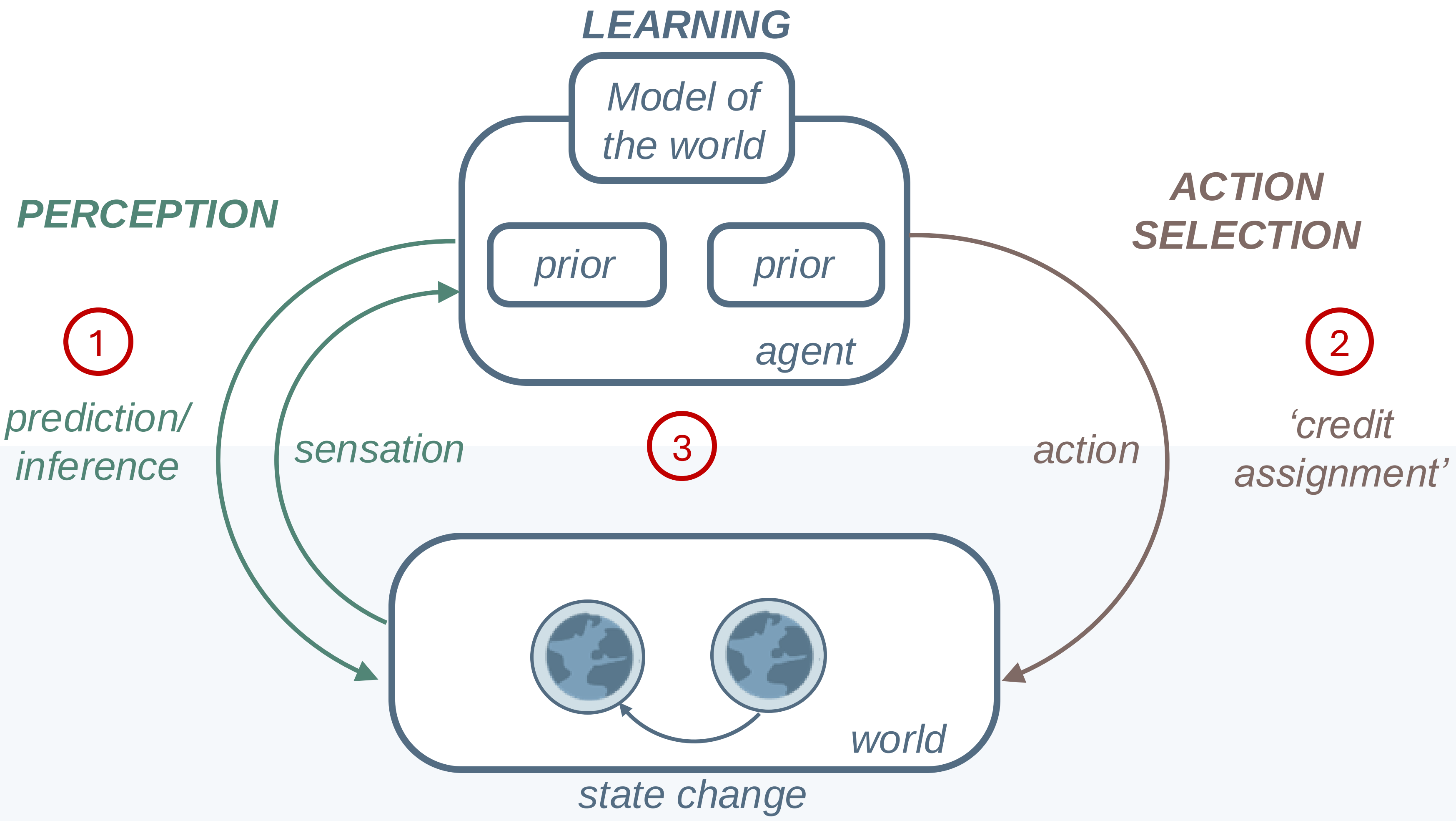
Data-driven Models

1. Disease insights
Mechanistic Models

2. Predictive validity
Data-driven Models

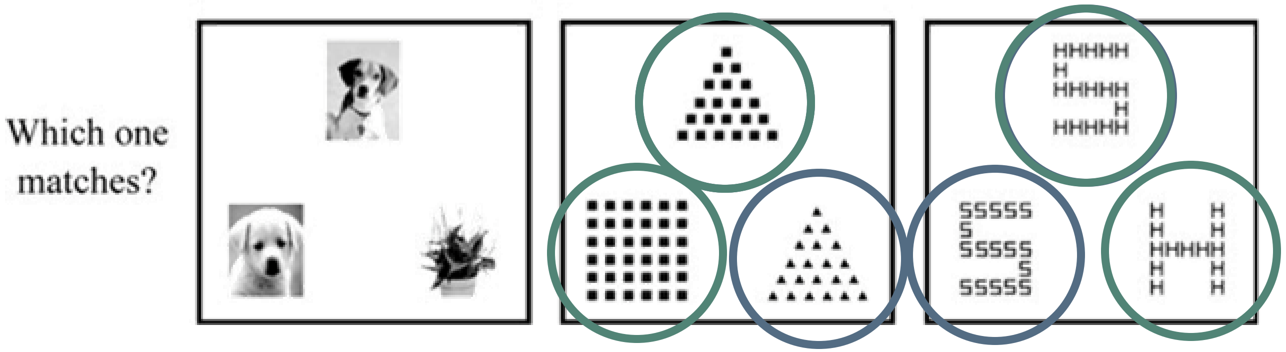
Combination

Bordersen et al., *PlosCB, 2011*
Huys *et al., Nat. Neuro., 2016;*
Geana *et al., Biol. Psych., 2021;*
Wiecki *et al. Plos One, 2016;*
Wiecki *et al., Clin Psychol Science, 2015*



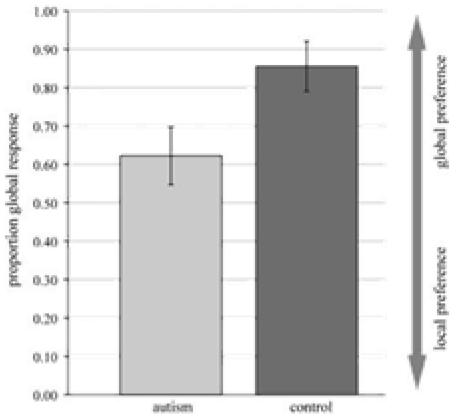
Petzschner, Weber et al., *Biol Psych, 2017*

Autism Spectrum Disorder



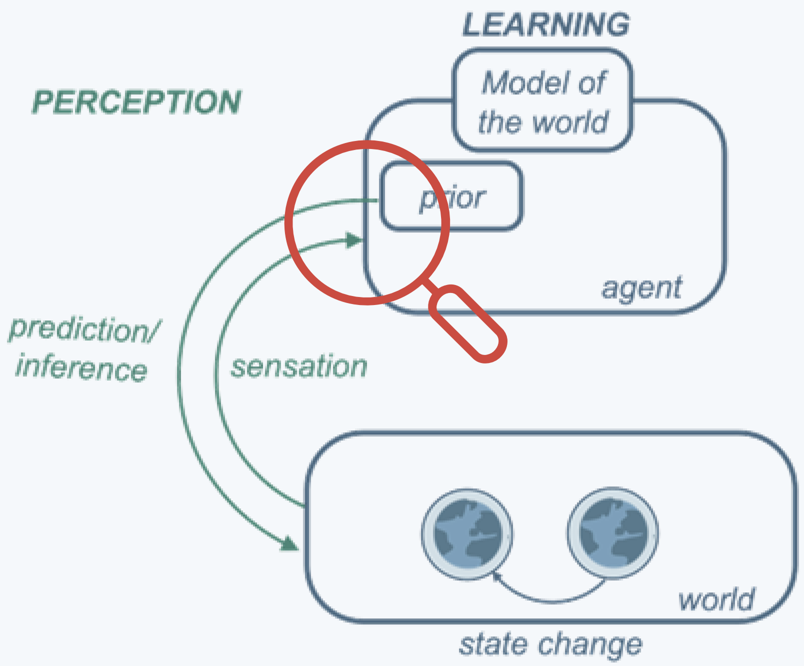
global

local



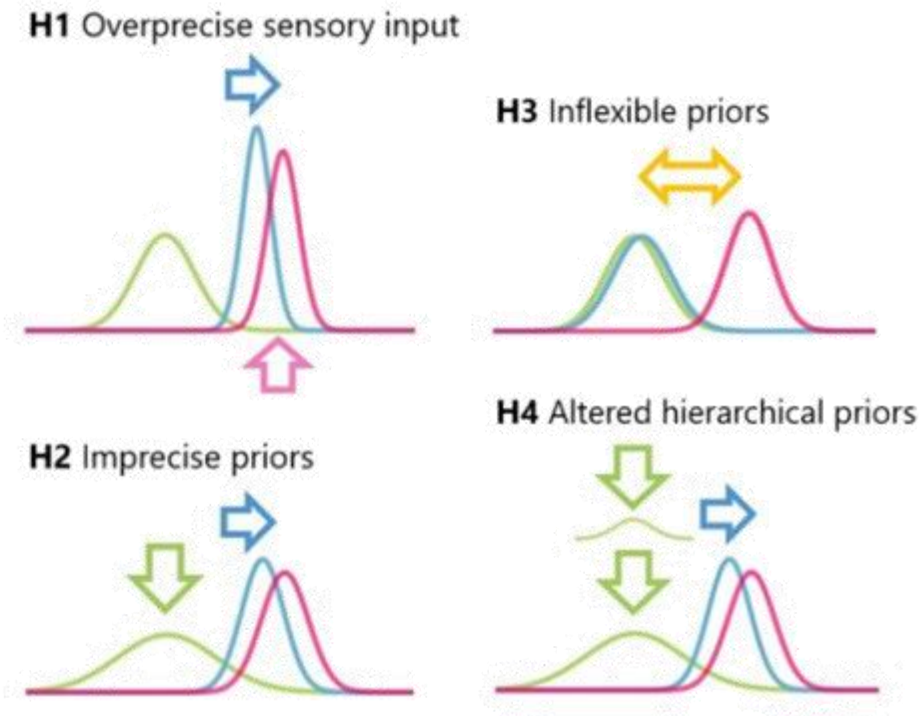
global

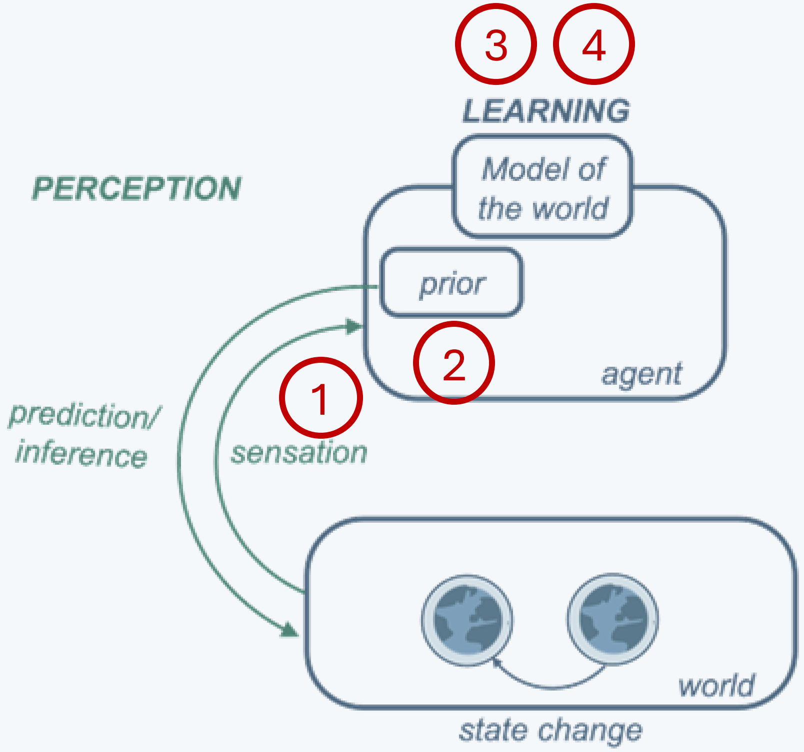
local



Koldewyn et al., *J Autism Dev Disord, 2013*

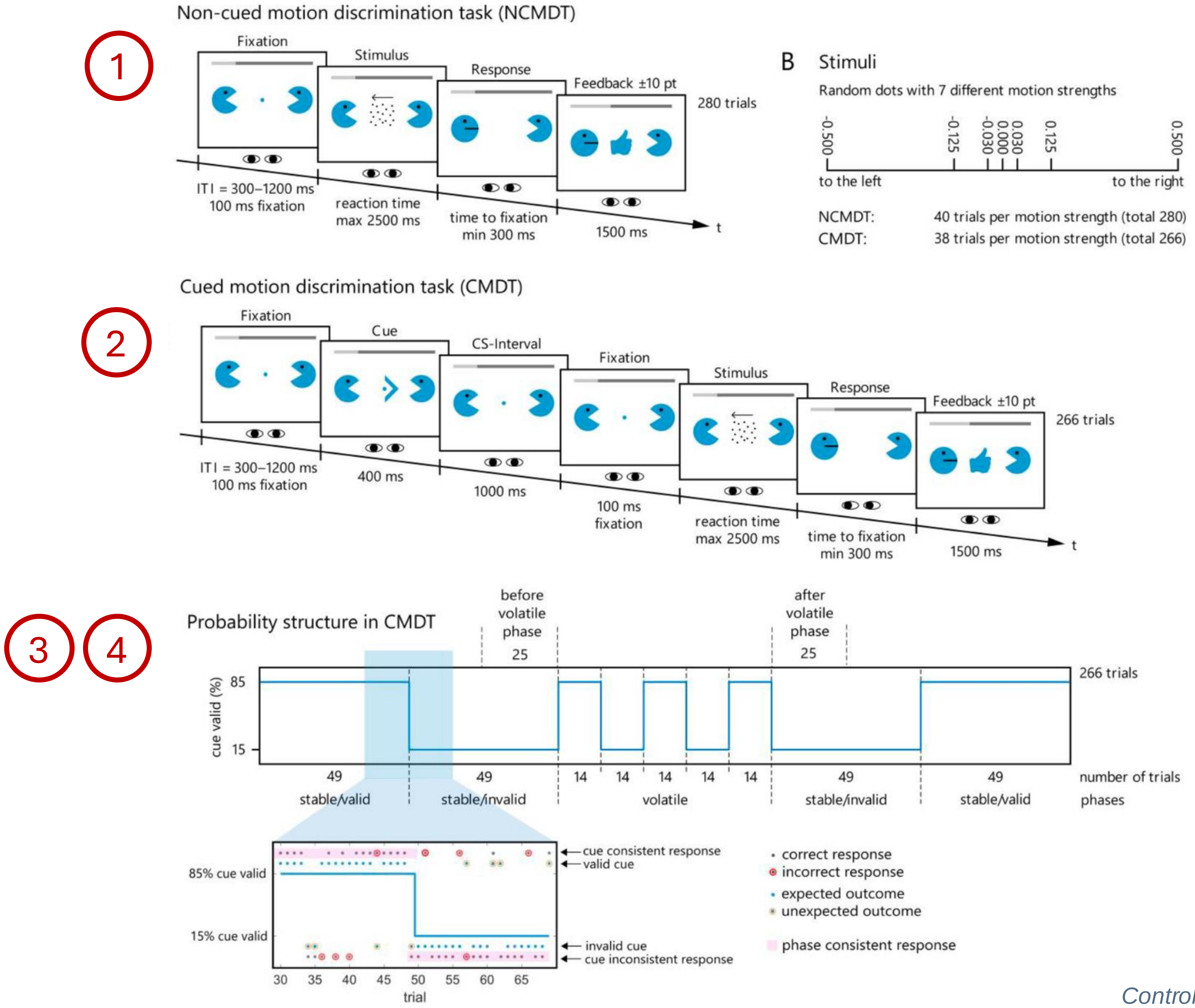
Hypothesis about Perceptual Deficits in Autism Spectrum Disorder





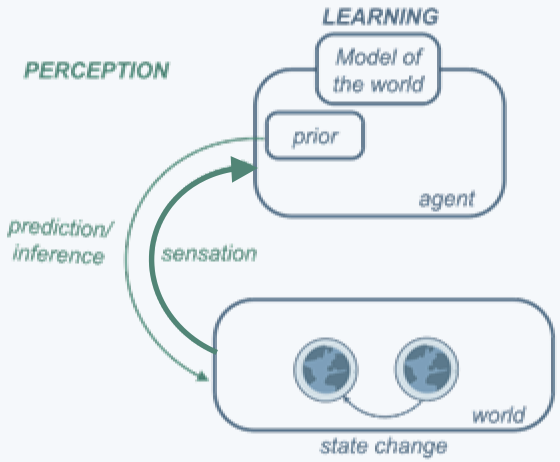
Schneebeli et al. *medRxiv, 2022;* ***Haker et al.,*** *Front Psych, 2016****; Lawson et al.,*** *Front Hum Neuro, 2014*

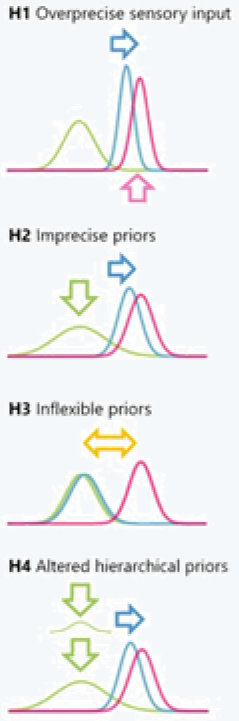
Testing the Hypothesis for Autism Spectrum Disorder



Control Group (n = 50)
Autism Group (n = 47)

Schneebeli et al. *medRxiv, 2022*

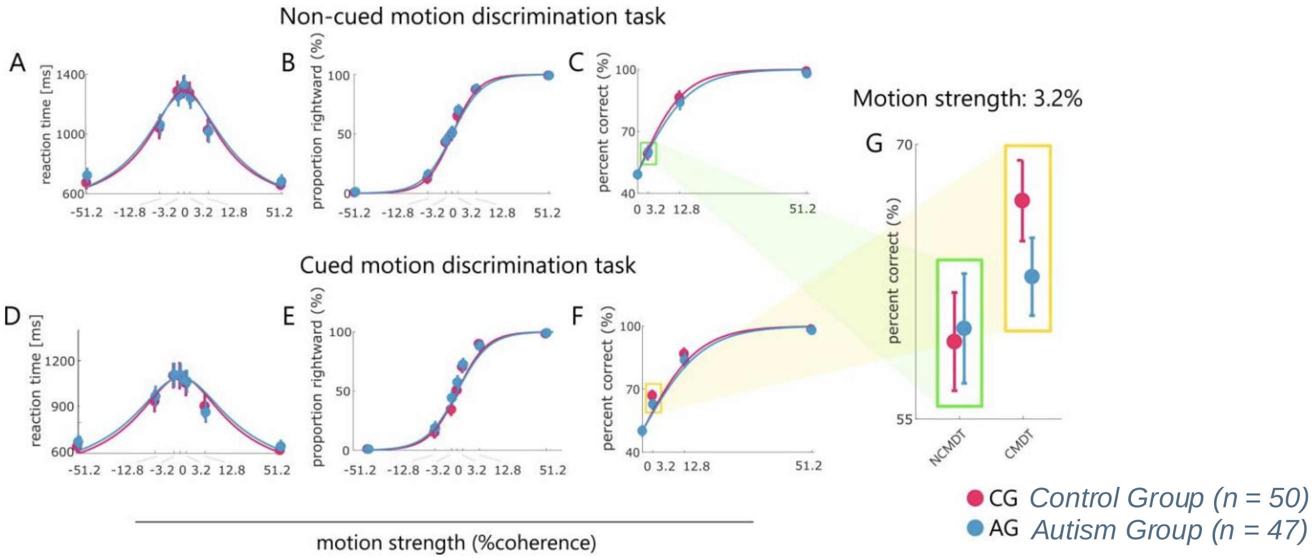




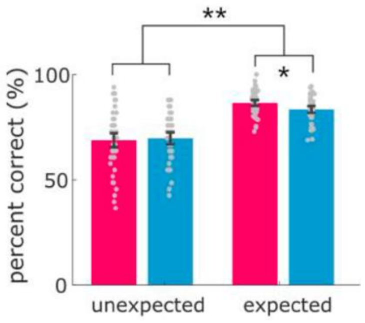
Haker et al., *Front Psych, 2016,*
Lawson et al., *Front Hum Neuro, 2014*

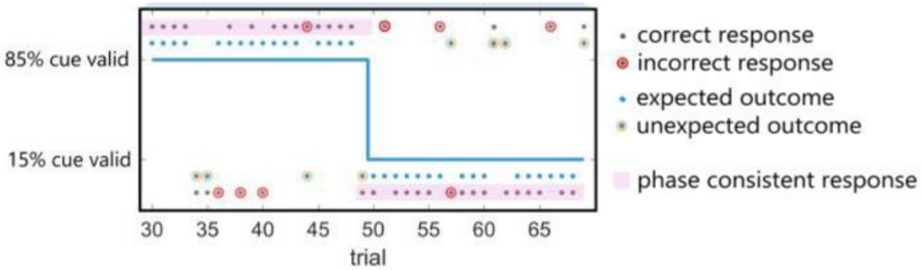
Maladaptive inference in Autism Spectrum Disorder

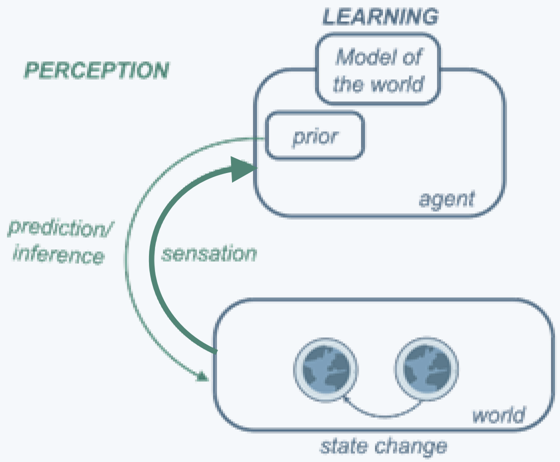
Patients with ASD rely less on prior information with sensory uncertainty is high

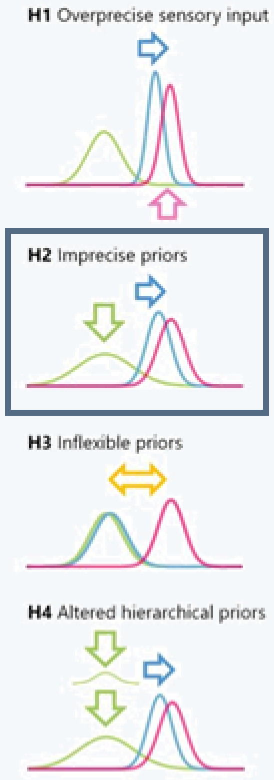


ASD did benefit less in trials where the cue was reliable









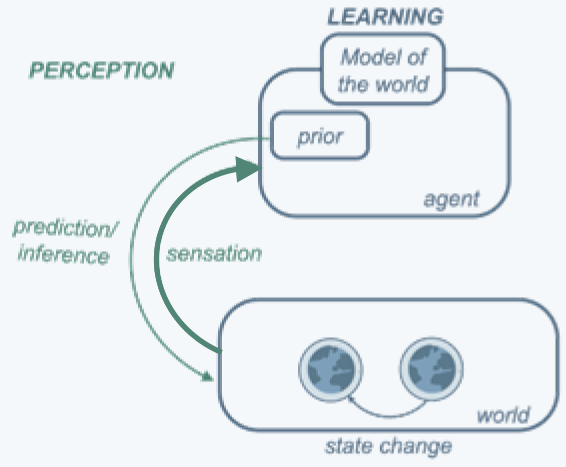
Schneebeli et al. *medRxiv, 2022*

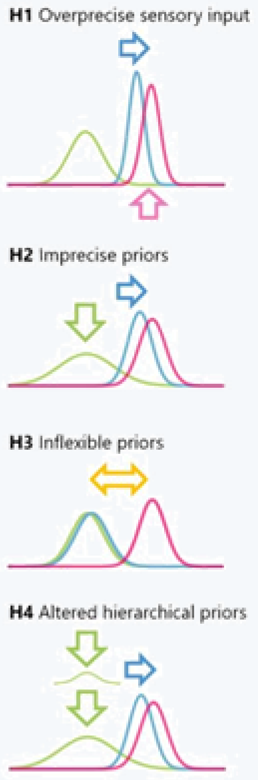
Computational Model: *DDM*

Maladaptive inference in Autism Spectrum Disorder

H1: Overprecise sensation hypothesis	H2: Imprecise prior hypothesis	H3: Inflexible prior hypothesis	H4: Hierarchical learning of priors
Does sensory processing and evidence accumulation differ between the AG and CG in the NCMDT?	*Does the AG use contextual prior information less than the CGs?*	*Does the AG have more difficulties than the CG in updating a contextual prior after learning it initially?*	*Is the use of prior information in the AG less modulated by the volatility of the contextual cue than in the CG?*
× **H1a** The AG and CG differ in accuracy and RT. × **H1b** The AG and CG differ in DDM parameter estimates (drift, threshold).	✓ **H2a** The AG benefits less than the CG from prior information provided by cues. ✓ **H2b** The AG shows a smaller difference in accuracy between expected and unexpected stimuli than the CG. ✓ **H2c** Responses of the AG are less phase-consistent on zero-coherence trials than response of the CG. ✓ **H2d** Responses of the AG are less phase-consistent on question trials than those of the CG. ✓ **H2e** The AG reports lower cue confidence than the CG on question trials.	× **H3a** The AG chooses options consistent with the cue more frequently (are more cue consistent) than the CG. × **H3b** The AG is more cue consistent in their reports on question trials than the CG.	✓ **H4a** Stability modulates the accuracy difference between expected and unexpected trial outcomes less in the AG than in the CG. × **H4b** Stability modulates the phase consistency less in the AG than in the CG. × **H4c** Stability modulates the reported phase consistency less in the AG than in the CG. ✓ **H4d** Stability of the phase modulates the reported cue confidence less in the AG than in the CG.

Autism Paper





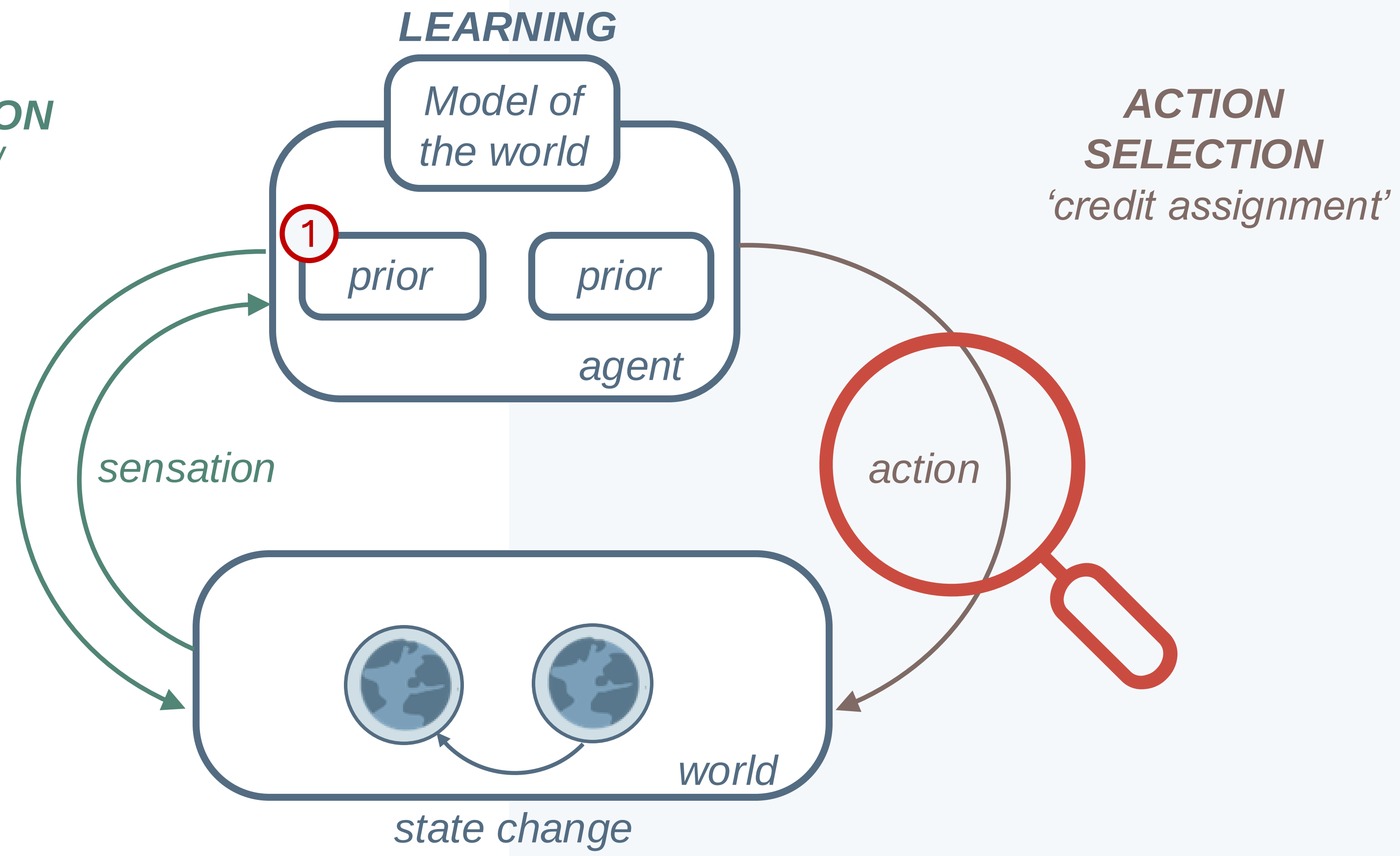
Schneebeli et al. *medRxiv, 2022*

Computational Model: *DDM*

PERCEPTION
prediction/ inference

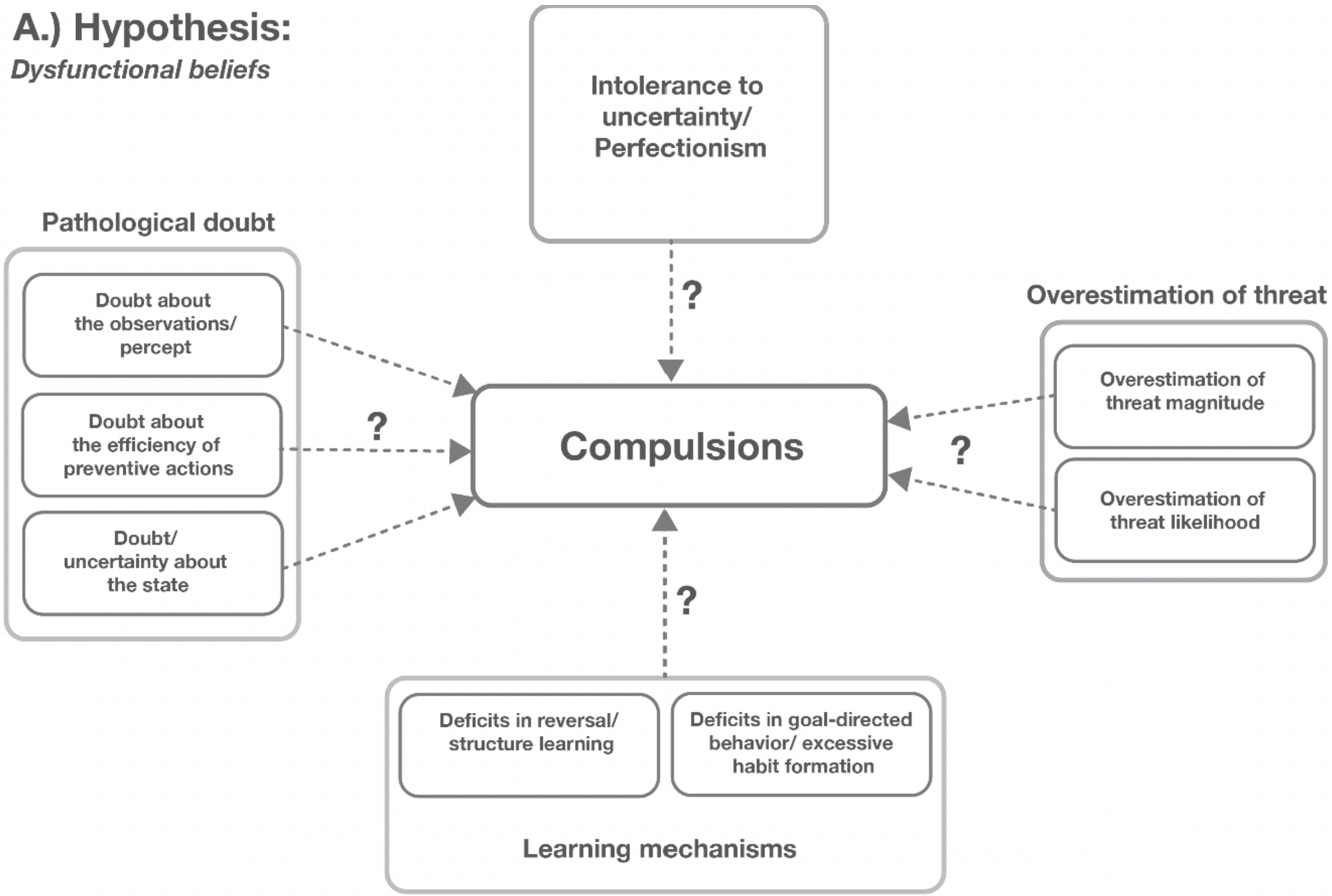
1 ***Autism:*** *Imprecise priors may underlie perceptual symptoms in Autism Spectrum Disorder*

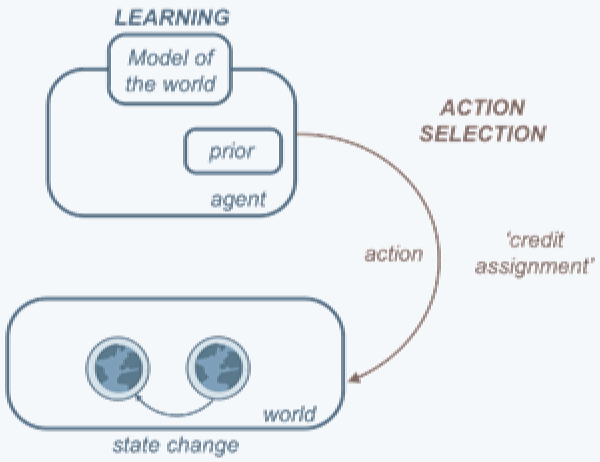
Autism Paper



Petzschner, Weber et al., Biol Psych, 2017

Obsessive-Compulsive Disorder



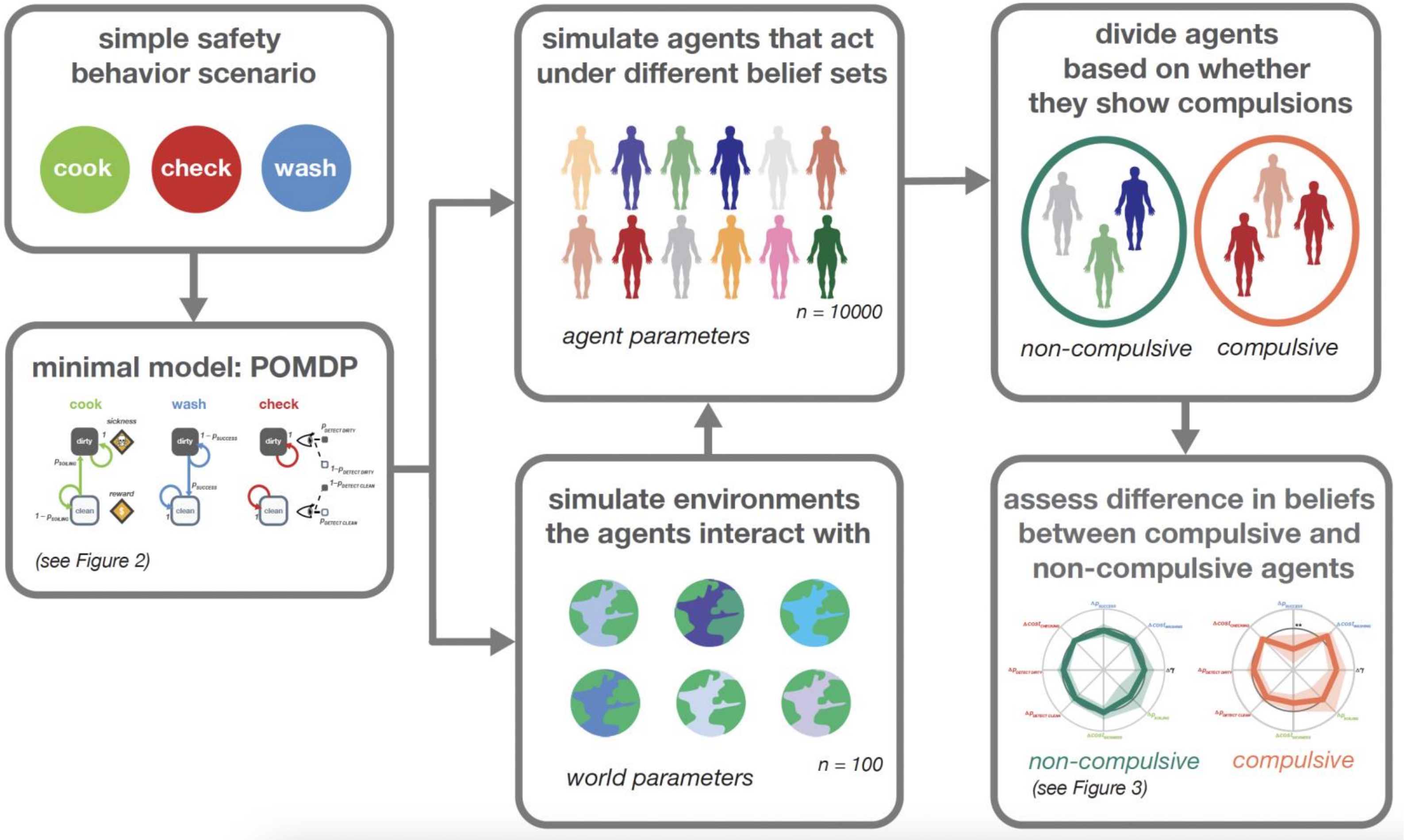


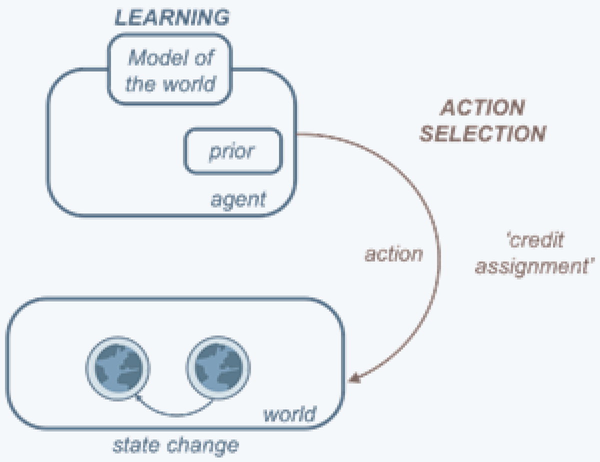

Klaas Enno Stephan


Lionel Rigoux

Rigoux, Stephan, Petzschner, *PlosCB, 2024*

A model of compulsions

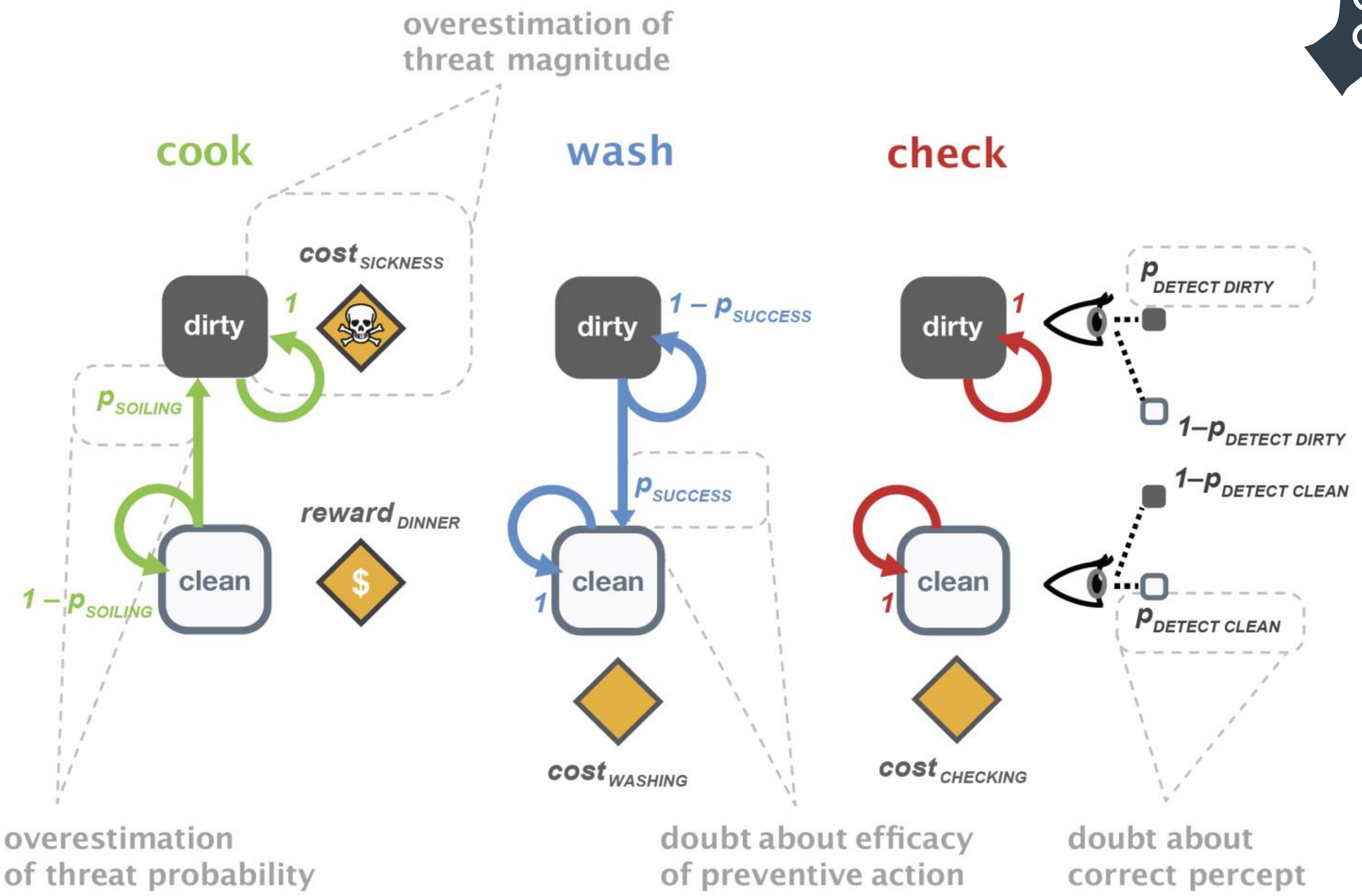


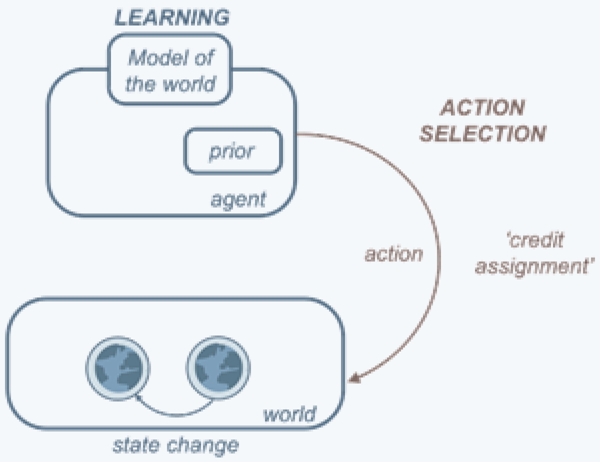


Rigoux, Stephan, Petzschner, PlosCB, 2024

Computational Model: POMDP

Modeling the impact of beliefs on behavior

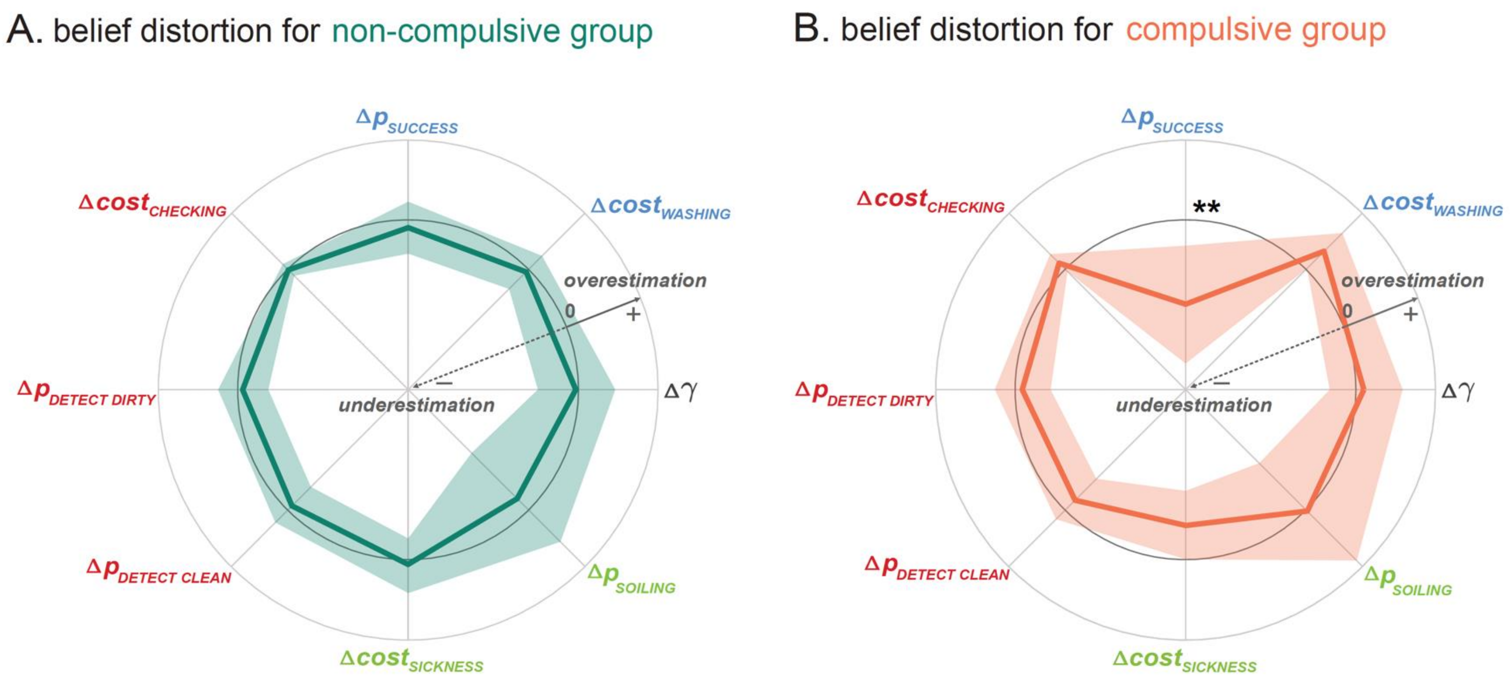


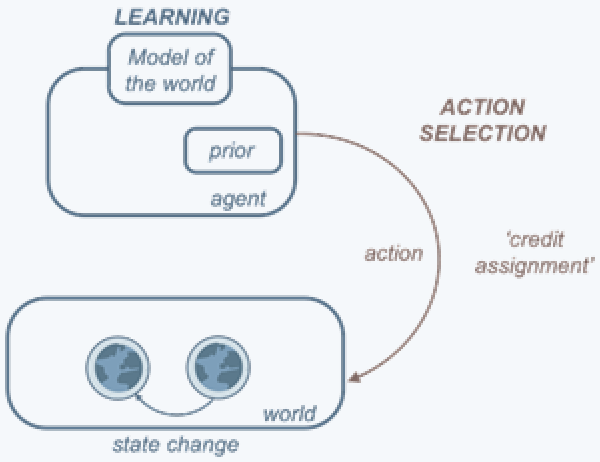


Rigoux, Stephan, Petzschner, PlosCB, 2024

Computational Model: *POMDP*

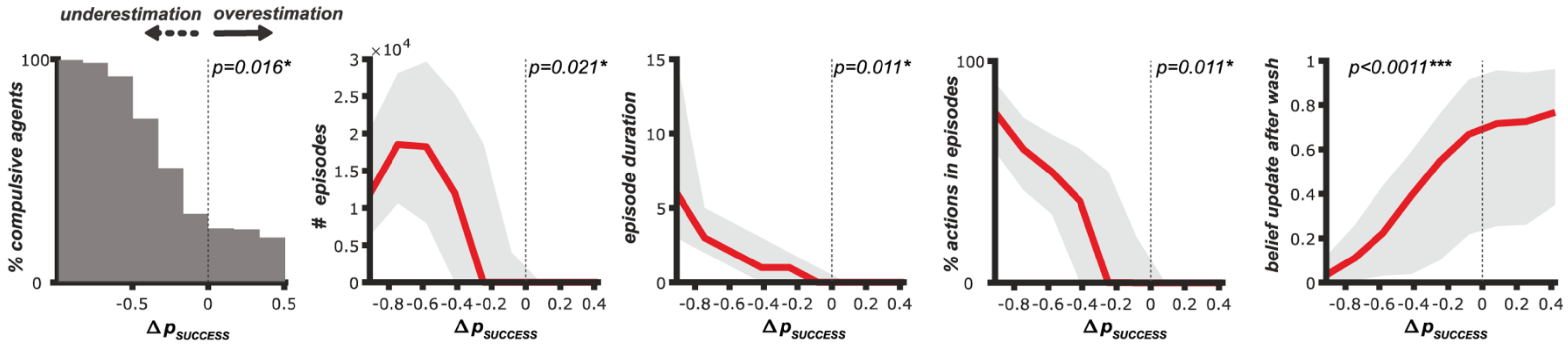
Compulsive behavior is driven by a distrust in effective avoidance



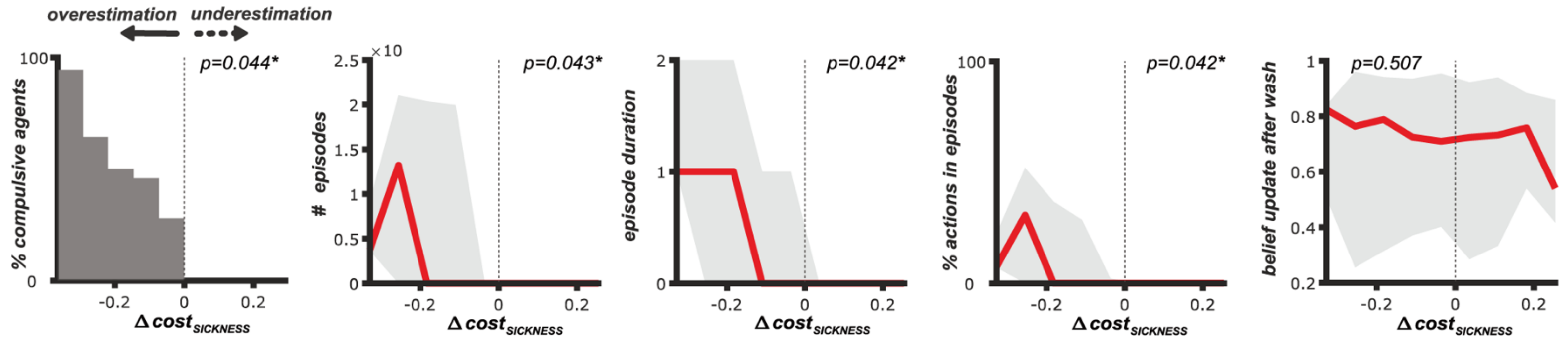


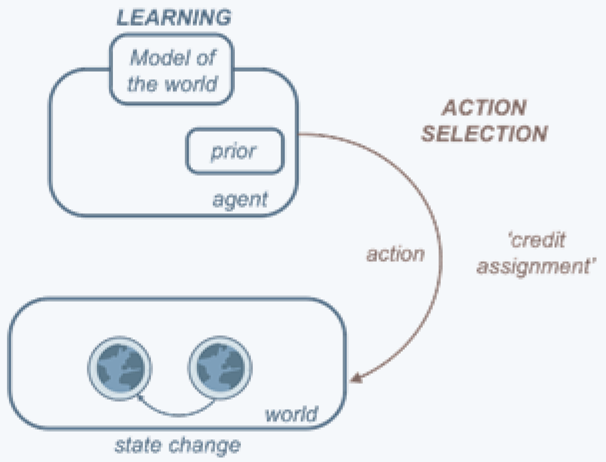
Rigoux, Stephan, Petzschner, *PlosCB, 2024*

Distrust in avoidance effectiveness is sufficient to cause compulsions and correlated with increases in compulsion severity.



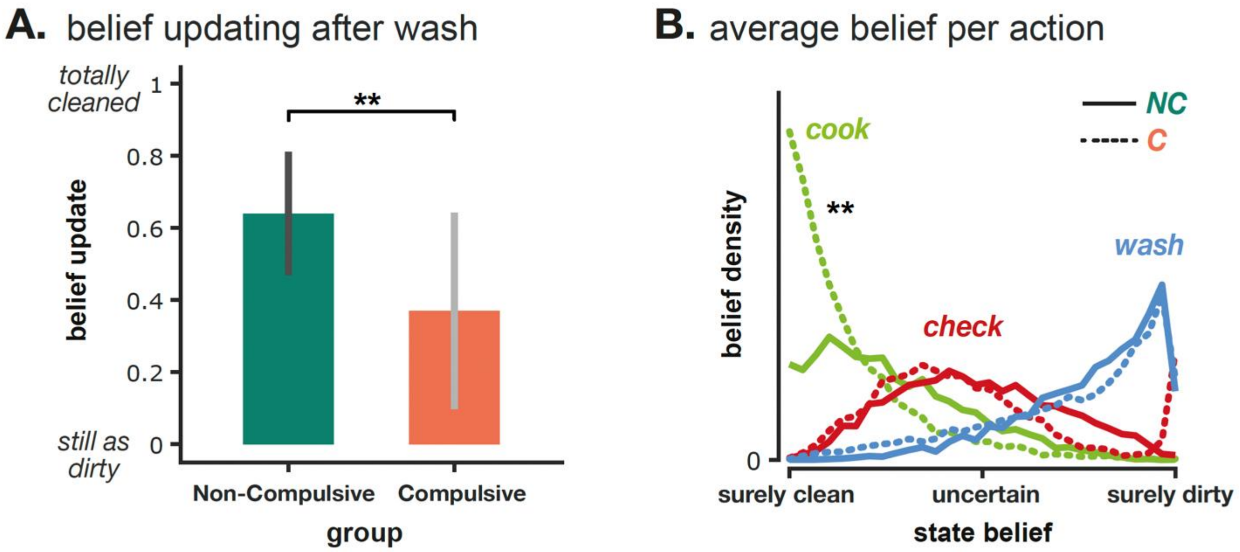
Overestimation of threat can trigger the onset of compulsive episodes, but does not sustain compulsions

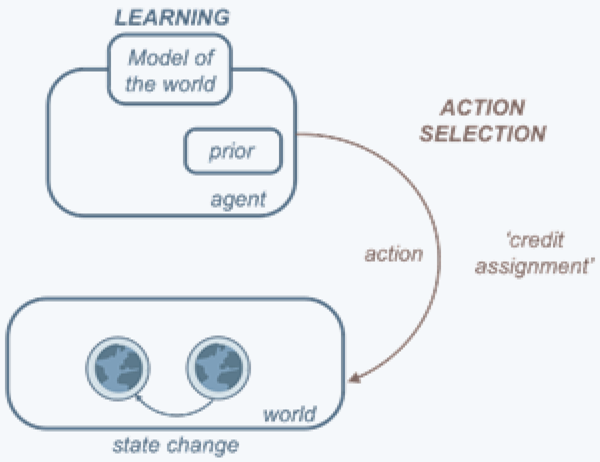




Rigoux, Stephan, Petzschner, *PlosCB, 2024*

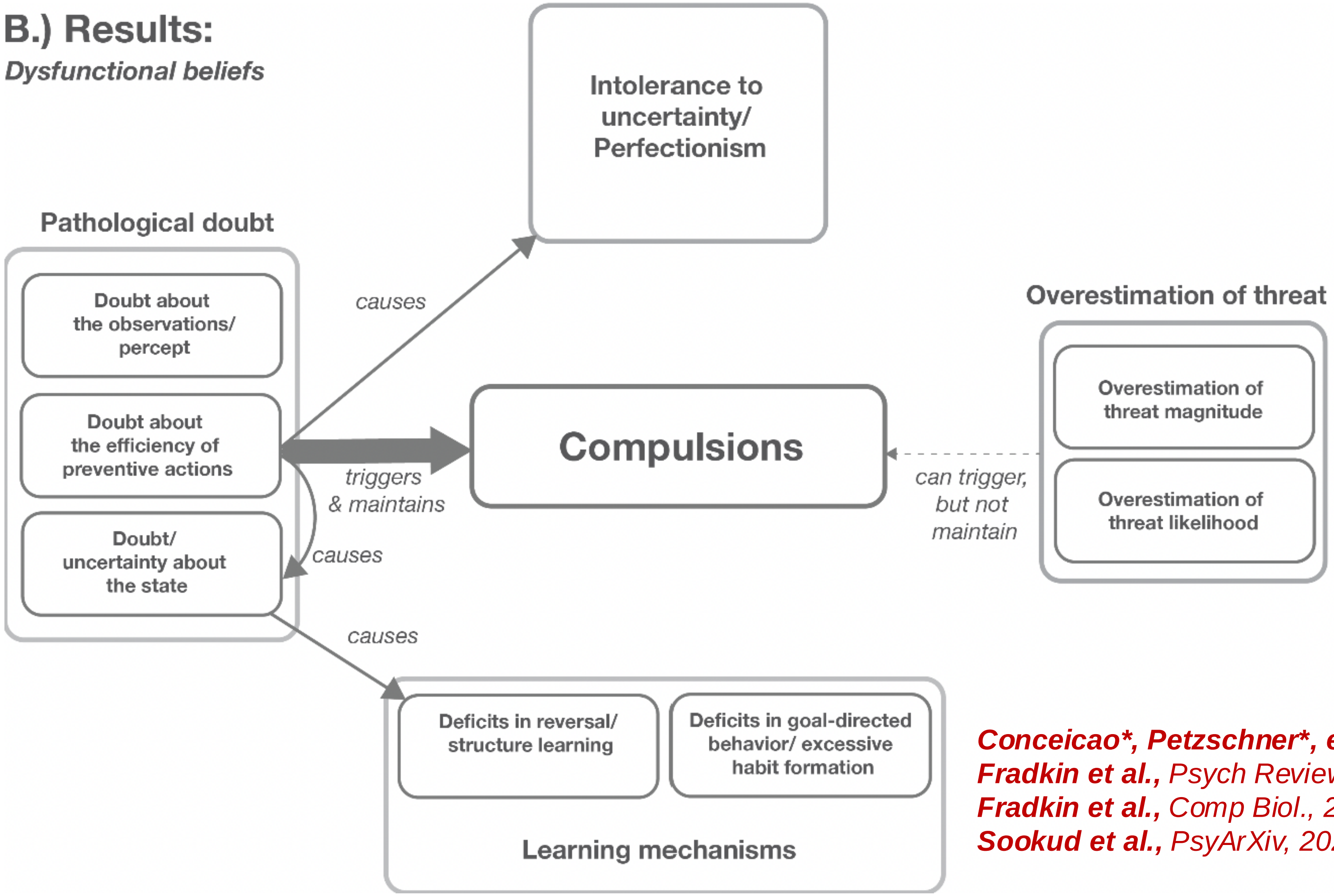
Underestimation of avoidance success leads to slowed belief updating and pathological doubt

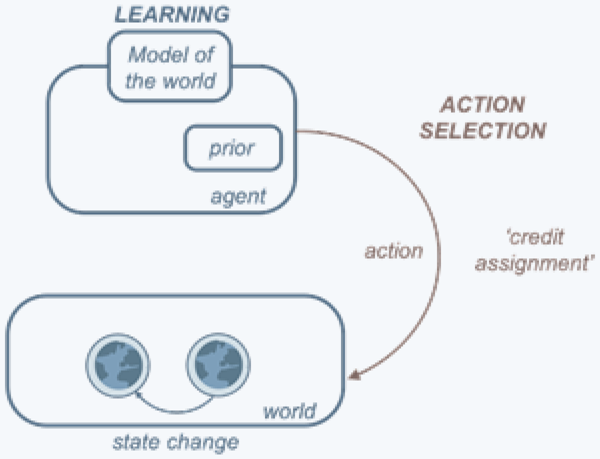




Rigoux, Stephan, Petzschner, *PlosCB, 2024*

B.) Results:
Dysfunctional beliefs





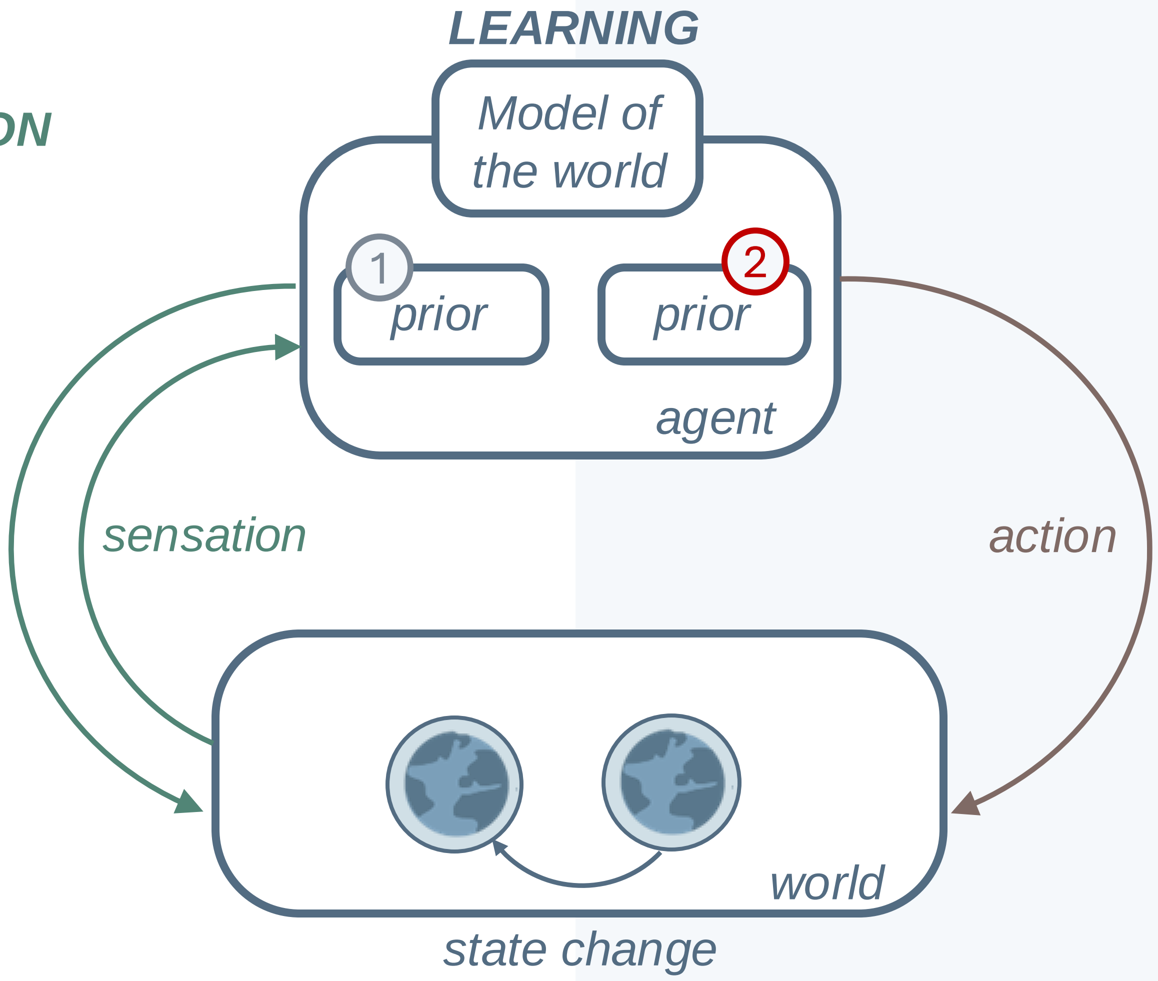
Conceicao*, Petzschner*, et al. , *BioRxiv, 2023*
Fradkin et al., *Psych Review, 2020*
Fradkin et al., *Comp Biol., 2020*
Sookud et al., *PsyArXiv, 2024*

Get the Paper

Rigoux, Stephan, Petzschner*, PlosCB, 2024*

PERCEPTION
prediction/ inference

1 ***Autism:*** *Imprecise priors may underlie perceptual symptoms in Autism Spectrum Disorder*



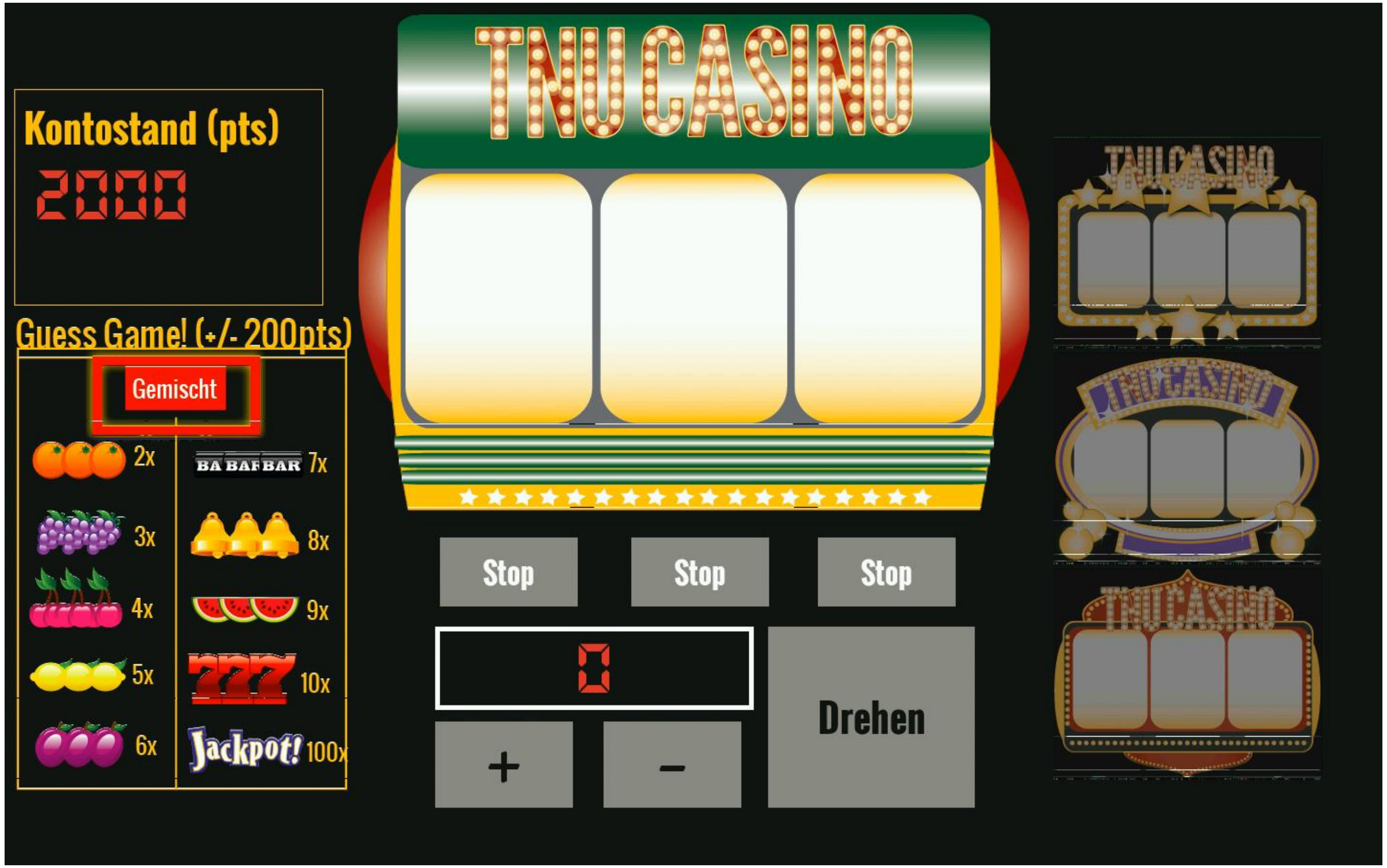
ACTION SELECTION
'credit assignment'

2 ***OCD:*** *decreased belief about control can cause compulsion (harm avoidance)*

OCD Paper

Petzschner, Weber *et al., Biol Psych, 2017*

Maladaptive Credit Assignment in Pathological Gambling



Recreational Gamblers (n = 43)
Pathological Gamblers (n = 44)

Saee Paliwal

Gina Paolini

Stephanie Olayia

Independent manipulation of reward and control

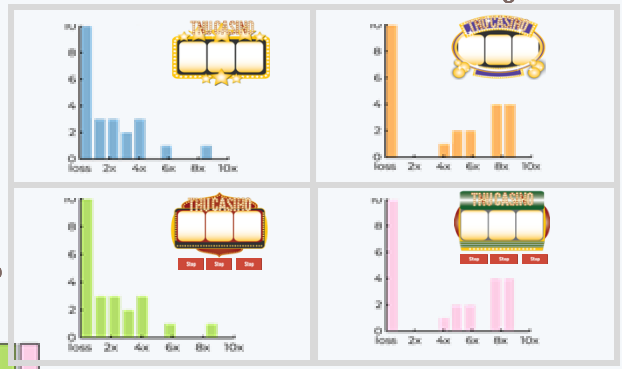
Reward (magnitude)

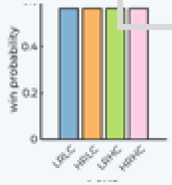
low high

(illusion of) control

low

high





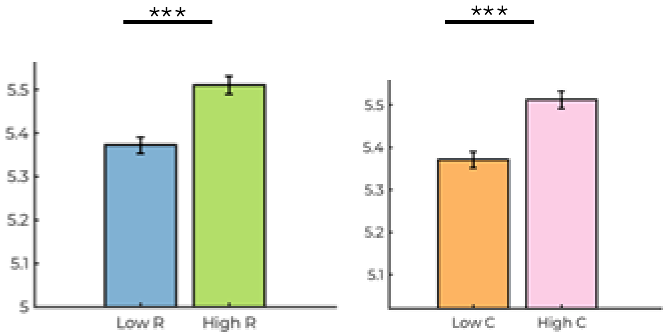
Same win probability across machines!

Petzschner*, Paliwal* et al., (in prep)

Beliefs about control increase bet size

Effect of reward magnitude

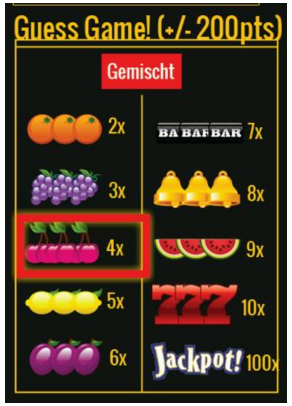
Effect of illusion of control



LME for log(betsize):
Main effect of reward magnitude
Main effect of control illusion
* Main effect of patient
Interaction reward magn. x control illusion
Interaction patient x control illusion
n.e. Interaction patient x reward magnitude

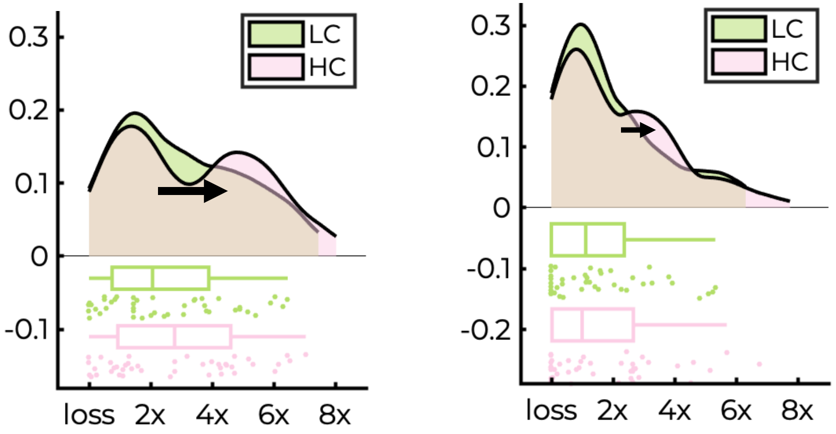
	reward magnitude	
(illusion of) control	Low/Low	Low/High
	High/Low	High/High

Beliefs about control increase outcome prediction



Pathological Gamblers

Recreational Gamblers

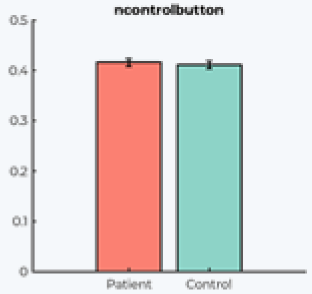


True Control:
P_{obj}(Outcome|Action)

Illusion of control belief:
P_{subj}(Outcome|Action)

LME gamma link for outcome prediction:
Main effect of control illusion
Main effect of reward magnitude
Main effect of patient
n.s. Interaction reward x control illusion
Interaction patient x reward
n.s. Interaction patient x control illusion

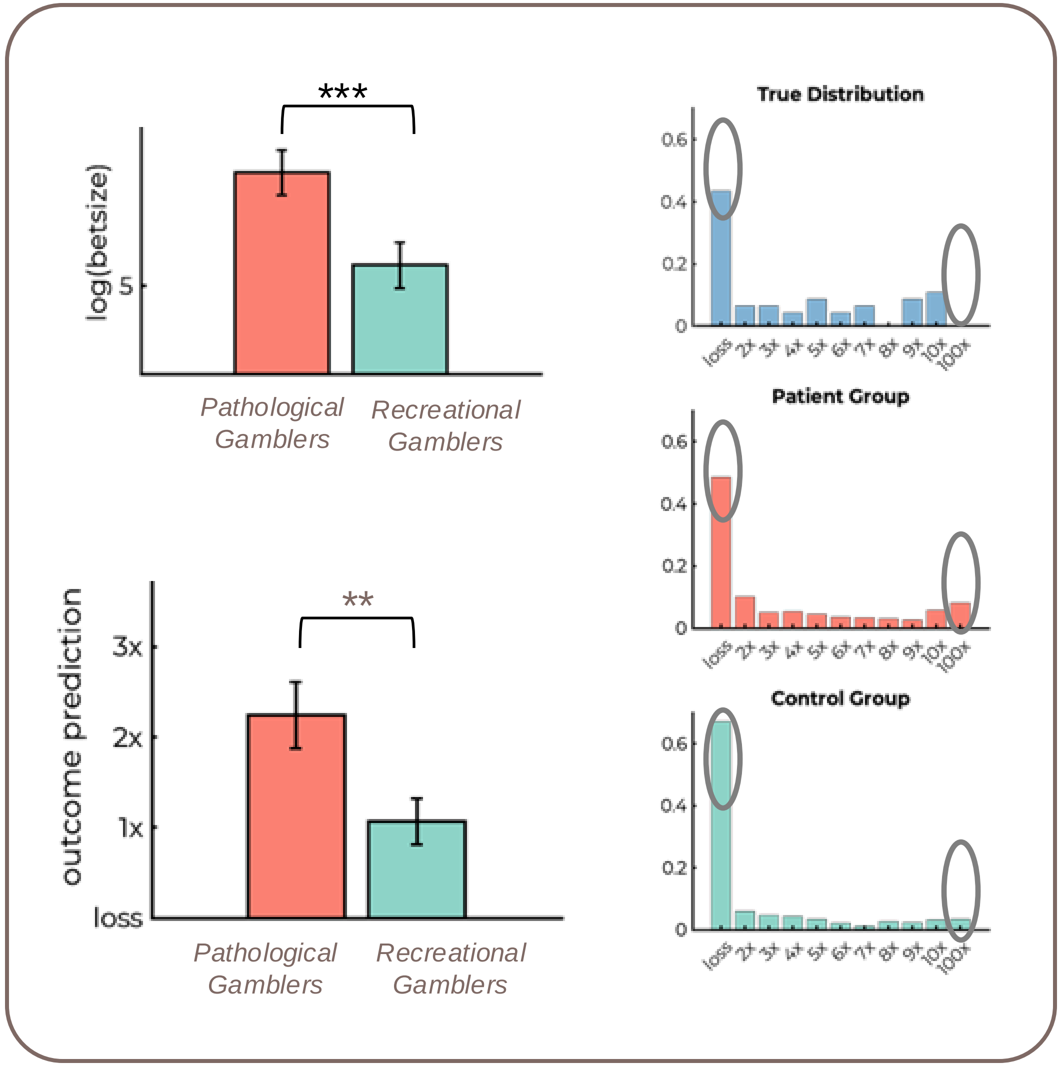
The effect of control does not depend on whether we execute control!

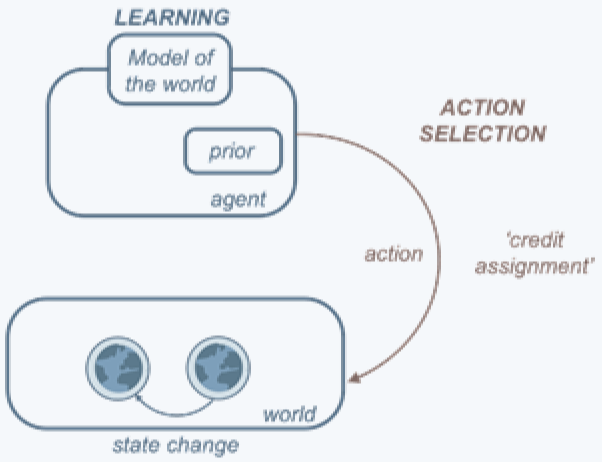


Recreational Gamblers (n = 43)
Pathological Gamblers (n = 44)

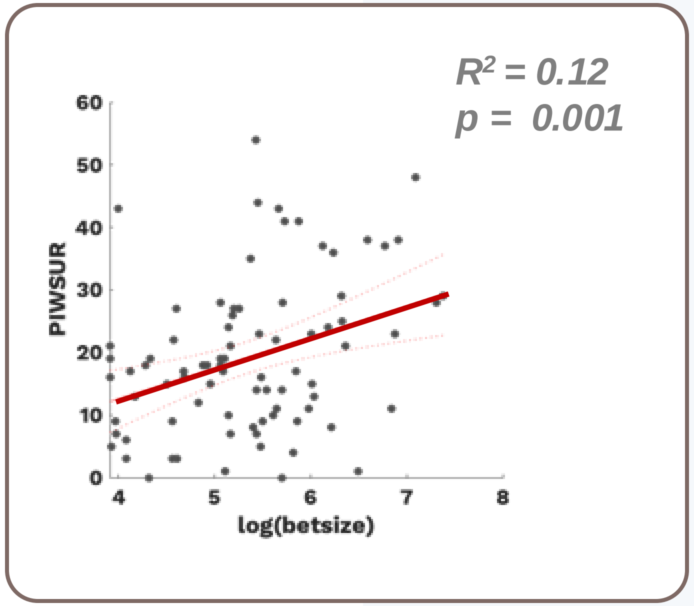
Petzschner*, Paliwal* et al., (in prep)

Group Differences





Baseline number of button presses should relate to compulsivity



Recreational Gamblers (n = 43)
Pathological Gamblers (n = 44)

Petzschner*, Paliwal* *et al., (in prep)*

Group Differences

Computational Model: *RL*

No learning

$Model\ 1:\ log(b_i) \sim \beta_1$

$Model\ 2:\ log(b_i) \sim \beta_1 + \beta_2 \cdot r_{t-1}$

Learning a value of the machine (context)

$Model\ 3:\ log(b_i) \sim \beta_1 + \beta_2 \cdot V_t$

$$V_{t+1}(s) = V_t(s) + \alpha_1 \delta_{V,t}$$

$Model\ 4:\ log(b_i) \sim \beta_1 + \beta_2 \cdot V_t$

$$if\ \delta_{V,t} \geq 0:\ V_{t+1}(s) = V_t(s) + \alpha_1 \delta_{V,t}$$

$$if\ \delta_{V,t} < 0:\ V_{t+1}(s) = V_t(s) + \alpha_2 \delta_{V,t}$$

Learning + Control as Value increase

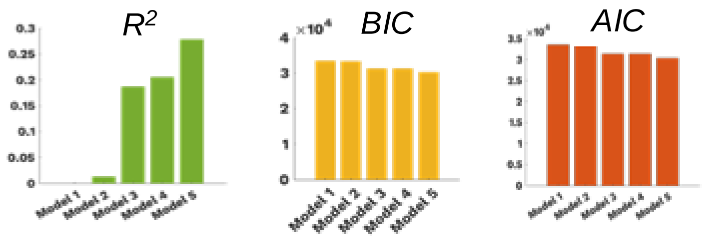
$Model\ 5:\ log(b_i) \sim \beta_1 + \beta_2 \cdot V_t$

$$if\ \delta_{V,t} \geq 0:\ V_{t+1}(s) = V_t(s) + \alpha_1 \delta_{V,t}$$

$$if\ \delta_{V,t} < 0:\ V_{t+1}(s) = V_t(s) + \alpha_2 \delta_{V,t}$$

$$if\ control\ high:\ V_{t+1}(s) = V_t(s) + \alpha_3 V_t(s)$$

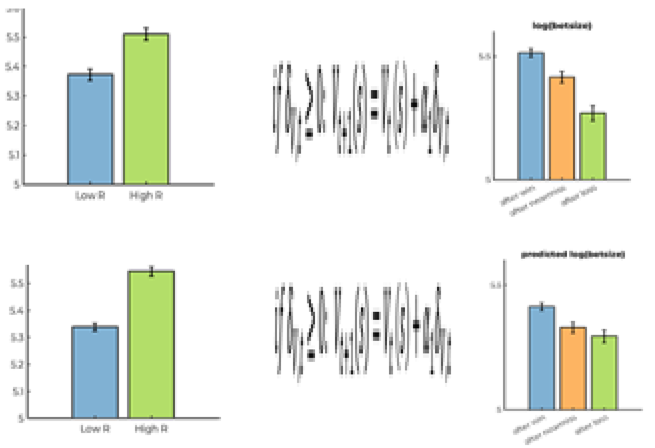
Model 5 with learning and control is winning model

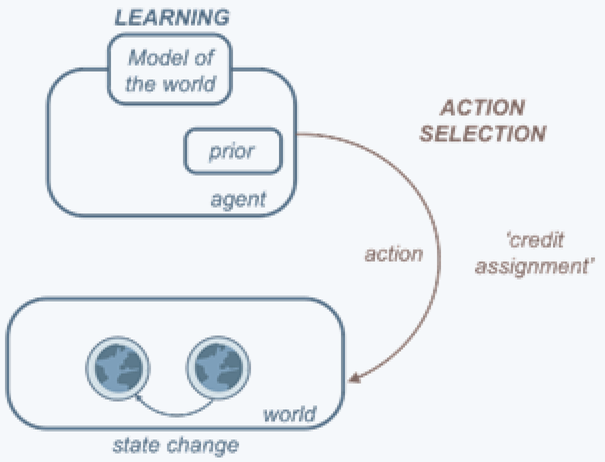


Winning model can capture the main effects in the data

Data

Model prediction



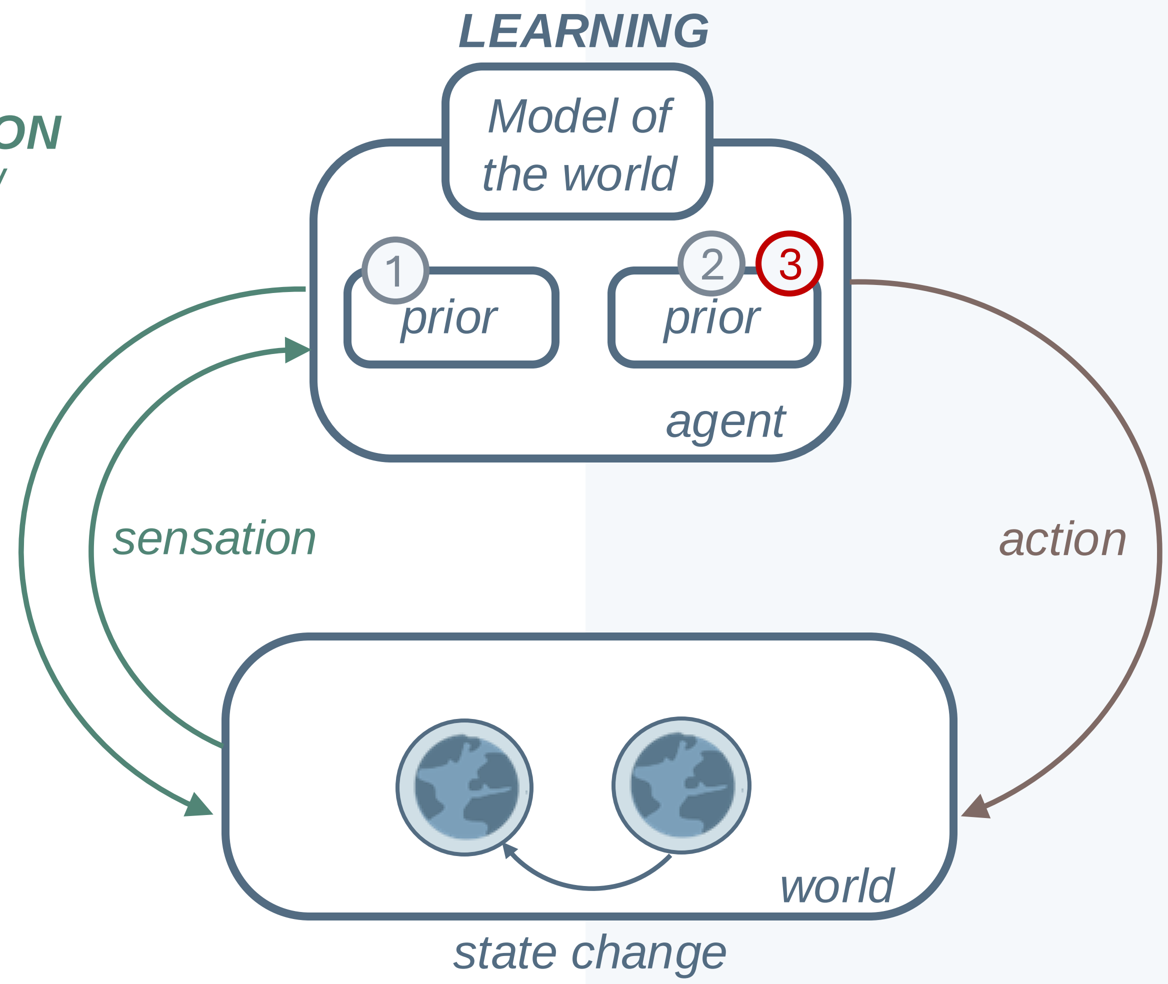


Recreational Gamblers (n = 43)
Pathological Gamblers (n = 44)

Petzschner*, Paliwal* et al., (in prep); **Gold** et al., 2012; **Palminteri** et al. 2015; Daw 2011

PERCEPTION
prediction/ inference

1 ***Autism:*** *Imprecise priors may underlie perceptual symptoms in Autism Spectrum Disorder*

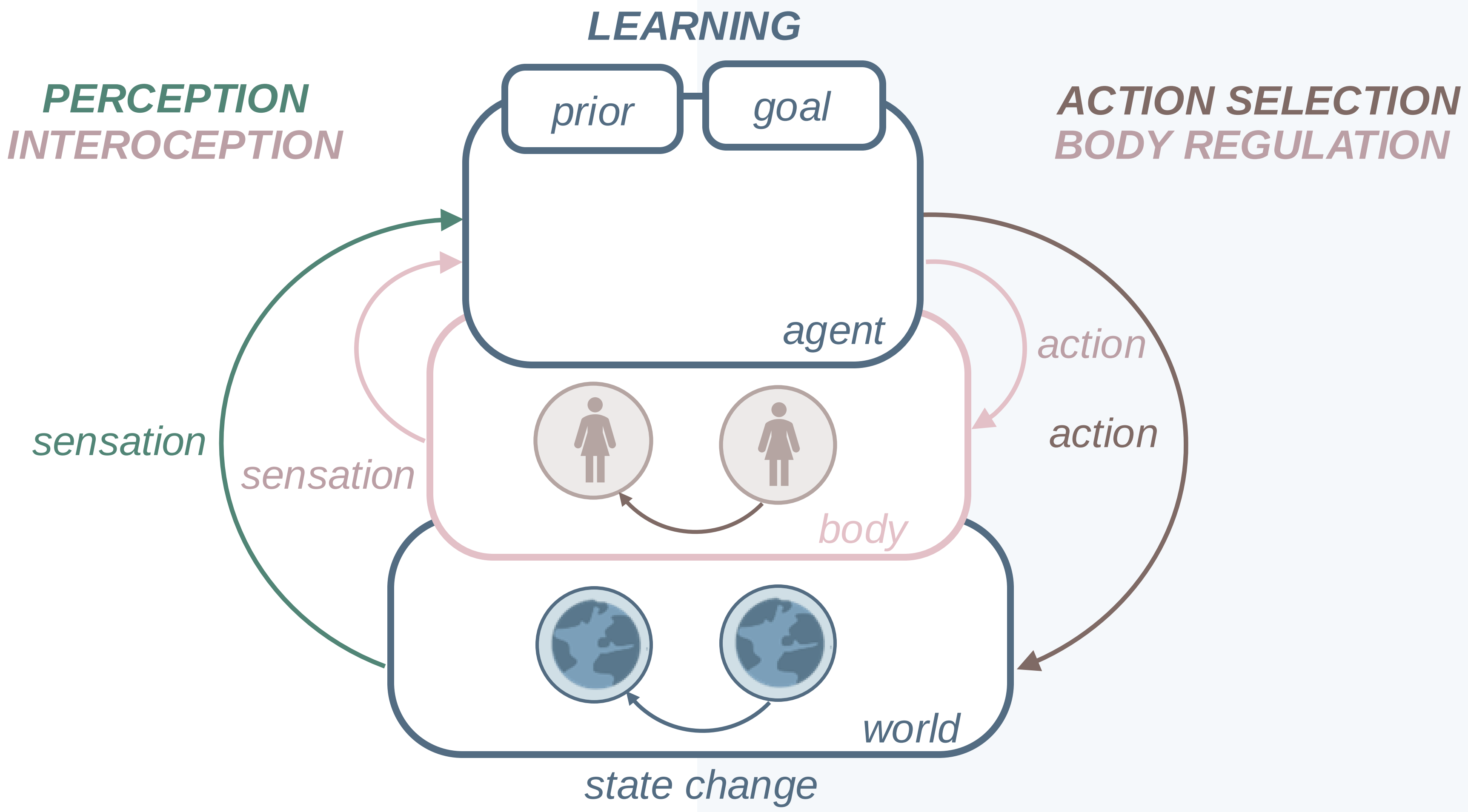


ACTION SELECTION
'credit assignment'

2 ***OCD:*** *decreased belief about control can cause compulsion (harm avoidance)*

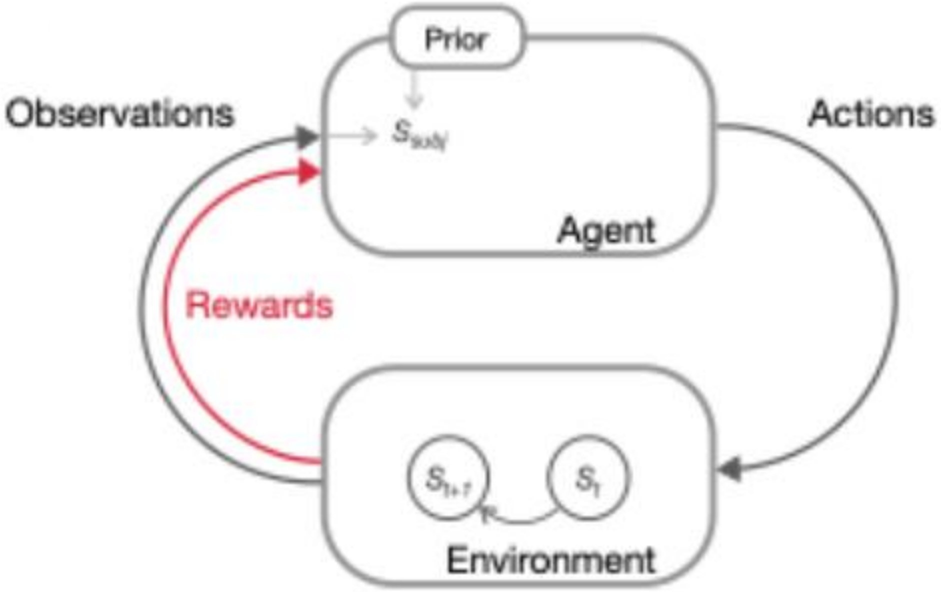
3 ***Pathological Gambling:*** *increased belief about control can cause compulsion (reward seeking)*

Petzschner, Weber *et al., Biol Psych, 2017*



Seth, *TiCS, 2012*
Khalsa et al., *Biol Psych, 2018*
Petzschner, Weber et al., *Biol Psych, 2017*
Petzschner et al. *TINS, 2021*

New Preprint:
“Rethinking reinforcement learning: The interoceptive origins of reward”



Reward Paper

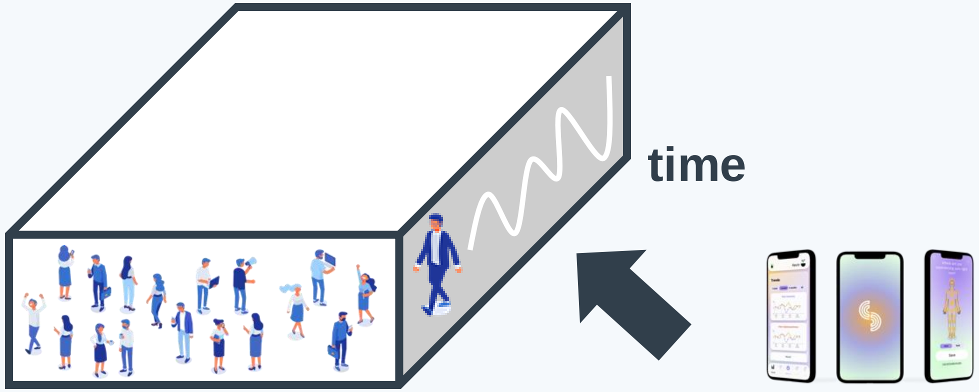
Weber, Yee, Small, Petzschner, *PsyArxiv, 2024 (invited at TiCS)*

1. Disease insights

Mechanistic Models

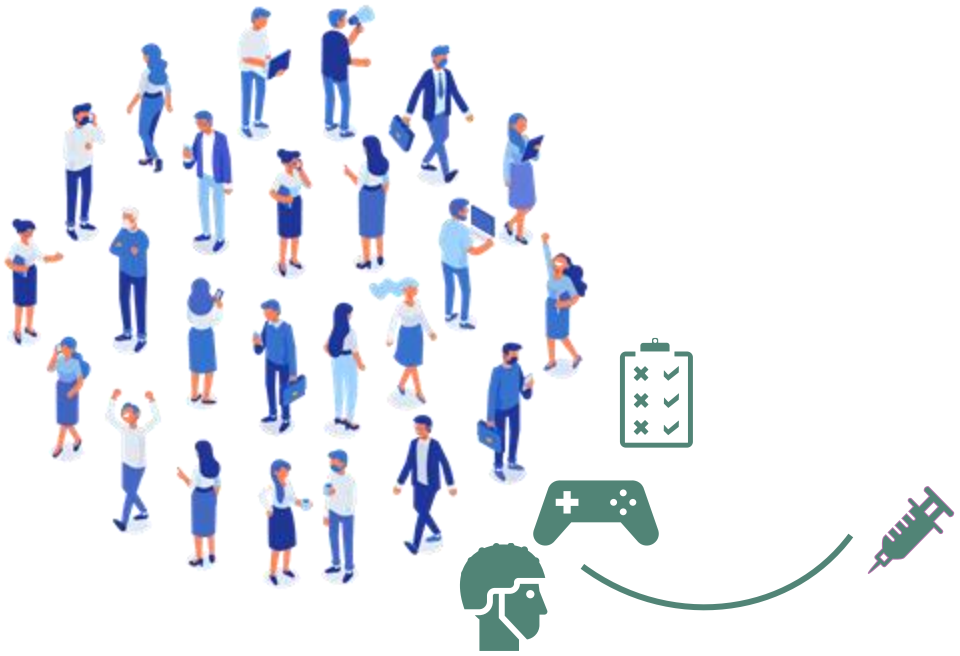
Big data

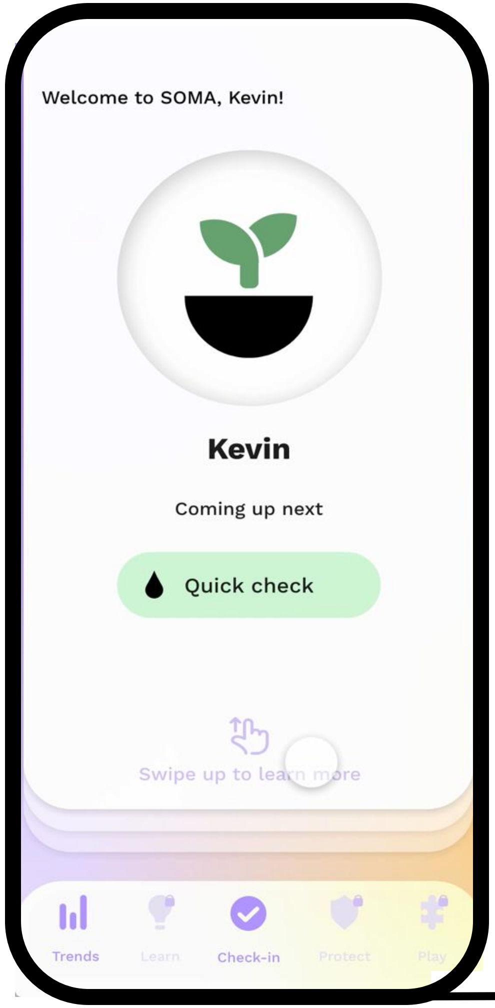
Prediction needs: Deep & wide data



2. Predictive validity

Data-driven Models





- Pain inten
- Pain i
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- Mood
- Emot
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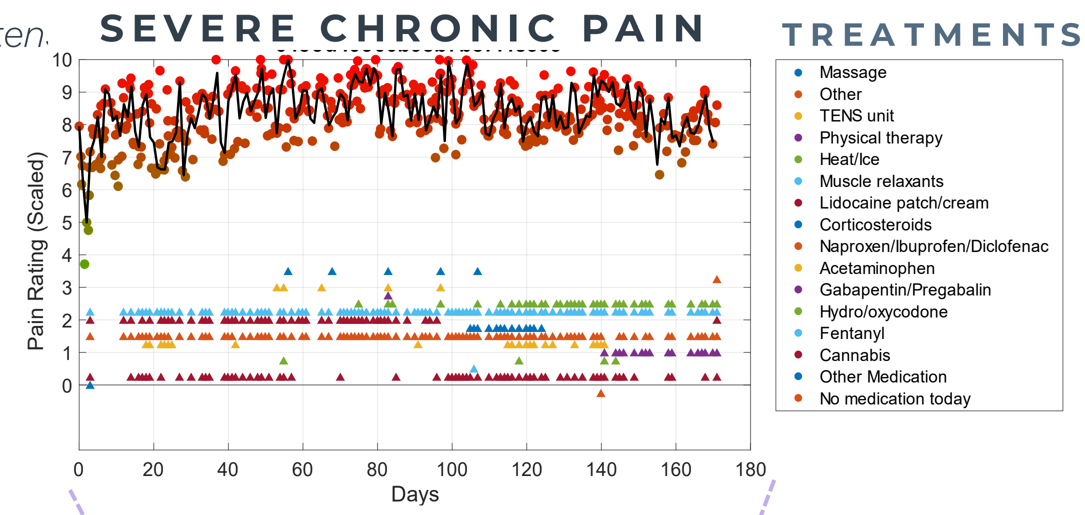

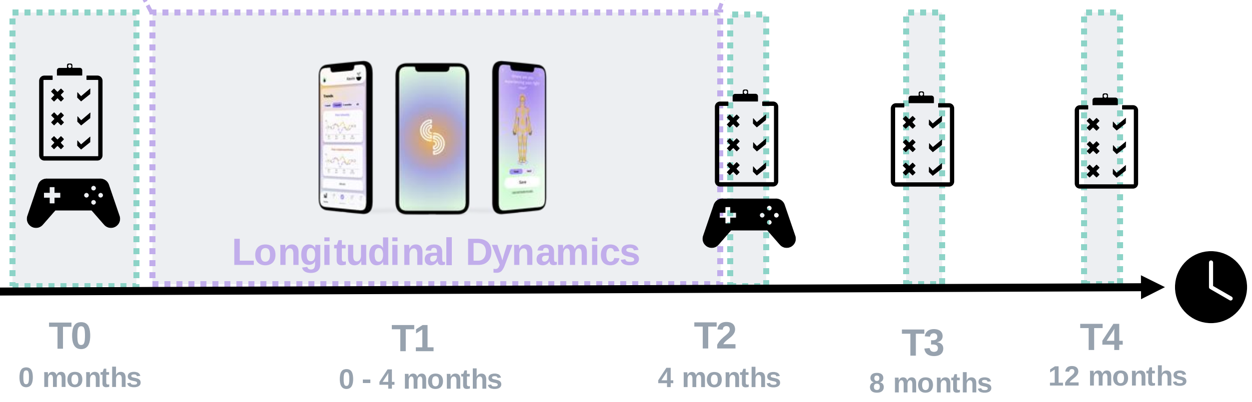

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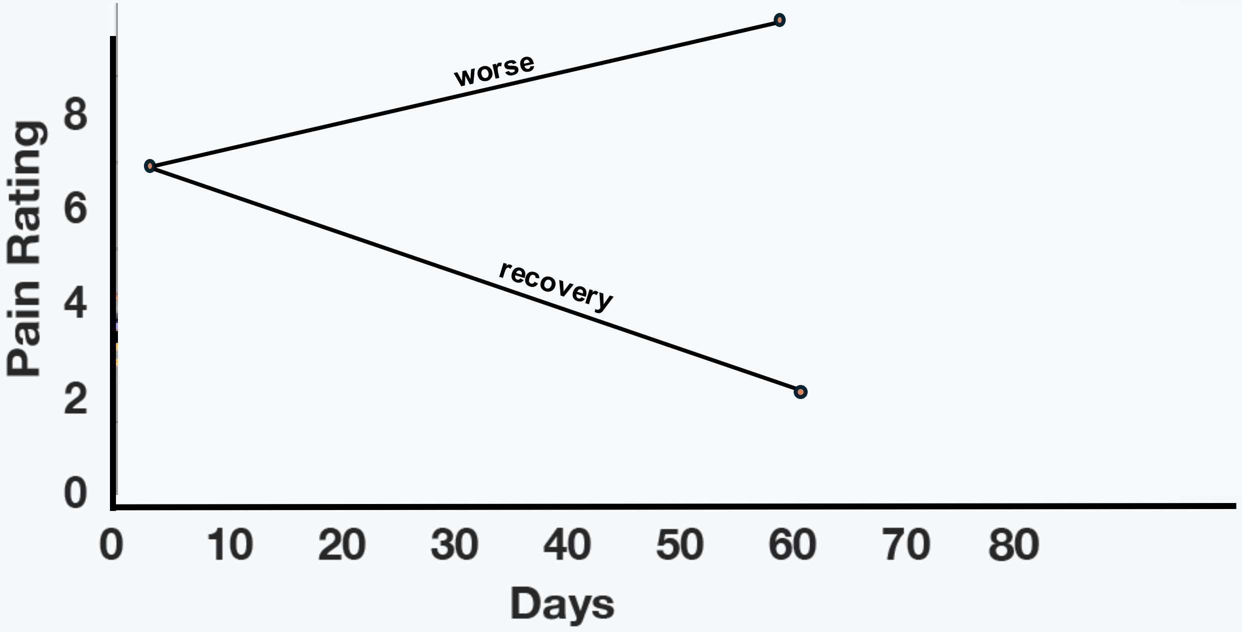
Zimmermann, …Petzschner, JMIR UHealth, 2024*

Pain and Mood are highly variable. Single ratings often fail to give a full picture of recovery.

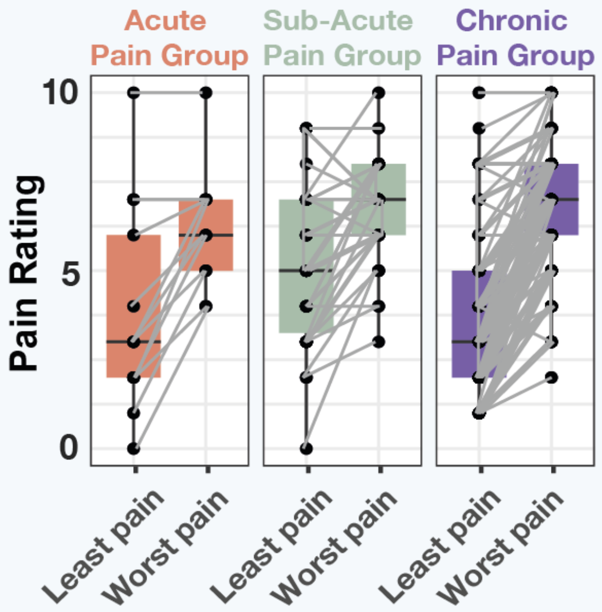
Patient A

Patient B

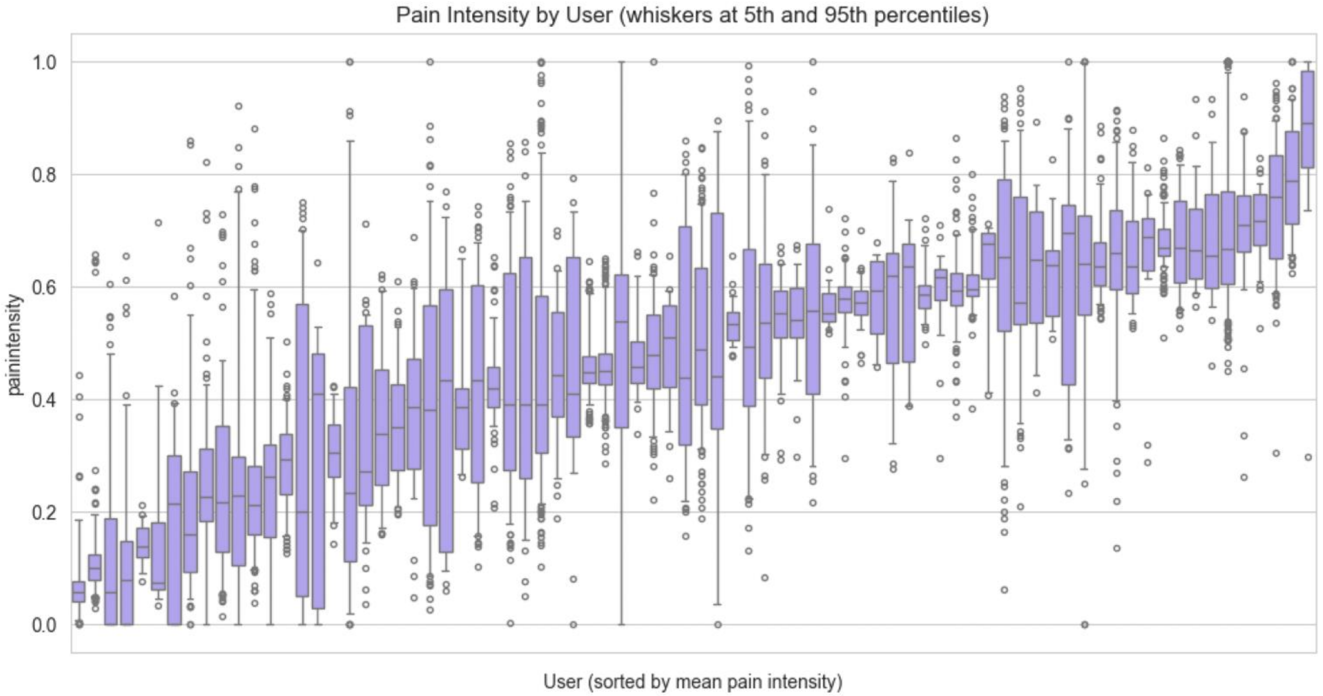


Variability with days and across months

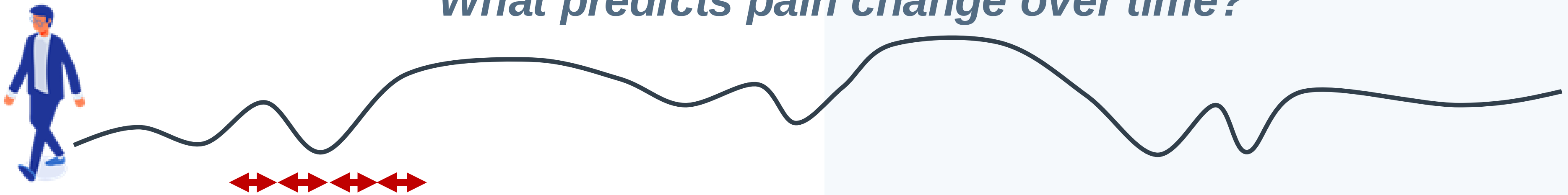
Within 24h



Within 4 month

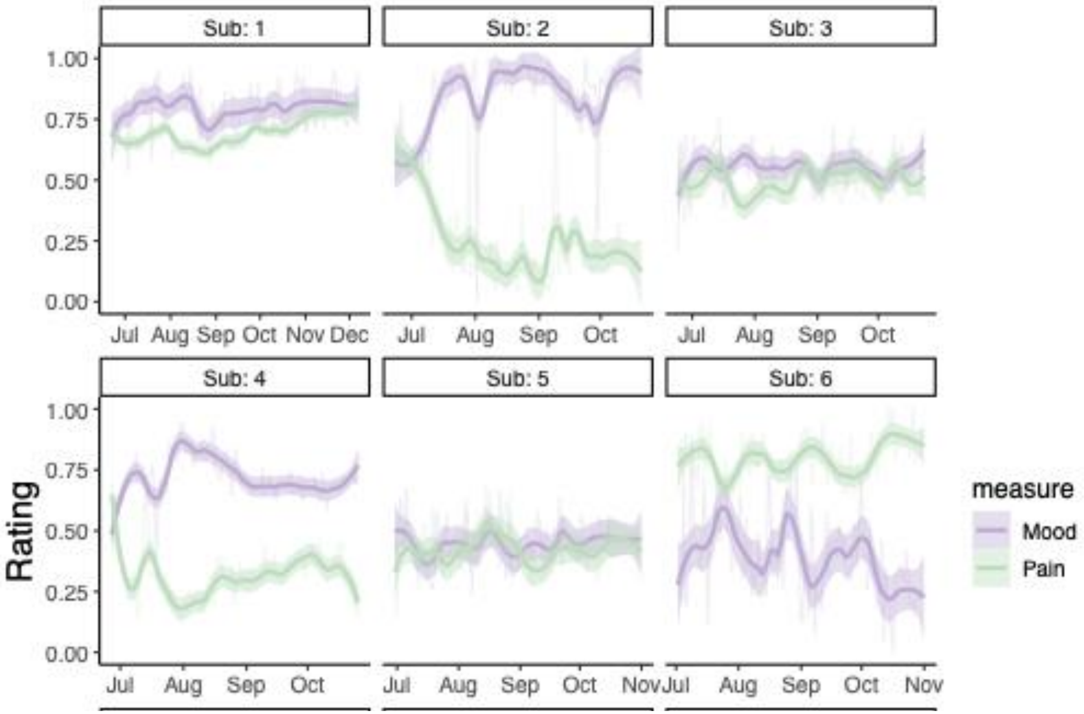


What predicts pain change over time?



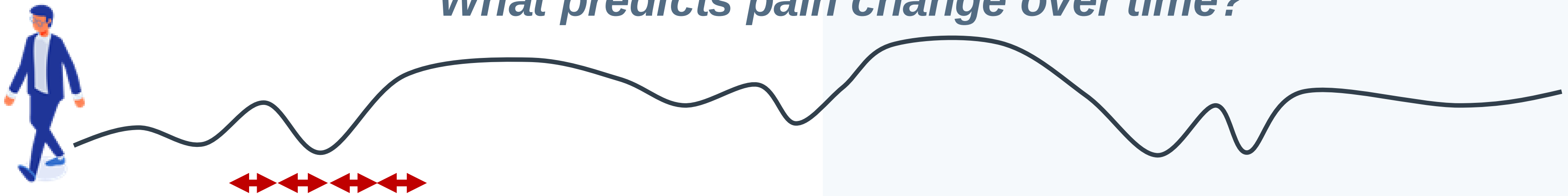
day to day

SHORTTERM:



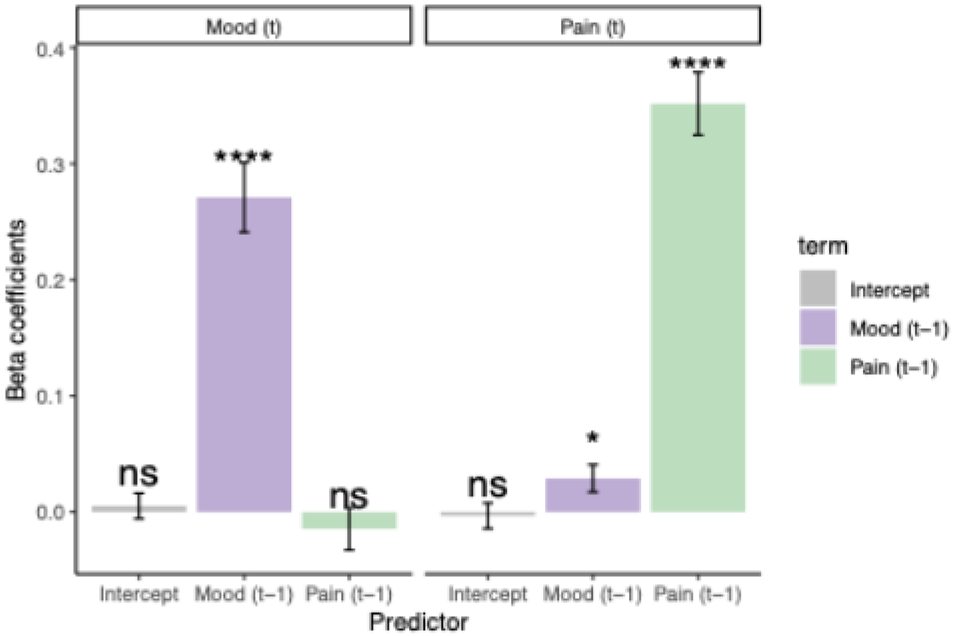
Chloe Gunsilius *Joseph Heffner*

What predicts pain change over time?



day to day

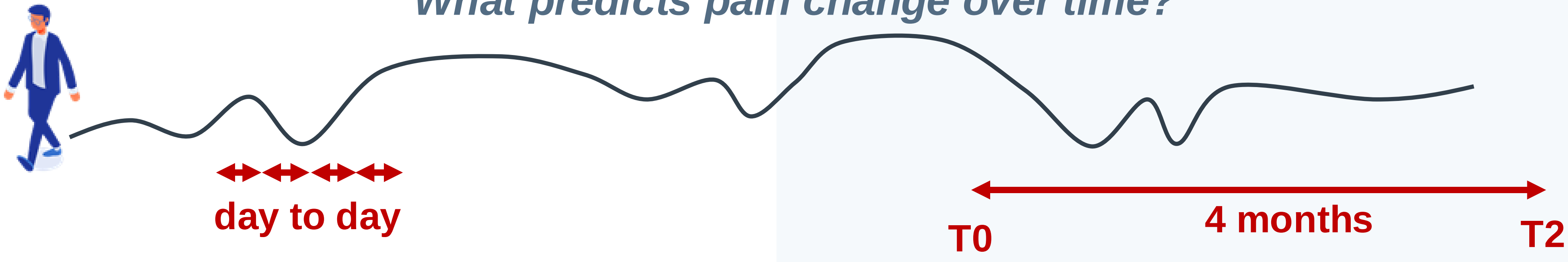
SHORTTERM:
Mood and expected pain best predict current pain,
but current pain does not predict future mood



Chloe Gunsilius

Joseph Heffner

What predicts pain change over time?



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Mood and expected pain best predict current pain,
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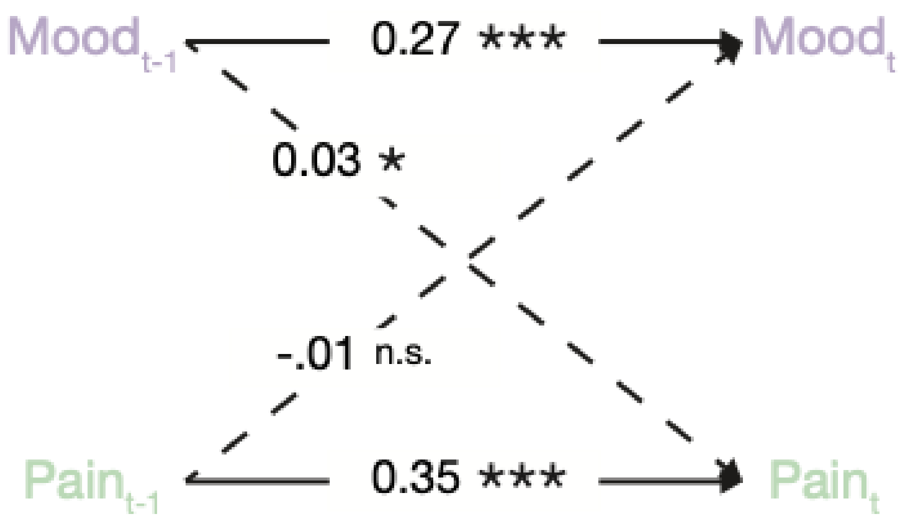
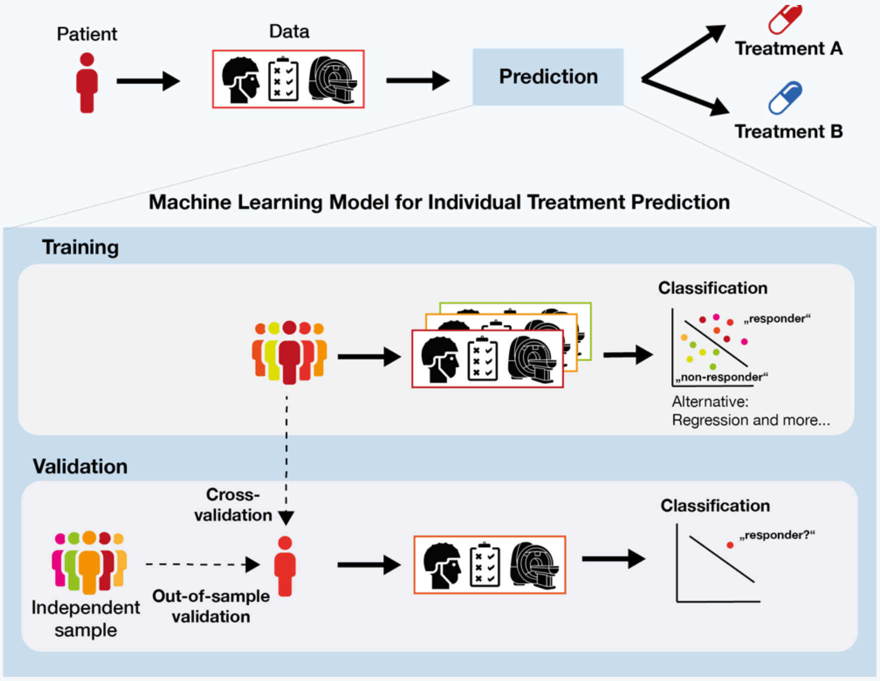


LONGTERM:



Petzschner, *Science, 2024*

n = 127

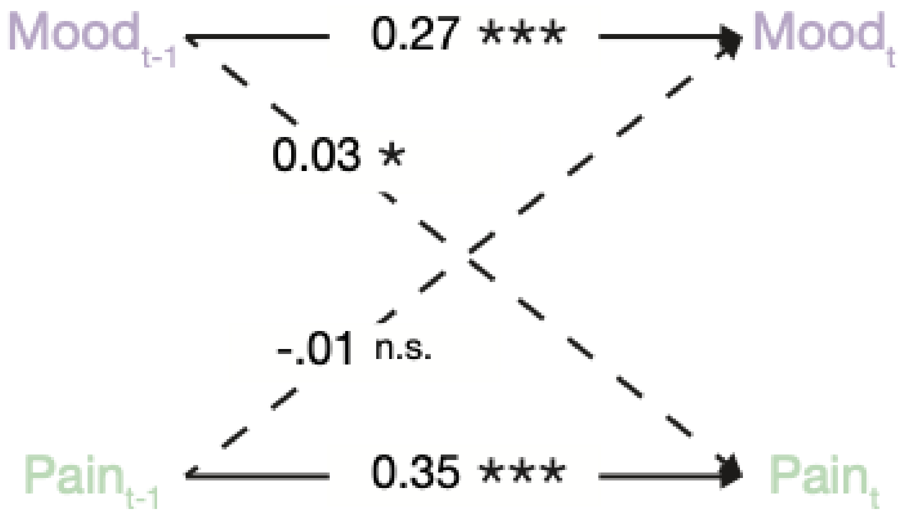
What predicts pain change over time?

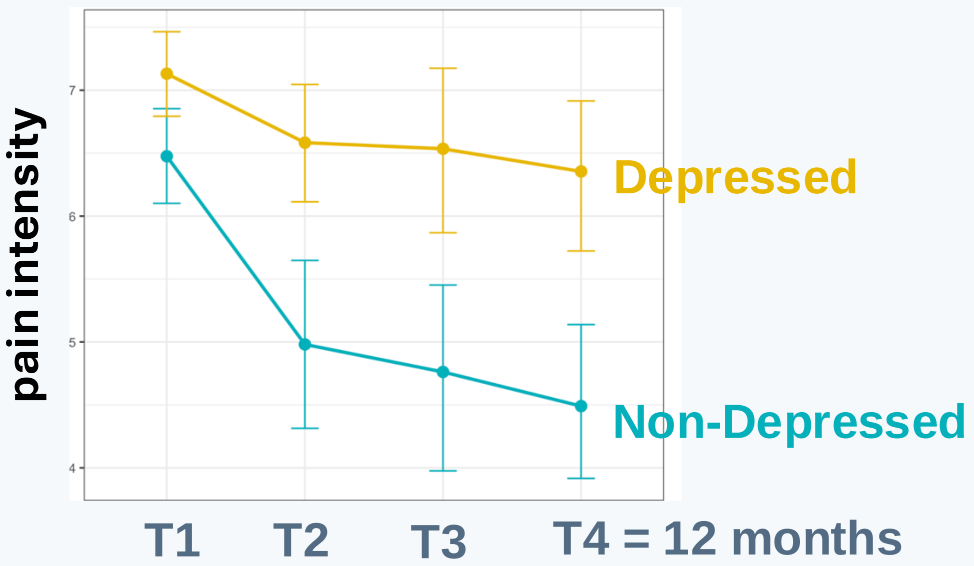
SHORTTERM:

Mood and expected pain best predict current pain, but current pain does not predict future mood

LONGTERM:

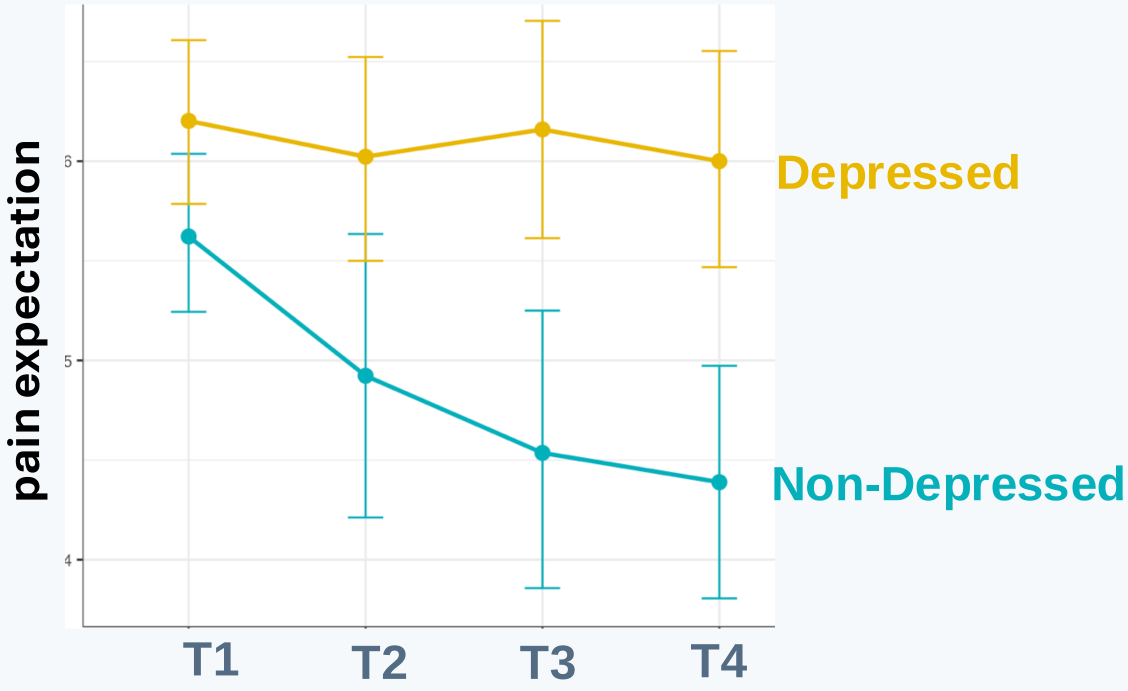
Depression and expected pain predict pain change over 4 months



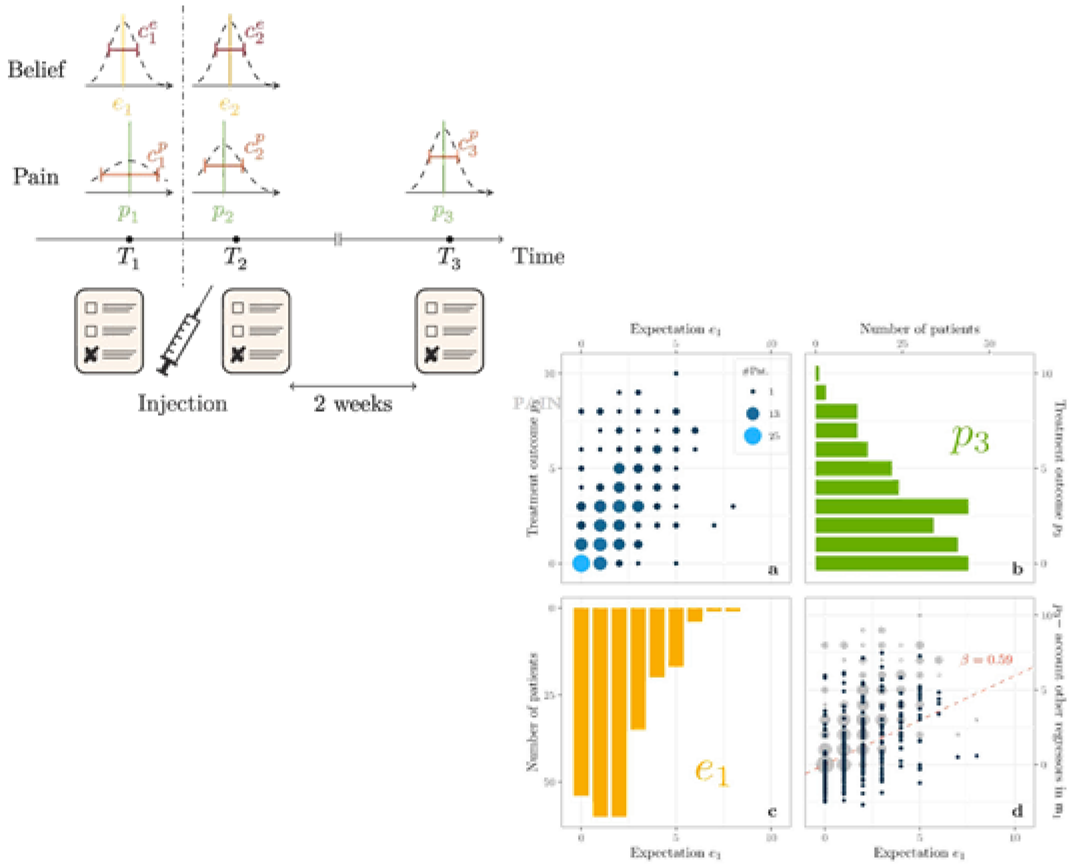


n = 127

Depression relates to negative pain expectations



Negative pain expectations predict treatment response

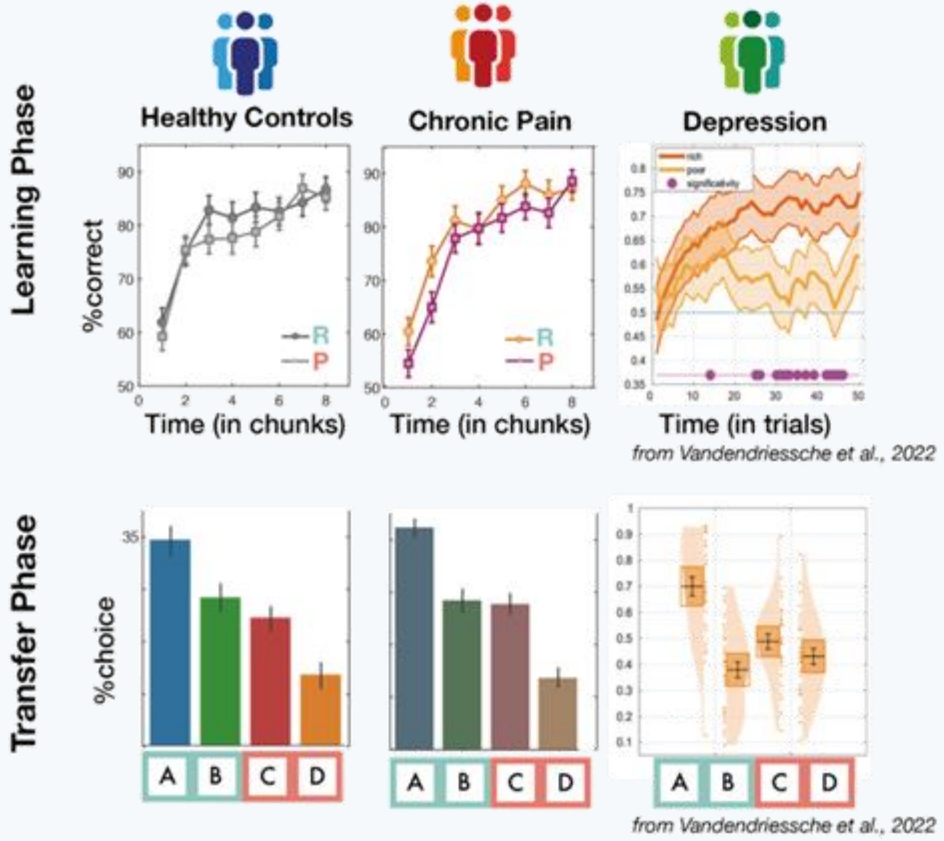


n = 252

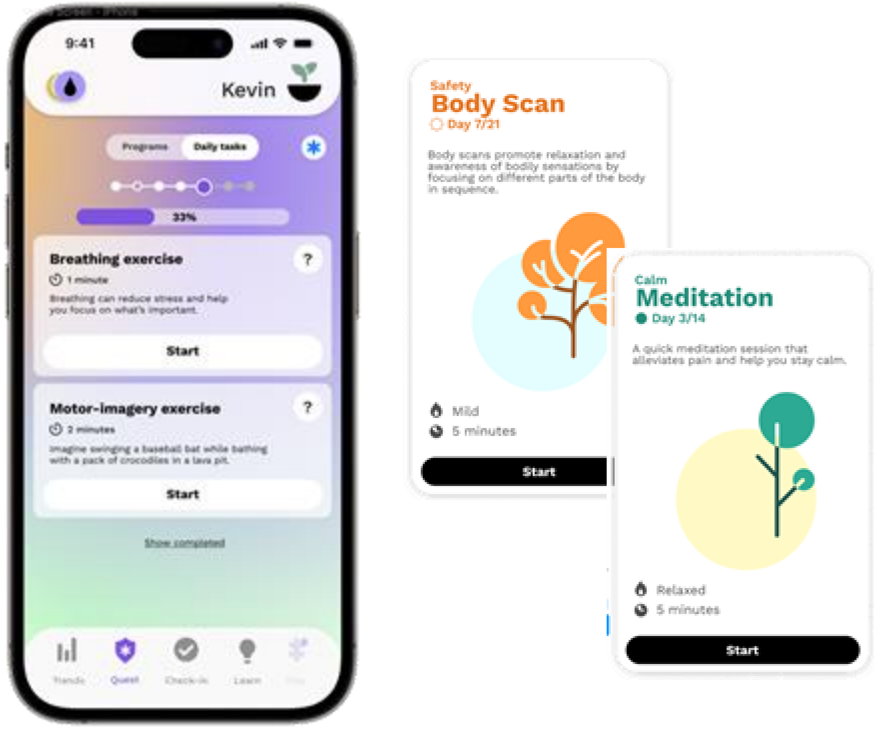
***Müller-Schrader** et al. Pain, 2023*

Next Steps

Understanding Comorbidity between Depression and Chonic Pain based on cortico-striatal function



Closed loop Mind-Body Intervention



1. Disease insights

Mechanistic Models

2. Predictive validity

Data-driven Models

Combination

Thank you!

Petzschner Lab:

- *Chloe Zimmerman*
- *Caroline McLaughlin*
- *Chad Williams*
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- *Bradford Roarr*
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- *Klaas Enno Stephan*
- *Matt Nassar*
- *Sienna Bruinsma*
- *Michael Frank*
- *Lionel Rigoux*
- *Stephanie Jones*
- *Lilian Weber*
- *Debbie Yee*
- *Dana Small*
- *Maya Schneebeli*
- *Tiago Maia*
- *Vasco Conceição*
- *Translational Neuromodeling Unit*

Reach out:

Website: fpetzschner.com/lab
SOMA Science: somatheapp.com
X: @rikepetzschner/ @peaclab/ @somatheapp

Lab Website

ROBERT J. & NANCY D. CARNEY INSTITUTE FOR BRAIN SCIENCE BROWN UNIVERSITY

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