Feedback please!

https://tnusurvey.ethz.ch/index.php/472246

RL in mental health

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No conflicts of interest.

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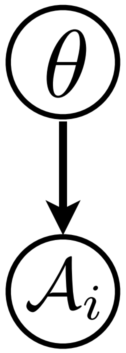
NYC

FNSNF DFG Deutsche Forschungsgemeinschaft minz Molecular Imaging Network Zurich

Disclaimer

- tutorial focus on analysing data with RL models
- very incomplete, selective and subjective review
- lots of my own work for exposition

Hierarchical estimation - “random” effects



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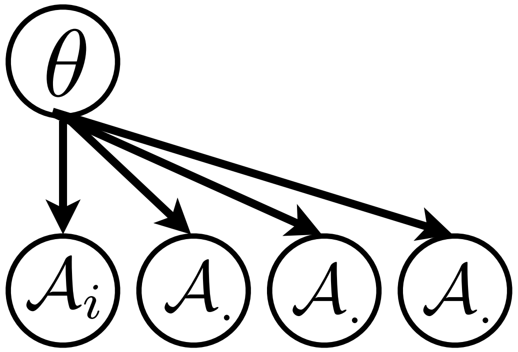

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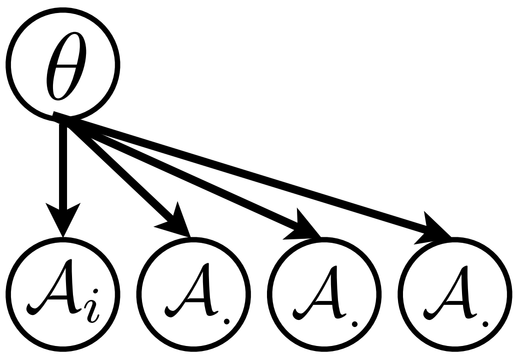

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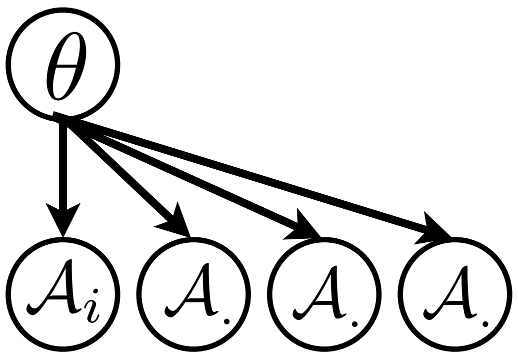

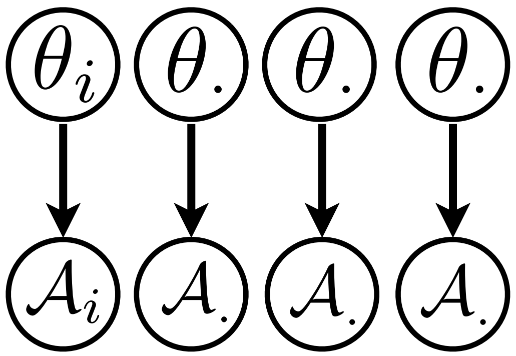

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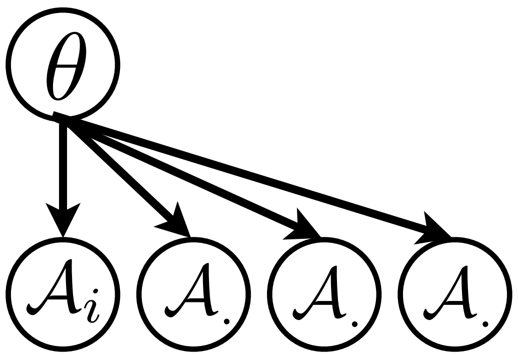

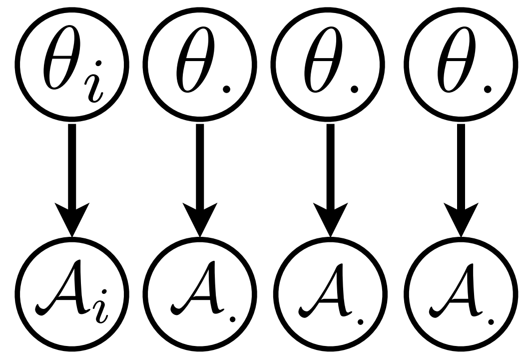

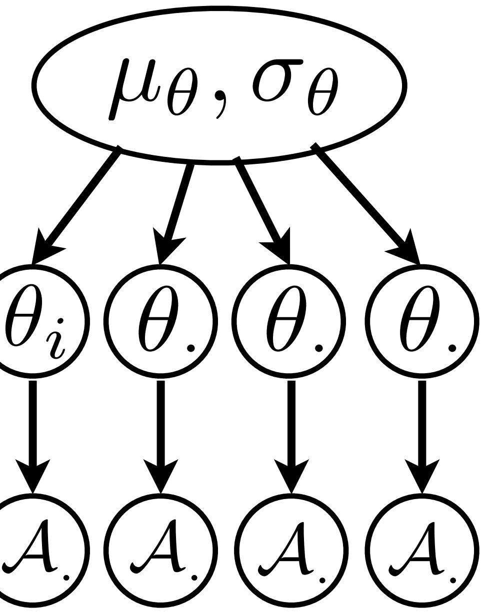

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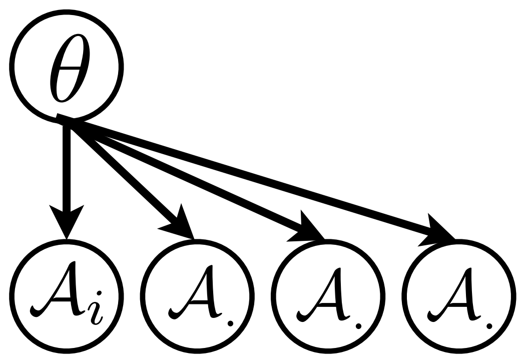

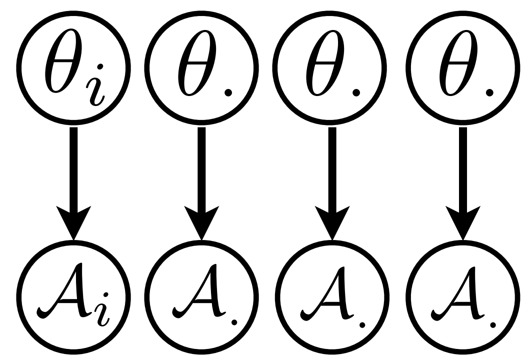

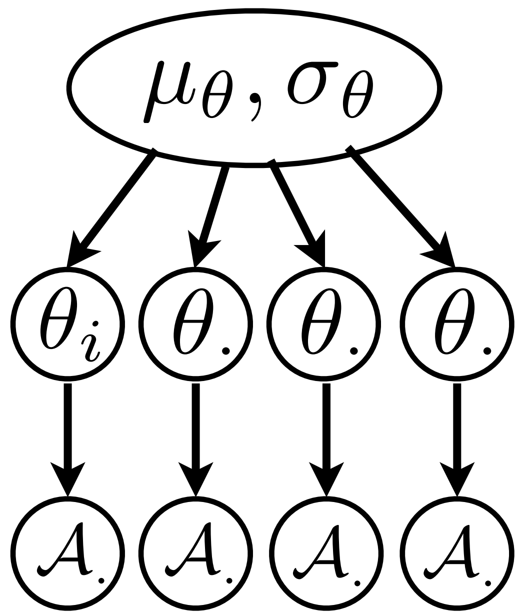

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$$p(\mathcal{A}_i|\mu_\theta,\sigma_\theta) = \int d\theta_i\, p(\mathcal{A}_i|\theta_i)\, p(\theta_i|\mu_\theta,\sigma_\theta)$$

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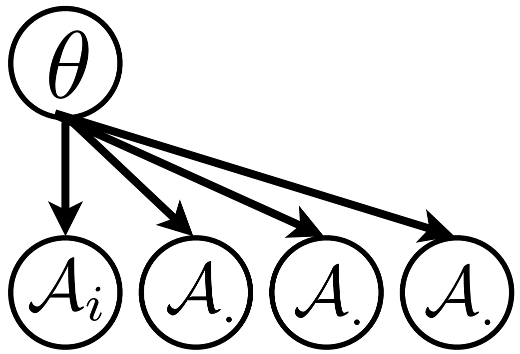

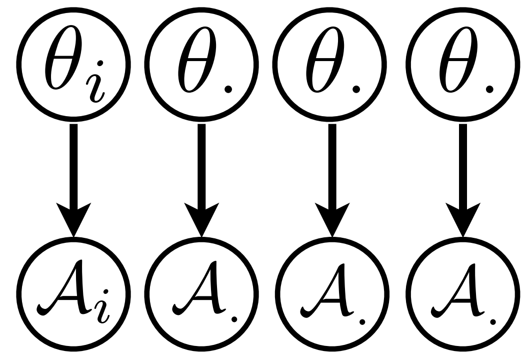

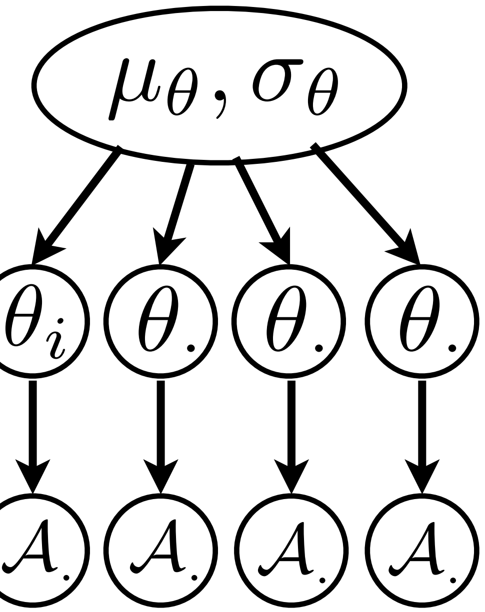

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Estimating the hyperparameters

- Effectively we now want to do gradient ascent on:

$$\frac{d}{d\zeta} p(\mathcal{A}|\zeta)$$

- But this contains an integral over individual parameters:

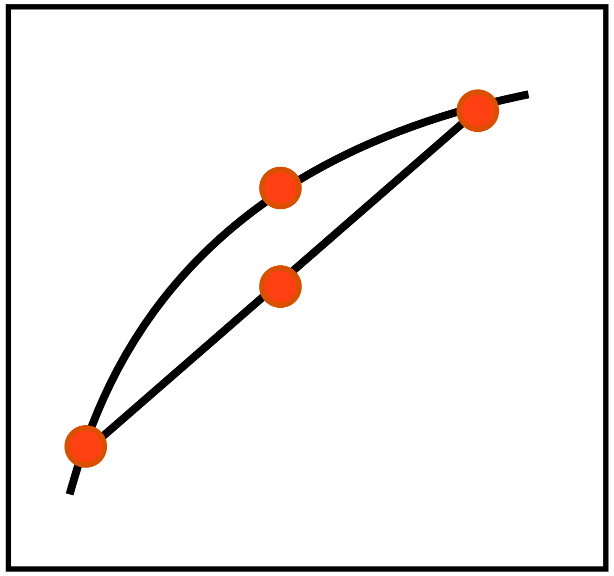
$$p(\mathcal{A}|\zeta) = \int d\theta p(\mathcal{A}|\theta)\, p(\theta|\zeta)$$

- So we need to:

$$\begin{aligned} \hat{\zeta} &= \underset{\zeta}{\operatorname{argmax}}\, p(\mathcal{A}|\zeta) \\ &= \underset{\zeta}{\operatorname{argmax}} \int d\,\theta p(\mathcal{A}|\theta)\, p(\theta|\zeta) \end{aligned}$$

Expectation Maximisation

$$\begin{aligned}
\log p(\mathcal{A}|\zeta) &= \log \int d\theta\, p(\mathcal{A},\theta|\zeta) \\
&= \log \int d\theta\, q(\theta) \frac{p(\mathcal{A},\theta|\zeta)}{q(\theta)} \\
&\geq \int d\theta\, q(\theta) \log \frac{p(\mathcal{A},\theta|\zeta)}{q(\theta)} \\
k^{\text{th}} \text{ E step: } q^{(k+1)}(\theta) &\leftarrow p(\theta|\mathcal{A},\zeta^{(k)}) \\
k^{\text{th}} \text{ M step: } \zeta^{(k+1)} &\leftarrow \underset{\zeta}{\operatorname{argmax}} \int d\theta\, q(\theta) \log p(\mathcal{A},\theta|\zeta)
\end{aligned}$$



Jensen's inequality

- Iterate between
  - Estimating MAP parameters given prior parameters
  - Estimating prior parameters from MAP parameters

EM with Laplace approximation

Prior mean = mean of MAP estimates

$$\text{M step:} \quad \zeta_\mu^{(i+1)} = \frac{1}{K}\sum_k \mathbf{m}_k$$

$$\zeta_{\nu^2}^{(i+1)} = \frac{1}{N}\sum_i \left[(\mathbf{m}_k)^2 + \mathbf{S}_k\right] - (\zeta_\mu^{(i+1)})^2$$

Take uncertainty of estimates into account

Prior variance depends on inverse Hessian S and variance of MAP estimates

Simulations

- emfit toolbox
  - models and fitting for six experiments
    - basic Rescorla-Wagner
    - probabilistic reward task Pizzagalli et al., 2005
    - Affective Go/Nogo Guitart et al. 2012
    - Twostep Daw et al., 2011
    - Effort Gold et al., 2013
    - Pruning Huys et al, 2012, Lally et al., 2017
  - wrapper scripts
  - key function is emfit.m

- www.cmod4mh.org/emfit.zip

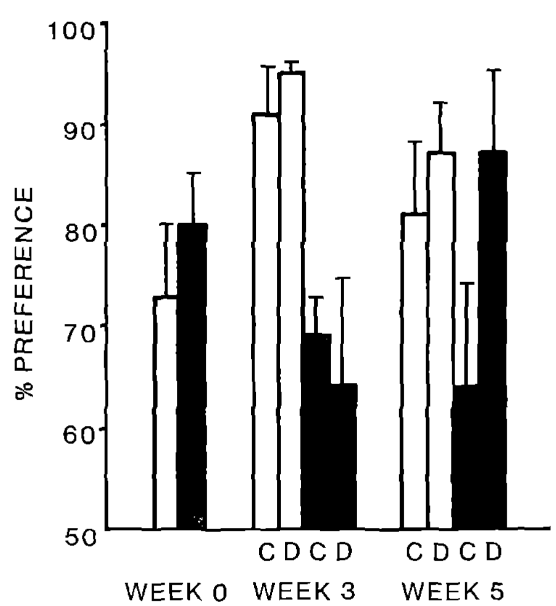
Outline

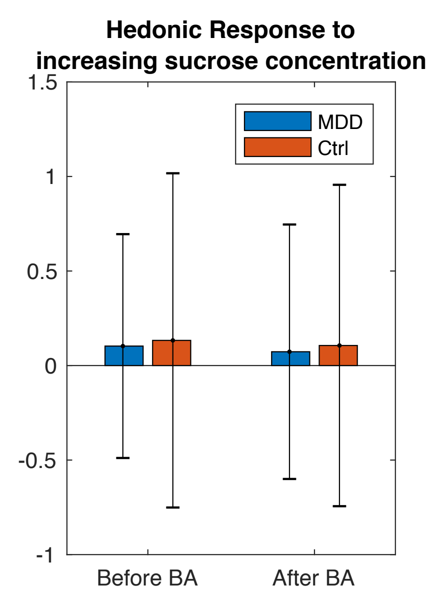
Depression	Addiction
OCD	Anxiety
Schizophrenia	Parkinson’s
Mood	Metareasoning

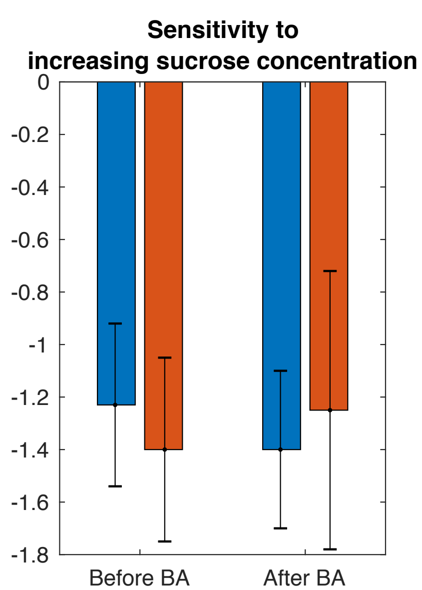
Anhedonia in depression

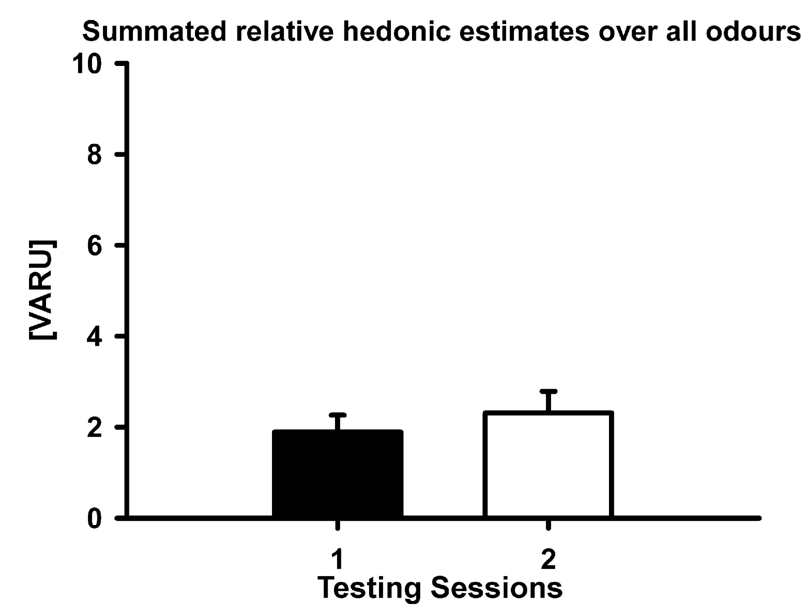
- Diminished interest or pleasure in response to **stimuli** that were previously perceived as rewarding
- What is “stimuli”? What “states” does this correspond to in terms of RL?

$$\mathcal{V}(s) = \arg\max_a \sum_{s'} \mathcal{T}^a_{ss'}[\mathcal{R}^a_{ss'} + \gamma \mathcal{V}(s')]$$









Willner et al., 1987; Dichter et al., 2010; Klepce et al., 2010

Anhedonia in depression

- Anhedonia
  - inability to enjoy rewards
  - but assessed by introspection / recollection
  - maybe due to the expected values accessed?
  - the problem then must be learning

$$\mathcal{Q}_t(a,s) = \mathcal{Q}_{t-1}(a,s) + \epsilon(r_t - \mathcal{Q}_{t-1}(a,s))$$

Montague et al., 1996, Dunlop and Nemeroff 2007; Gard et al., 2006

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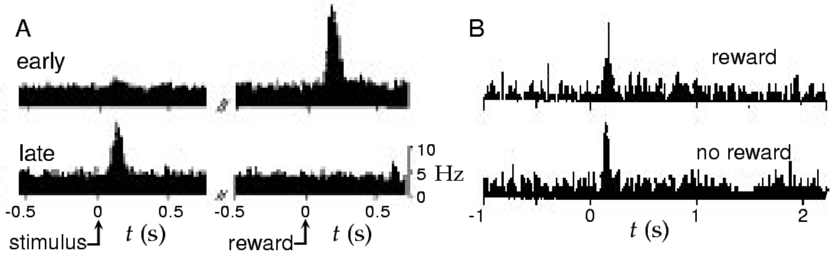
Dopamine



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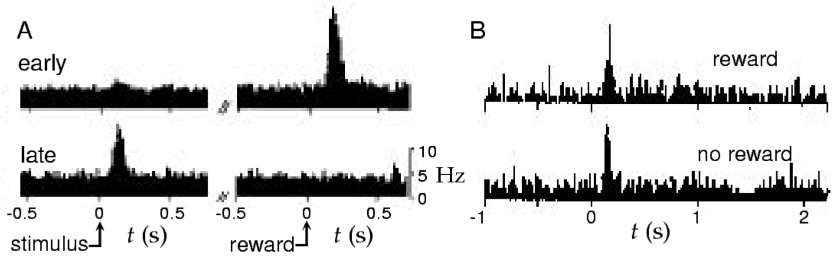

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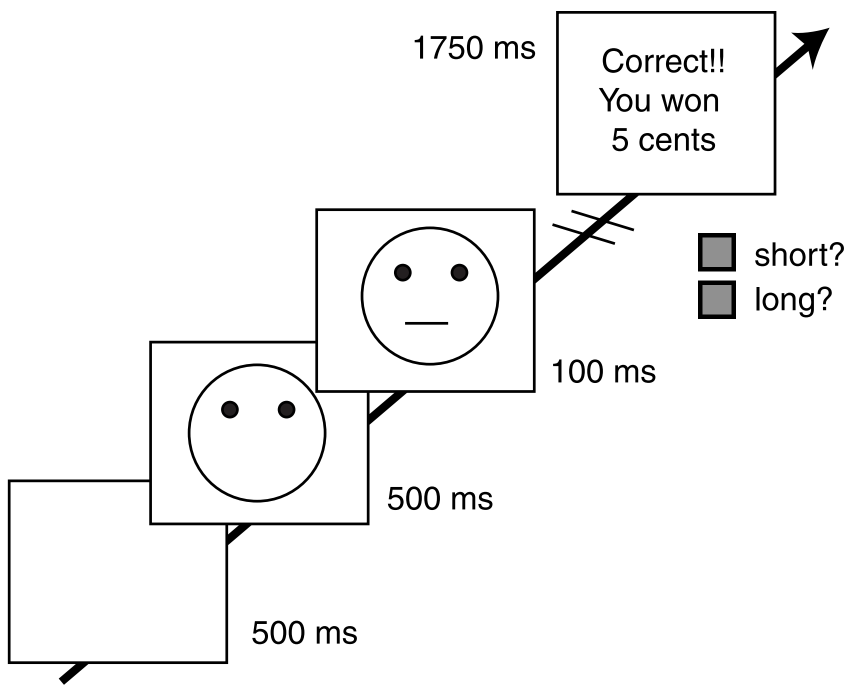
Reward expectation



Long = rich:	Long correct:	75% rewarded
	Short correct:	30% rewarded

Short = rich:	Long correct:	30% rewarded
	Short correct:	75% rewarded

Pizzagalli et al., 2005 Biol Psych

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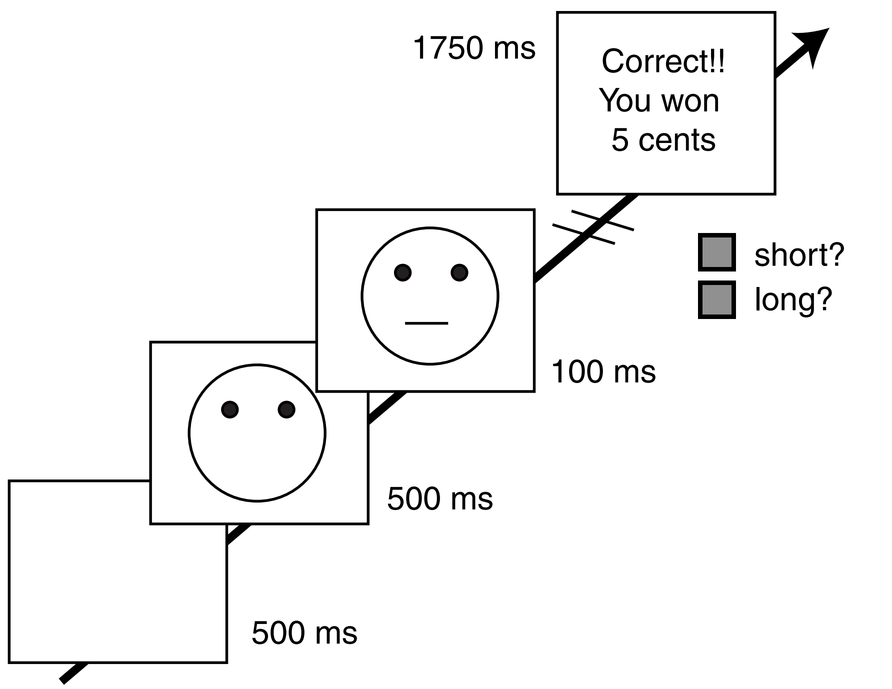

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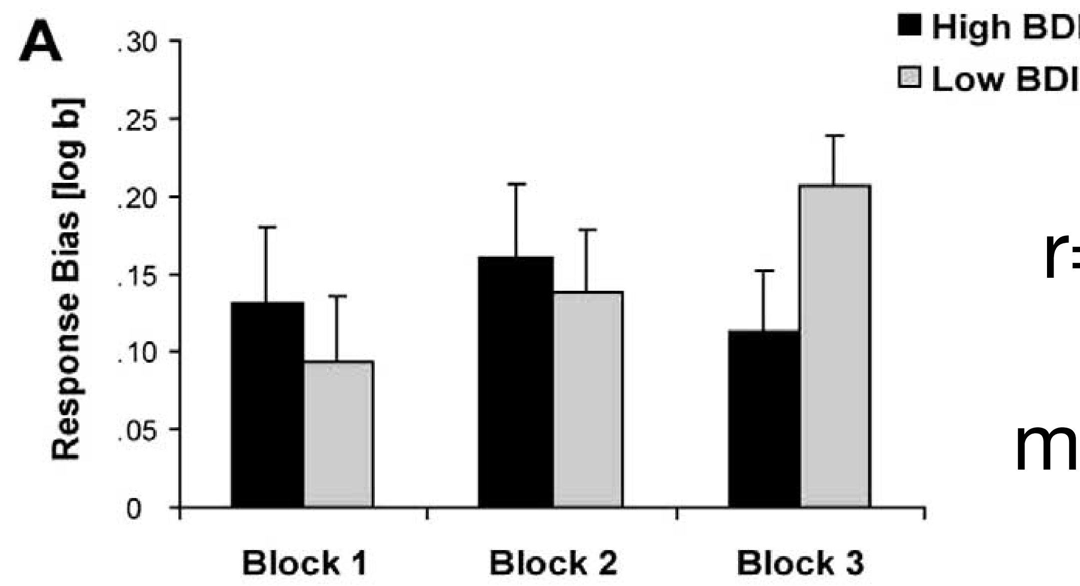

r=-0.28 w/ BDI melancholia

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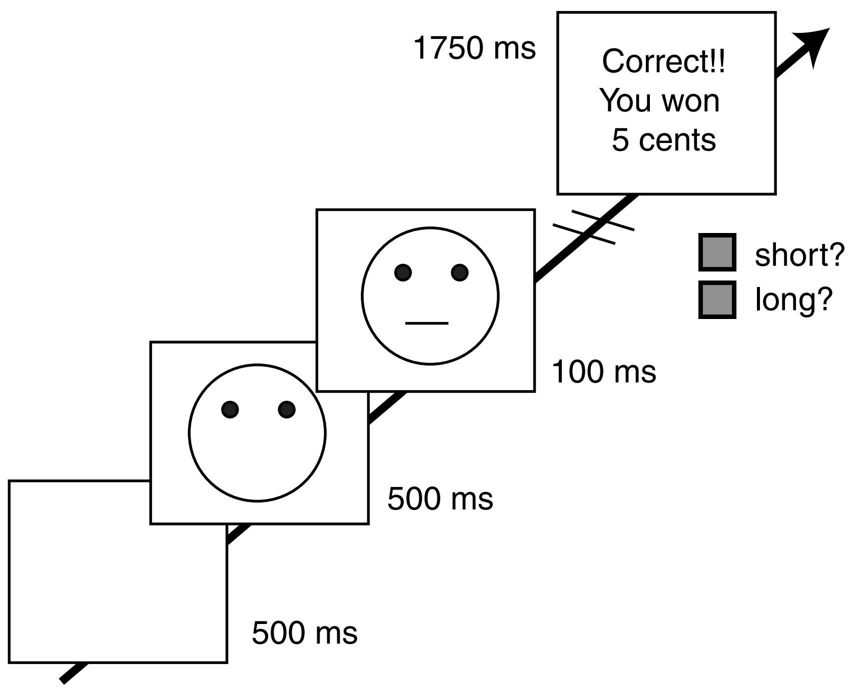
Reward expectation



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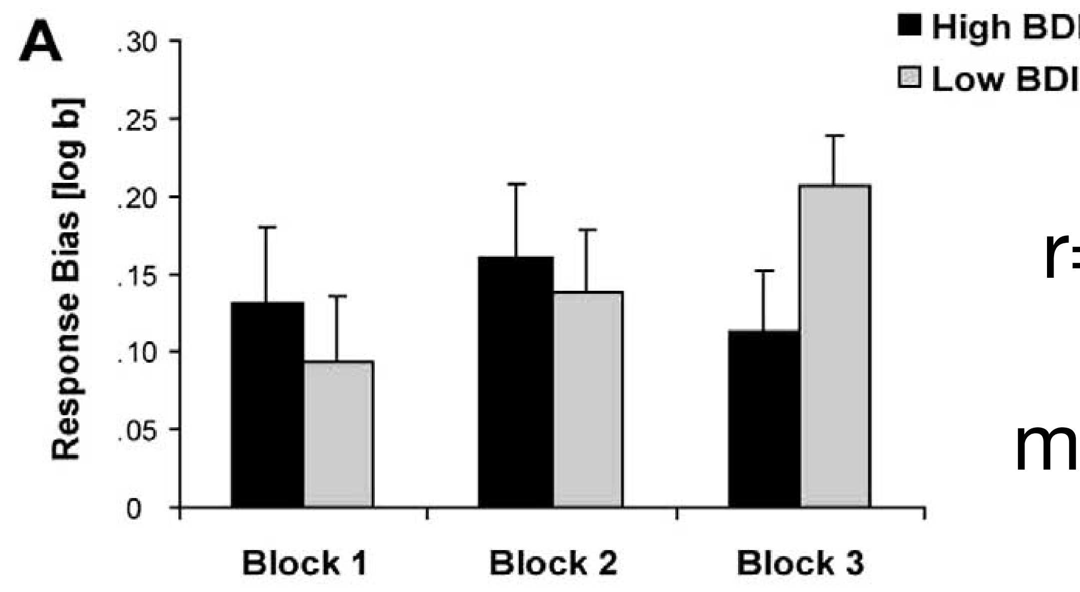

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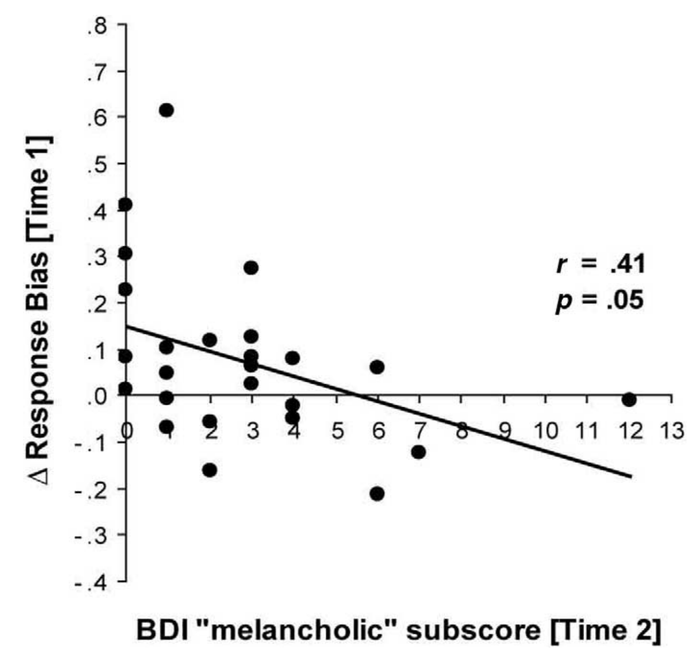
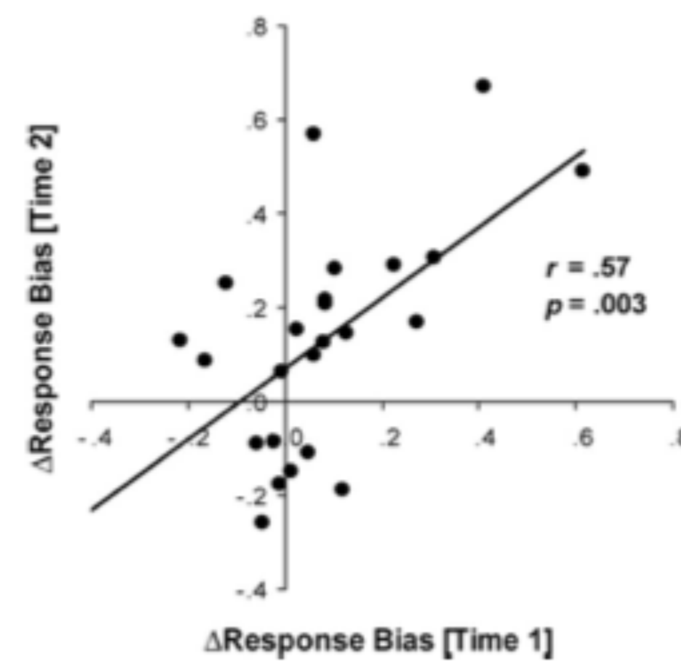
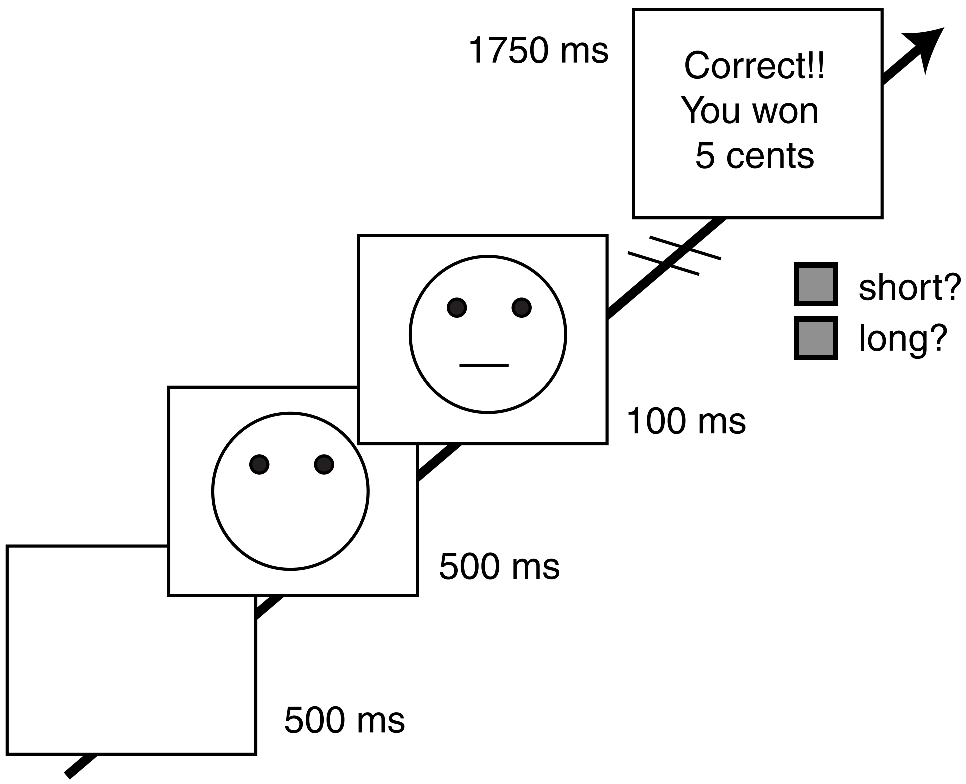




Pizzagalli et al., 2005 Biol Psych

Modelling: first get the task



Huys et al., 2013 Biol Mood Anx

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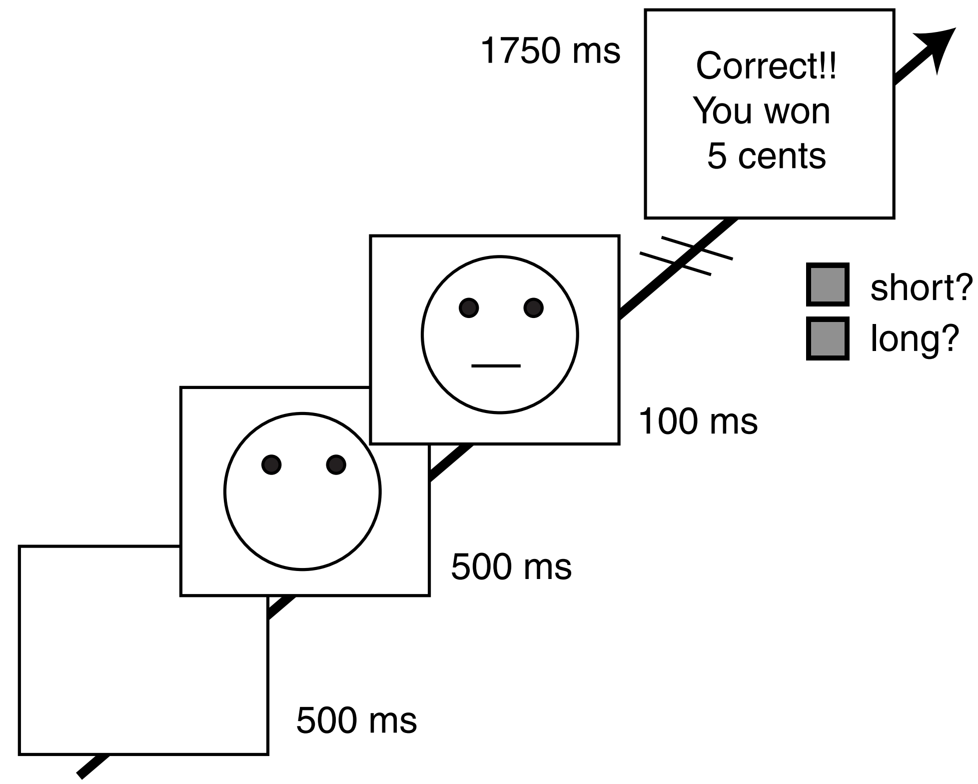

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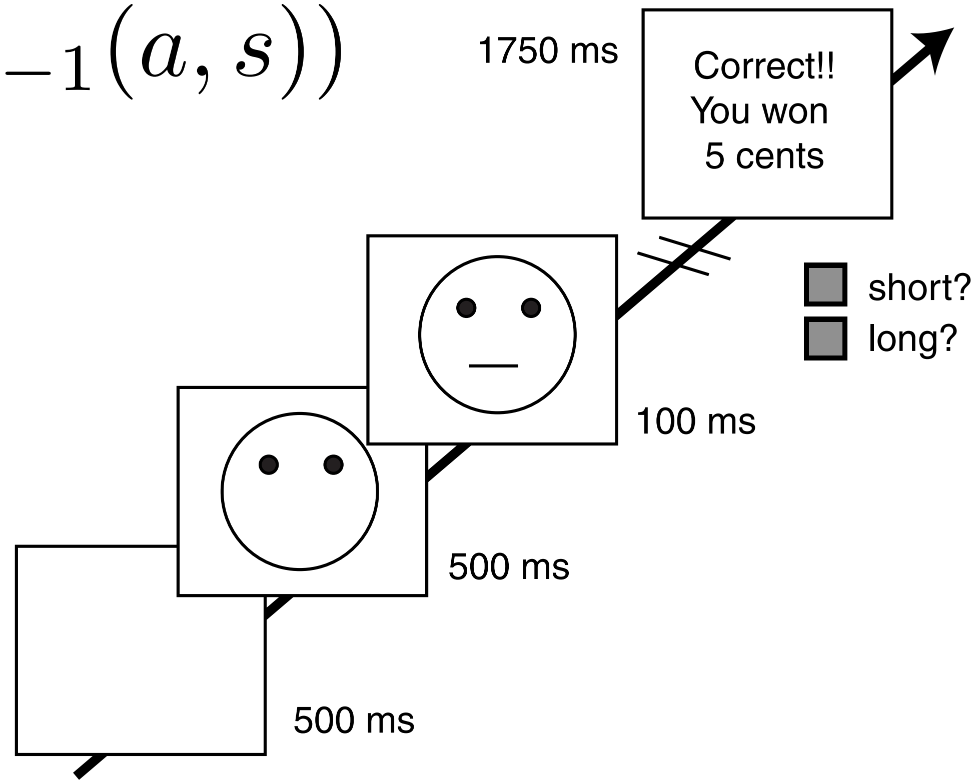

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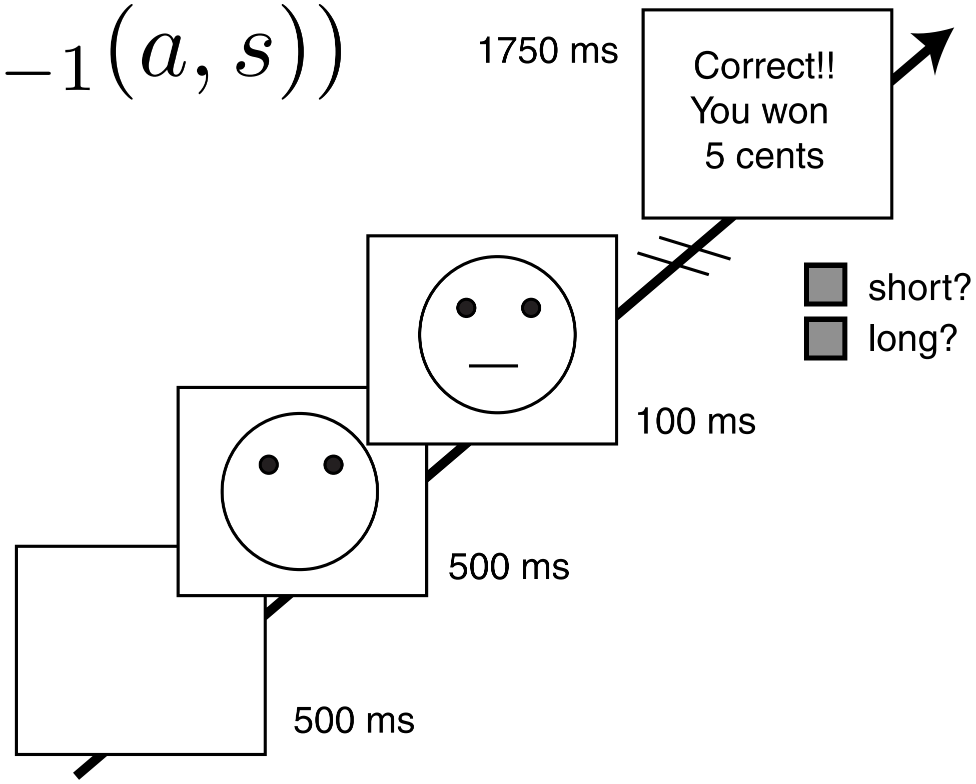

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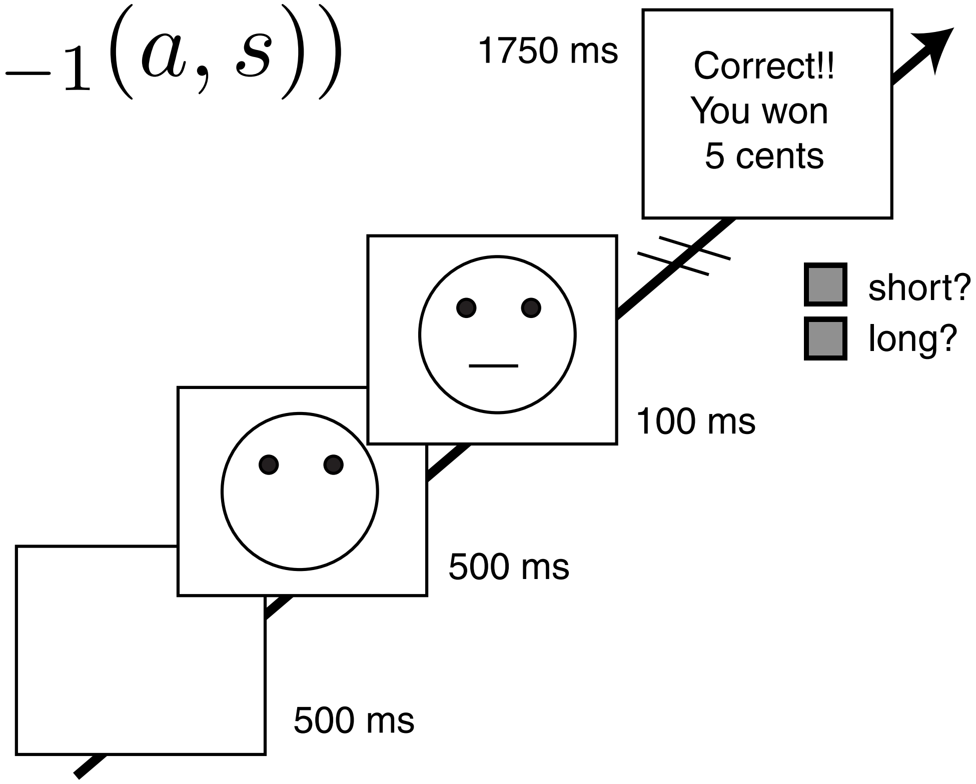


with instructions

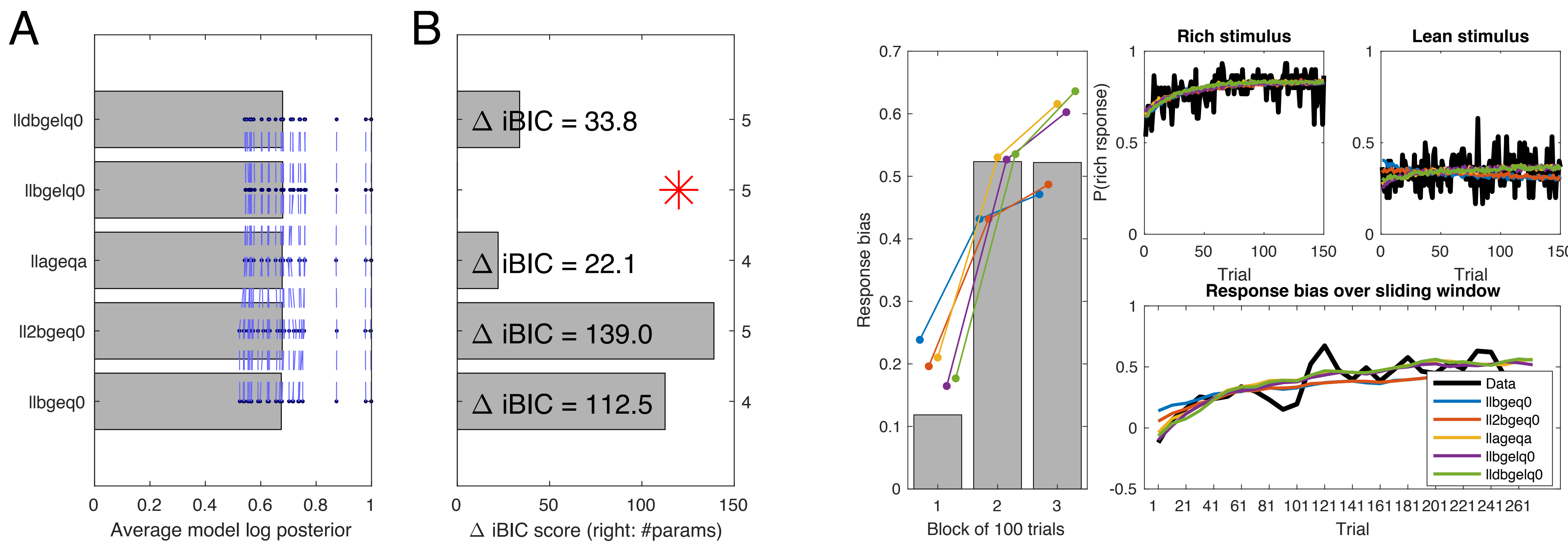
$$p(a|s) = \frac{e^{\mathcal{Q}(a,s)+\gamma\mathcal{I}(a,s)}}{\sum_{a'} e^{\mathcal{Q}(a',s)+\gamma\mathcal{I}(a',s)}}$$

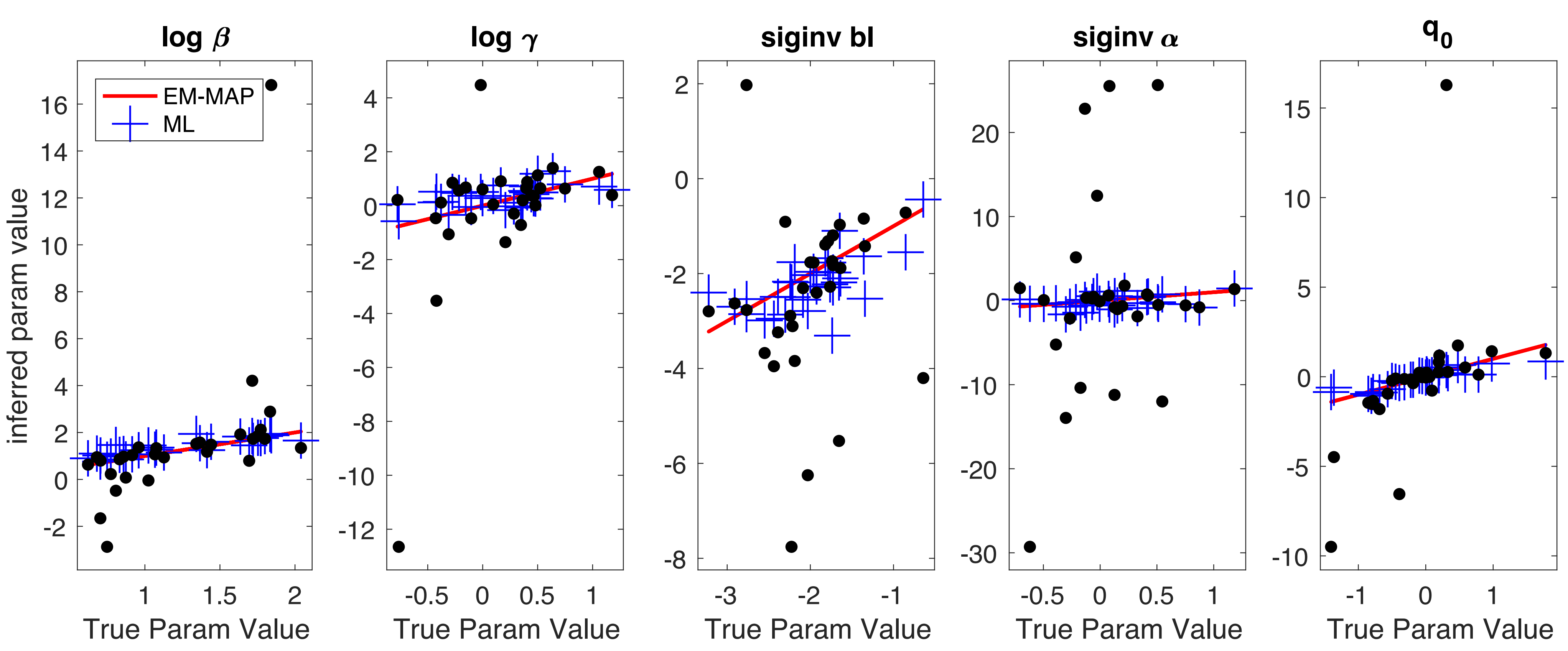
with state uncertainty

$$p(a|s) = \frac{e^{\zeta\mathcal{Q}(a,s)+(1-\zeta)\mathcal{Q}(a,s')+\gamma\mathcal{I}(a,s)}}{\sum_{a'} e^{\zeta\mathcal{Q}(a',s)+(1-\zeta)\mathcal{Q}(a,s')+\gamma\mathcal{I}(a',s)}}$$

Huys et al., 2013 Biol Mood Anx

Hierarchical fitting





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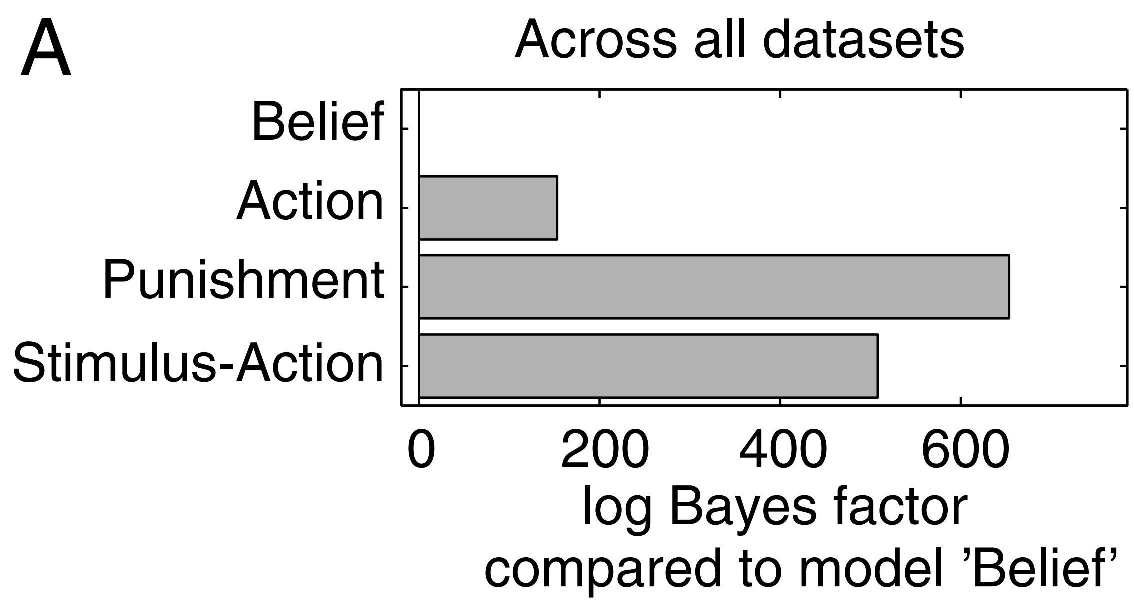
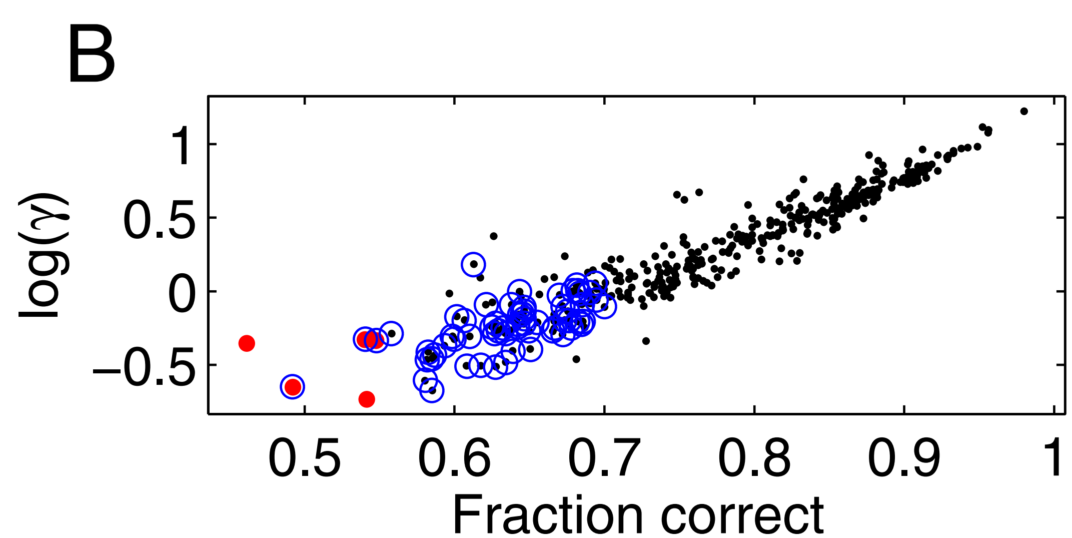
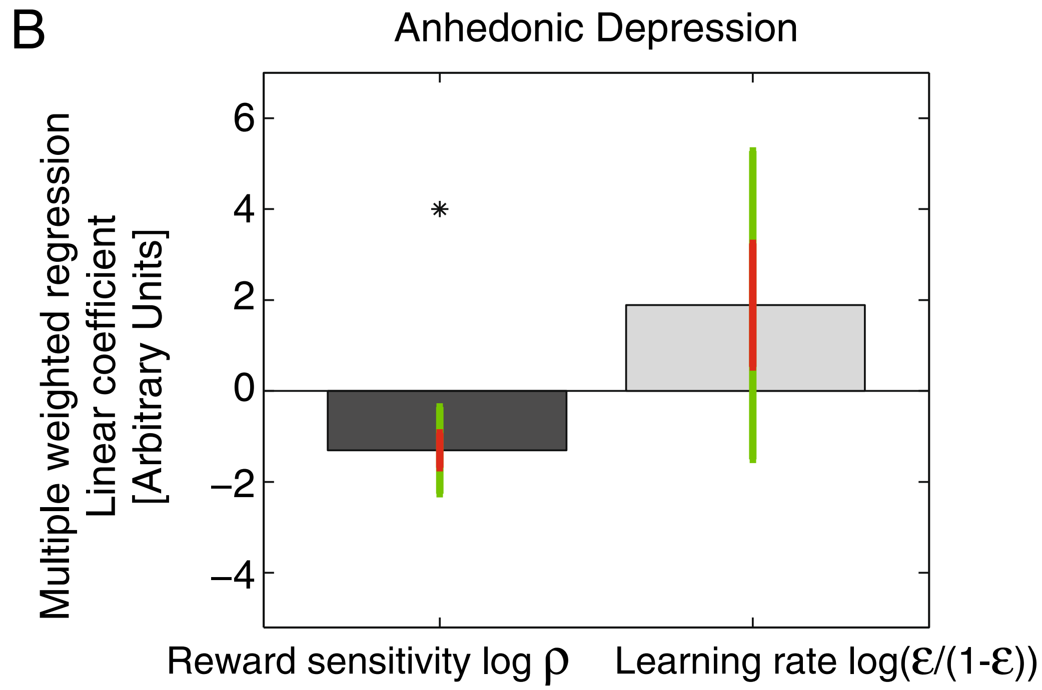




Huys et al., 2013 Biol Mood Anx

Anhedonia correlates with reward sensitivity



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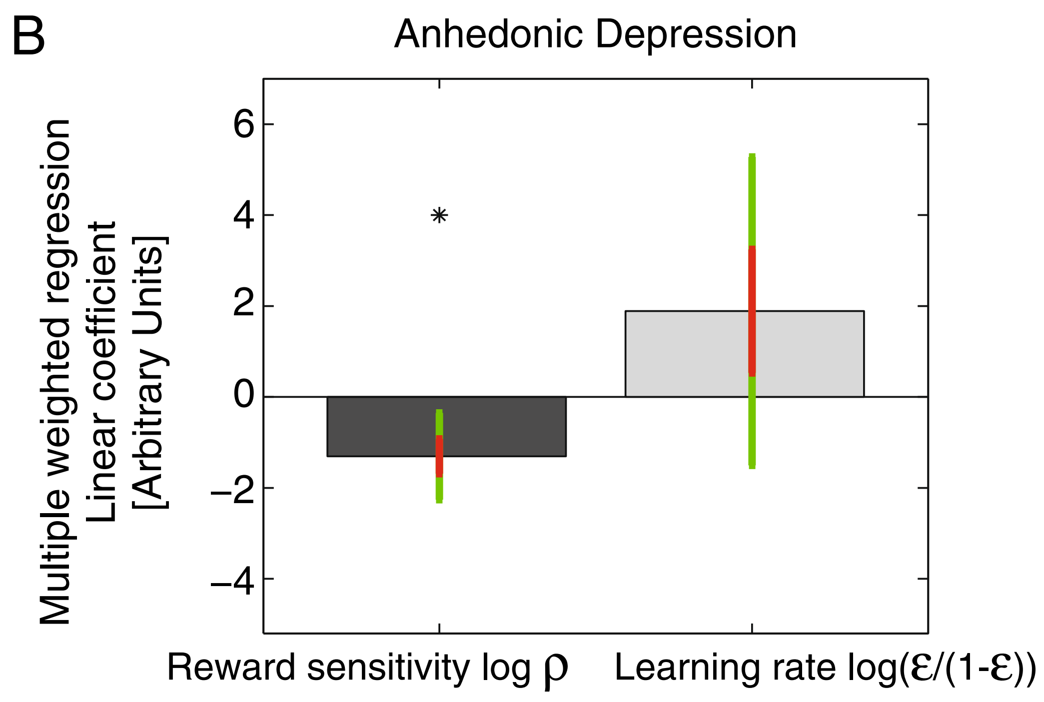

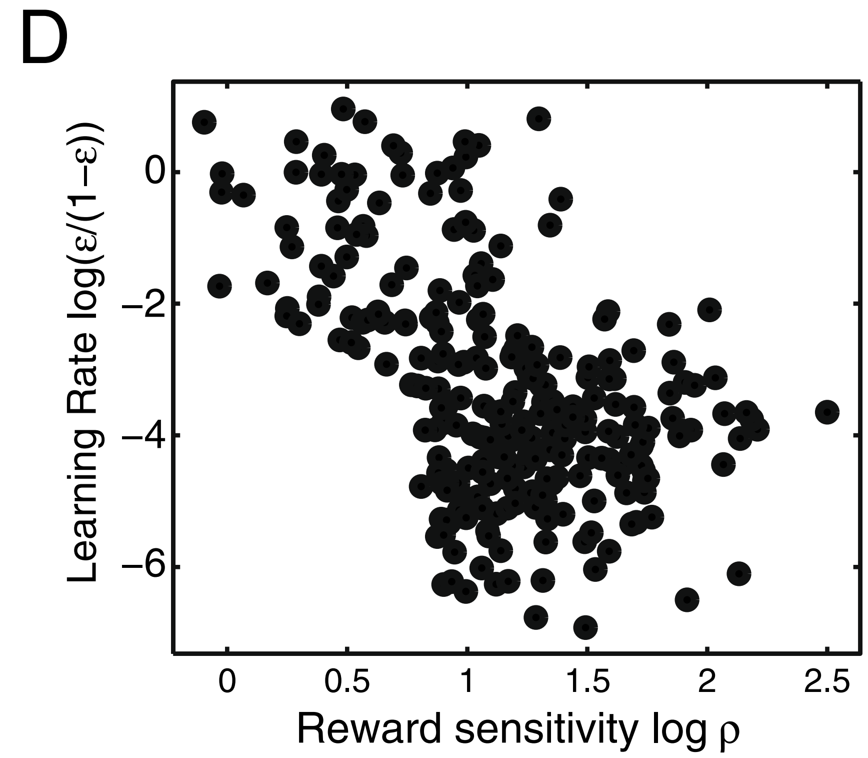

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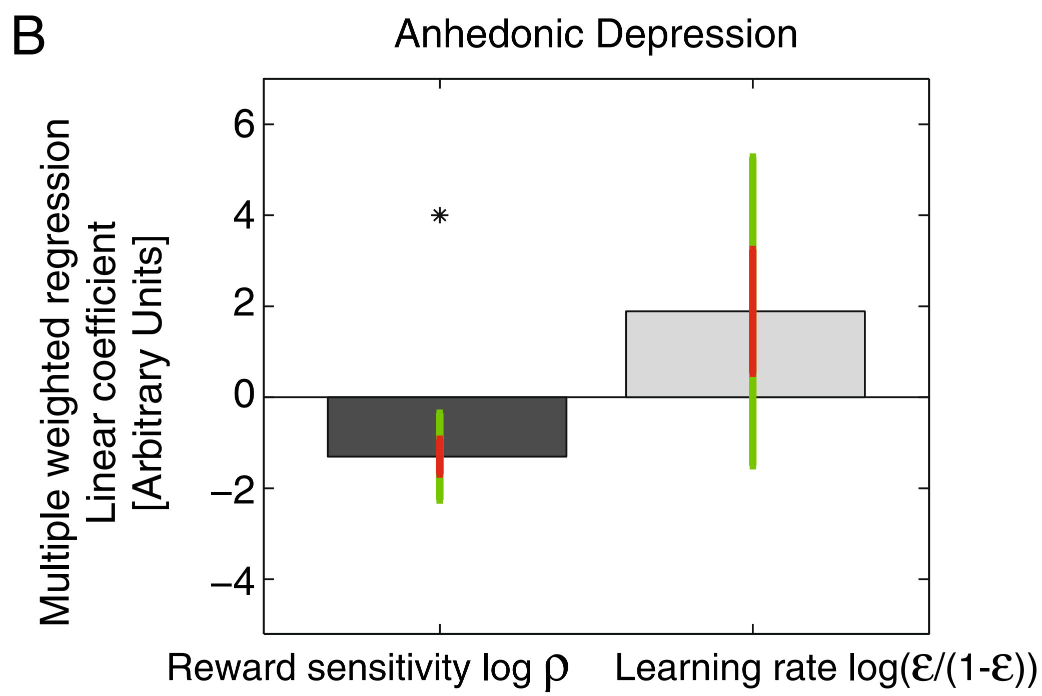
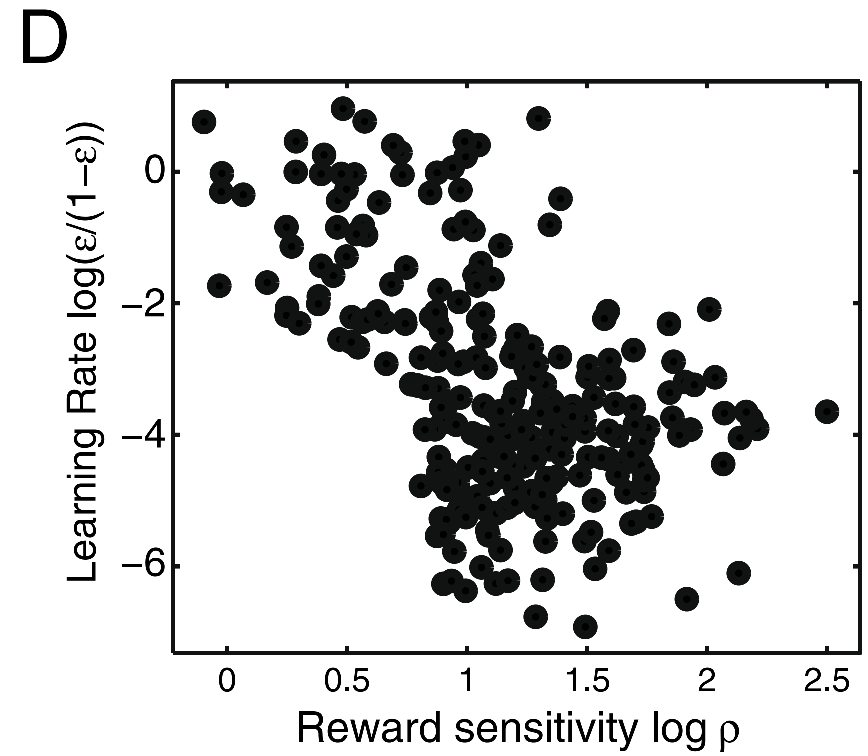
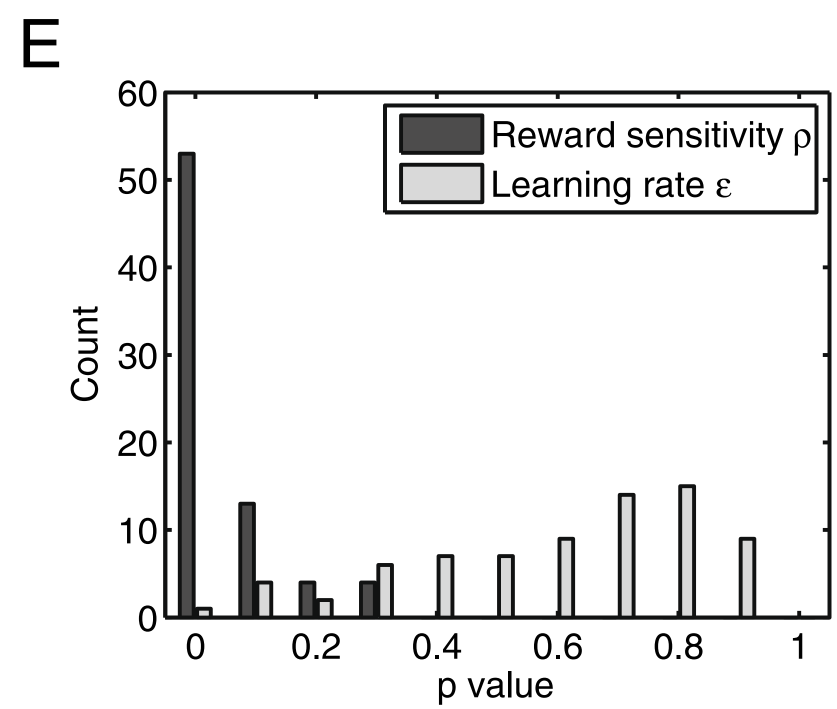


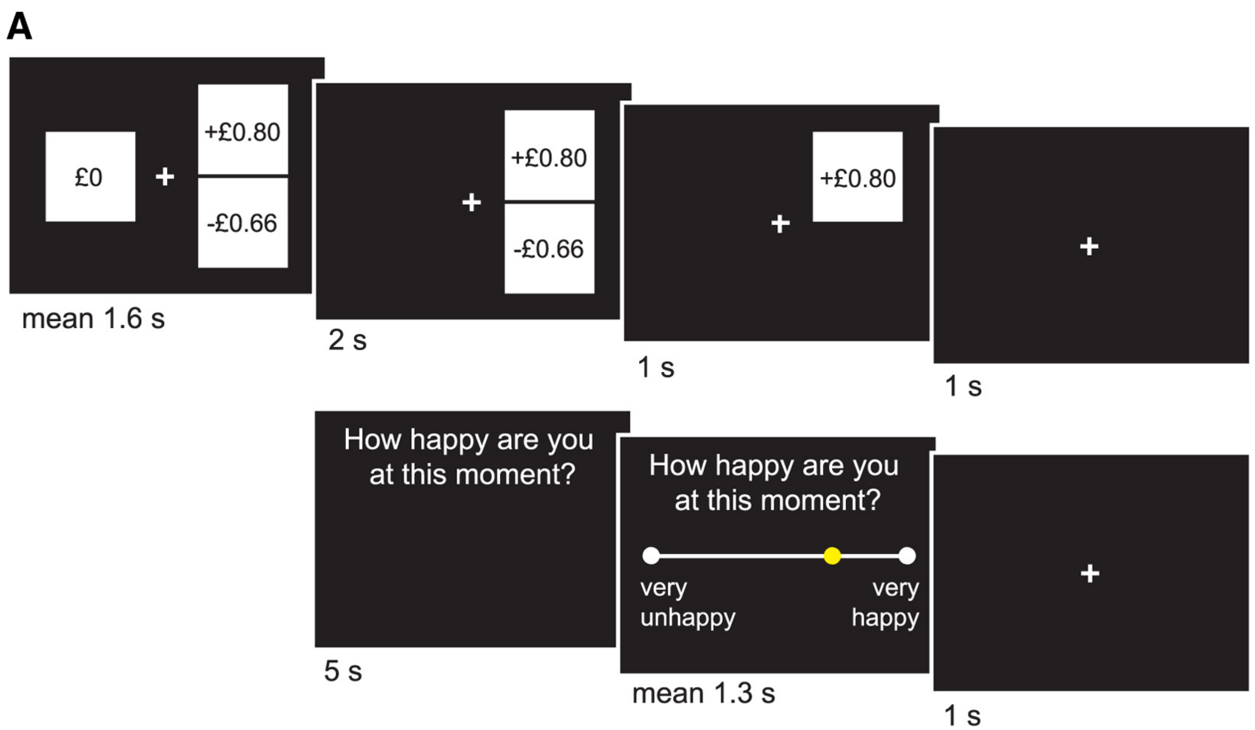


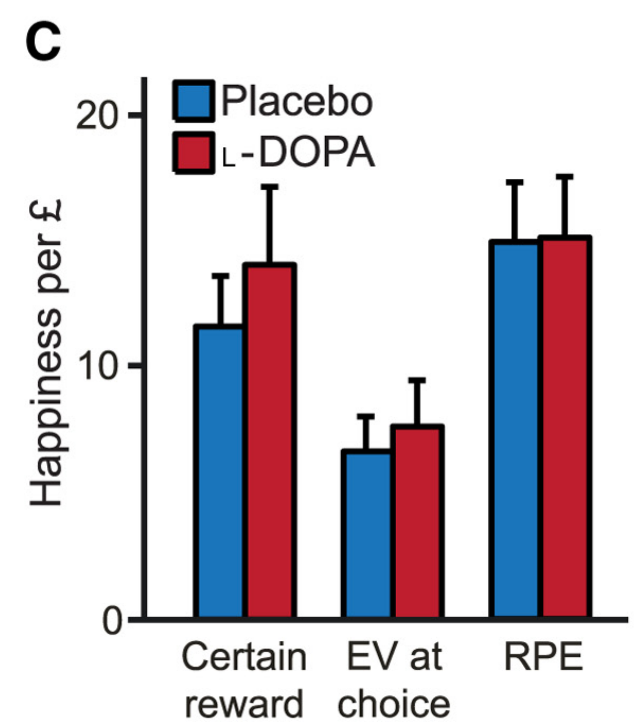
Data
↓
Parameters ⟶ correlation
↓
Surrogate data
↓
Parameters ⟶ correlation



Huys et al., 2013 Biol Mood Anx

Happiness?





$$\text{Happiness}(t) = w_0 + w_1 \sum_{j=1}^{t} \gamma^{t-j}\,\text{CR}_j + w_2 \sum_{j=1}^{t} \gamma^{t-j}\,\text{EV}_j + w_3 \sum_{j=1}^{t} \gamma^{t-j}\,\text{RPE}_j$$

Rutledge et al., 2015 J Neurosci

Happiness?

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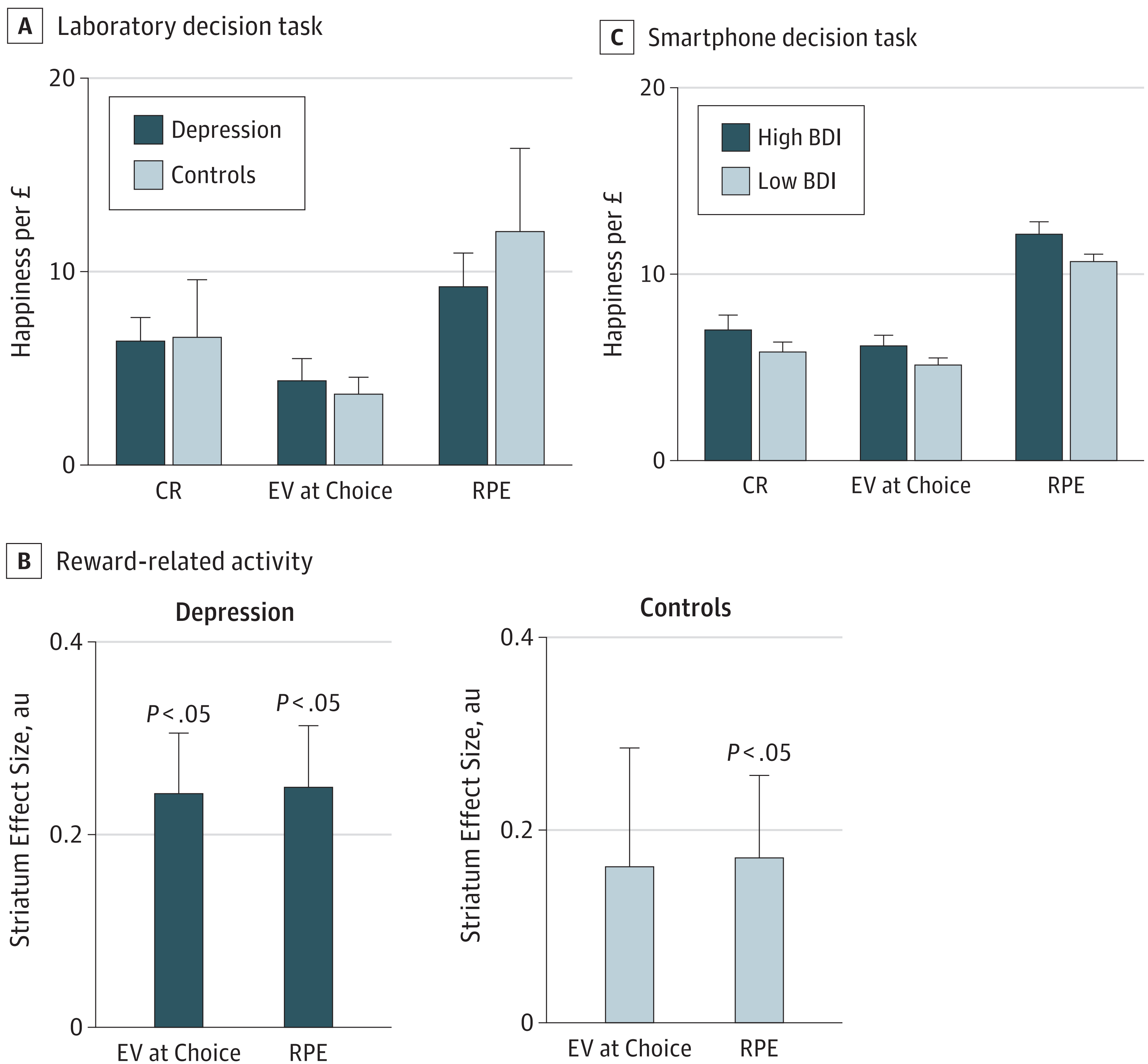


Rutledge et al., 2017 JAMA Psych

Anhedonia

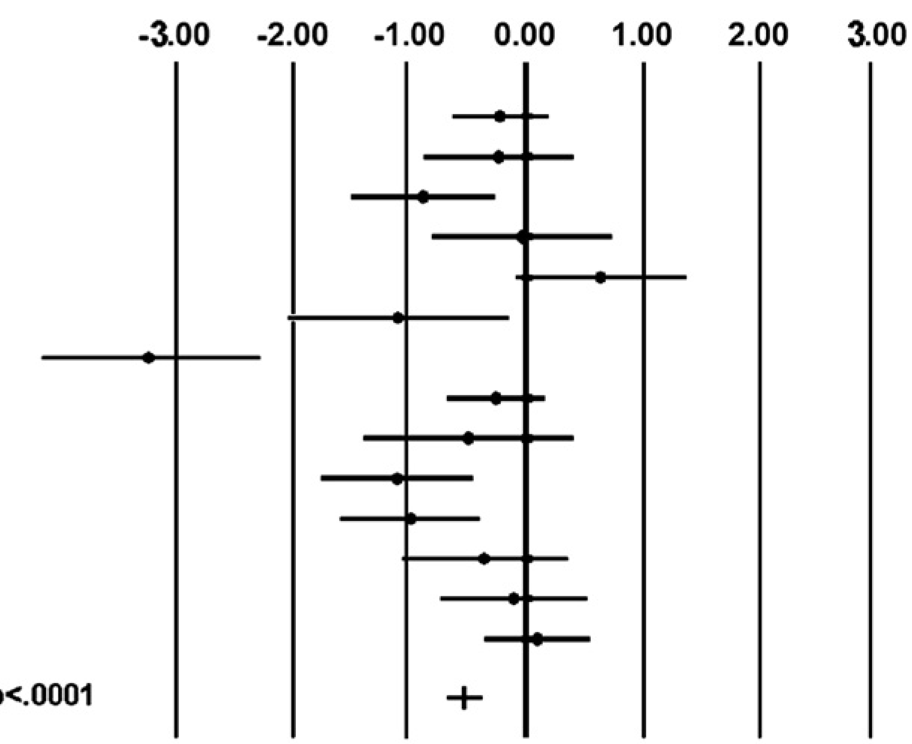
- No impairment in primary sensitivity (sucrose)
- No impairment in learning
- No impairment in computing prediction errors
- Anhedonia related to sensitivity to complex stimuli (here monetary)

Bylsma et al., 2008

Anhedonia

- No impairment in primary sensitivity (sucrose)
- No impairment in learning
- No impairment in computing prediction errors
- Anhedonia related to sensitivity to complex stimuli (here monetary)

	Citation	Year	MDD	Ctrl		
Positive Emotional Reactivity	Greden	1986	63	37		
	Sigmon	1992	20	20		
	Sloan	1997	24	23		
	Allen	1999	14	14		
	Henriques	2000	18	15		
	Gehricke	2000	11	11		
	Sloan	2001	20	20		
	Rottenberg	2002	72	32		
	Tsai	2003	12	10		
	Kaviani	2004	22	22		
	Dunn	2004	25	25		
	Dichter	2004	17	16		
	Rottenberg	2005	19	22		
	Forbes	2005	38	38		
PER (14)			375	305	d=-.530	p<.0001



Bylsma et al., 2008

Example code

- www.cmod4mh.org/emfit.zip

- batchRunEMfit('mProbabilisticReward')
  - will generate example data
  - fit all models in modelList.m
  - perform model comparison
  - generate surrogate data
  - generate plots for basic sanity checks

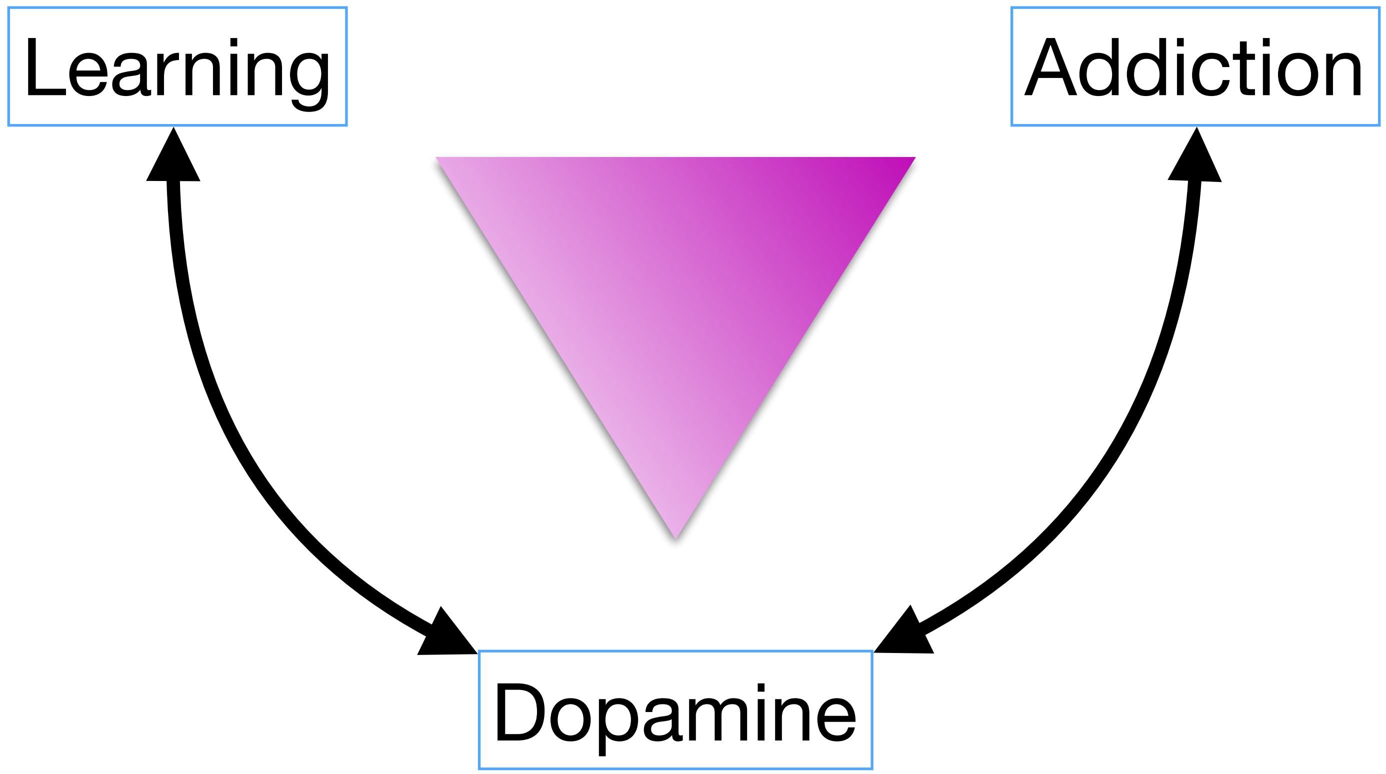
- basic model is llbeq0.m

Outline

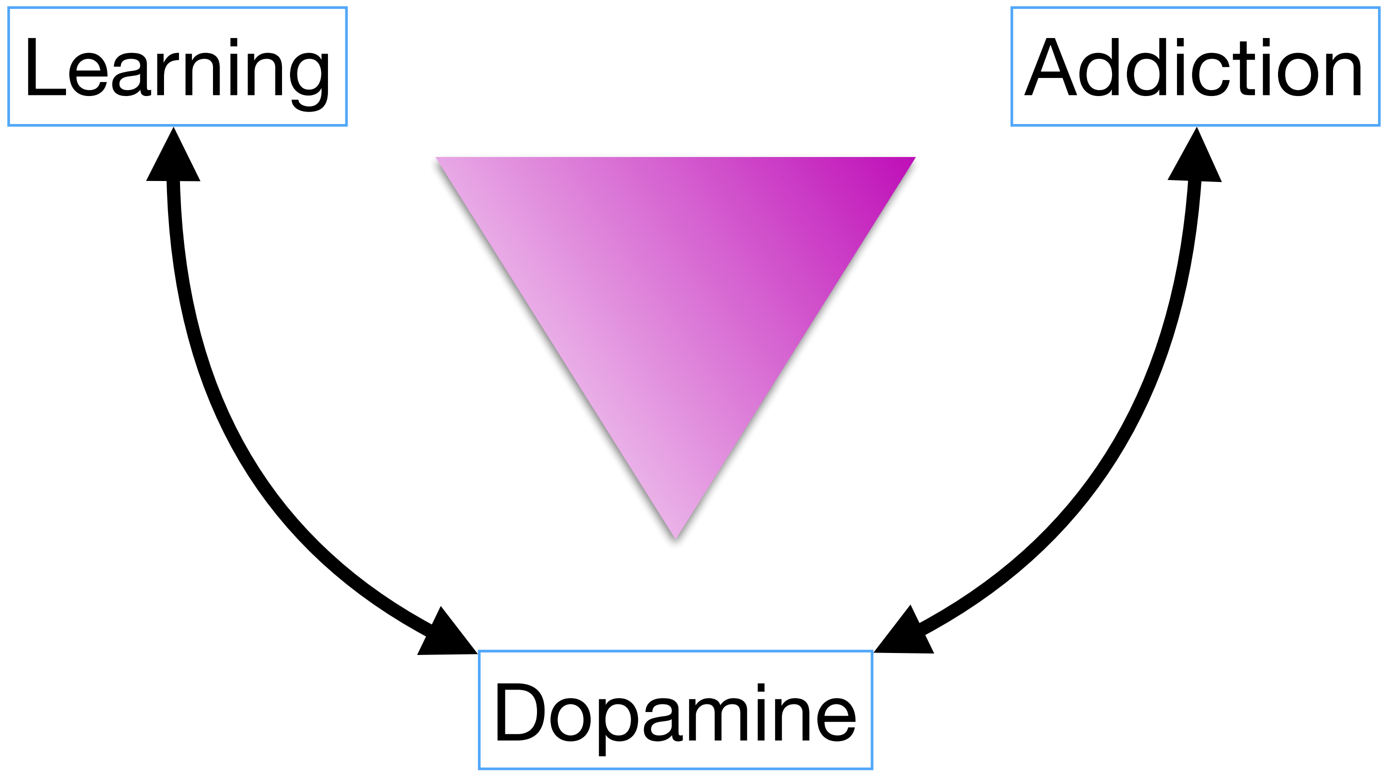
Depression	Addiction
OCD	Anxiety
Schizophrenia	Parkinson’s
Mood	Metareasoning

Dopamine, learning & addiction

Dopamine, learning & addiction



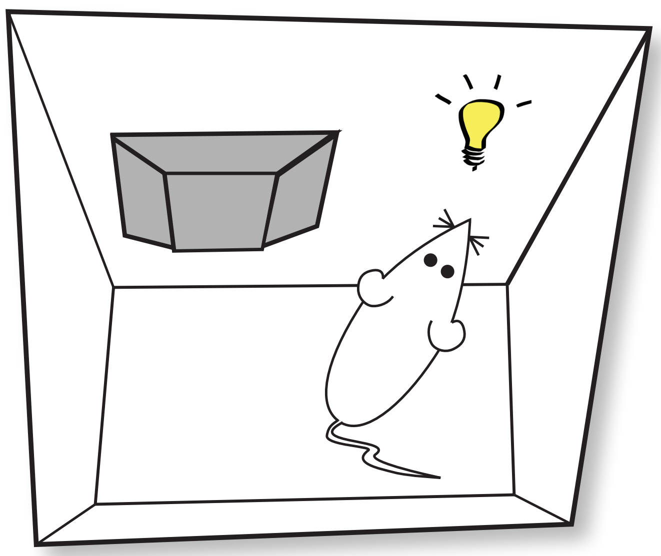
Dopamine, learning & addiction



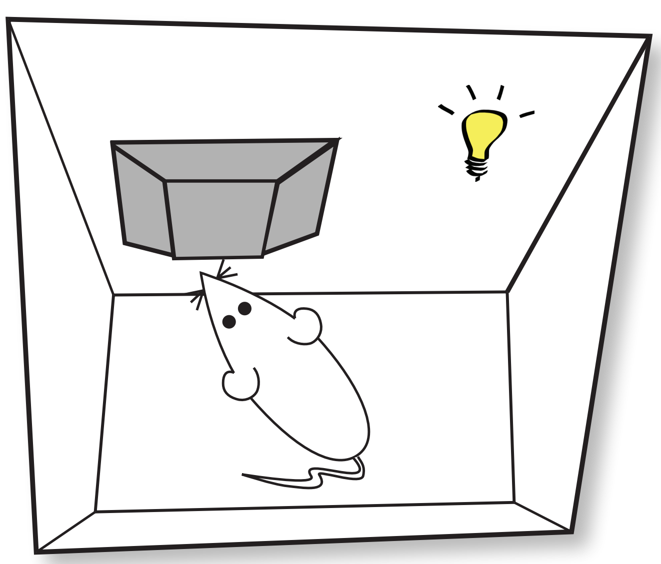
Is dopamine's role in addiction mediated by its role in learning?

Addictive Pavlovian values

A

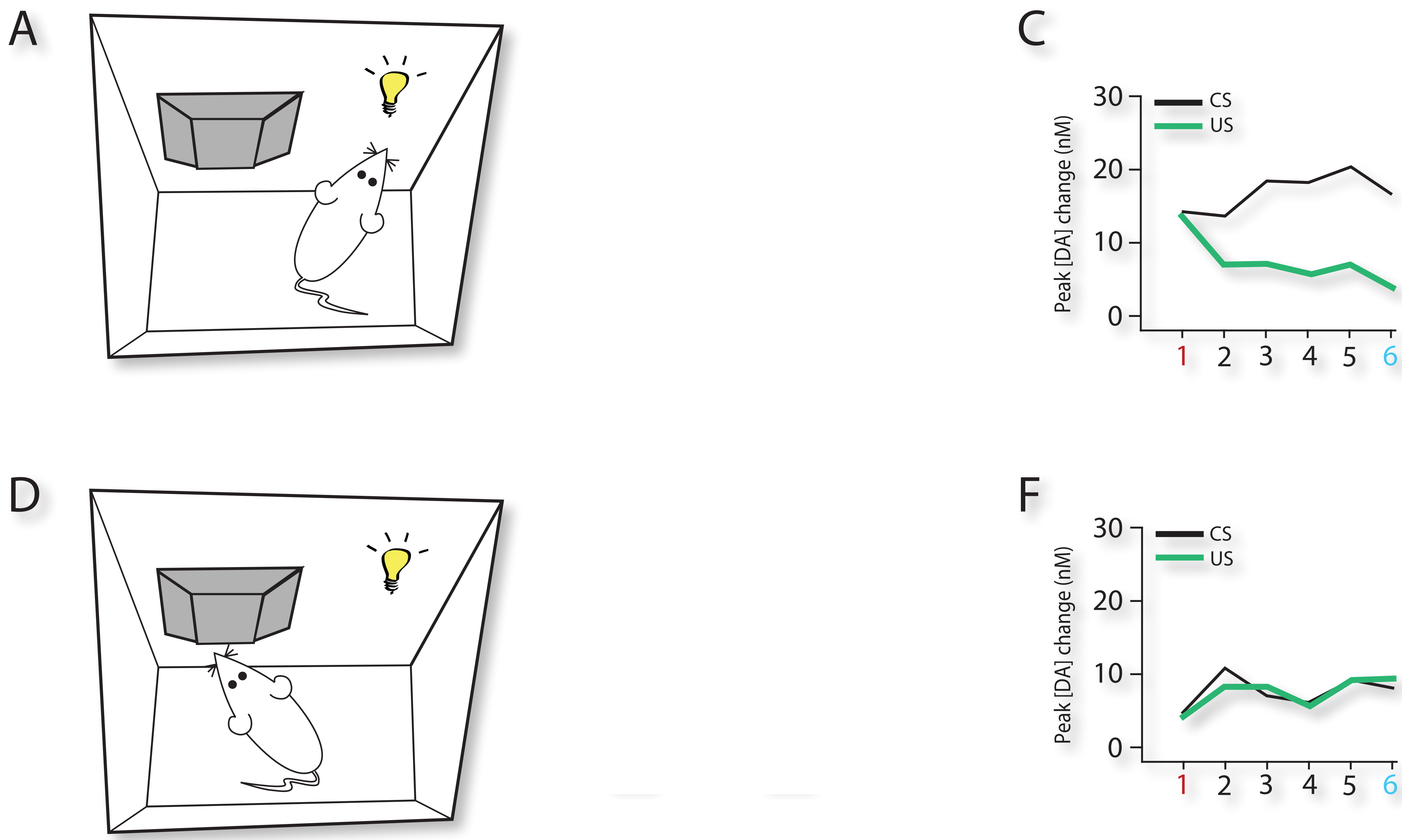


D



Flagel et al., 2011 Nature, Huys et al., 2014 Prog. Neurobiol.

Addictive Pavlovian values



Flagel et al., 2011 Nature, Huys et al., 2014 Prog. Neurobiol.

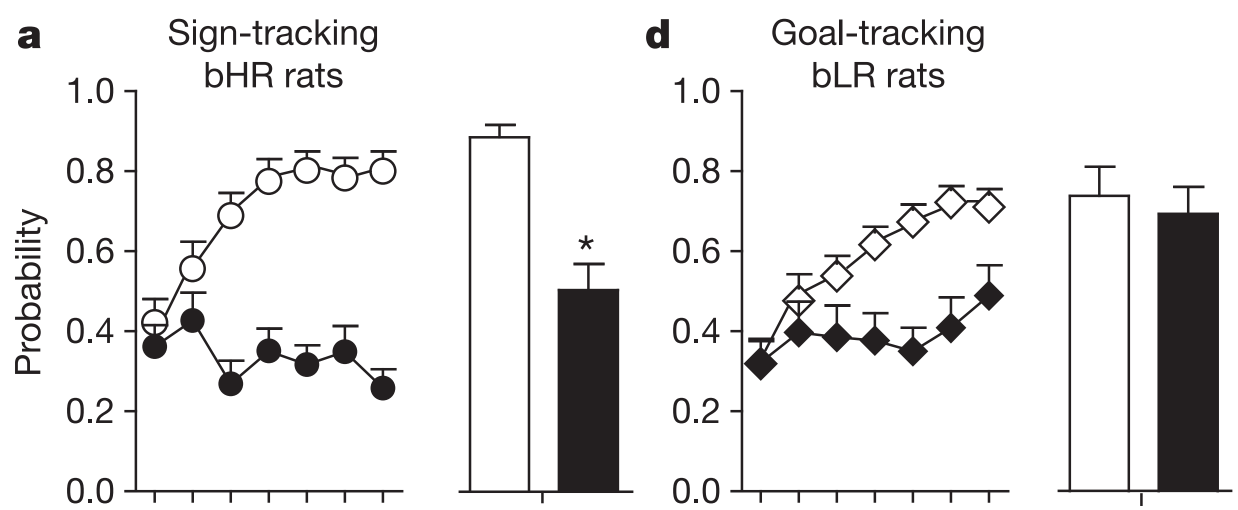
Dopamine

Sign trackers Goal trackers

Flagel et al., 2011 Nature

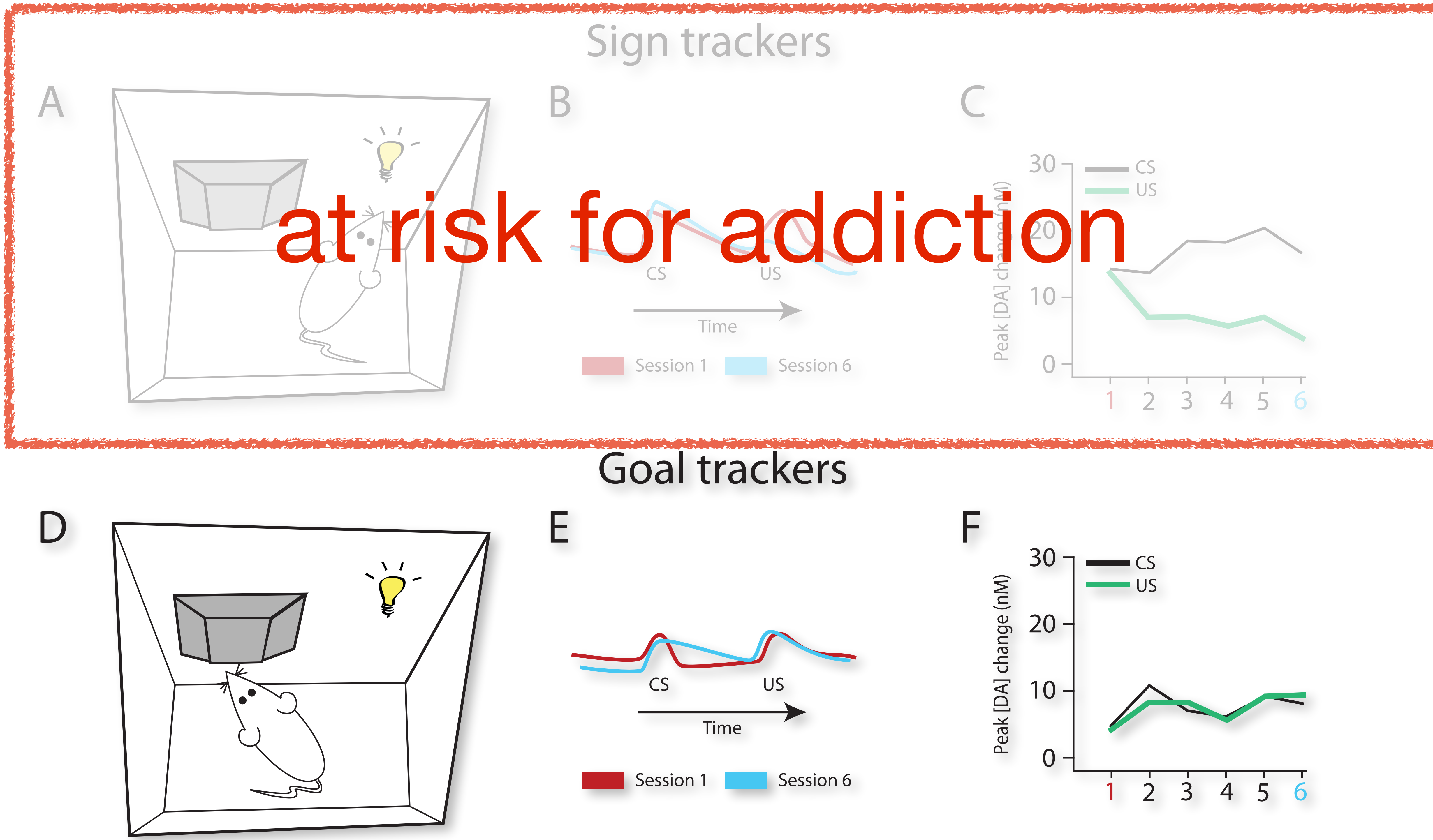
Dopamine

Sign trackers   Goal trackers



Flagel et al., 2011 Nature

Pavlovian state values: sign tracking

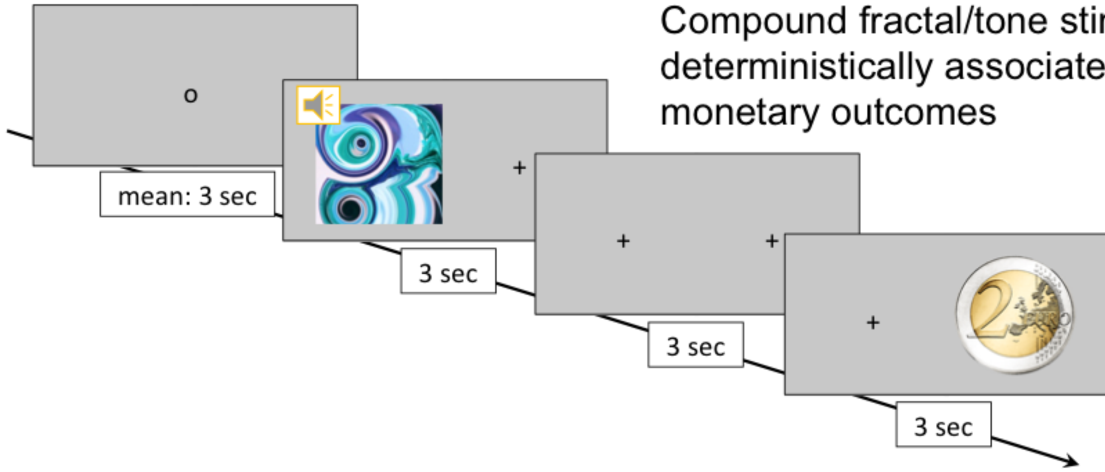


Flagel et al., 2011 Nature

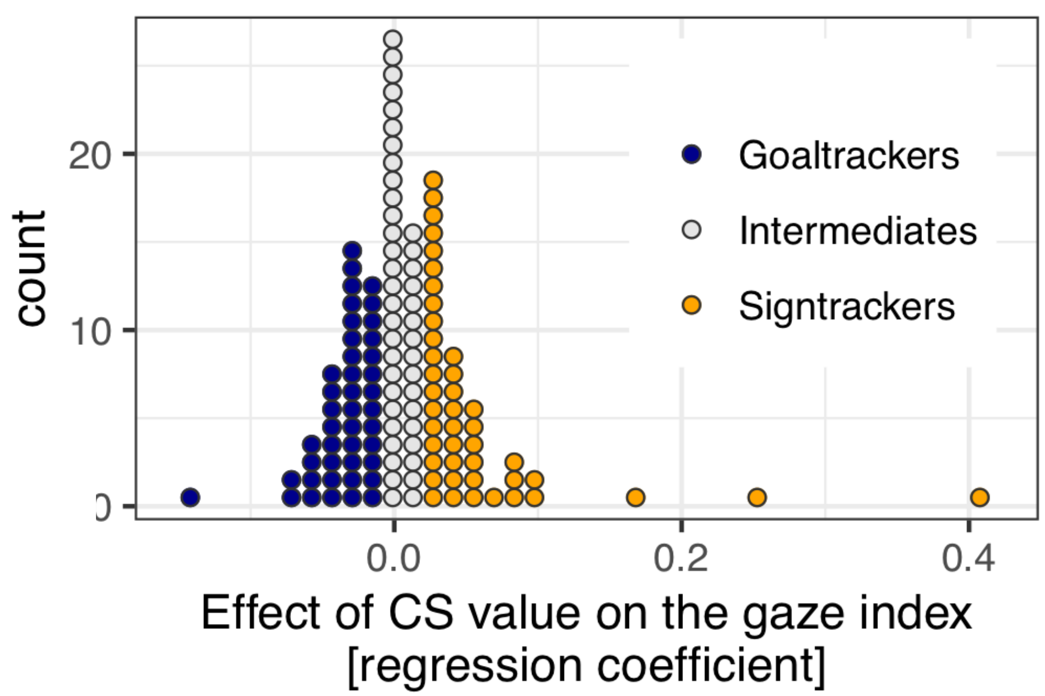
Sign-tracking in humans?

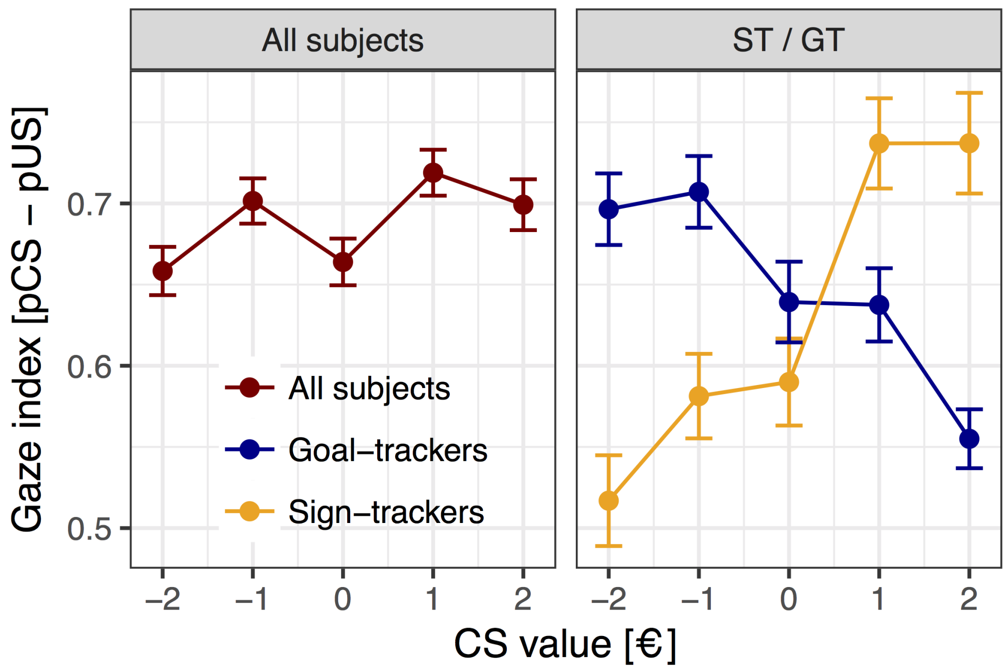
Experimental Paradigm
Pavlovian Conditioning

n=129



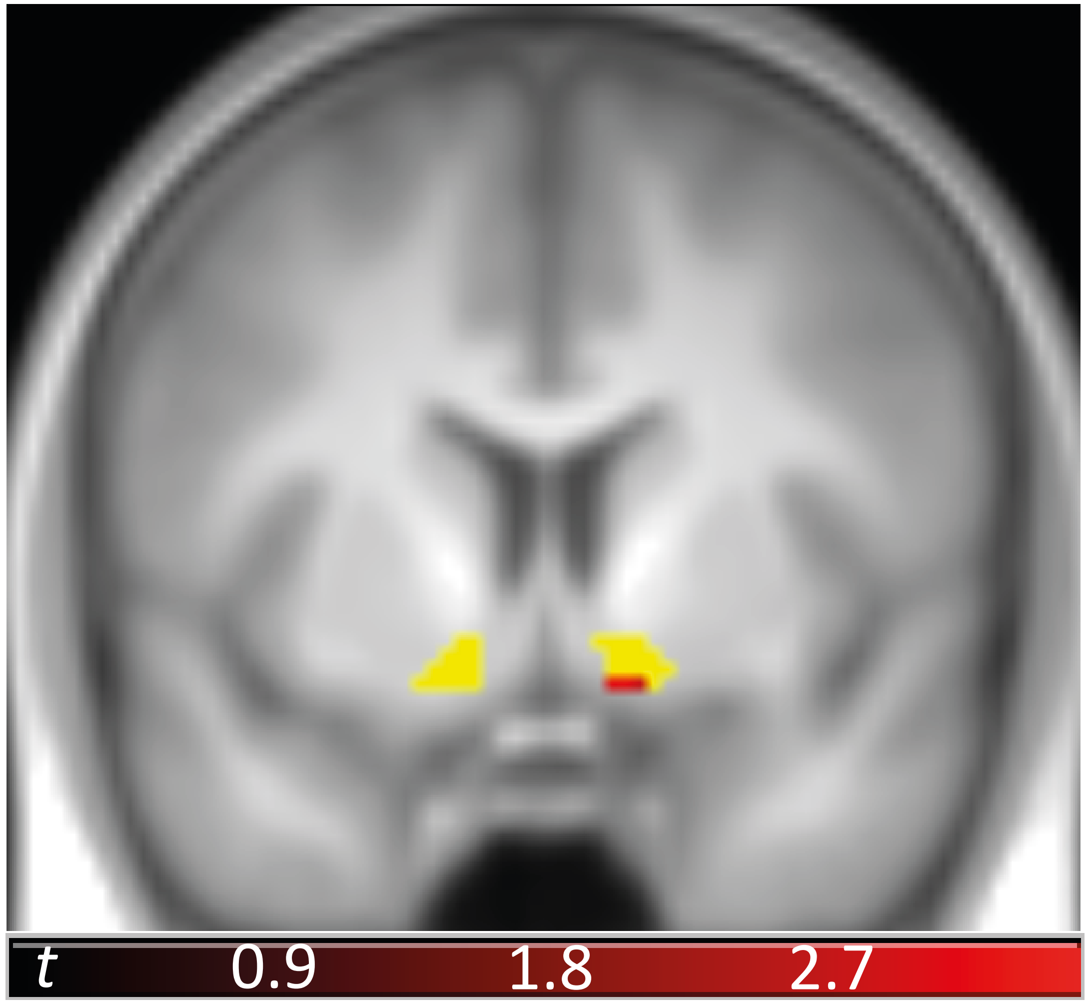
Compound fractal/tone stimuli deterministically associated with monetary outcomes

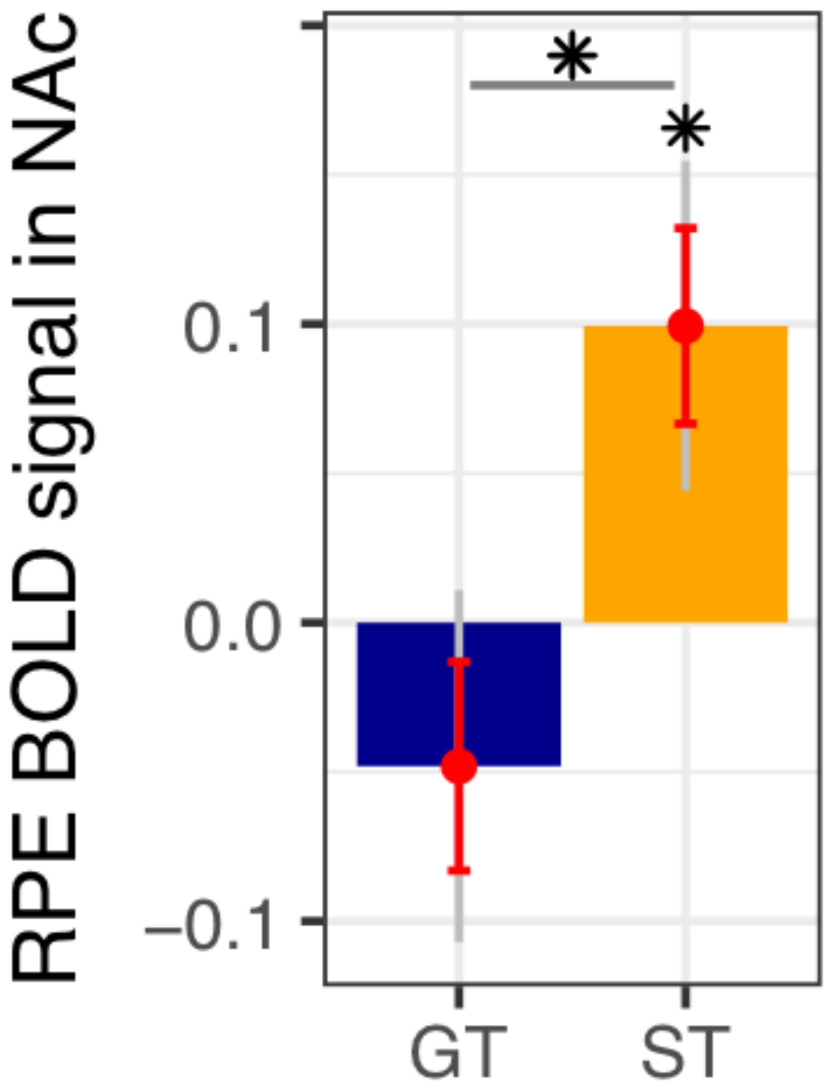




Schad et al., in prep

STs only show BOLD RPE





Schad et al., in prep

RPEs in Pavlovian setting?

- No behaviour - cannot fit the usual models
- Early results: fMRI relatively insensitive to learning rate used. 0.3 as ‘default’
- Here, assumed slower one as Pavlovian trace conditioning paradigm

What should we expect?

- Assume data generated as follows

$$\mathbf{Y} = \beta \mathbf{x}_g + \epsilon,$$

- and use wrong regressor

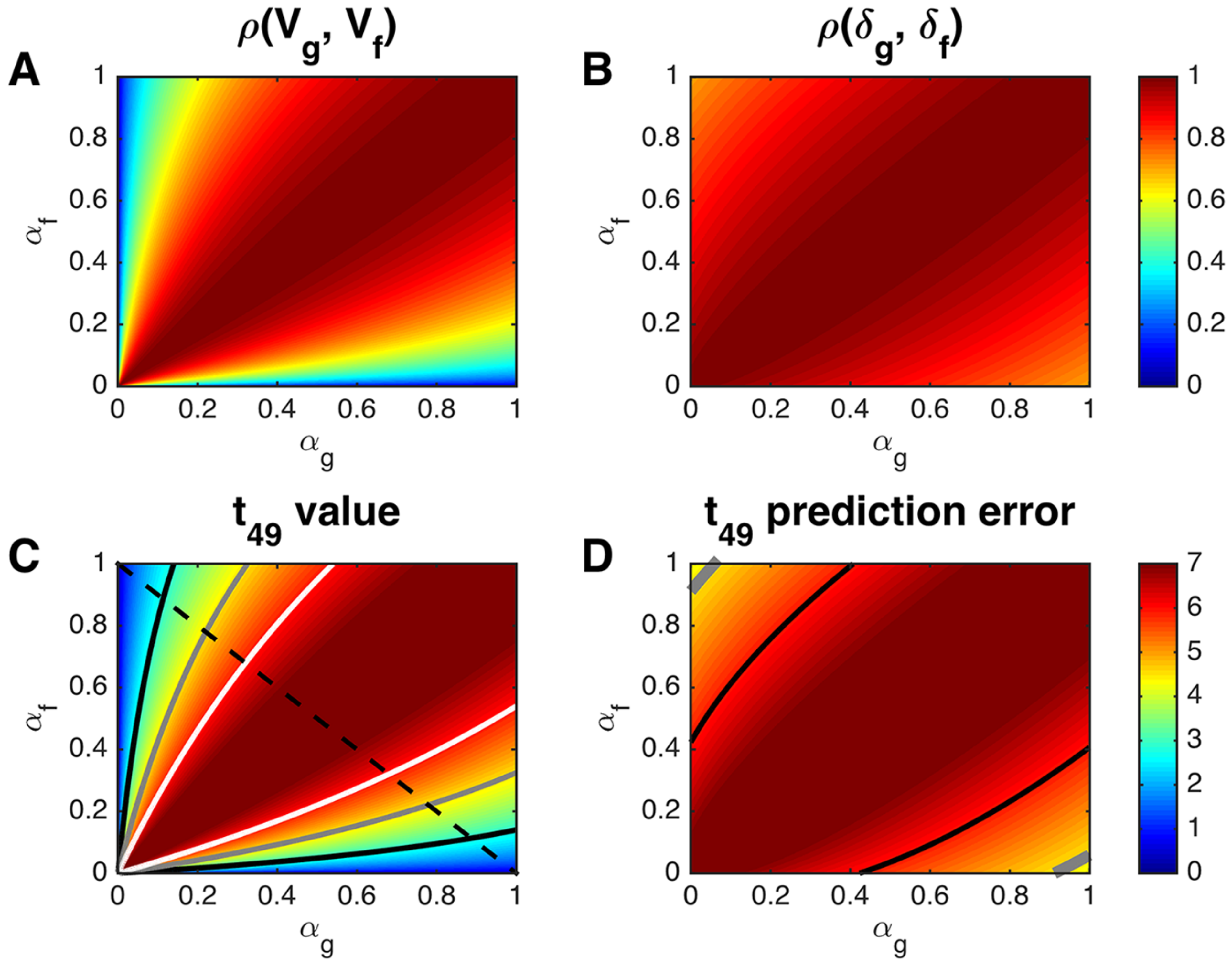
$$\begin{aligned} \hat{\beta} &= (\mathbf{x}_f^T \mathbf{x}_f)^{-1} \mathbf{x}_f^T \mathbf{Y} \\ &= (\mathbf{x}_f^T \mathbf{x}_f)^{-1} (\mathbf{x}_f^T \beta \mathbf{x}_g) \\ &= \beta \rho(\mathbf{x}_g, \mathbf{x}_f) \frac{\sigma(\mathbf{x}_g)}{\sigma(\mathbf{x}_f)} \end{aligned}$$

- the resulting t/p values

$$\hat{t} = \frac{\hat{\beta}}{s(\hat{\beta})} = \rho(\mathbf{x}_g, \mathbf{x}_f)\mathrm{CNR}\sqrt{\frac{T-2}{1+\mathrm{CNR}^2(1-\rho(\mathbf{x}_g, \mathbf{x}_f)^2)}}$$

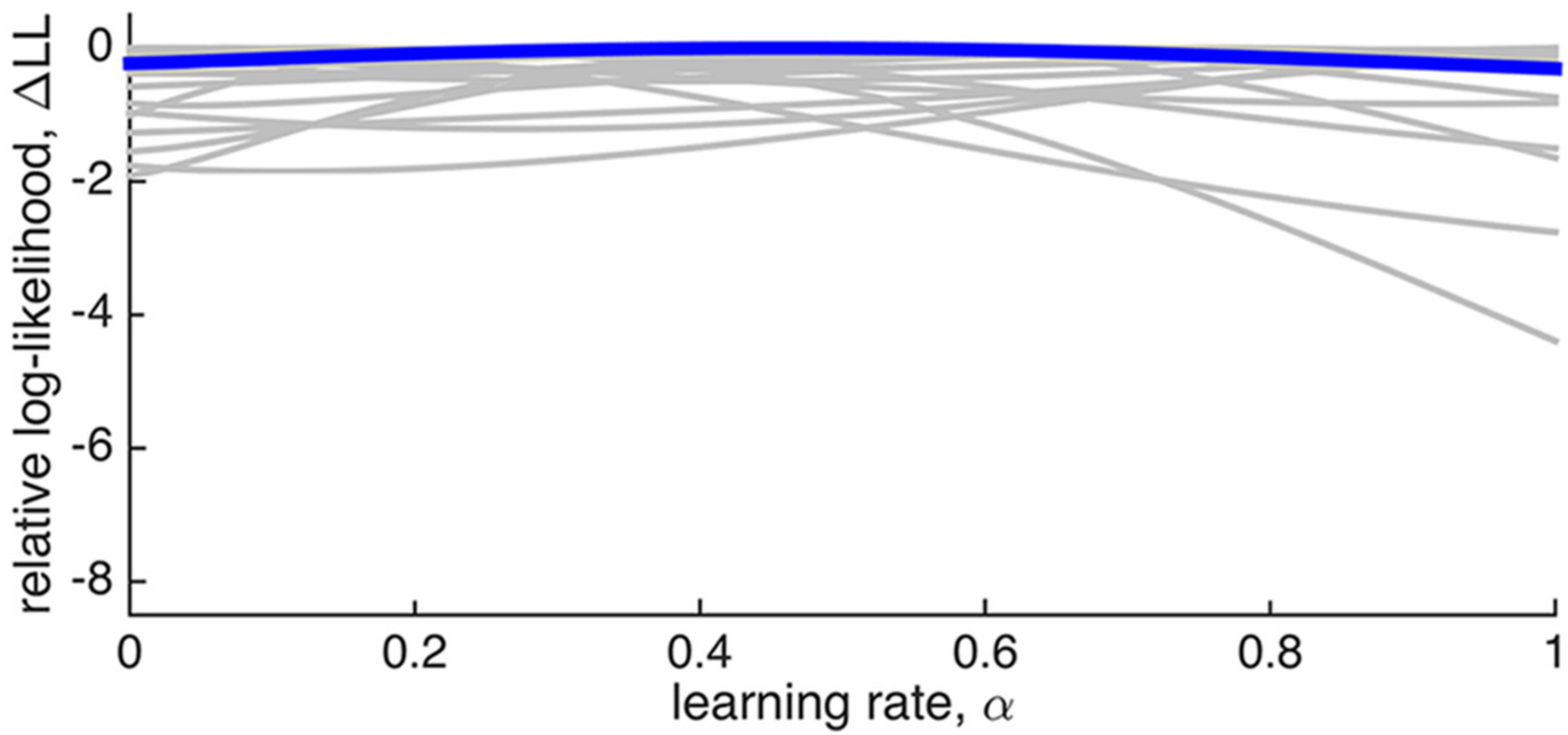
Wilson and Niv 2017 PLoS CB

For static reward probability



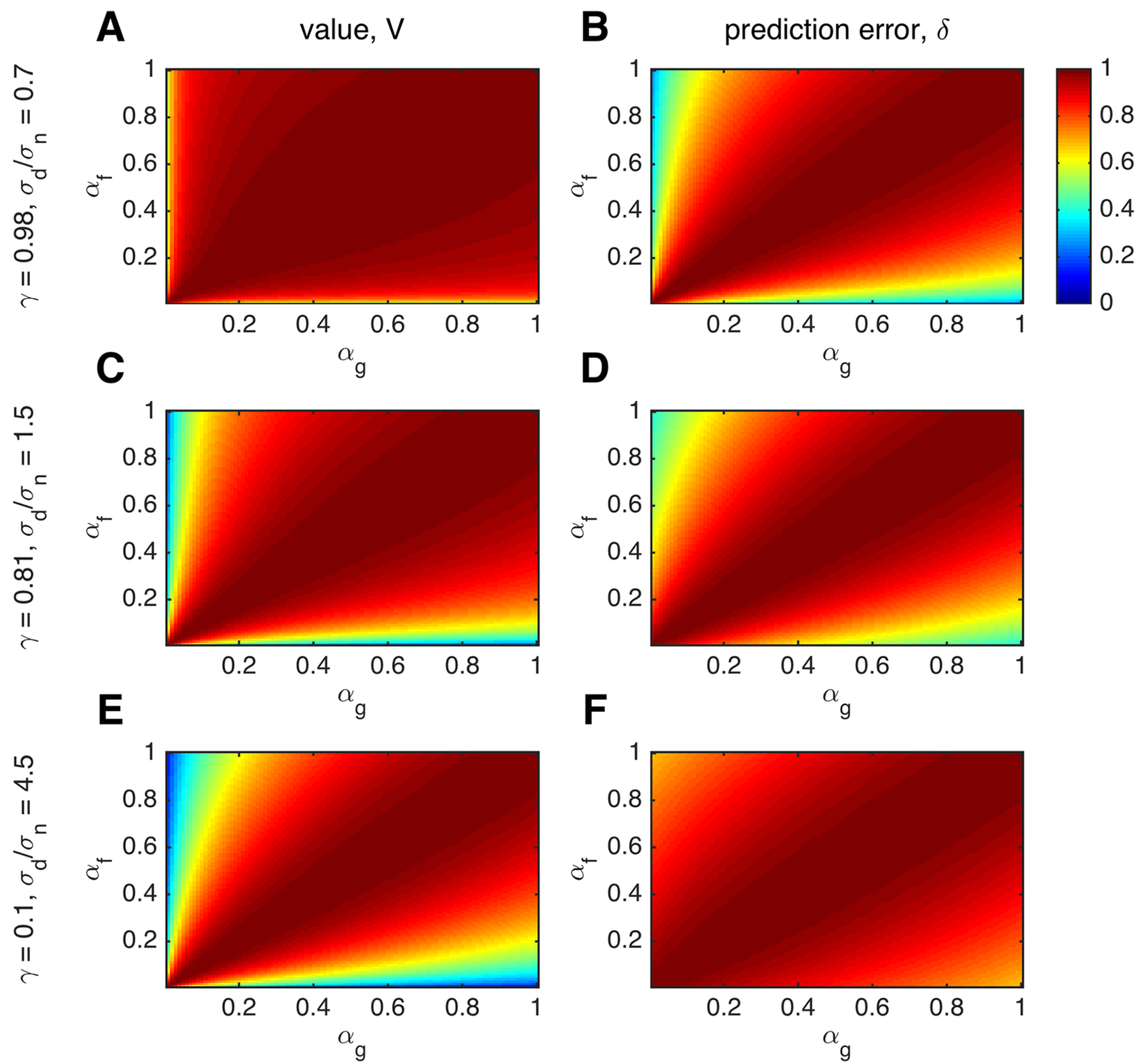
Wilson and Niv 2017 PLoS CB

There is little information



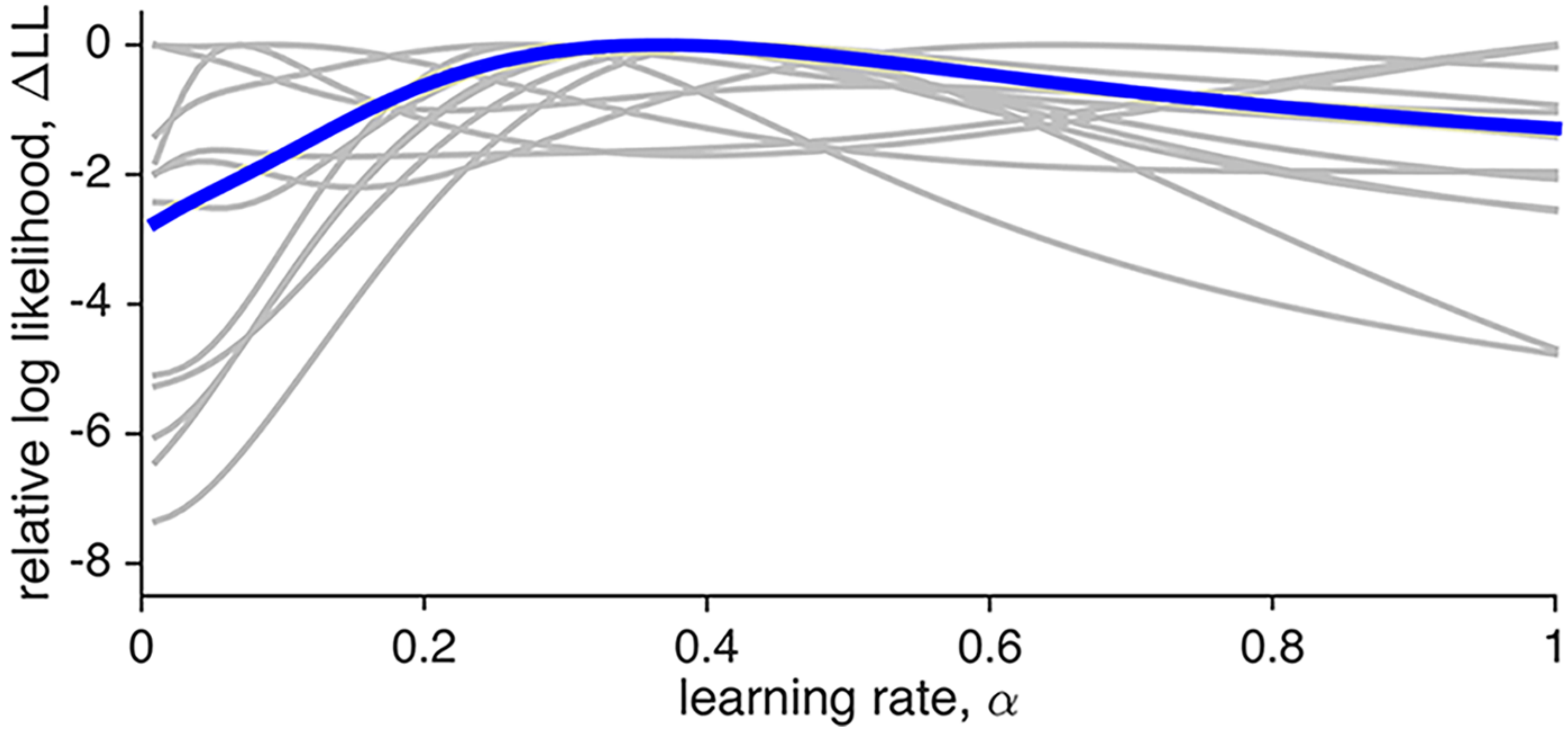
Wilson and Niv 2017 PLoS CB

For drifting reward probability



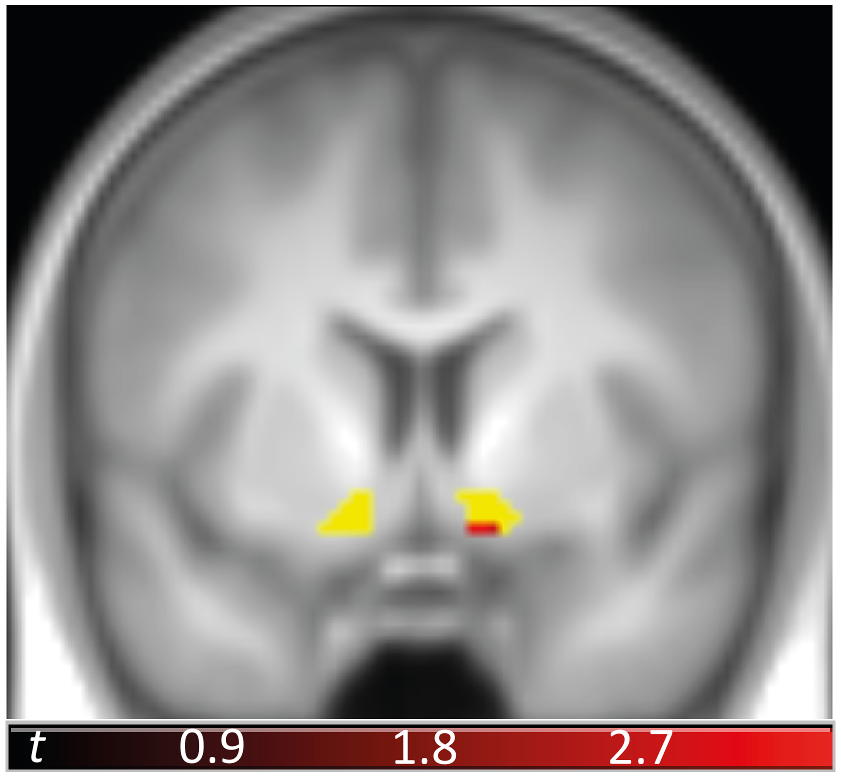
Wilson and Niv 2017 PLoS CB

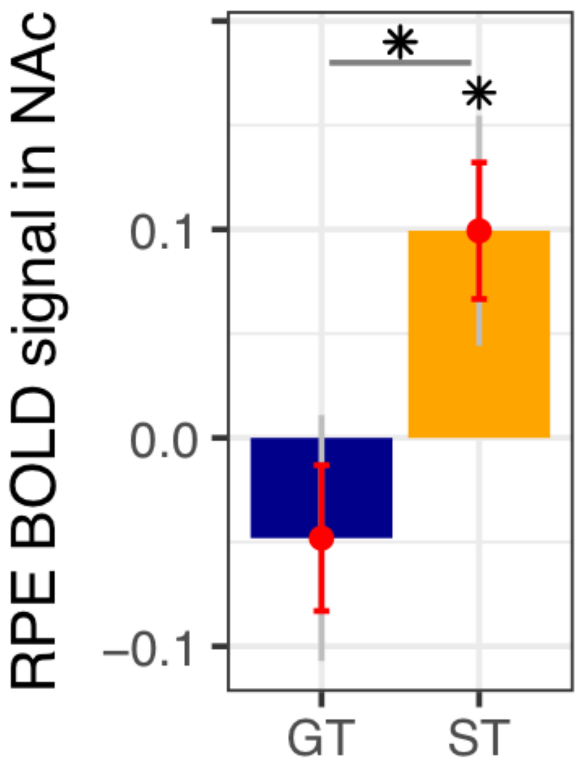
There is some information



Wilson and Niv 2017 PLoS CB

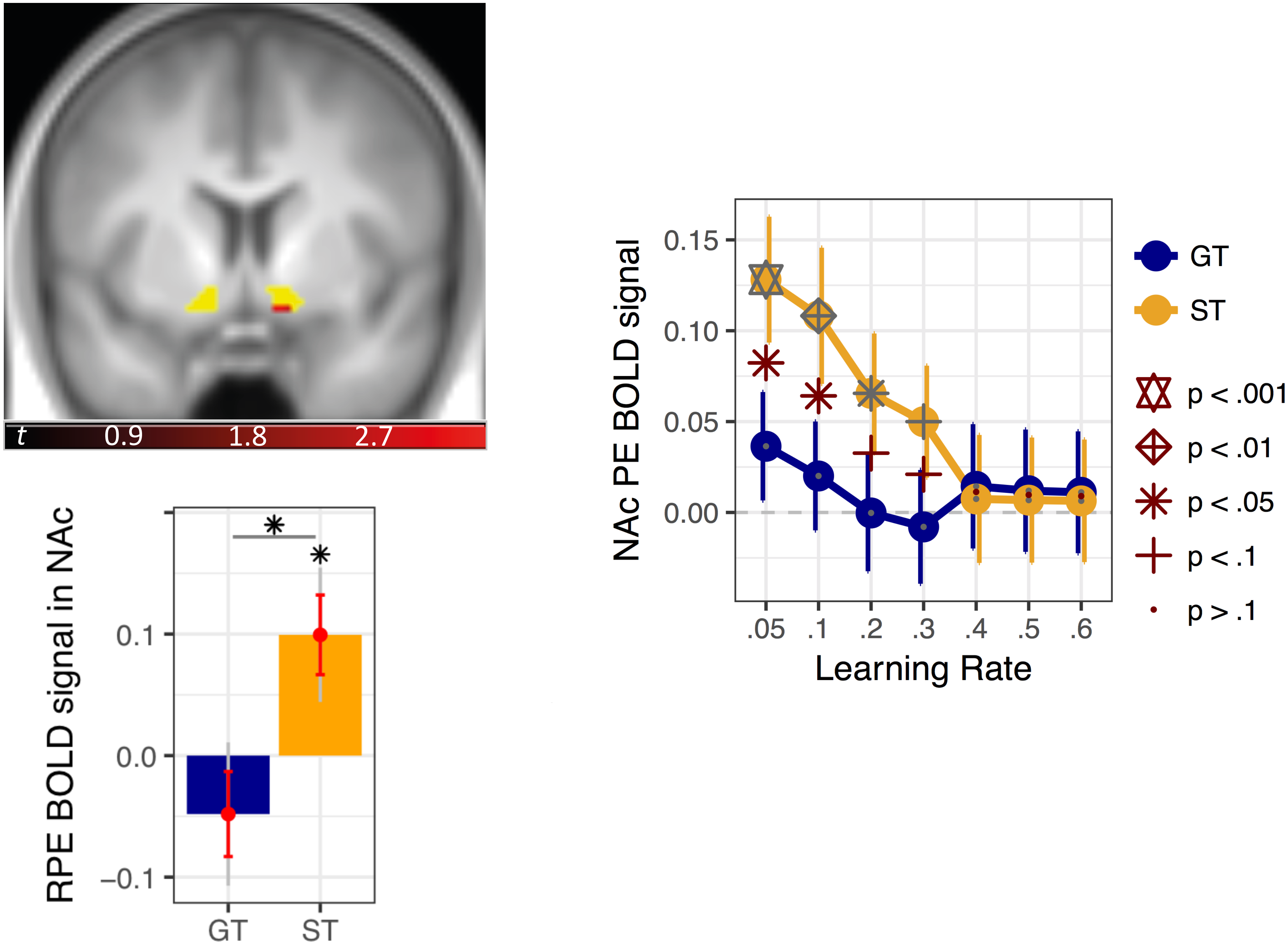
STs only show BOLD RPE





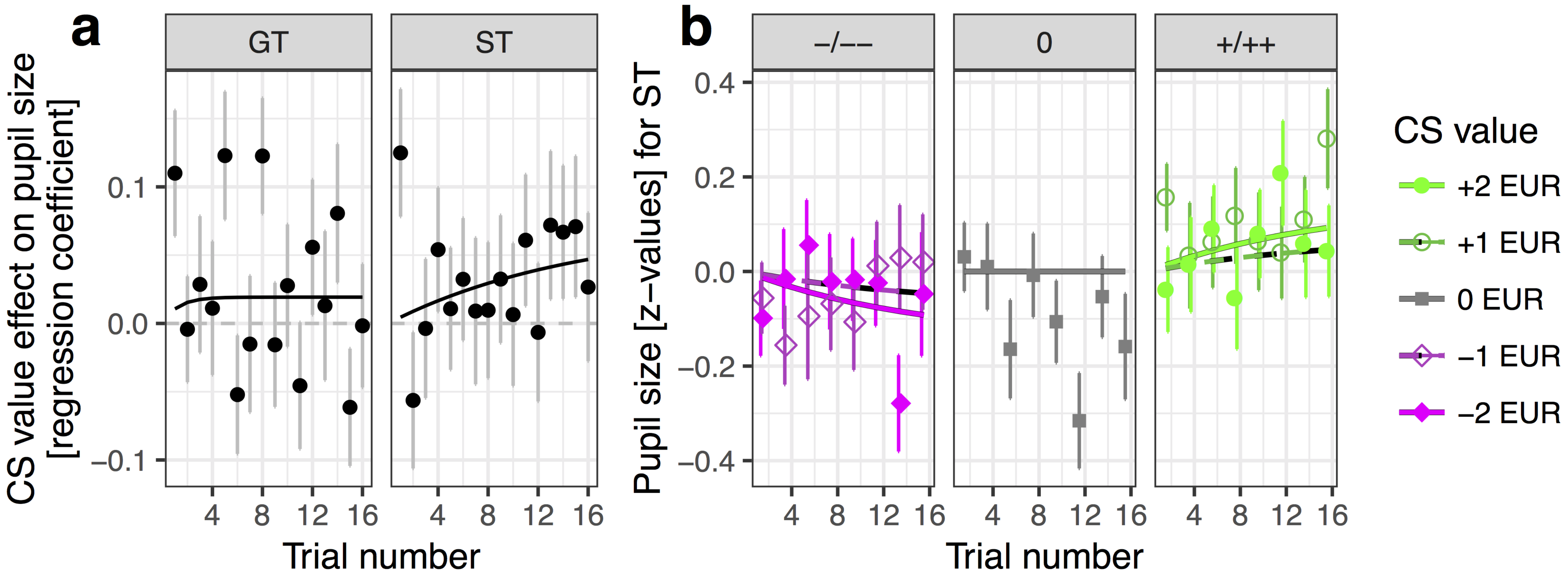
Schad et al., in prep

STs only show BOLD RPE



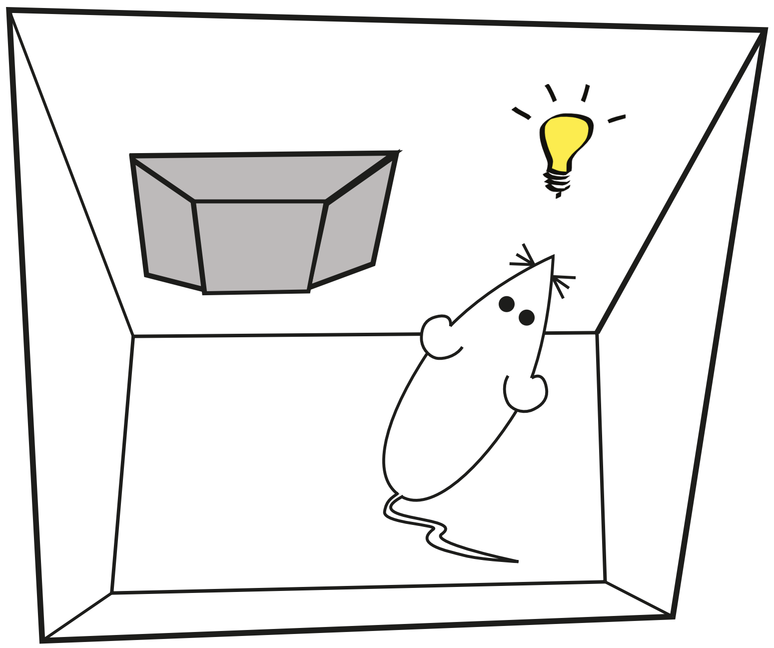
Schad et al., in prep

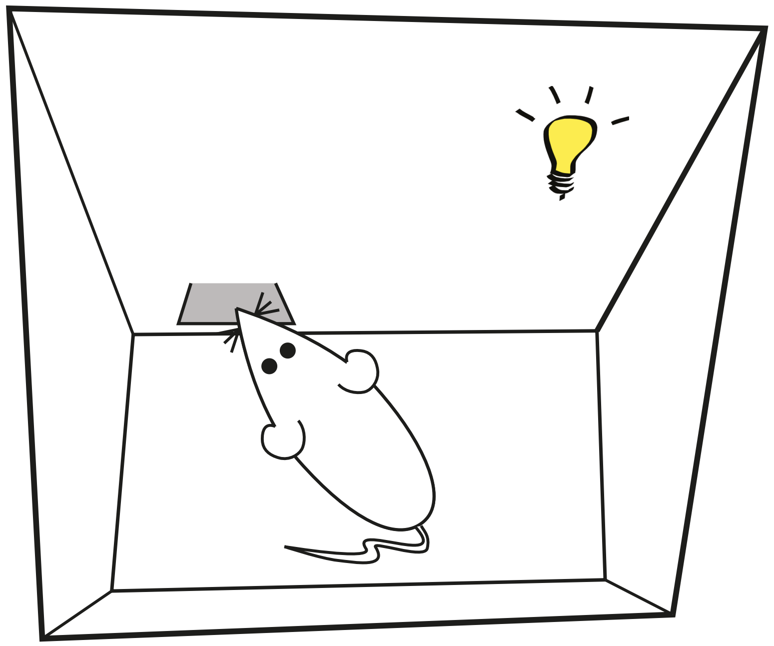
Pupil size accommodates in STs only



Schad et al., in prep

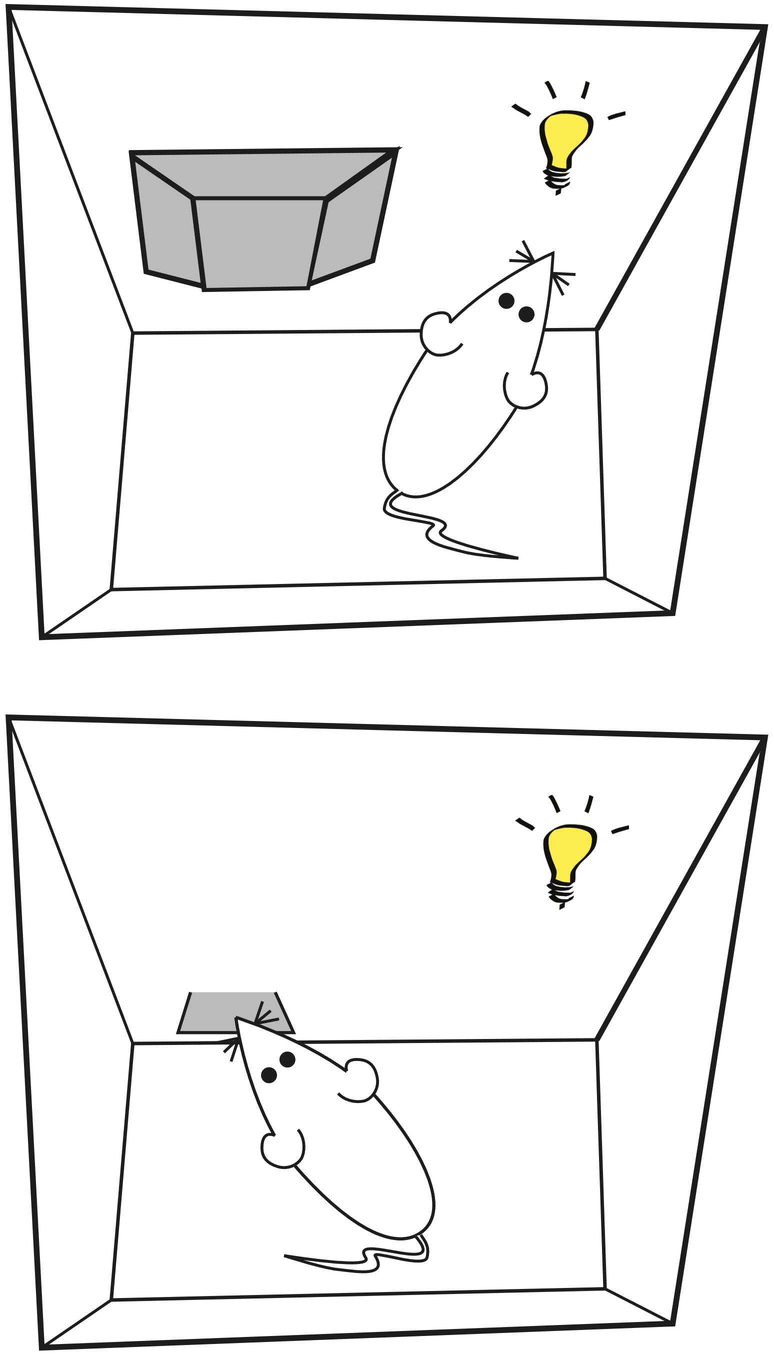
Pavlovian-Instrumental Transfer





Schad et al., in prep

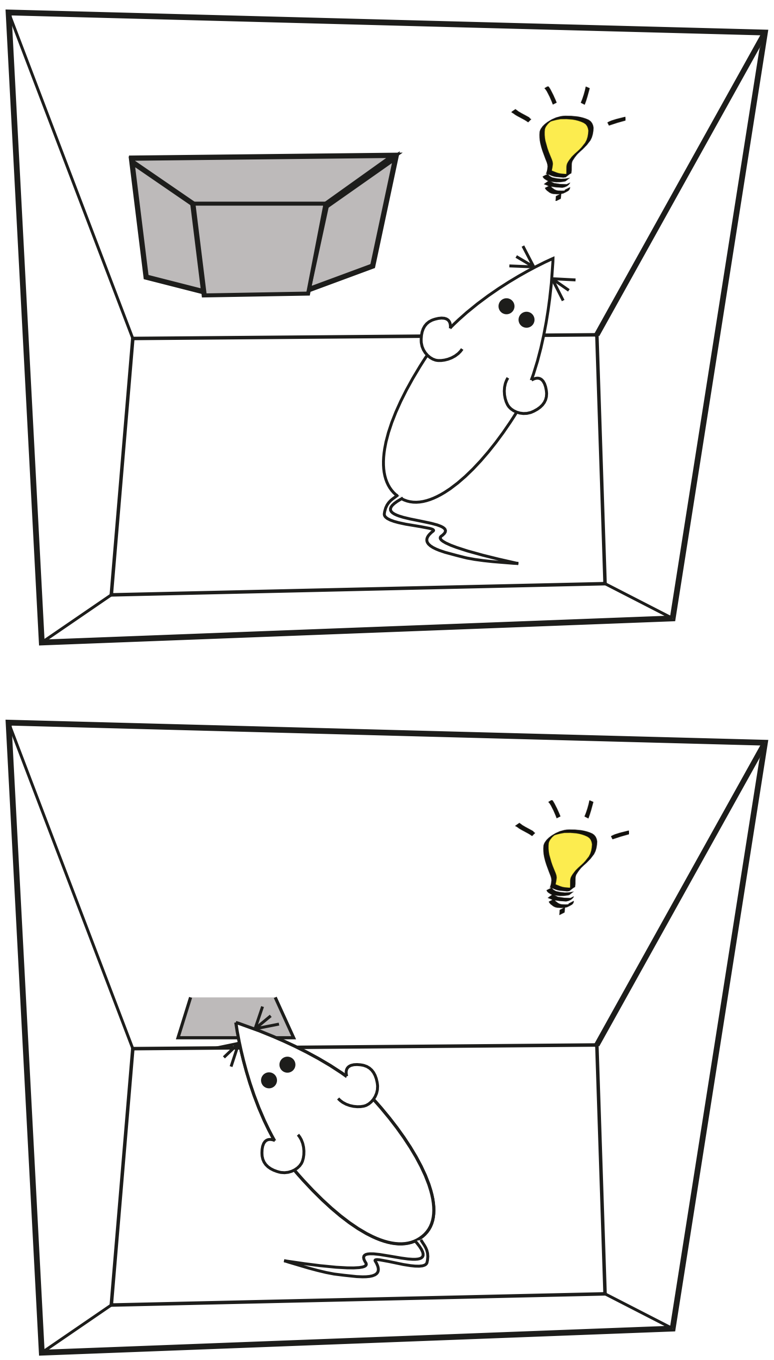
Pavlovian-Instrumental Transfer



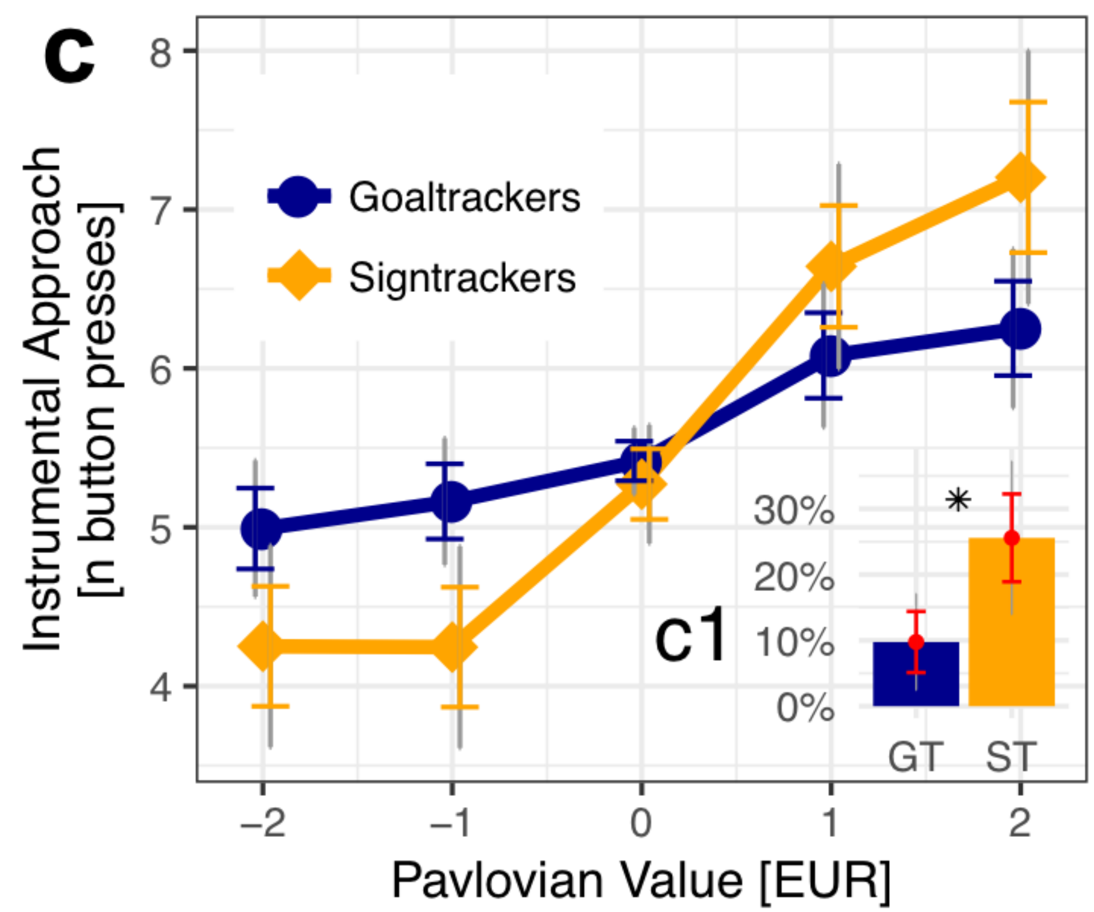
Stimulus control

Schad et al., in prep

Pavlovian-Instrumental Transfer



Stimulus control

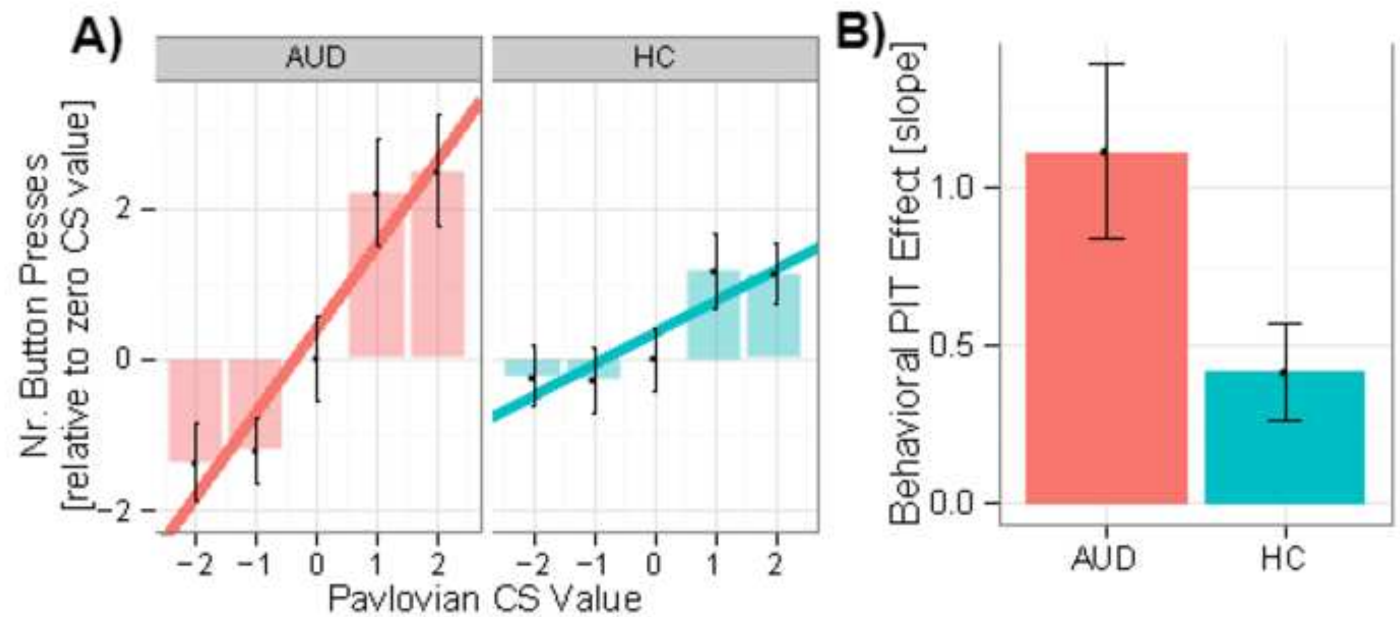


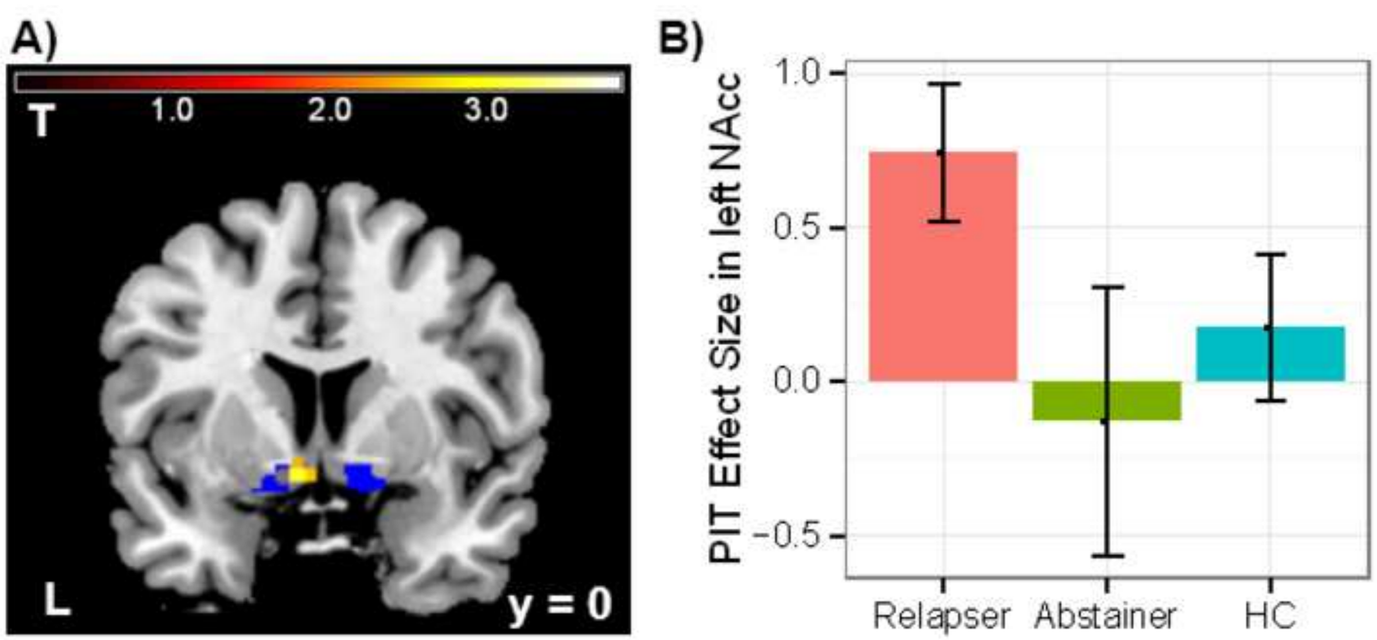
Schad et al., in prep

PIT in alcohol use disorder

31 AUD → 13 abstainers, 11 relapsers

24 HC

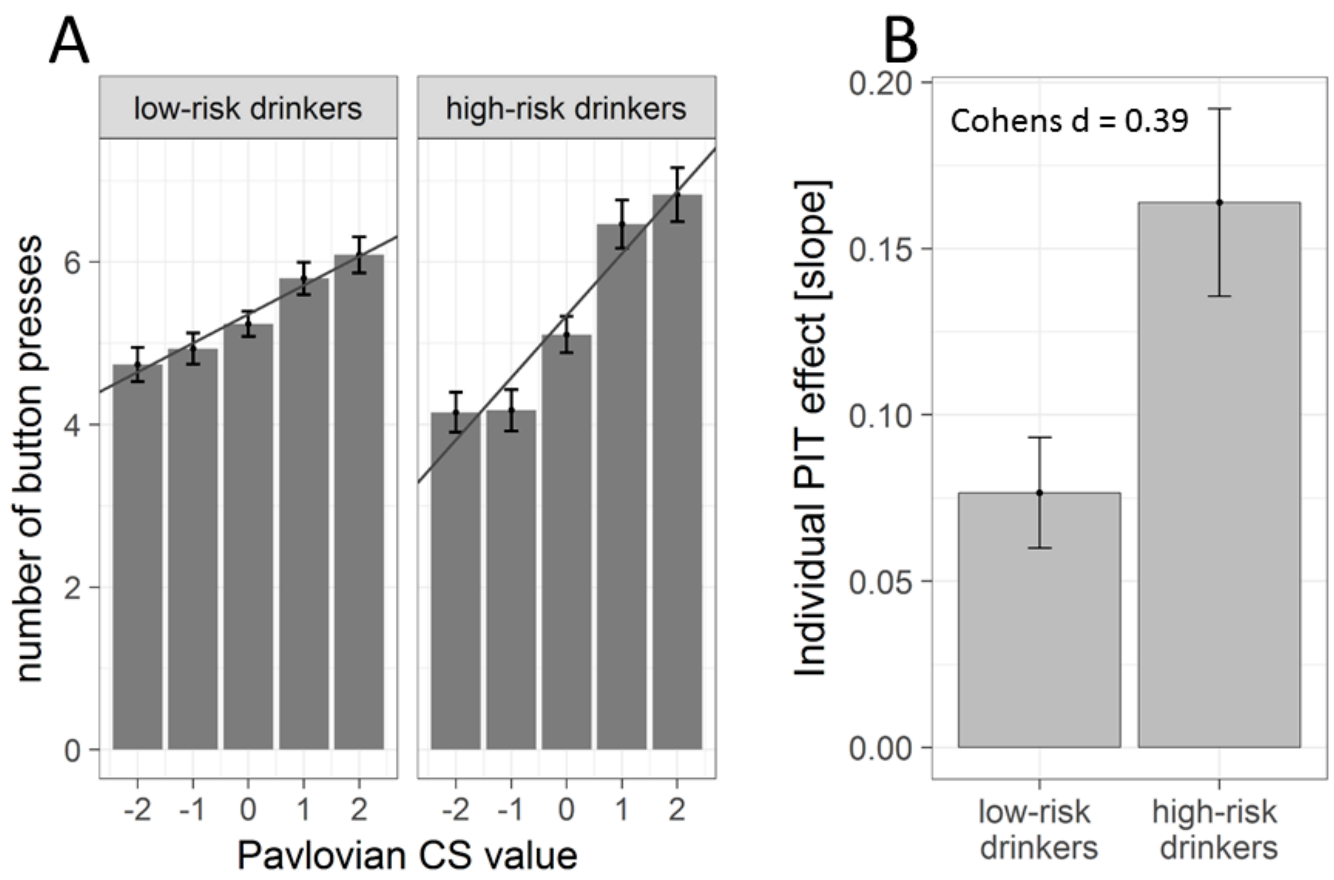


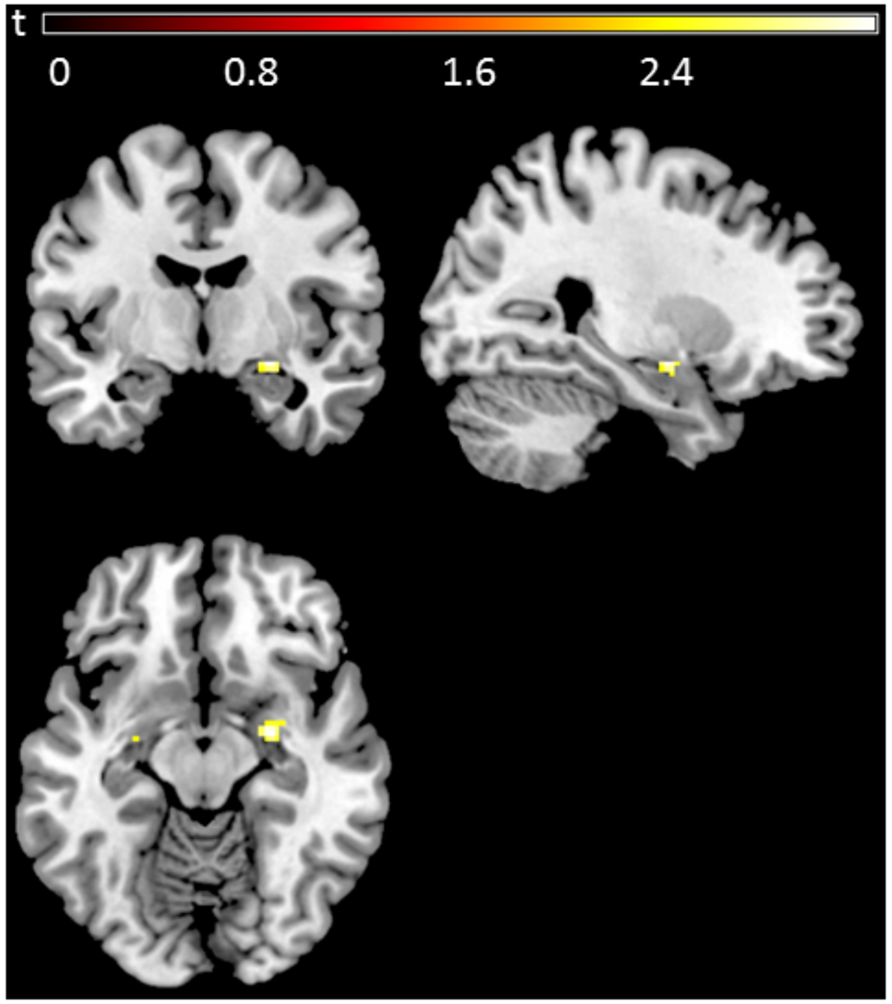


Garbusow et al., 2016 Addiction

PIT in at-risk young males

201 HC





Garbusow et al., 2017 under rev.

The point

- A model “processes” information
- Cannot increase it
- If it’s not there, the model won’t put it there

Outline

Depression

Addiction

OCD

Anxiety

Schizophrenia

Parkinson’s

Mood

Metareasoning

Obsessive-compulsive disorder

- Overwhelming urge to think certain thoughts or perform certain actions

- A “habit” driving urges to think and to act?

Review

Cell PRESS

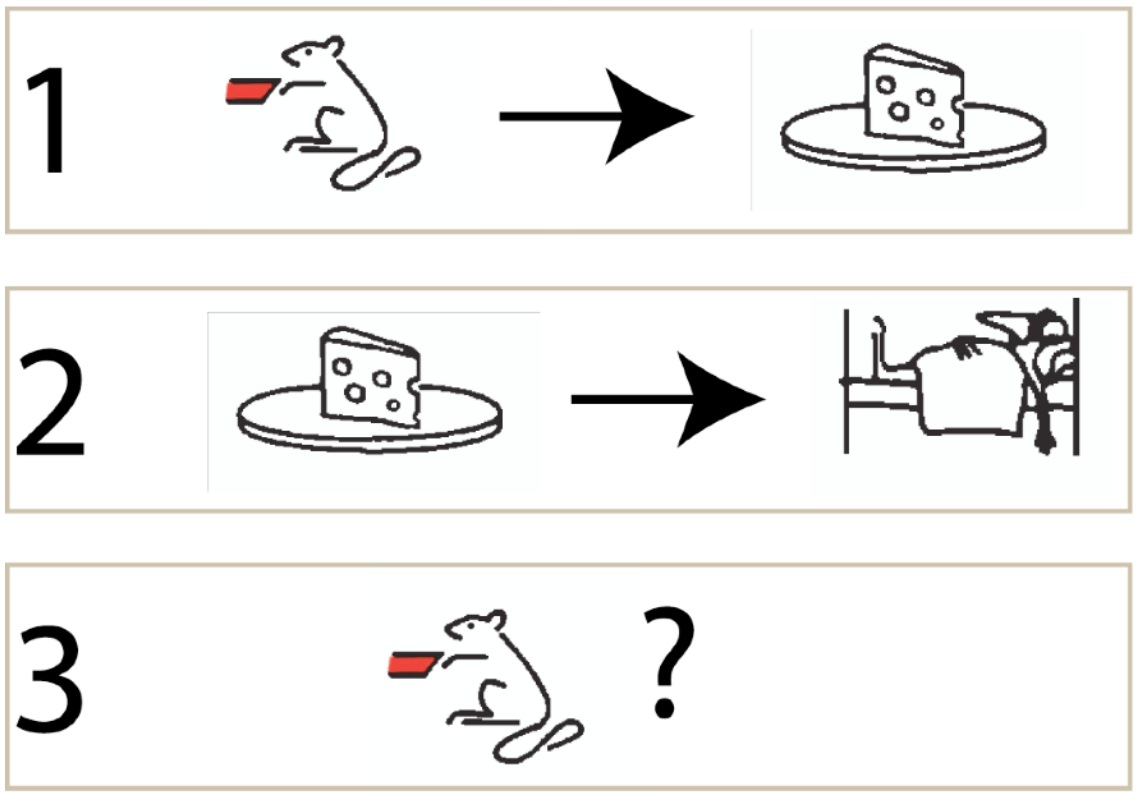
Special Issue: Cognition in Neuropsychiatric Disorders

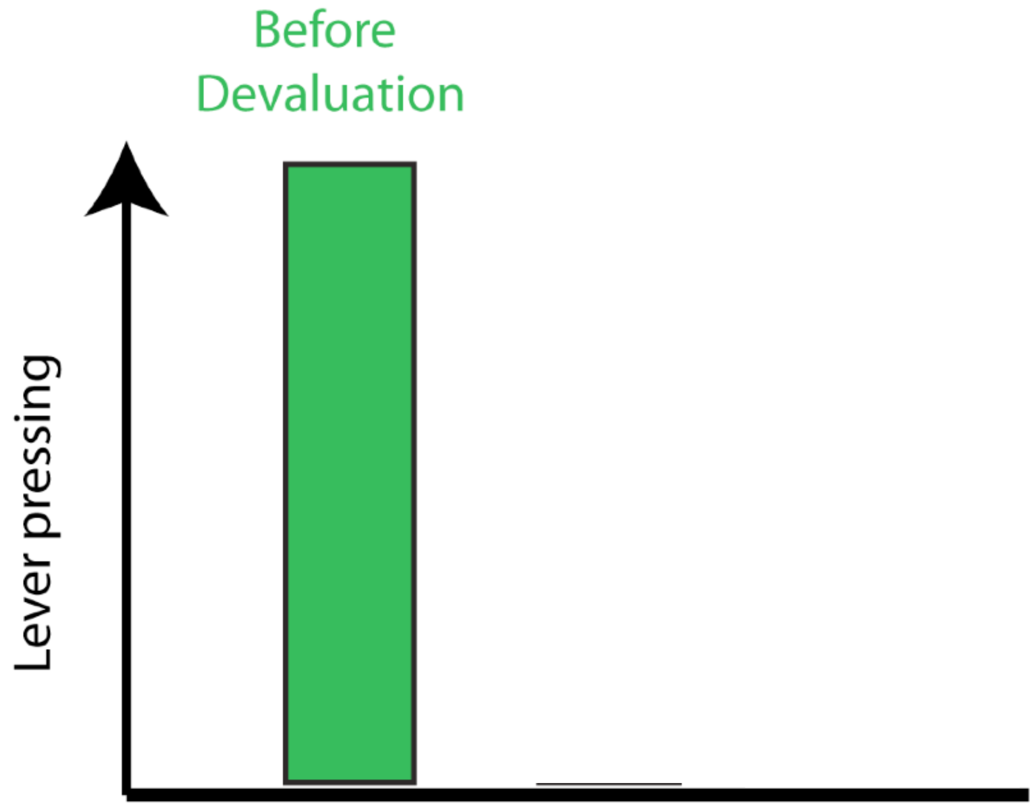
Neurocognitive endophenotypes of impulsivity and compulsivity: towards dimensional psychiatry

Trevor W. Robbins[1,2], Claire M. Gillan[1,2], Dana G. Smith[1,2], Sanne de Wit[4] and Karen D. Ersche[1,3]

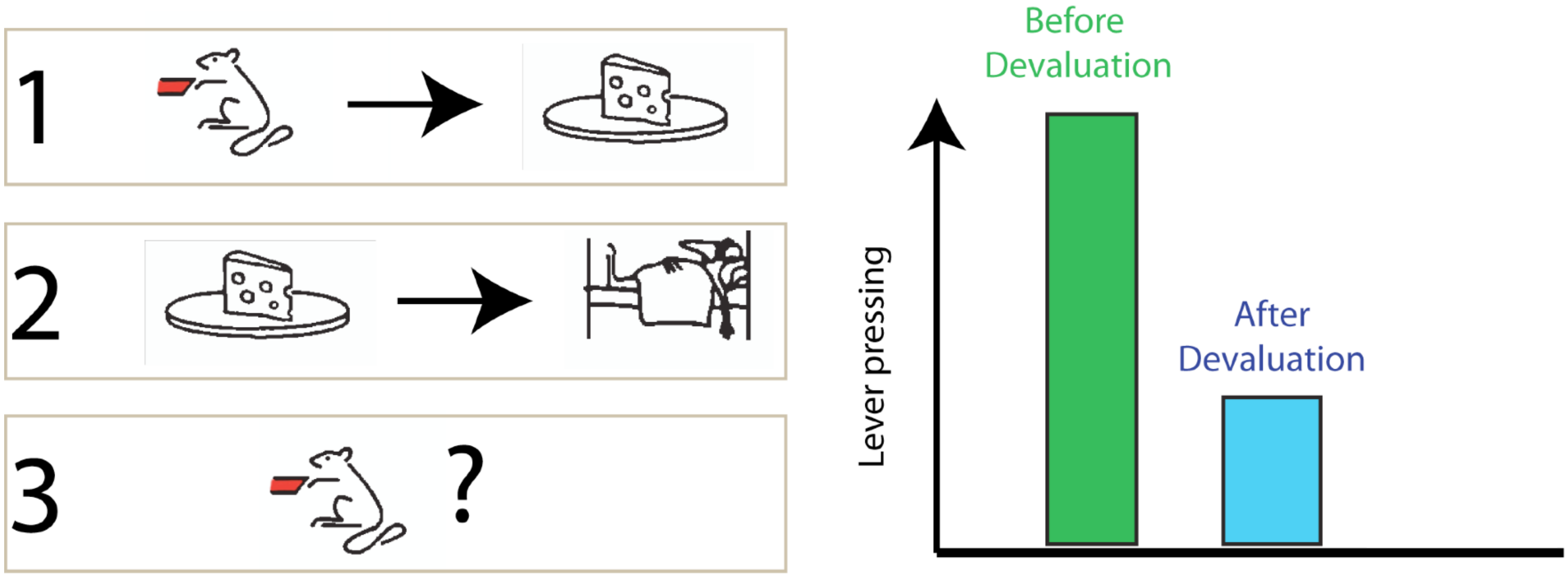
[1] Behavioural and Clinical Neuroscience Institute, University of Cambridge, Cambridge CB2 3EB, UK
[2] Department of Experimental Psychology, University of Cambridge, Cambridge CB2 3EB, UK
[3] Department of Psychiatry, School of Clinical Medicine, Addenbrookes Hospital, Cambridge CB2 0SP, UK
[4] Department of Clinical Psychology and Cognitive Science Center Amsterdam, University of Amsterdam, 1018 TV Amsterdam, The Netherlands

Habitization





Habitization



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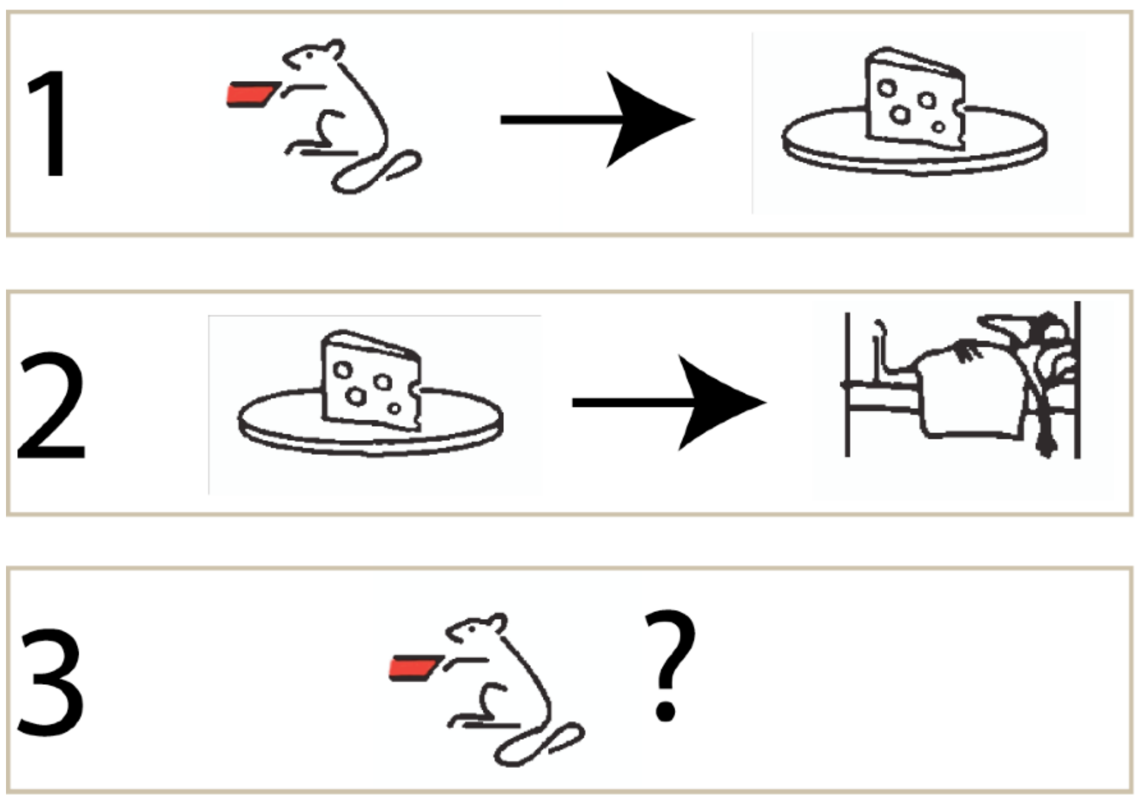
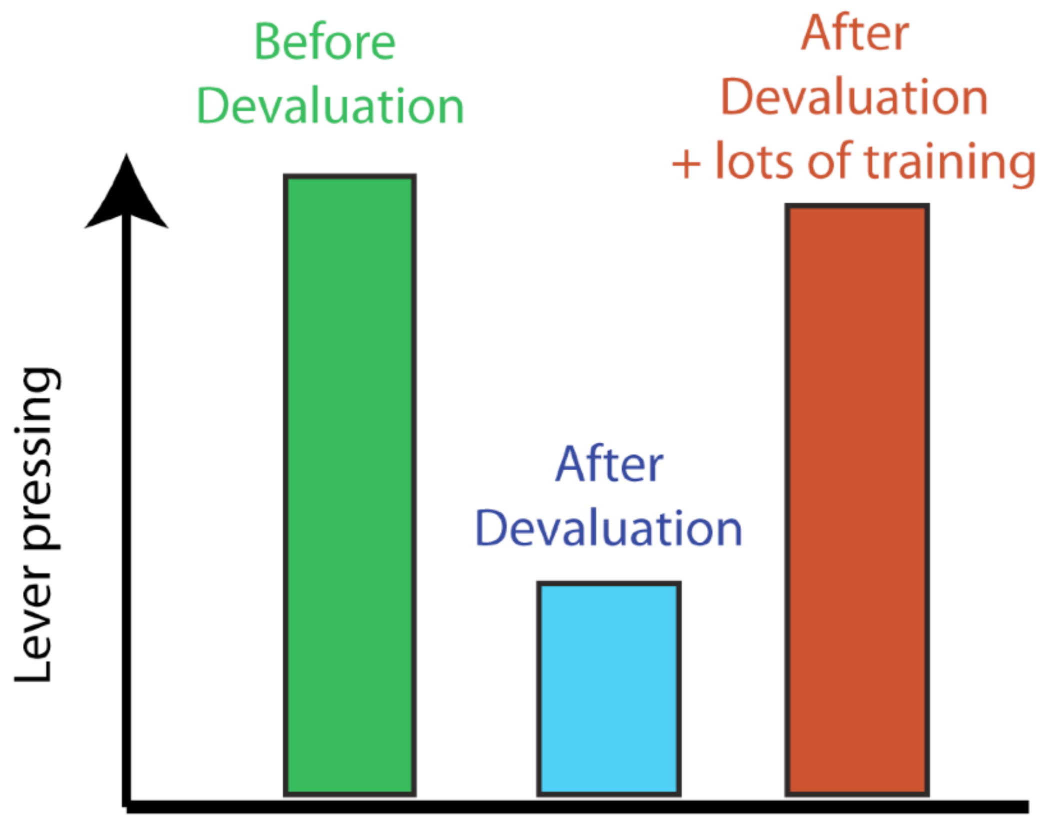
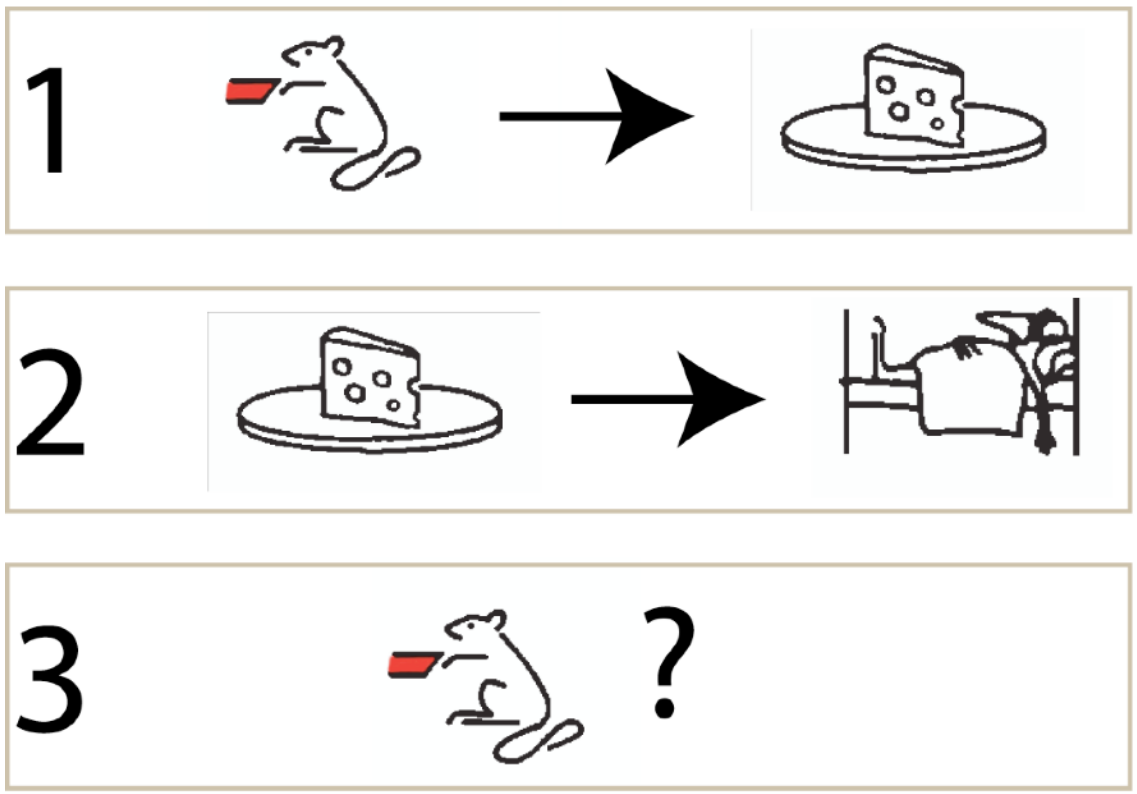
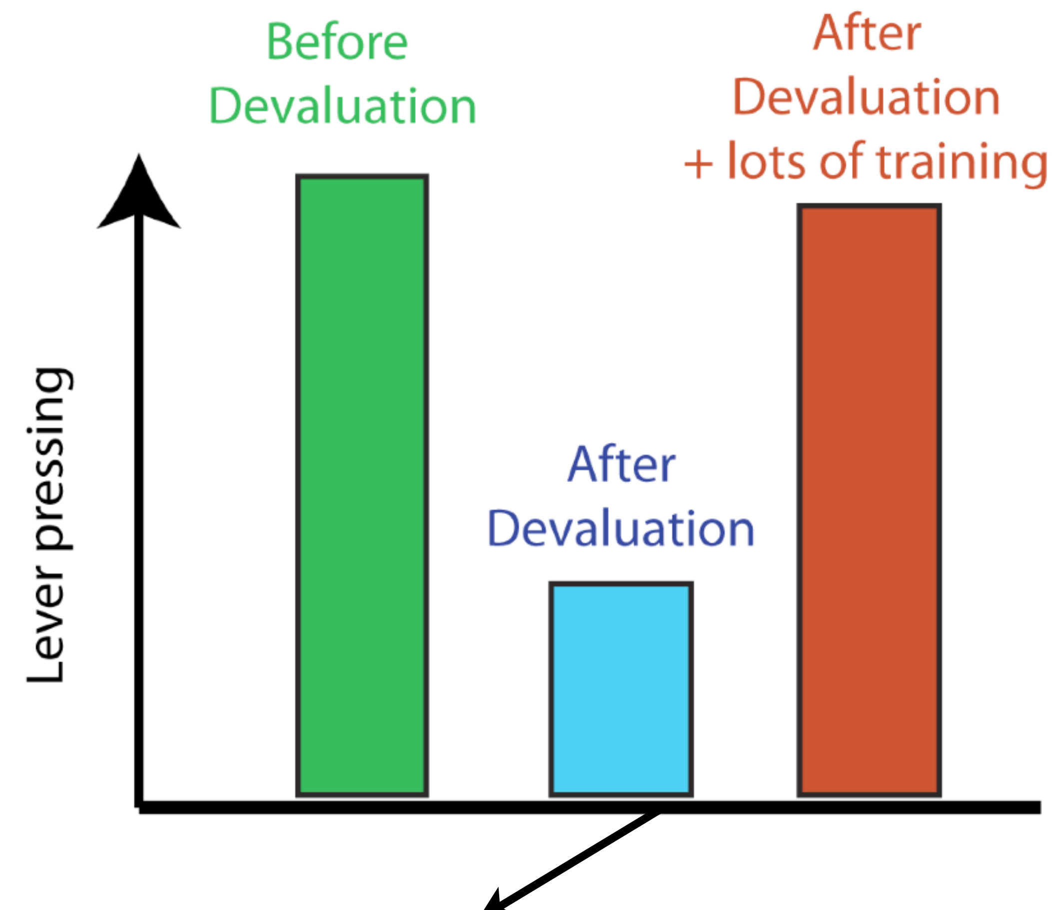




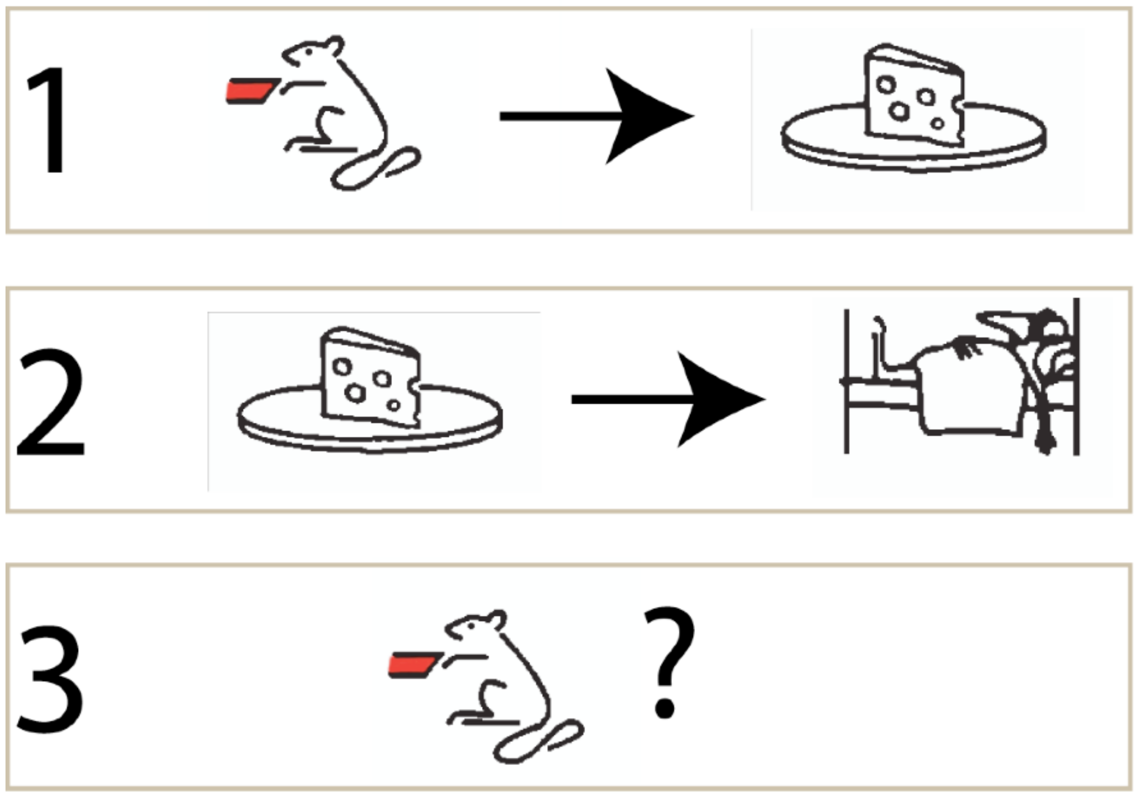
Habitization

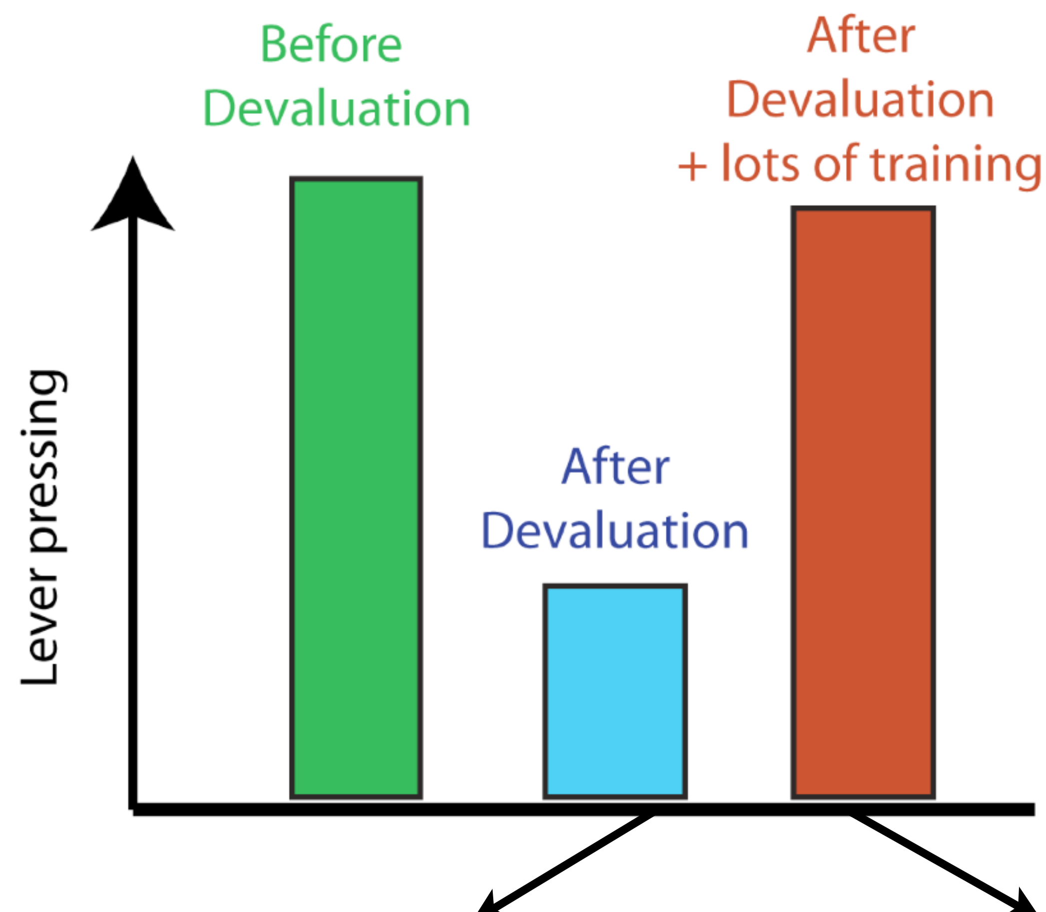




Get this pattern late if lesion infralimbic cortex

Habitization

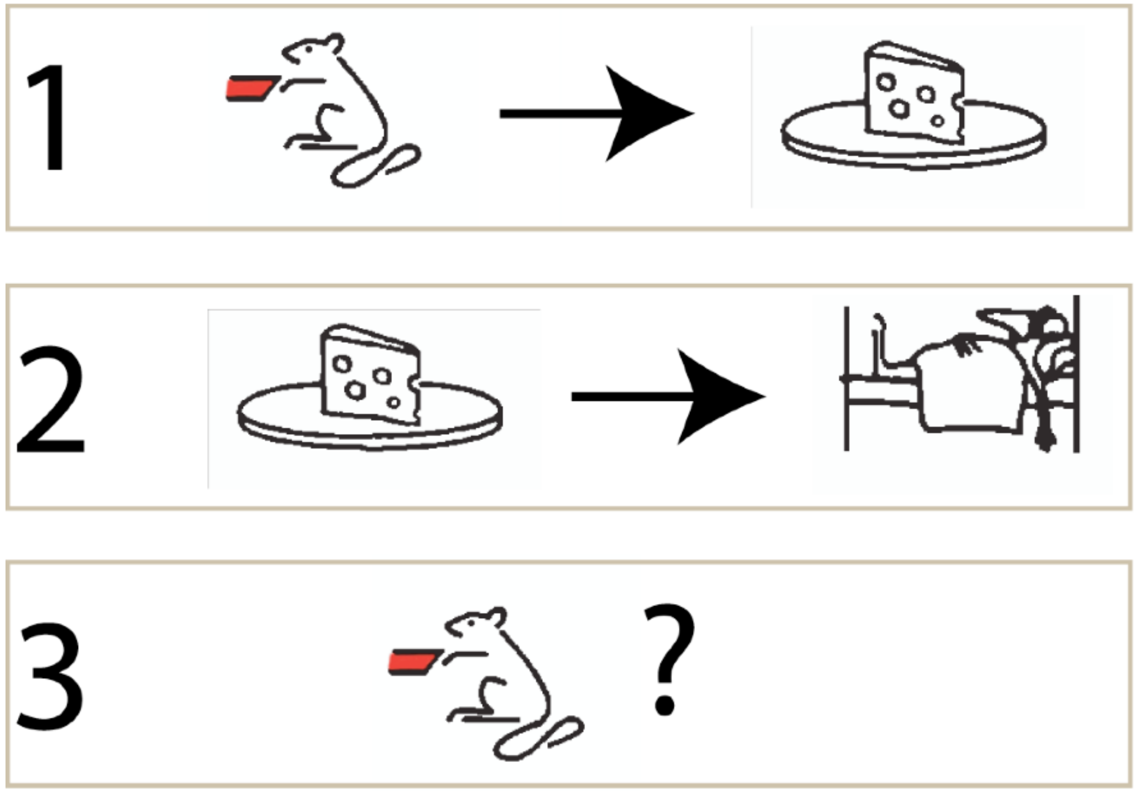


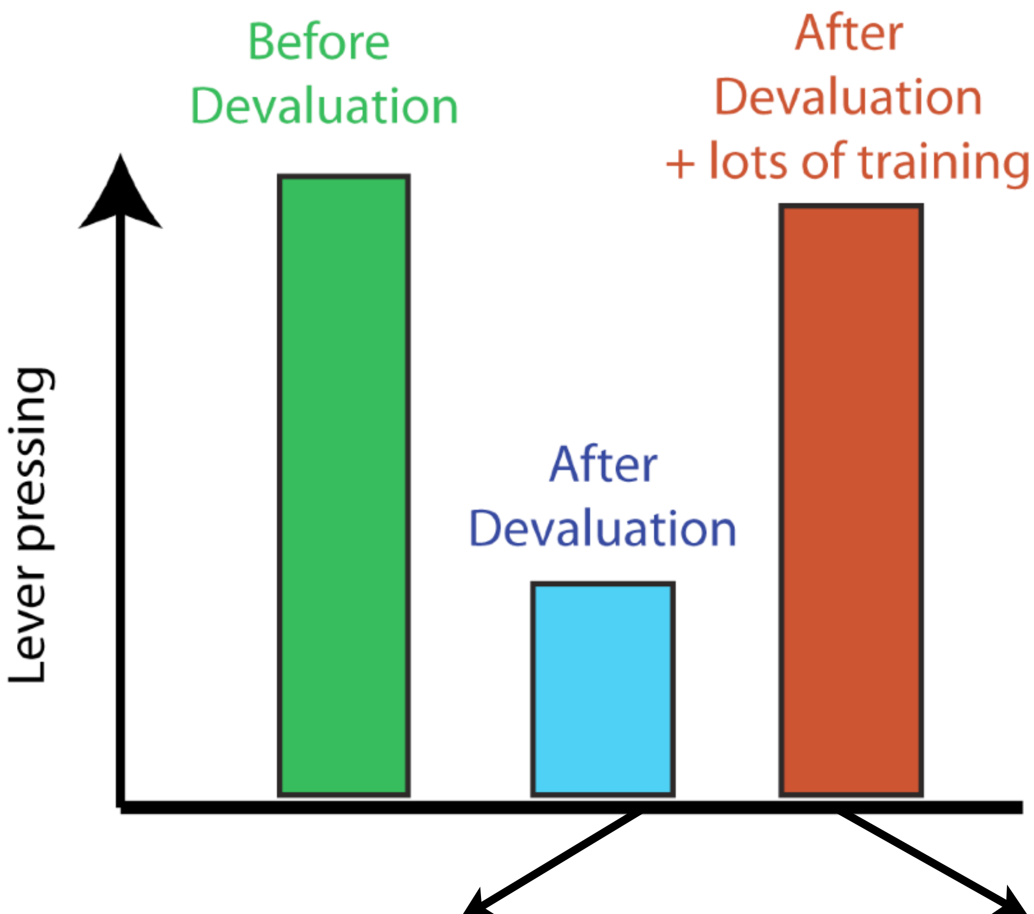


Get this pattern late if lesion infralimbic cortex

Get this pattern early if lesion prelimbic cortex

Habitization



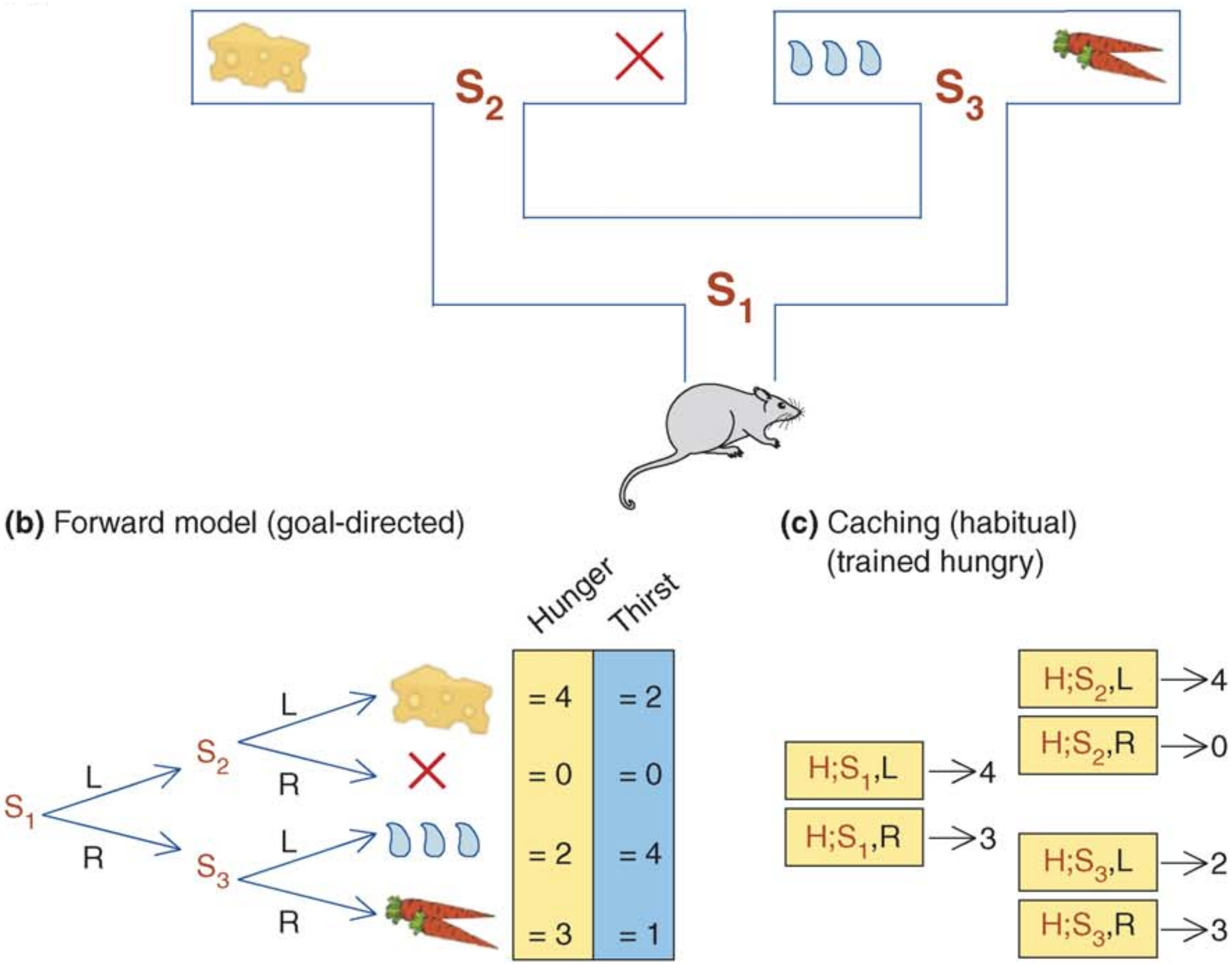


Get this pattern late if lesion infralimbic cortex

Get this pattern early if lesion prelimbic cortex

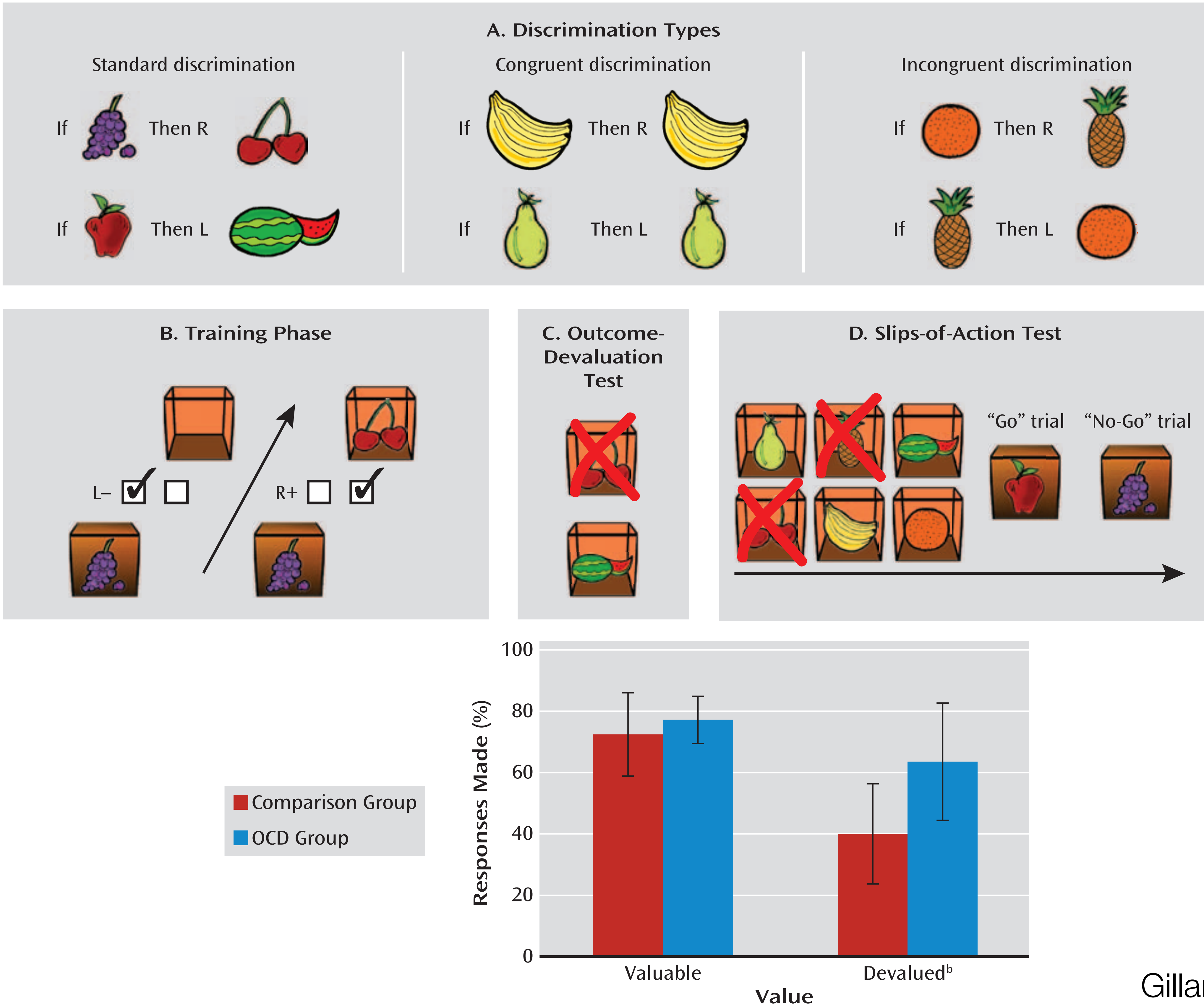
PEL ETOH

Model-free vs model-based valuation



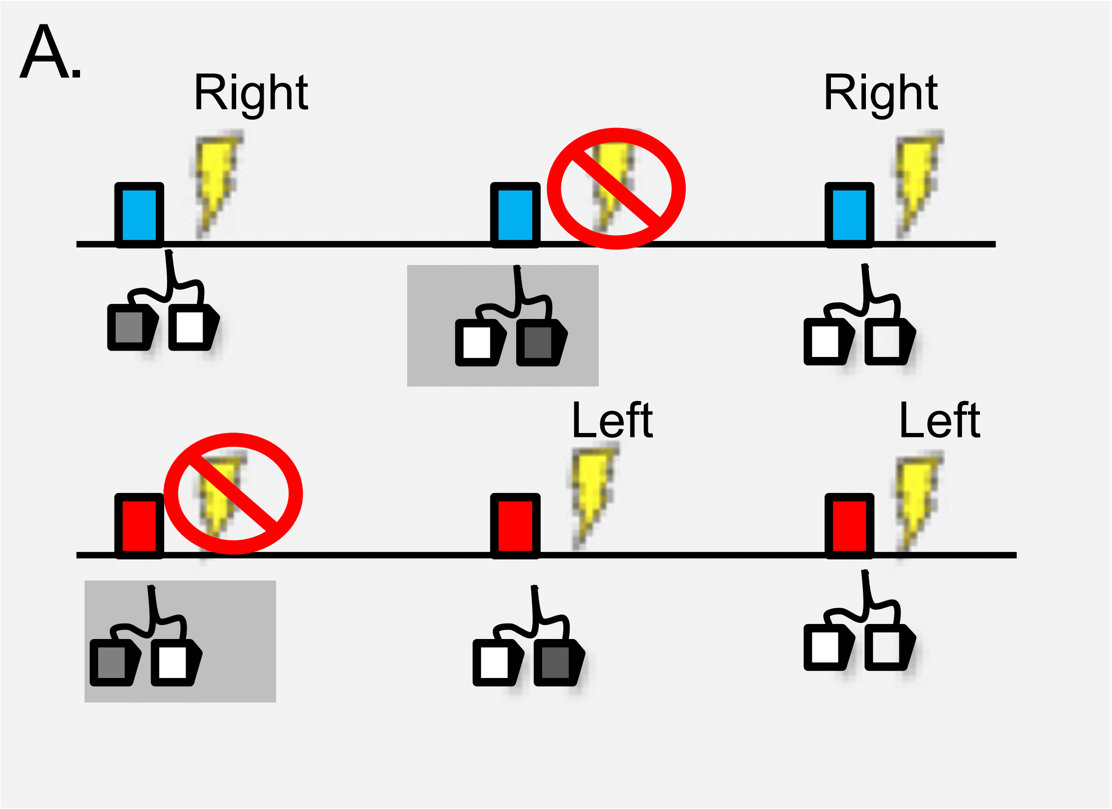
Niv et al., 2008 TICS

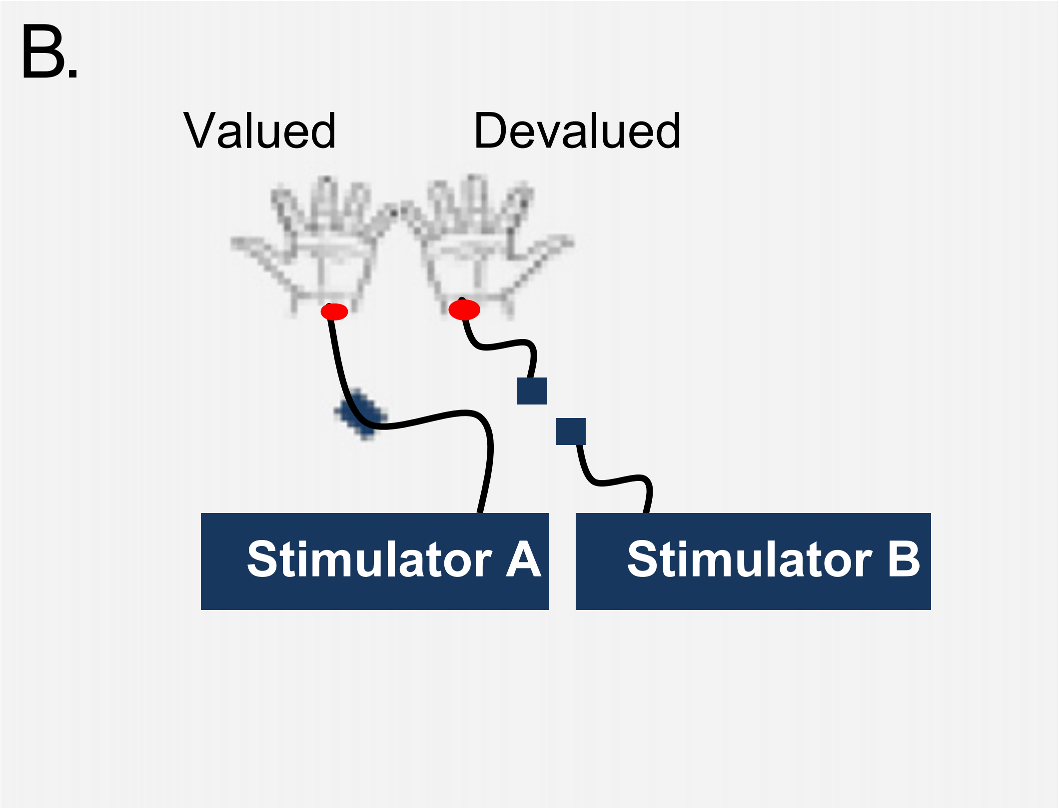
Devaluation is impaired in OCD



Gillan et al., 2011 AJP

Devaluation is impaired in OCD

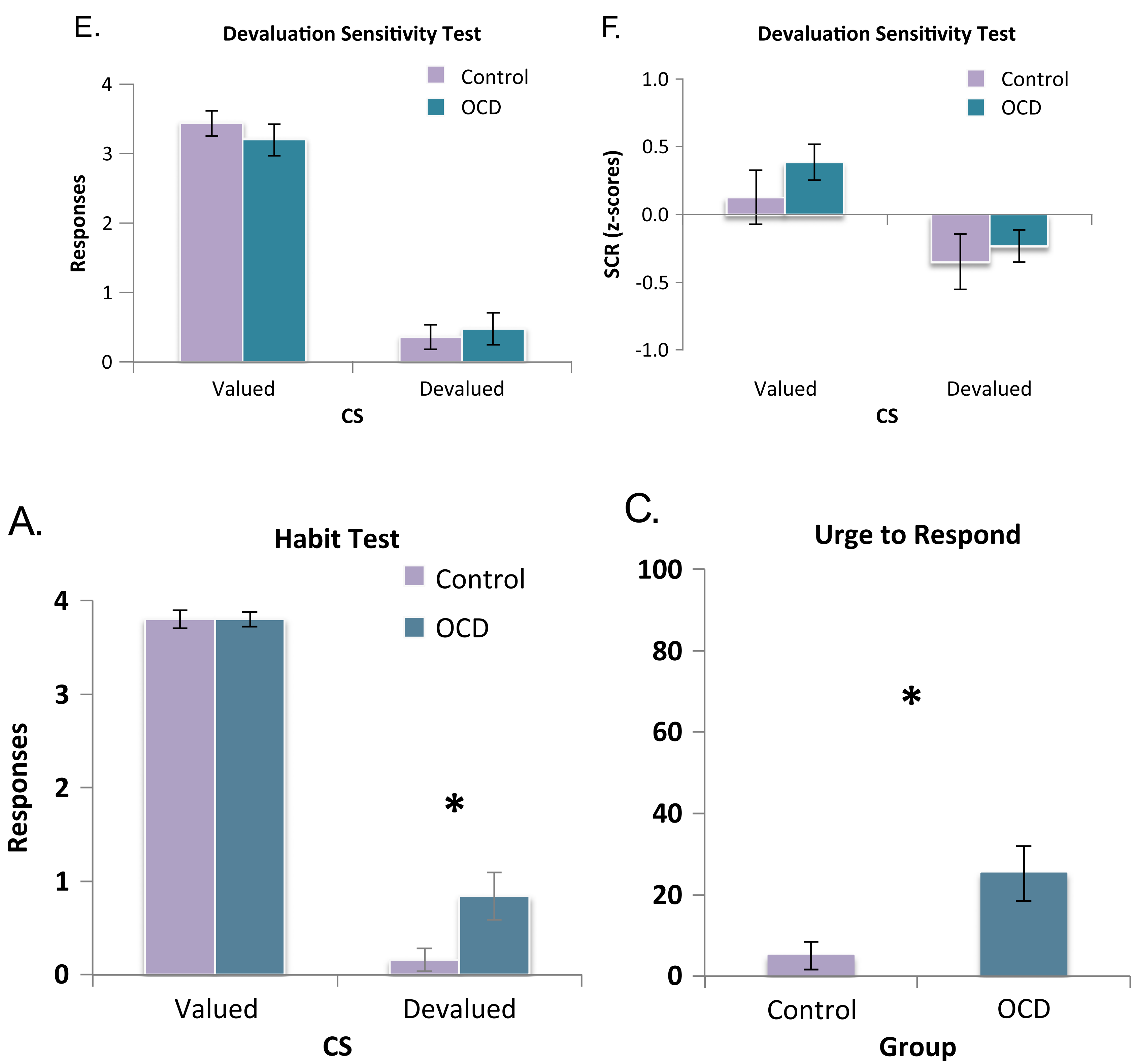




Initial training → Devaluation sensitivity test → Extended training → Habit test

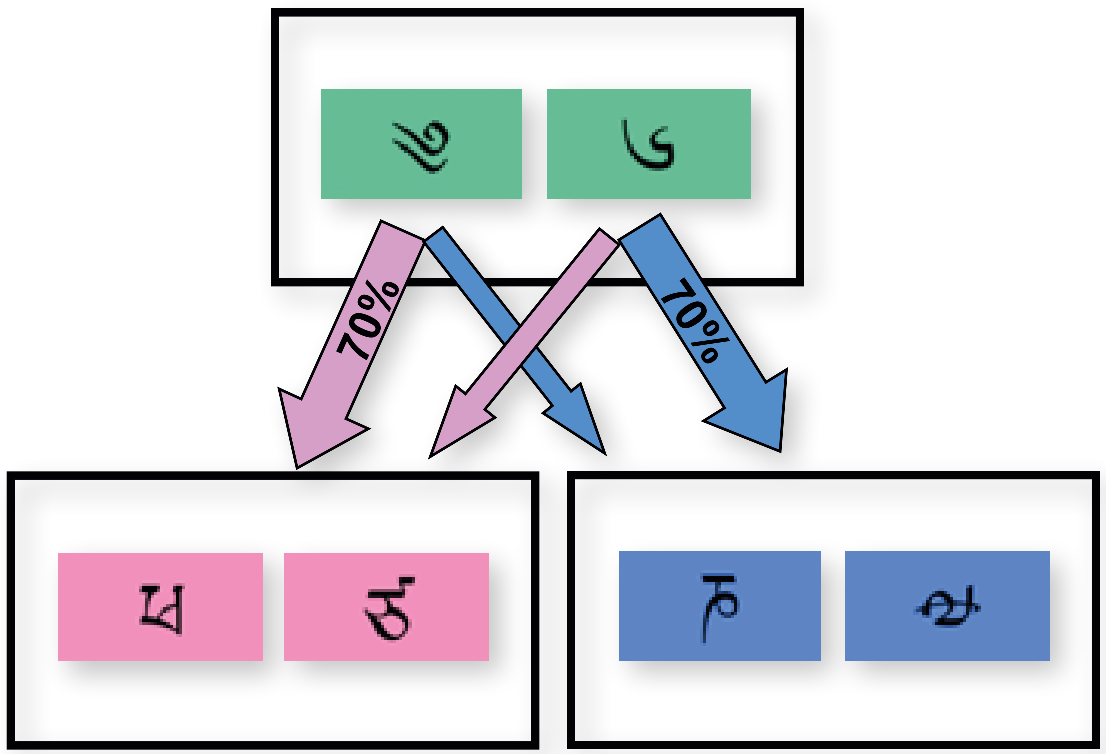
Gillan et al., 2013 Biol Psych

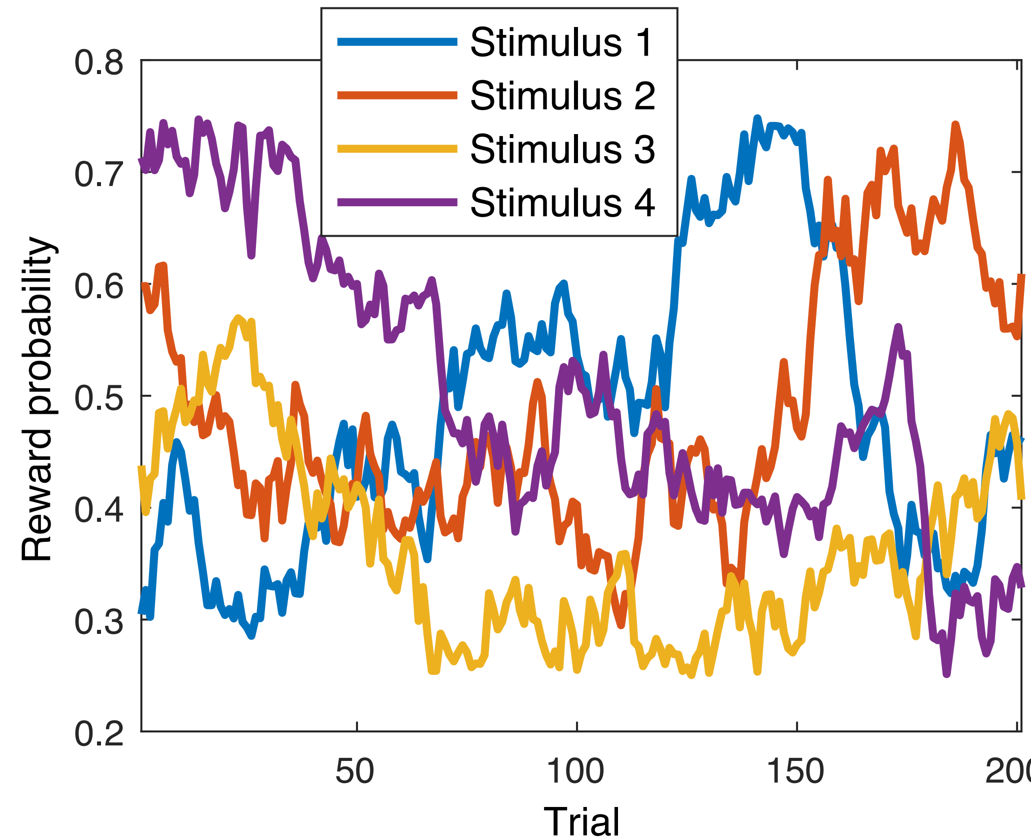
Devaluation is impaired in OCD

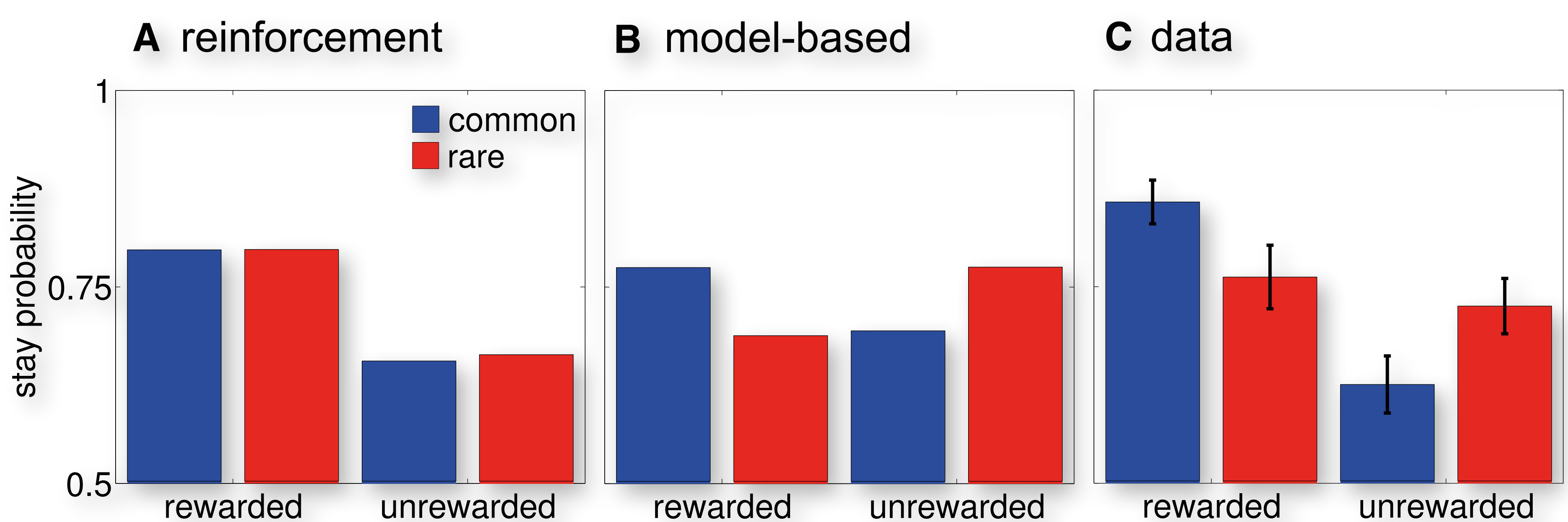


Gillan et al., 2013 Biol Psych

Two-step task

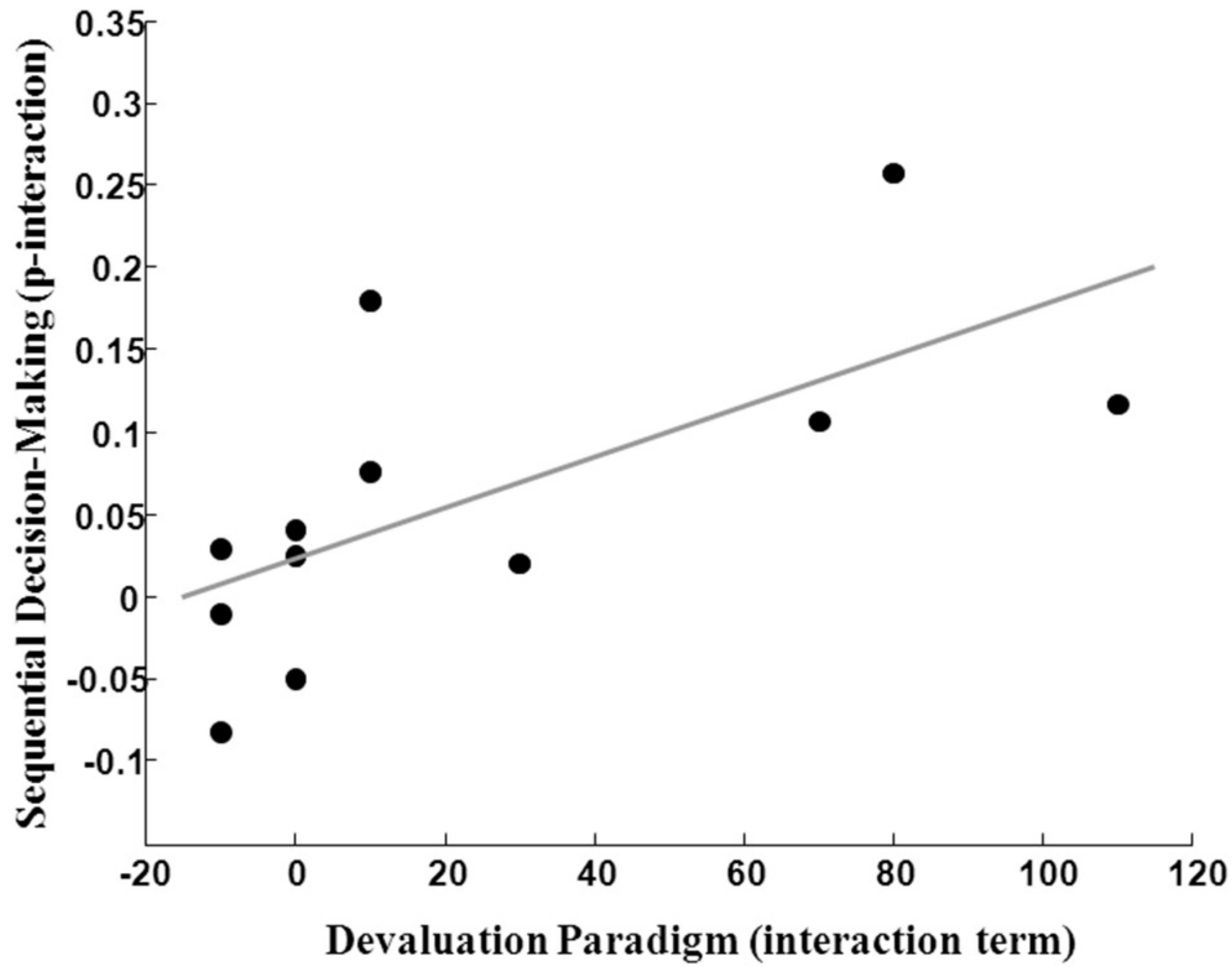






Daw et al., 2011 Neuron

Devaluation and two-step task



Friedel et al., 2014 Front Neurosci

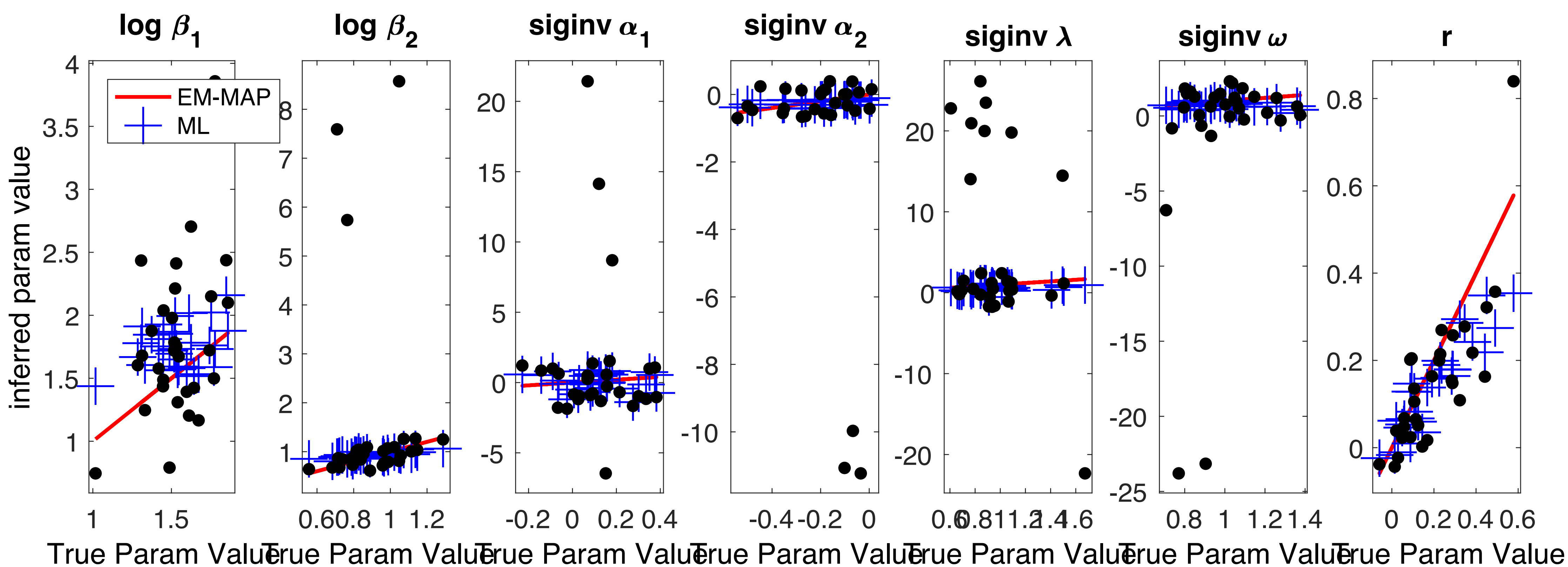
Example code

- www.cmod4mh.org/emfit.zip

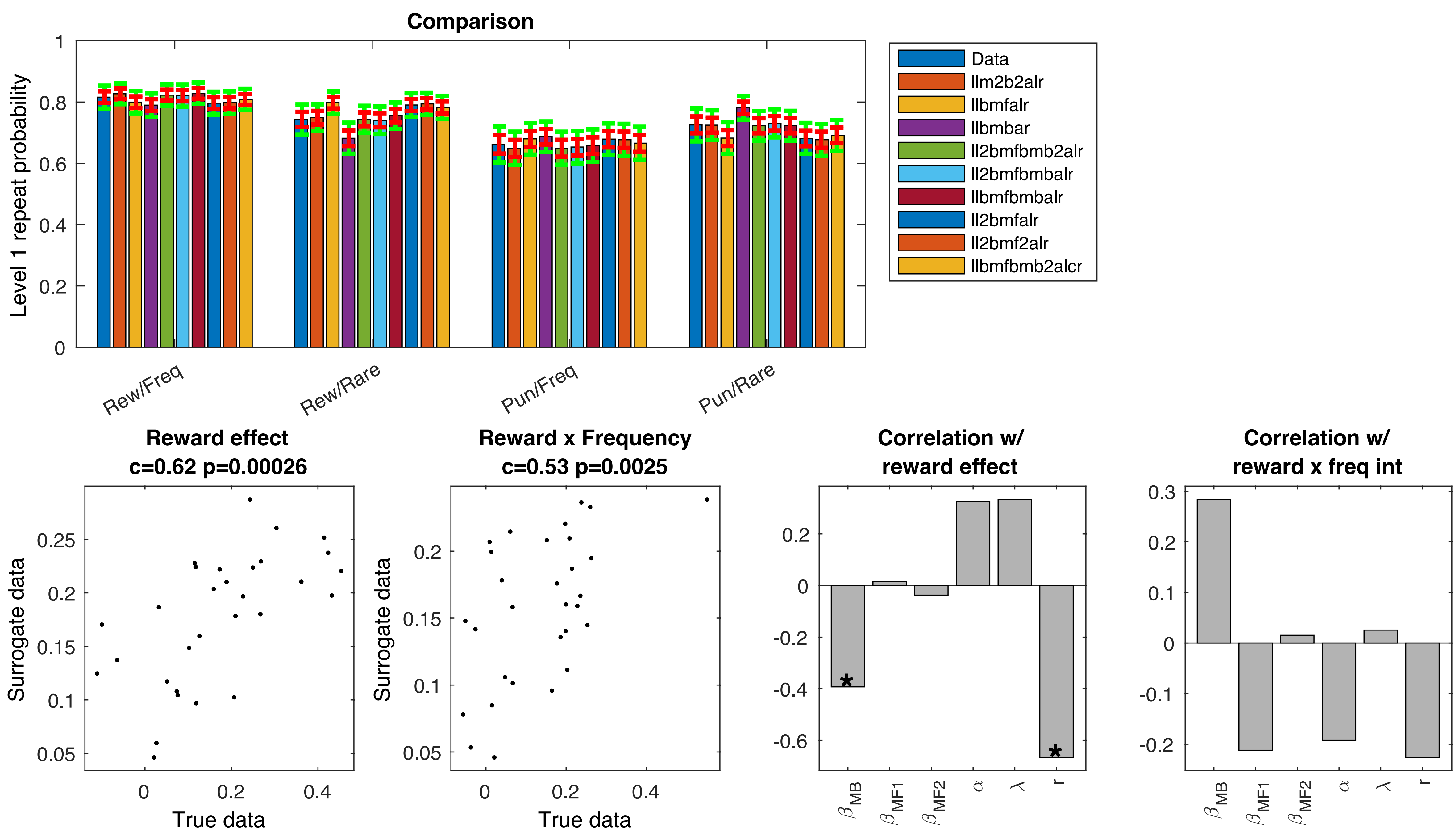
- batchRunEMfit('mTwostep')
  - will generate example data
  - fit all models in modelList.m
  - perform model comparison
  - generate surrogate data
  - generate plots for basic sanity checks

- basic model is llm2b2alr.m

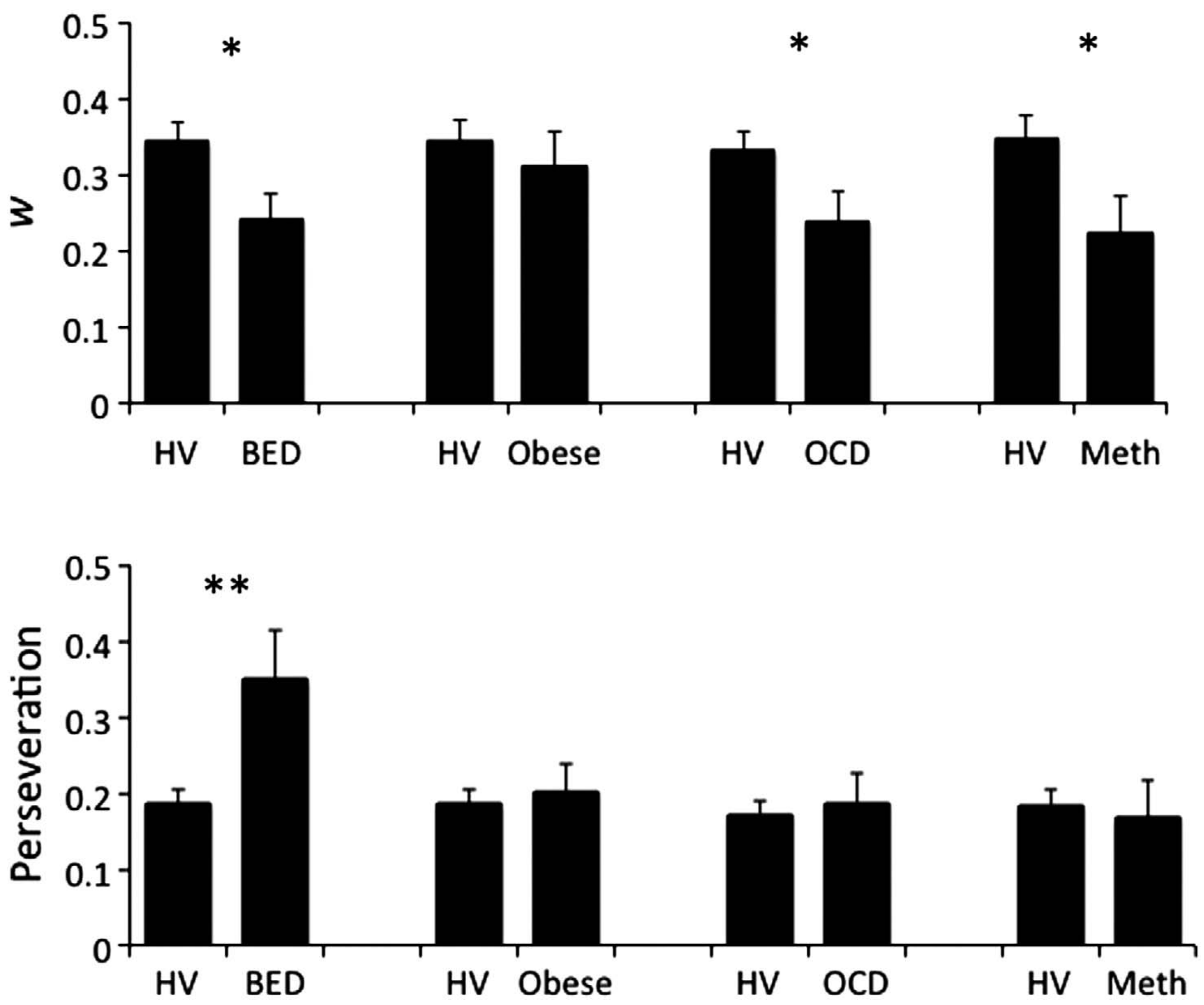
Hierarchical is definitely better



Twostep statistics



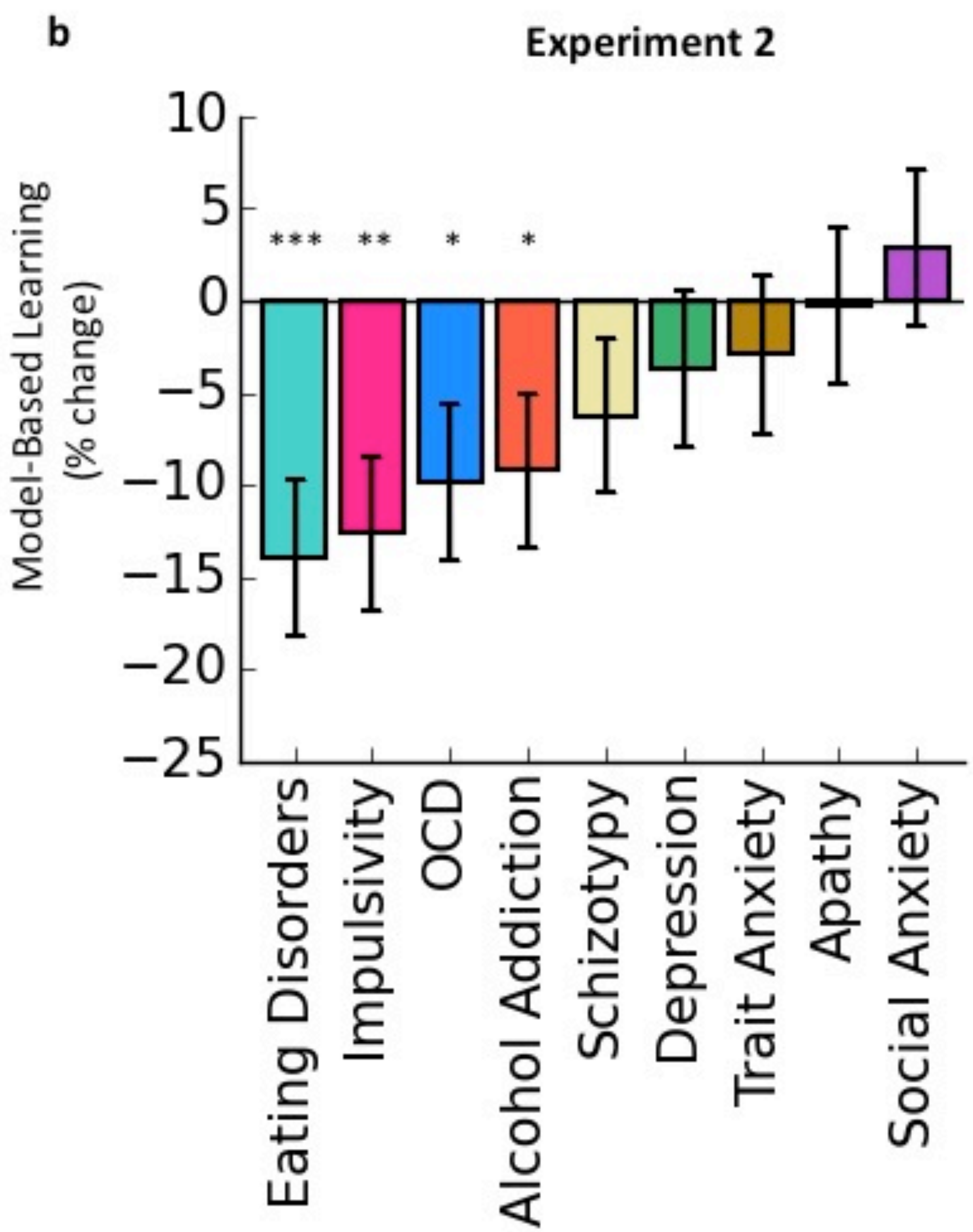
“Compulsive” disorders



Alcohol: no effect

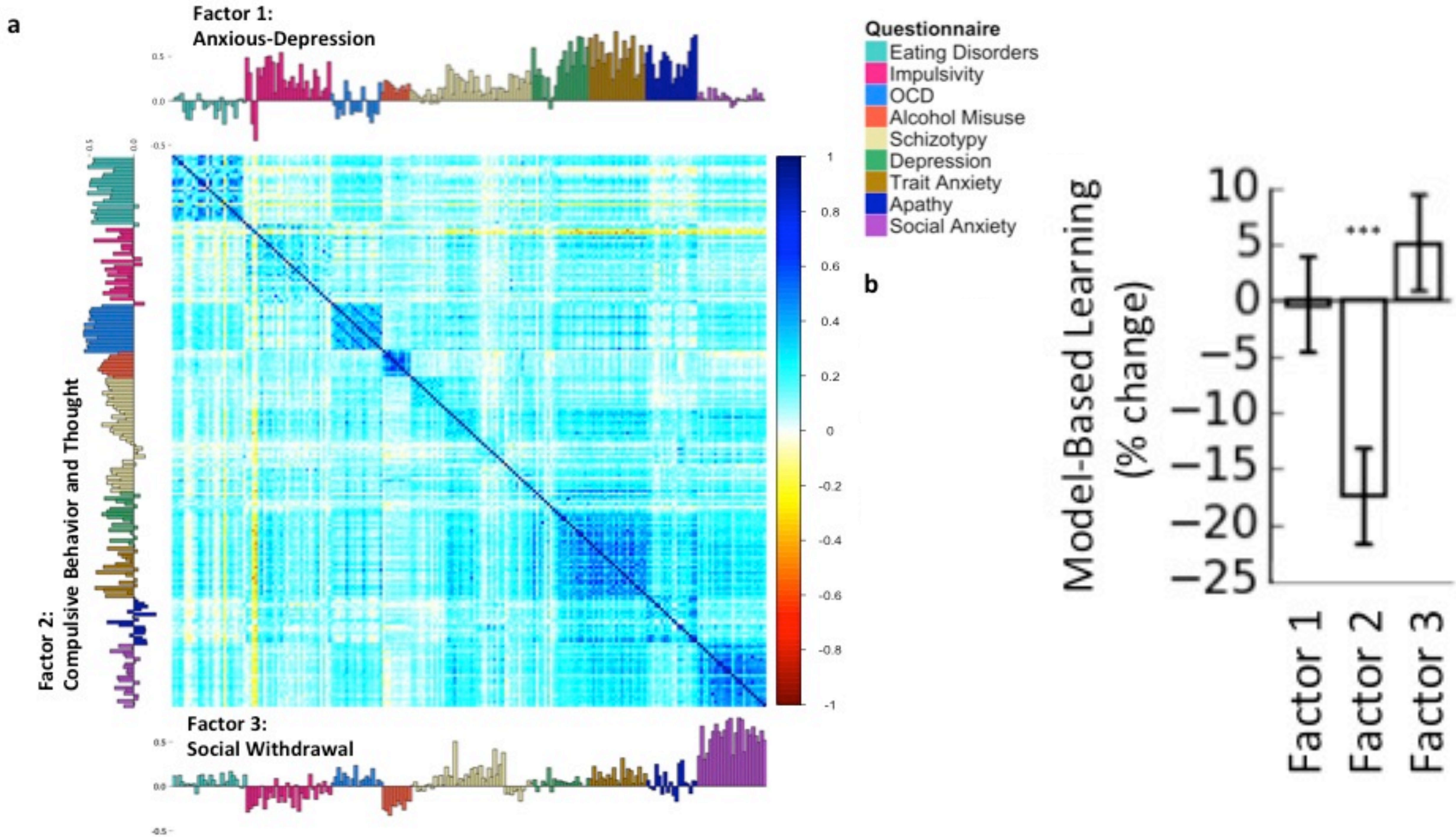
Voon et al., 2015 Mol. Psychiatry

Validation in large online sample

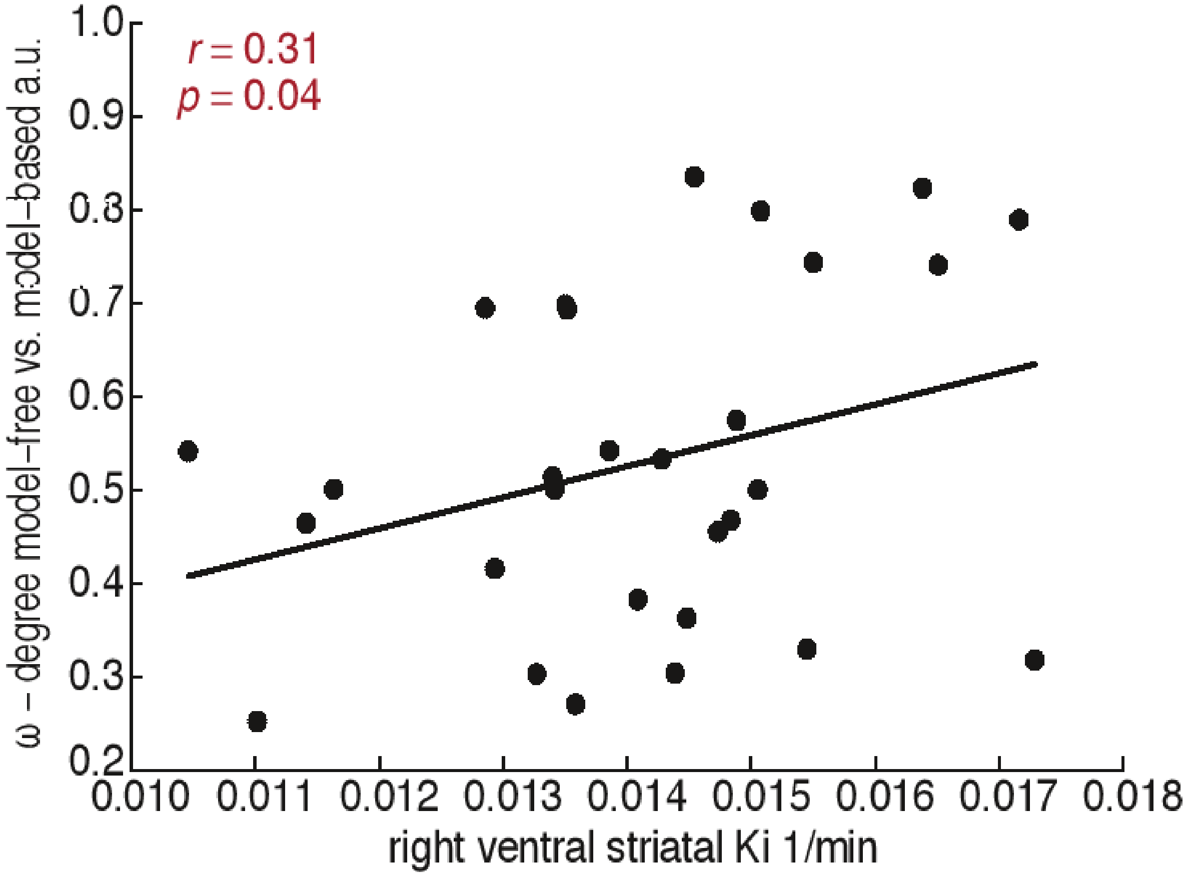


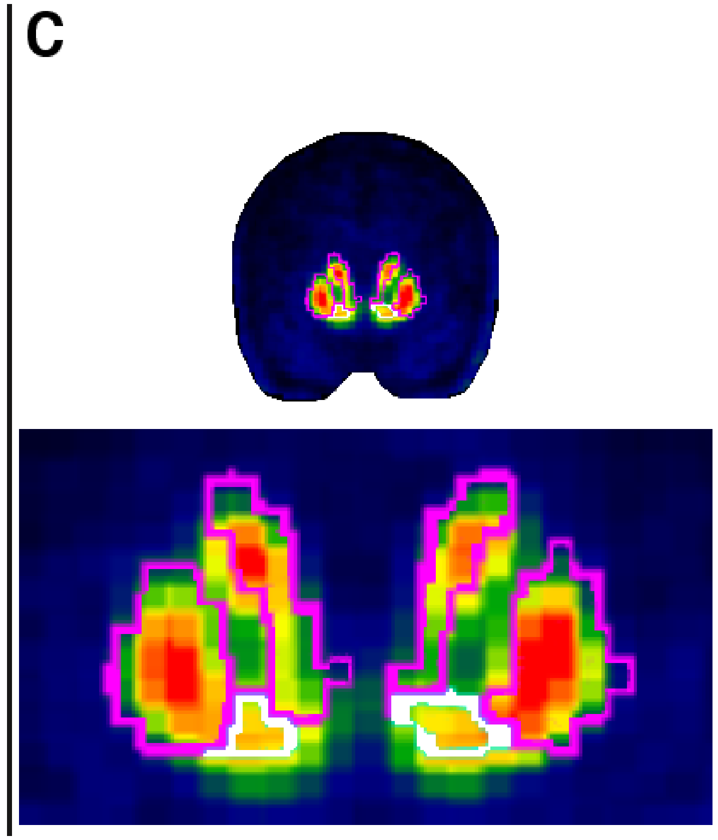
Gillan et al., 2016 eLife

Across questionnaires



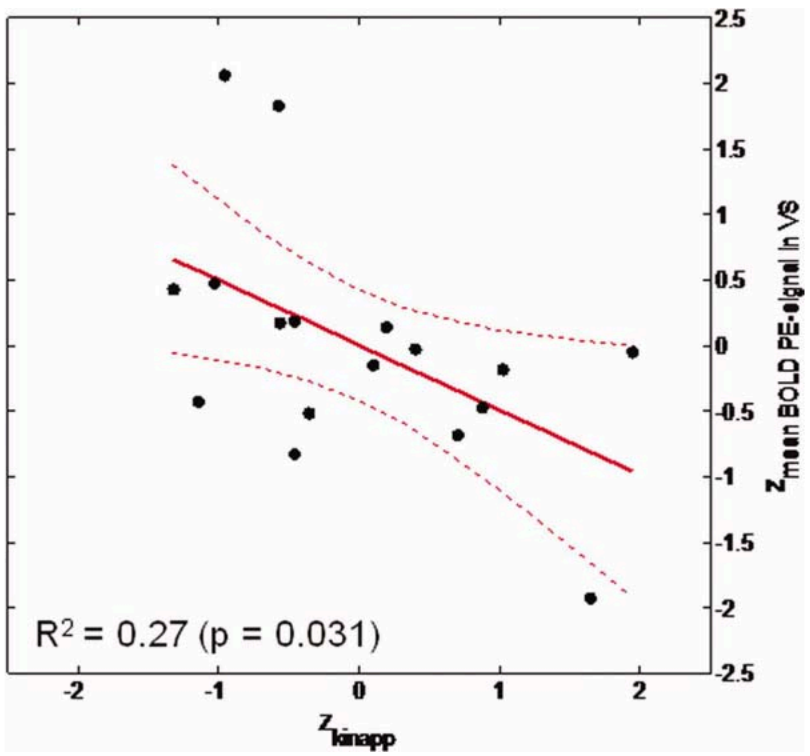
Ventral Striatal F-DOPA promotes MB choices

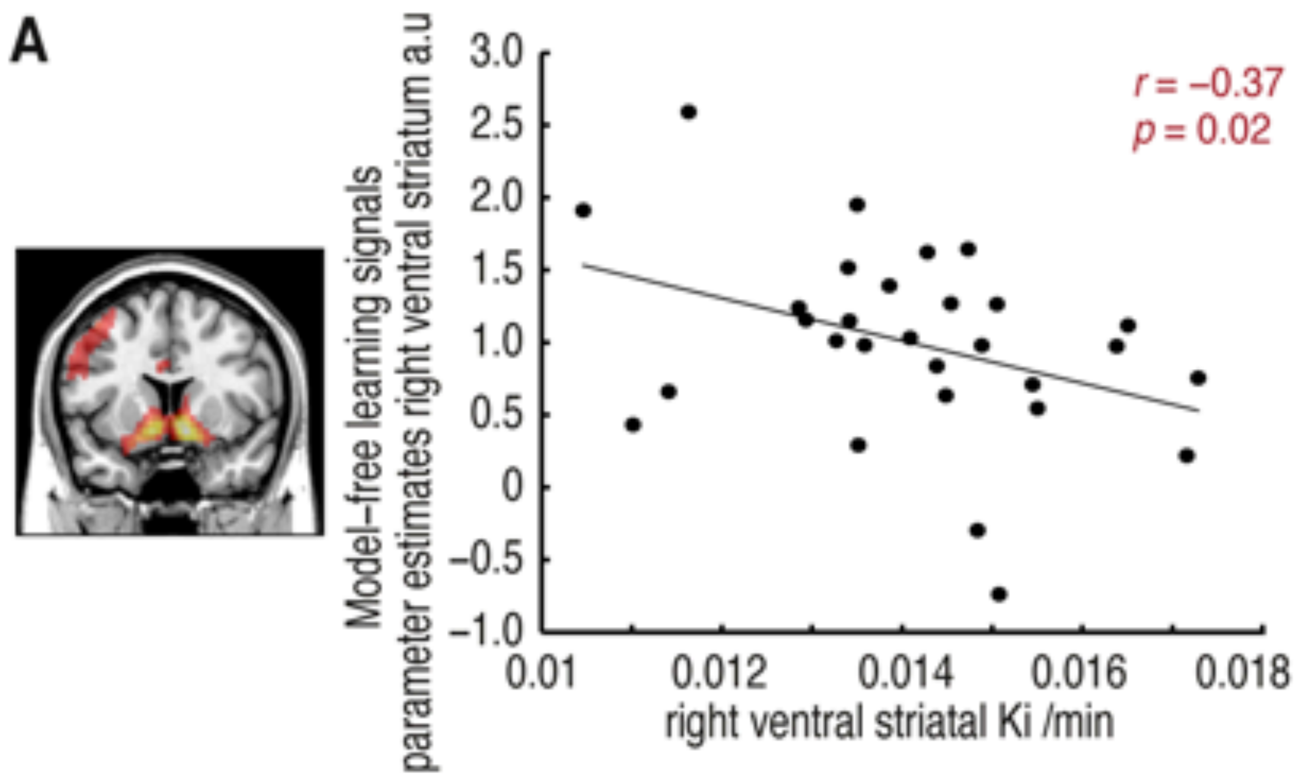




Deserno et al., 2015 PNAS

FDOPA and RPE betas: -ve correlation





Deserno et al., 2015 PNAS

No shift in at-risk drinking

Descriptive statistics of sample						
Age	188	18.07	18.24	18.33	18.50	18.93
Years in school	187	4	11	12	12	15
Measures of goal-directed/habitual control						
ω^a	188	0.00	0.20	0.59	0.80	1.00
MF_{score}	188	−0.42	−0.04	0.08	0.21	0.85
MB_{score}	188	−0.34	0.06	0.24	0.49	1.21
Measures of alcohol consumption						
CIDI measures						
$Drink_{score}$	188	−8.21	−3.54	−0.35	1.61	17.52
Age of first drink[a]	188	9	14	14	15	18
Age of first time drunk[a]	180	10	15	16	17	18
Estimated alcohol consumption in past year (g/day) [a]	188	0.00	3.21	6.43	15.43	112.50
Alcohol consumption in past year (g/drinking occasion)[a]	188	18	45	54	90	342
Age of first binge-drinking episode[a]	131	14	16	16	17	18
Number of binge-drinking episodes lifetime[a]	131	1	4	10	20	150
Alcohol consumption per binge-drinking episode (g)[a]	139	63	90	117	135	450
Questionnaire measures						
ADS sum score[a]	181	0	2	4	7	30
OCDS-G sum Score[a]	183	0	1	3	5	18
Blood markers						
AST (μKat/l)[a]	183	0.17	0.35	0.40	0.48	2.51
ALT (μKat/l)[a]	182	0.11	0.27	0.35	0.45	1.59
γ-GT (μKat/l)[a]	183	0.13	0.23	0.27	0.33	0.89
PEth[a]	158	10	10	60	60	1180
Measures of impulsivity						
BIS-15 sum score	185	18	27	30	34	45
SURPS Impulsivity[a]	186	5	9	10	11	17

Nebe et al., 2017 Addiction

No shift in at-risk drinking

	ω	MF_{score}	MB_{score}	RPE_{MF}		$RPE_{\Delta MB}$		BIS-15	SURPS
				vS	vmPFC	vS	vmPFC	SUM	IMP
$Drink_{score}$	−.067	.000	−.004	−.019	.014	−.058	−.023	.256***	.246***
Age of first drink	−.011	.042	.057	−.184*	−.143	−.063	−.008	−.125	−.263***
Age of first time drunk	.066	.052	.048	−.044	−.011	−.040	.059	−.182*	−.155*
Estimated alcohol consumption in past year (g/day)	−.070	−.071	.038	−.101	.021	−.105	−.048	.088	.116
Alcohol consumption in past year (g/drinking occasion)	−.026	−.081	.101	−.087	−.006	−.038	−.018	.133	.081
Age of first binge-drinking episode	.098	−.033	.019	.075	.040	.076	.047	−.156	−.126
Number of binge-drinking episodes lifetime	−.033	.038	.044	.001	.047	−.090	−.035	.232**	.179*
Alcohol consumption per binge-drinking episode (g)	−.064	.096	−.018	−.015	.048	.035	.059	.210**	.245***
ADS sum score	−.061	.007	.029	.006	.115	−.040	−.099	.211**	.298***
OCDS-G sum score	.000	−.011	.031	.088	.182*	.021	.073	.223**	.228**
AST	.015	.015	−.047	−.025	.059	−.008	−.042	.039	.165*
ALT	−.072	.061	−.080	.003	.029	.010	.030	−.018	.159*
γ-GT	−.066	−.011	−.160*	−.074	−.089	−.075	−.005	−.205**	−.092
PEth	.041	−.048	.052	−.091	−.016	−.019	.005	−.150	.005

Nebe et al., 2017 Addiction

No shift in clinical AUD sample

Variable	HCs (n = 96)		Abstainers (n = 37)		Relapsers (n = 53)	
Gender	Female: 16; male: 80		Female: 7; male: 30		Female: 6; male: 47	
Site	Berlin: 56; Dresden: 40		Berlin: 24; Dresden: 13		Berlin: 28; Dresden: 25	
	Mean (SD)	NA	Mean (SD)	NA	Mean (SD)	NA
Demographic Variables						
Education, years	11.9 (1.5)	2	10.8 (1.5)	2	10.6 (3.5)	2
Age, years	43.6 (10.9)	0	45.7 (12.0)	0	45.2 (9.9)	0
Income, €	1201 (686)	22	1150 (741)	0	1013 (621)	5
Smokers, %	65	0	75	0	75	0
Duration of abstinence at fMRI, days	66.5 (280.9)	0	21.4 (11.6)	0	22.3 (12.4)	0
Clinical Characteristics[e]						
No. of detoxifications	—	—	2.13 (2.06)	0	4.75 (5.03)	0
Positive alcohol expectancies	25.7 (4.6)	0	31.7 (4.4)	0	32.8 (3.9)	0
Depressive symptoms	1.9 (2.3)	1	3.9 (3.9)	0	4.2 (3.7)	0
Craving	2.7 (2.8)	1	10.3 (8.2)	1	12.9 (8.4)	3
Drinking motives	29 (7)	3	44 (11)	1	48 (14)	1
Time to relapse, days	—	—	—	—	87.1 (80.0)	4
Neuropsychological Testing						
Verbal IQ	28.3 (4.6)	3	28.6 (4.3)	0	28.2 (4.8)	1
Fluid IQ	10.7 (3.12)	0	9.9 (2.6)	1	9.1 (2.9)	0
Working memory	7.5 (2.04)	0	6.62 (1.91)	0	6.54 (1.89)	0
Blood Markers						
AST (μKat/L)	0.45 (0.17)	28	0.69 (0.53)	5	0.71 (0.52)	11
ALT (μKat/L)	0.43 (0.19)	28	0.88 (0.73)	5	1.08 (2.16)	11
γ-GT (μKat/L)	0.54 (0.67)	28	3.33 (6.71)	5	1.51 (1.38)	11
PEth (ng/mL)	203.24 (359.68)	16	447.85 (349.13)	16	806.15 (736.83)	31

Group

Sebold et al., 2017 Biol. Psychiatry

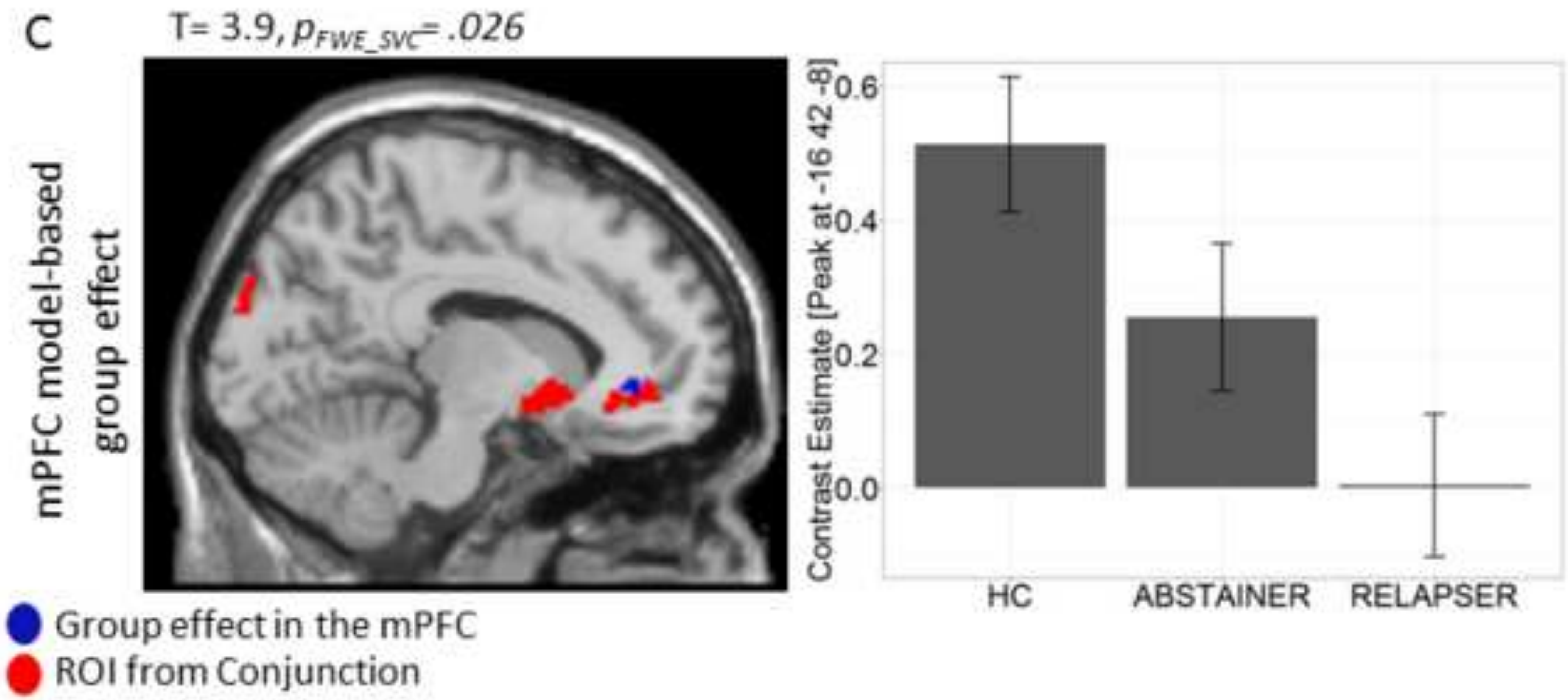
Neural impairments?

Sebold et al., 2017 Biol. Psychiatry

Neural impairments?

Sebold et al., 2017 Biol. Psychiatry

Neural impairments?



Sebold et al., 2017 Biol. Psychiatry

Alcohol expectancies

Motivational interviewing

Sebold et al., 2017 Biol. Psychiatry

Alcohol expectancies

Motivational interviewing

1. Drinking makes me feel warm and flushed.
2. Alcohol lowers muscle tension in my body.
3. A few drinks make me feel less shy.
4. Alcohol helps me to fall asleep more easily.
5. I feel powerful when I drink, as if I can really make other people do as I want.
6. I'm more clumsy after a few drinks.
7. I am more romantic when I drink.
8. Drinking makes the future seem brighter to me.
9. If I have had a couple of drinks, it is easier for me to tell someone off.
10. I can't act as quickly when I've been drinking.
11. Alcohol can act as an anesthetic for me, that is, it can stop pain.
12. I often feel sexier after I've had a few drinks.
13. Drinking makes me feel good.
14. Alcohol makes me careless about my actions.
15. Some alcohol has a pleasant, cleansing, tingly taste to me.

Sebold et al., 2017 Biol. Psychiatry

Alcohol expectancies

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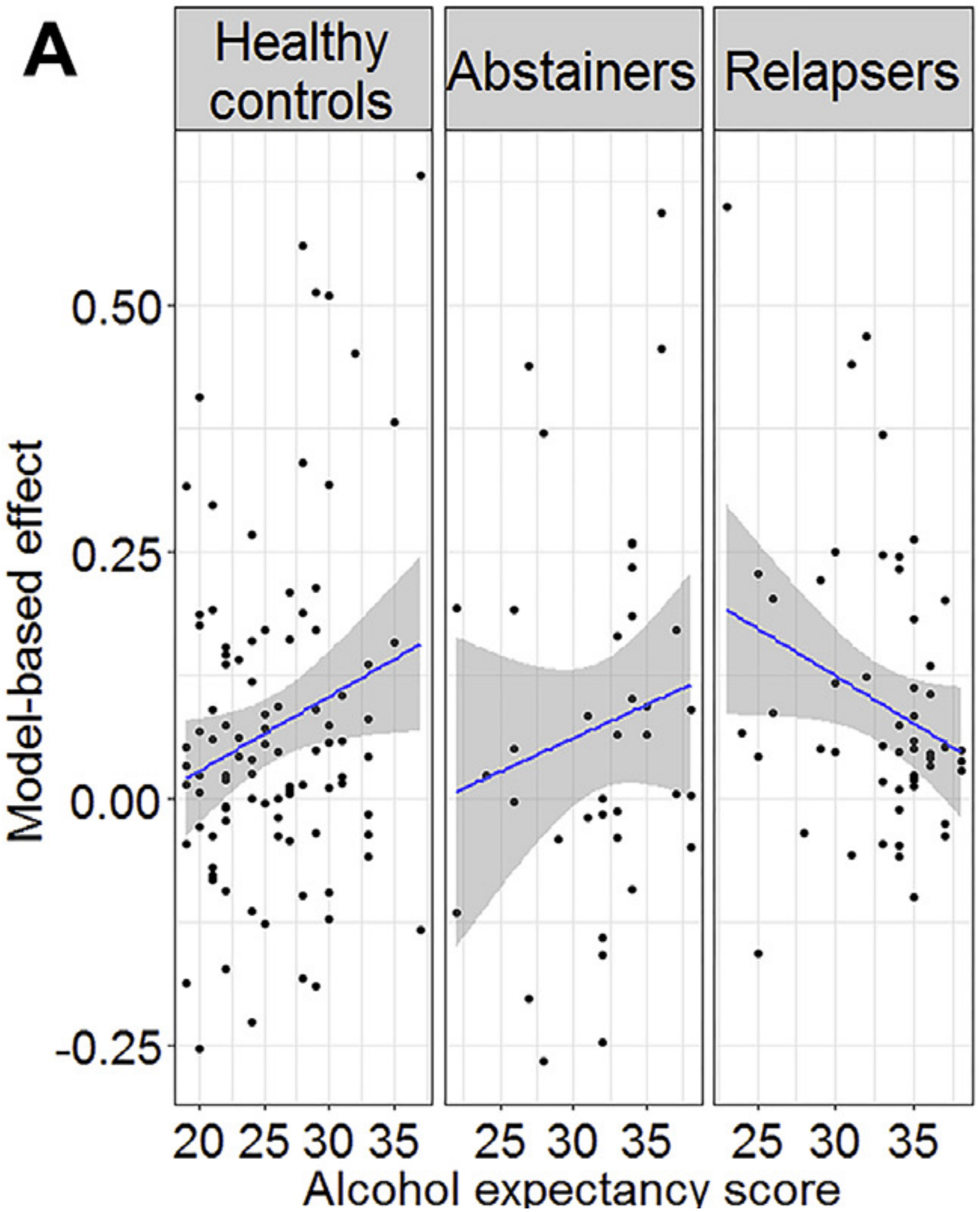
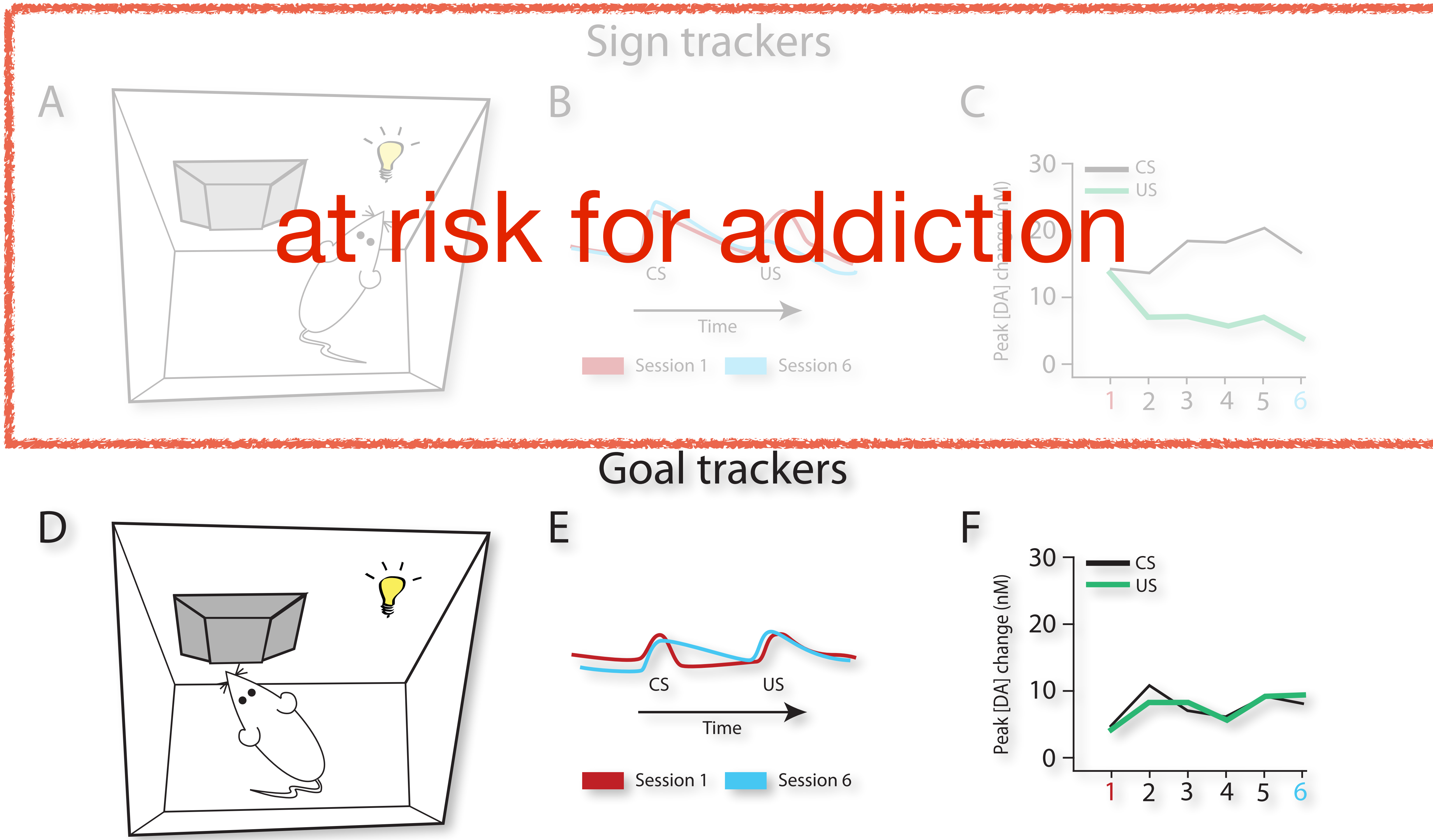


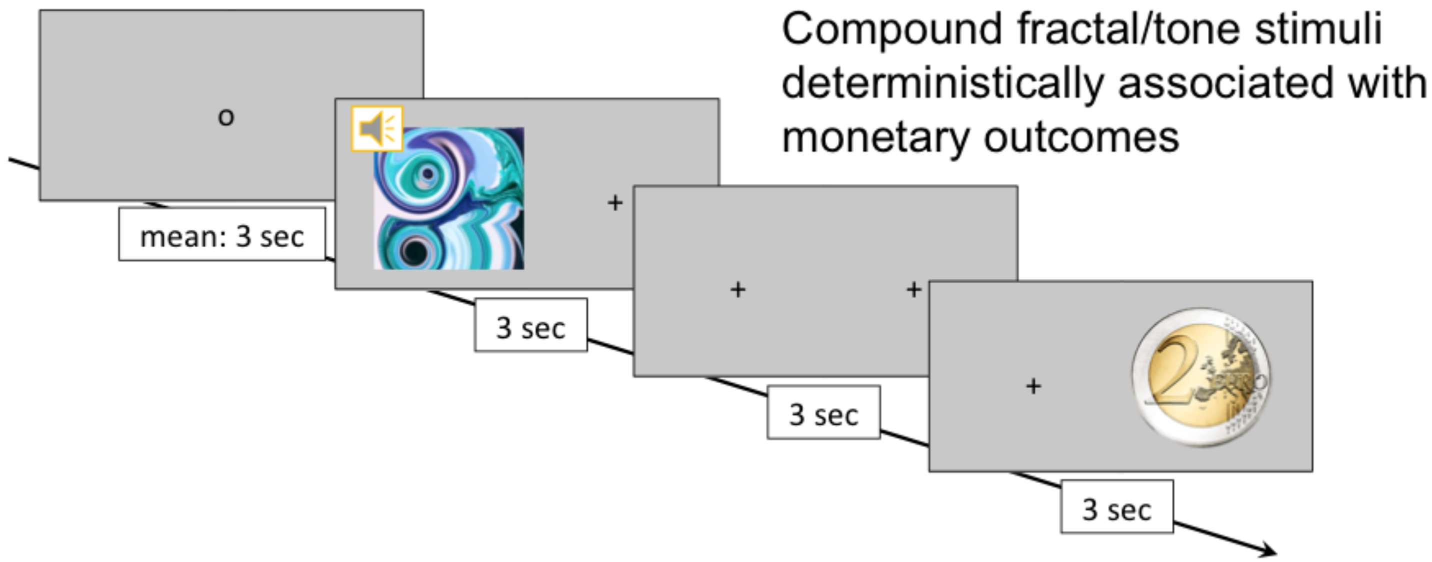
Sebold et al., 2017 Biol. Psychiatry

Pavlovian state values: sign tracking



Flagel et al., 2011 Nature

Goal-tracking in humans?



ST: learn expected value V
GT: learn mappings T from CS to US identity

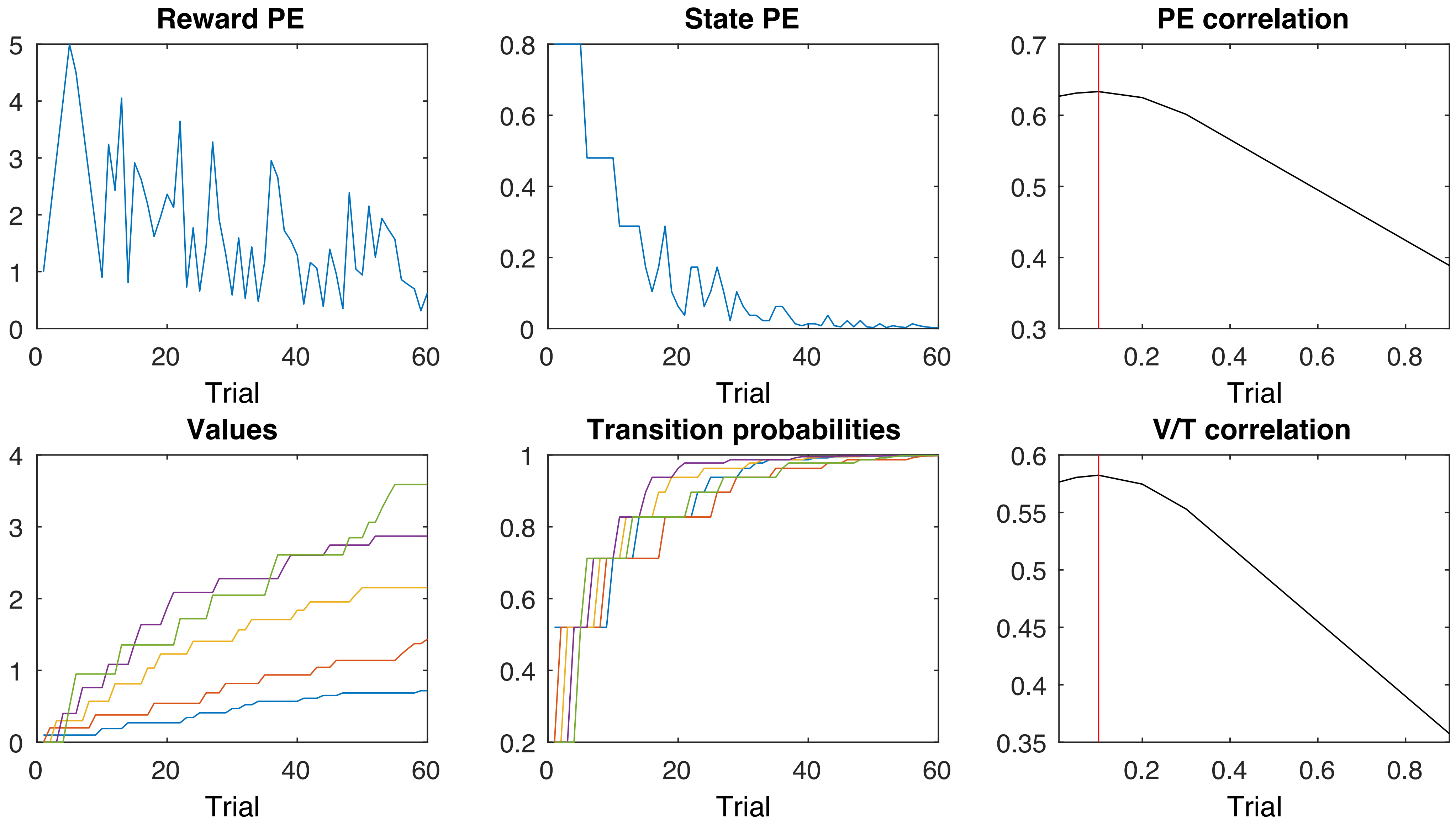
$$\mathcal{V}(s) = \sum_a \pi(a;s) \sum_{s'} \mathcal{T}(s'|s,a)[\mathcal{R}(s',a,s) + \mathcal{V}(s')]$$

Schad et al., in prep

Pavlovian learning in ST vs GT

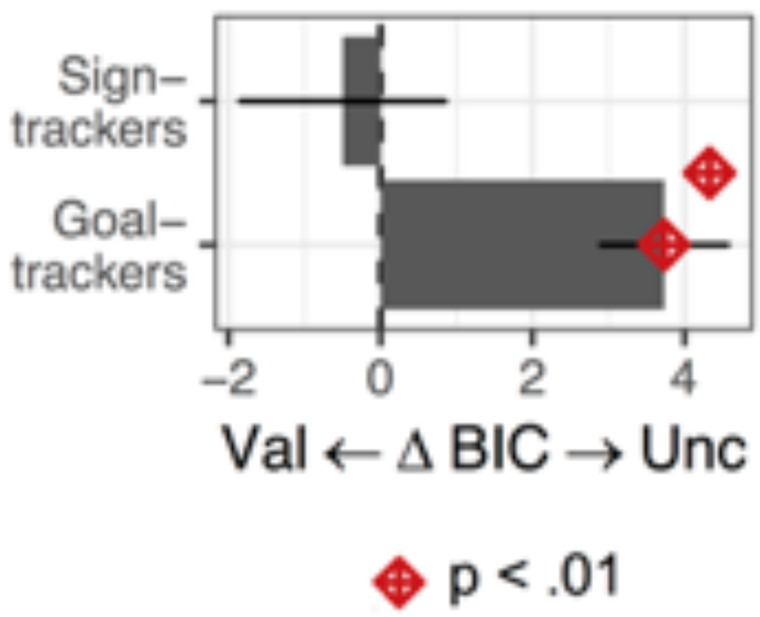
$$\mathcal{V}_t(s) = \mathcal{V}_{t-1}(s) + \alpha^r\,\delta^r_t \qquad \mathcal{T}_t(cs,us) = \mathcal{T}_{t-1}(cs,us) + \alpha^s\,\delta^s_t$$

$$\delta^r_t = r_t - \mathcal{V}_{t-1}(s) \qquad \delta^s_t = 1 - \mathcal{T}_{t-1}(cs,us)$$

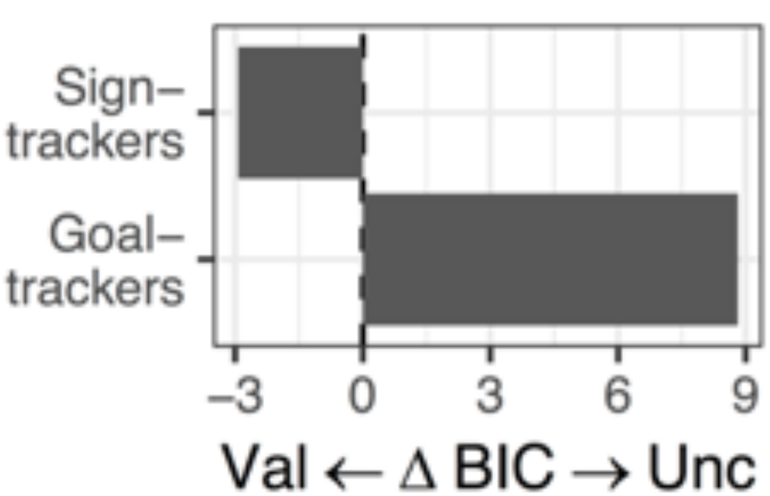


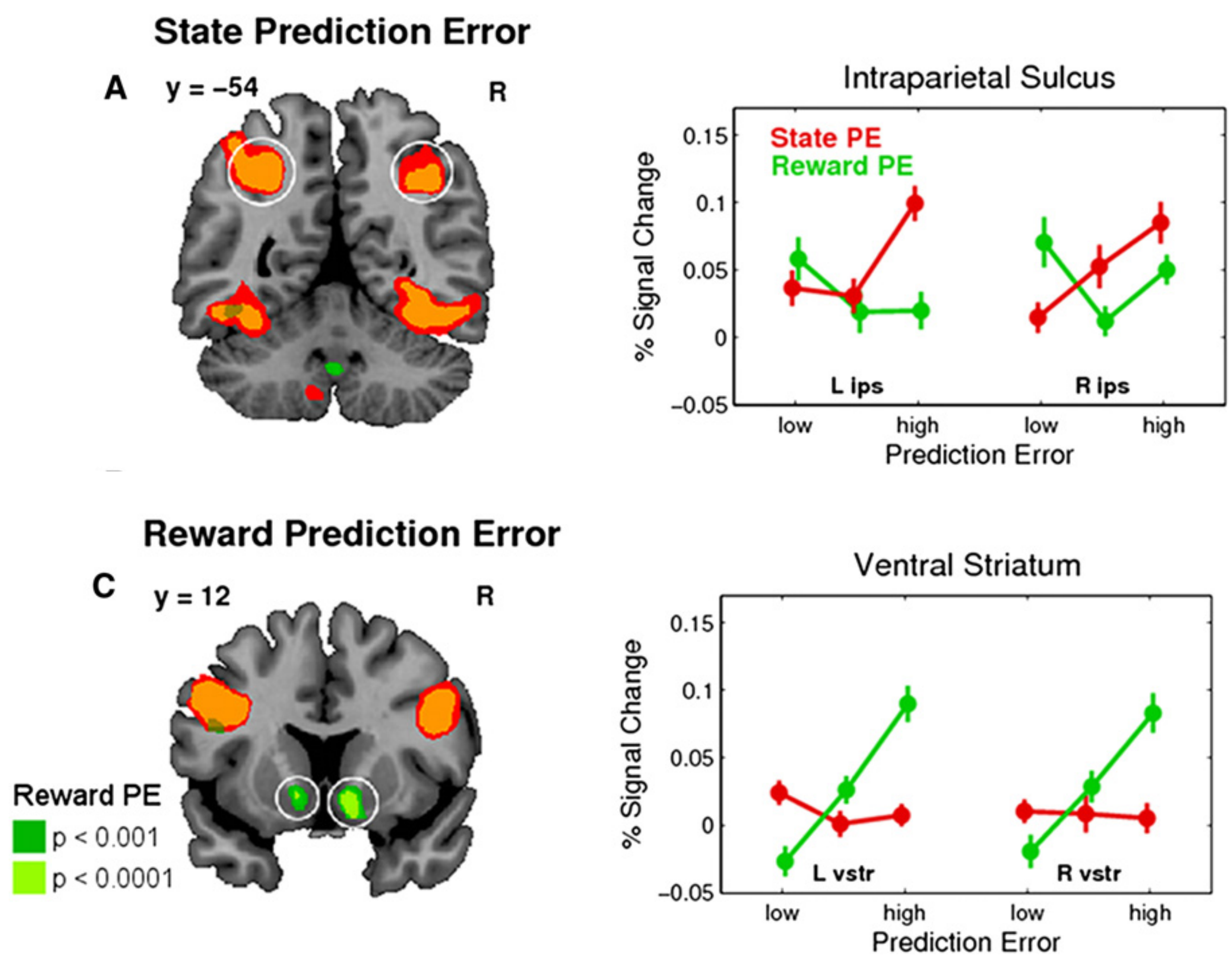
Goal-tracking signatures

Gaze



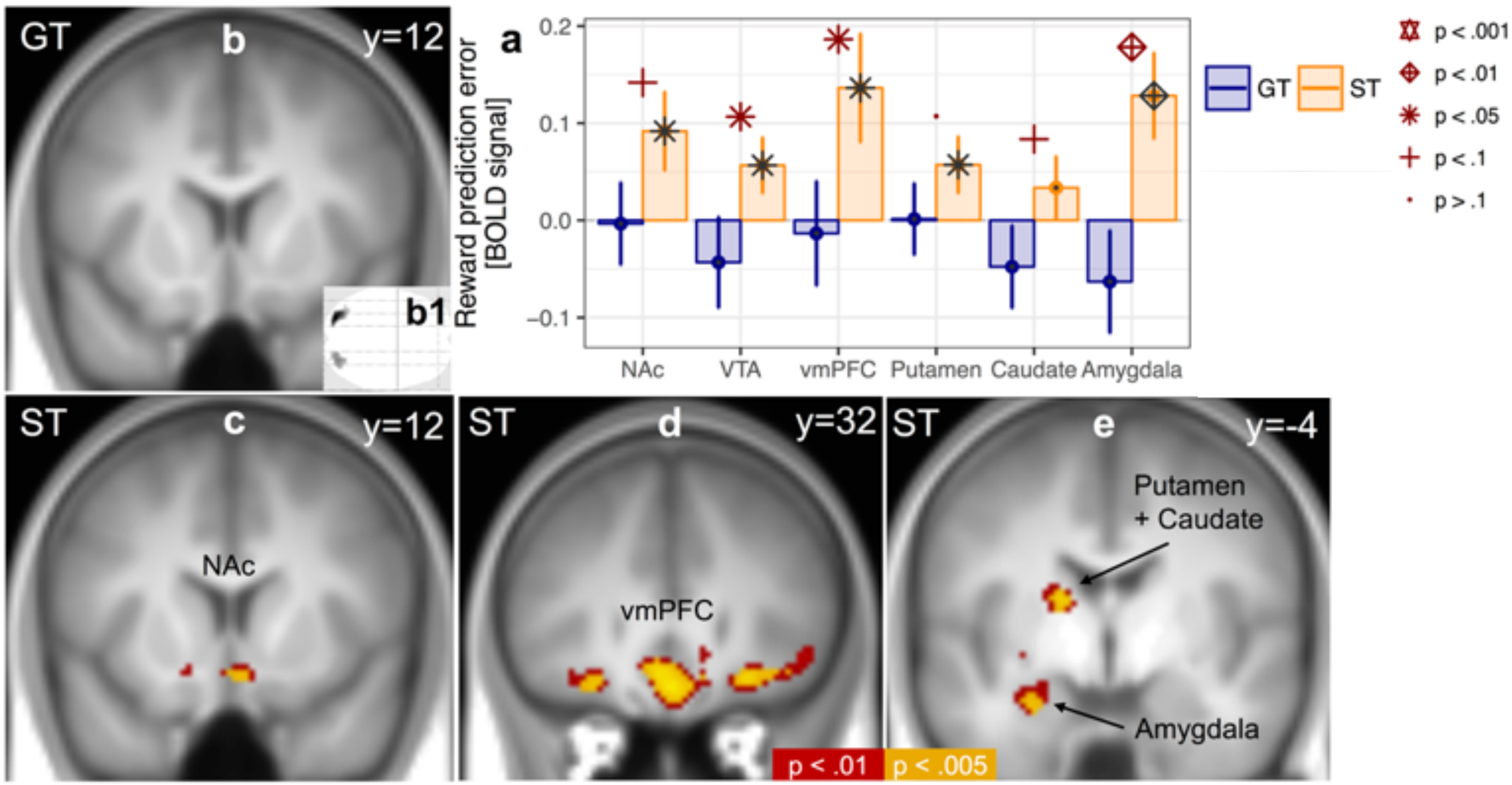
Pupil





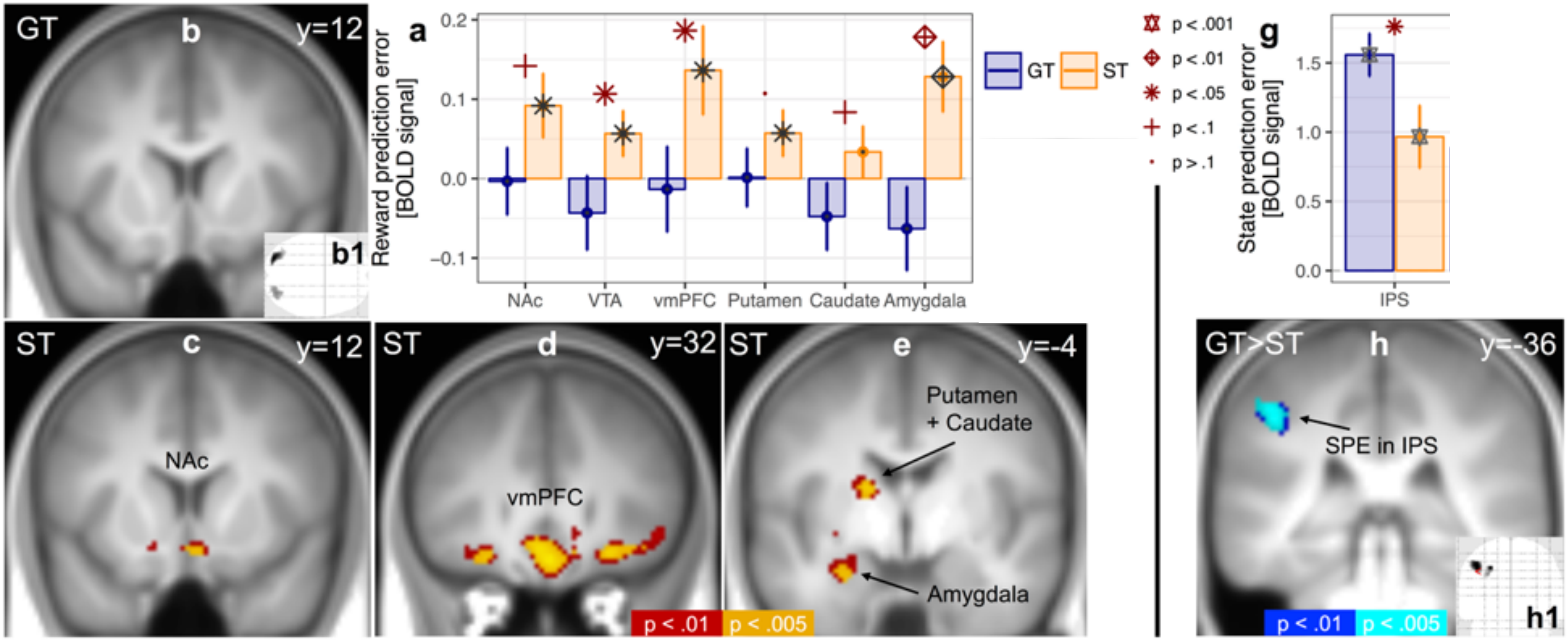
Schad et al., in prep, Gläscher et al. 2010 Neuron

Double dissociation between ST and GT



Schad et al., in prep

Double dissociation between ST and GT



Schad et al., in prep

Outline

Depression

Addiction

OCD

Anxiety

Schizophrenia

Parkinson's

Mood

Metareasoning

Pavlovian vs Instrumental paradigms

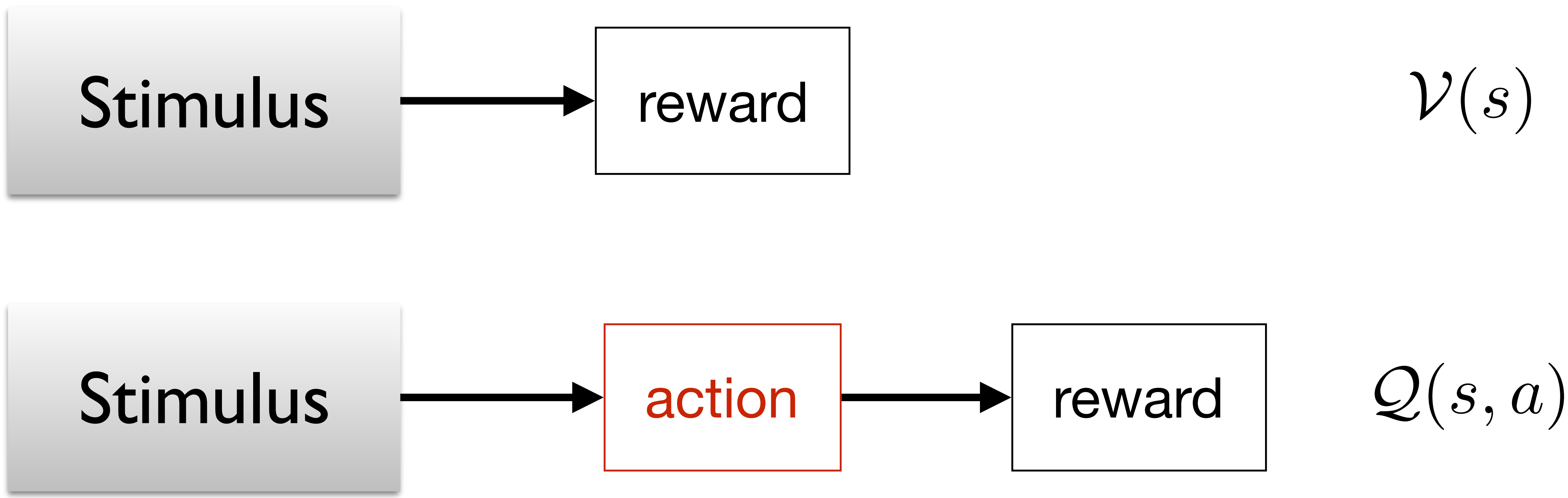
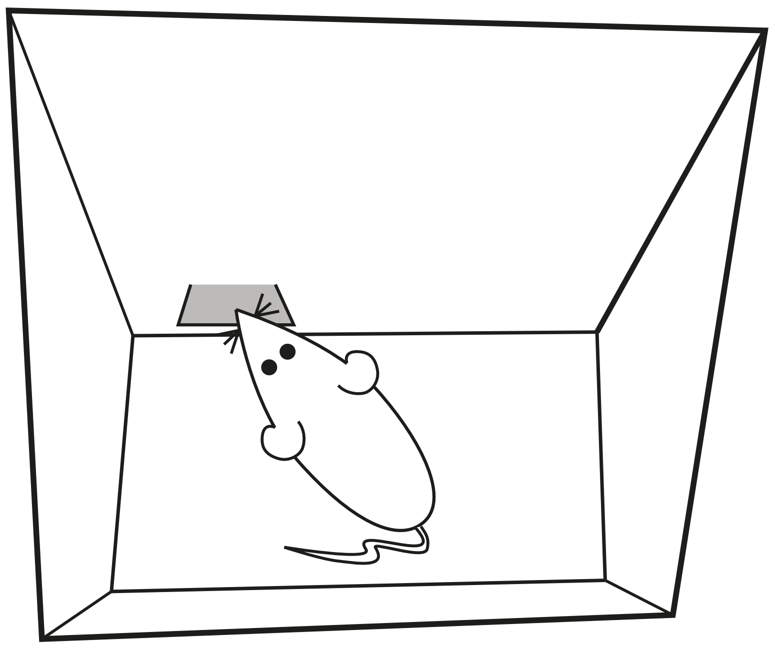


Table 1 Types of values

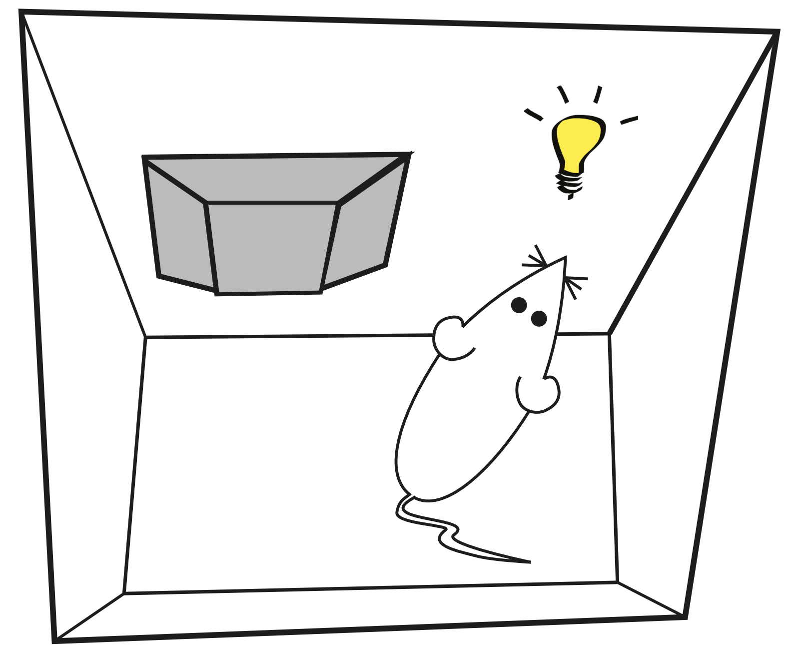
	Model-free	**Model-based**
Pavlovian (state) values	$\mathcal{V}^{\text{MF}}(s)$	$\mathcal{V}^{\text{MB}}(s)$
Instrumental (state-action) values	$\mathcal{Q}^{\text{MF}}(s,a)$	$\mathcal{Q}^{\text{MB}}(s,a)$

Huys et al., 2014 Prog Neurobiol

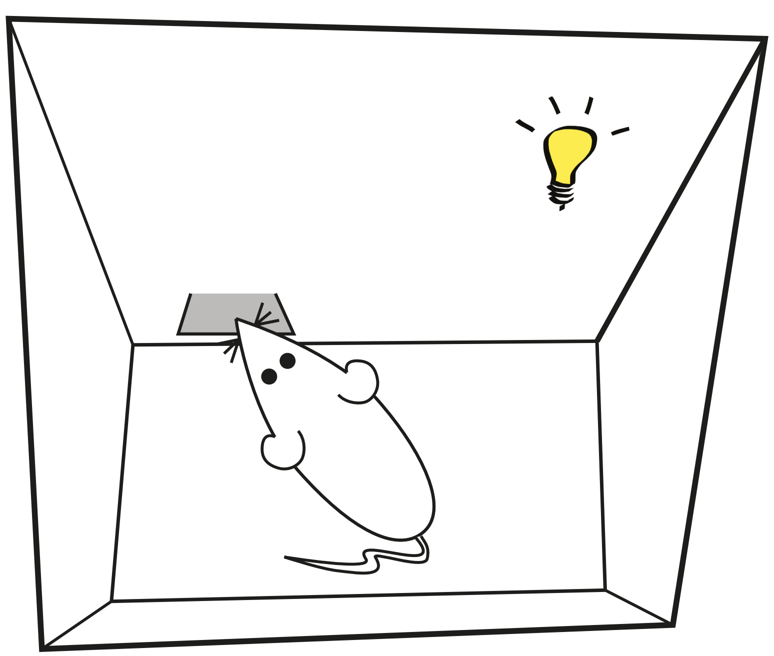
Pavlovian-Instrumental transfer



$$\mathcal{Q}(s,a)$$



$$\mathcal{V}(s)$$

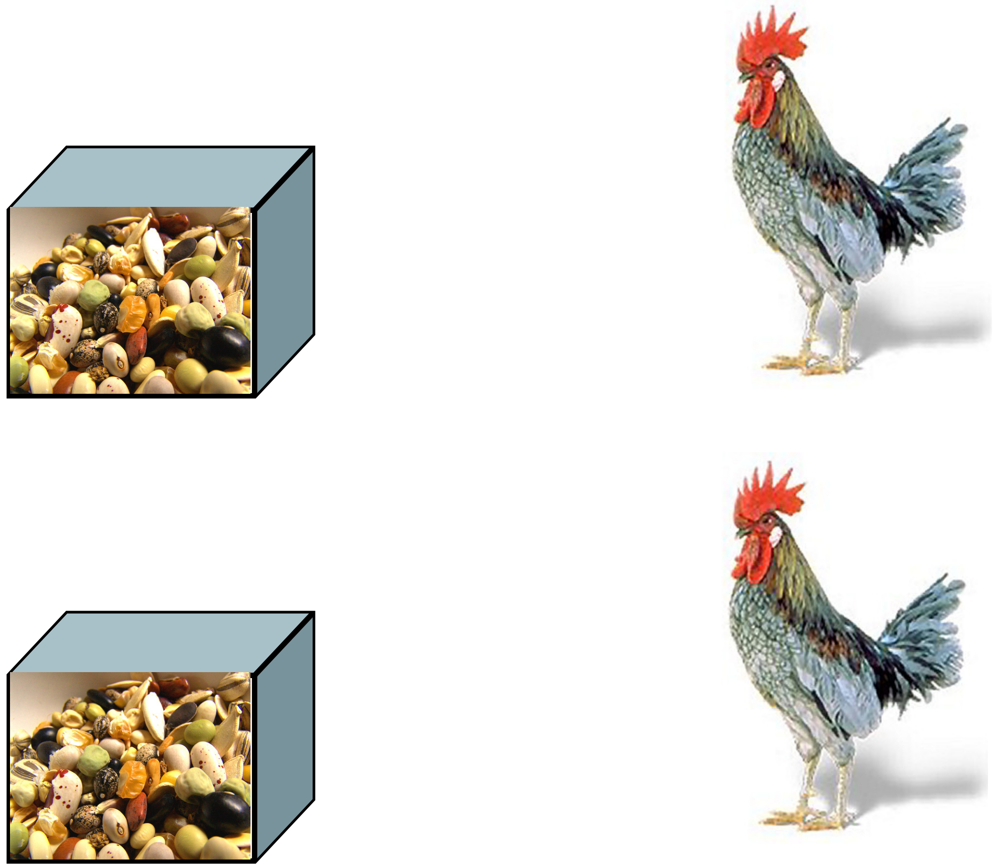


$$\begin{array}{ll} \mathcal{Q}(s,a)+\mathcal{V}(s) & \text{if natural} \\ \mathcal{Q}(s,a) & \text{else} \end{array}$$

“Pavlovian” unconditioned responses

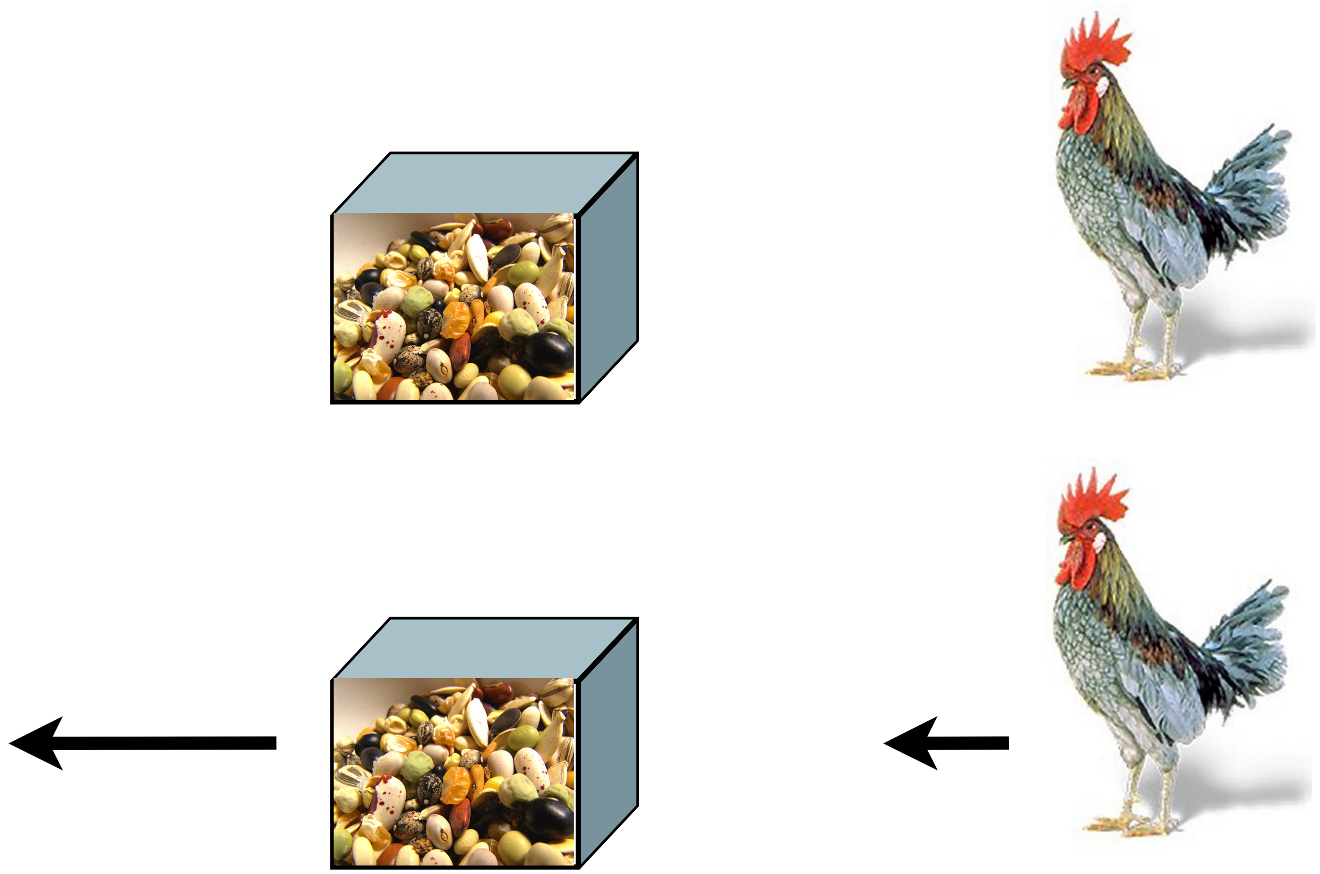
Hershberger 1986

“Pavlovian” unconditioned responses



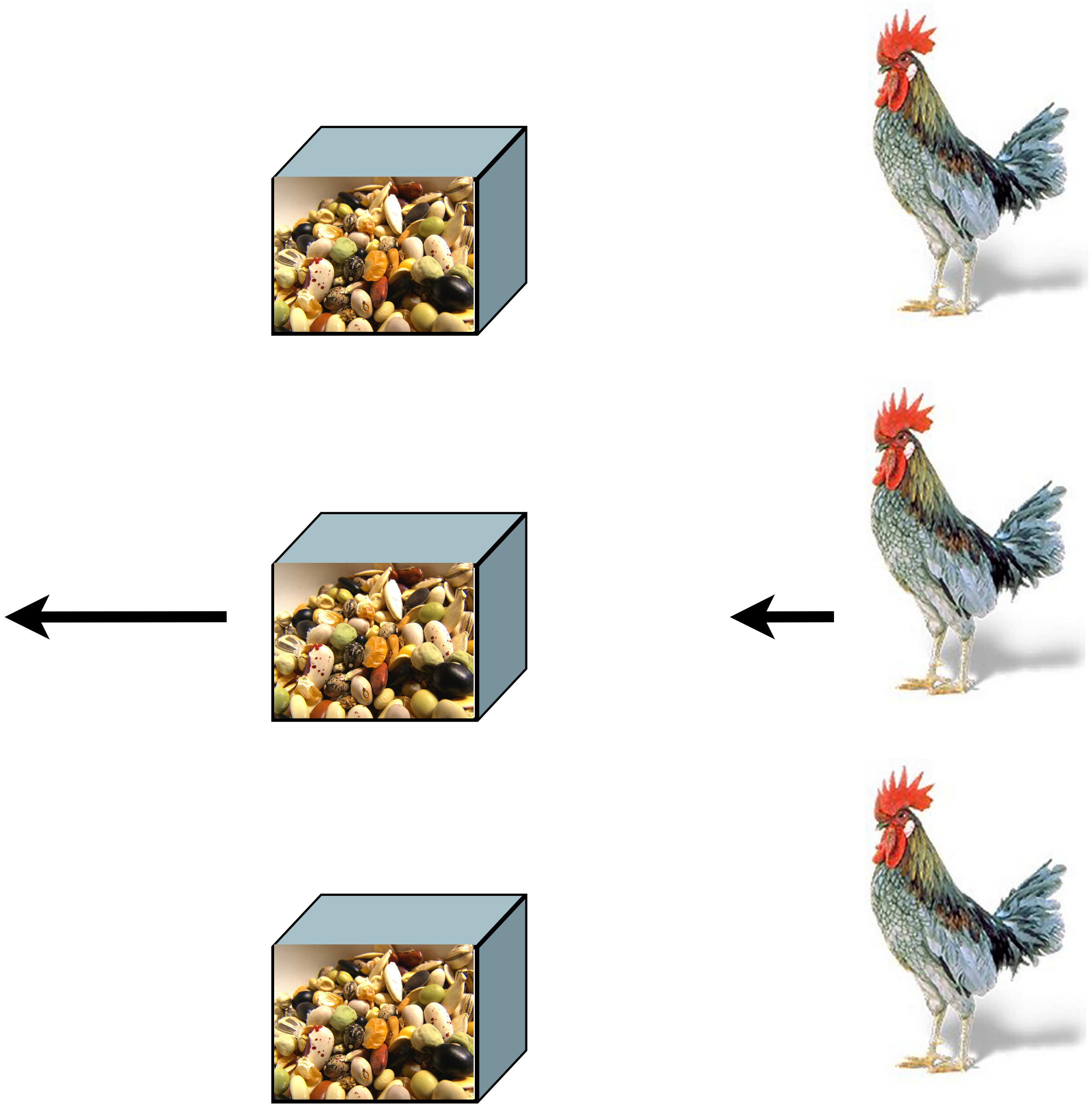
Hershberger 1986

"Pavlovian" unconditioned responses



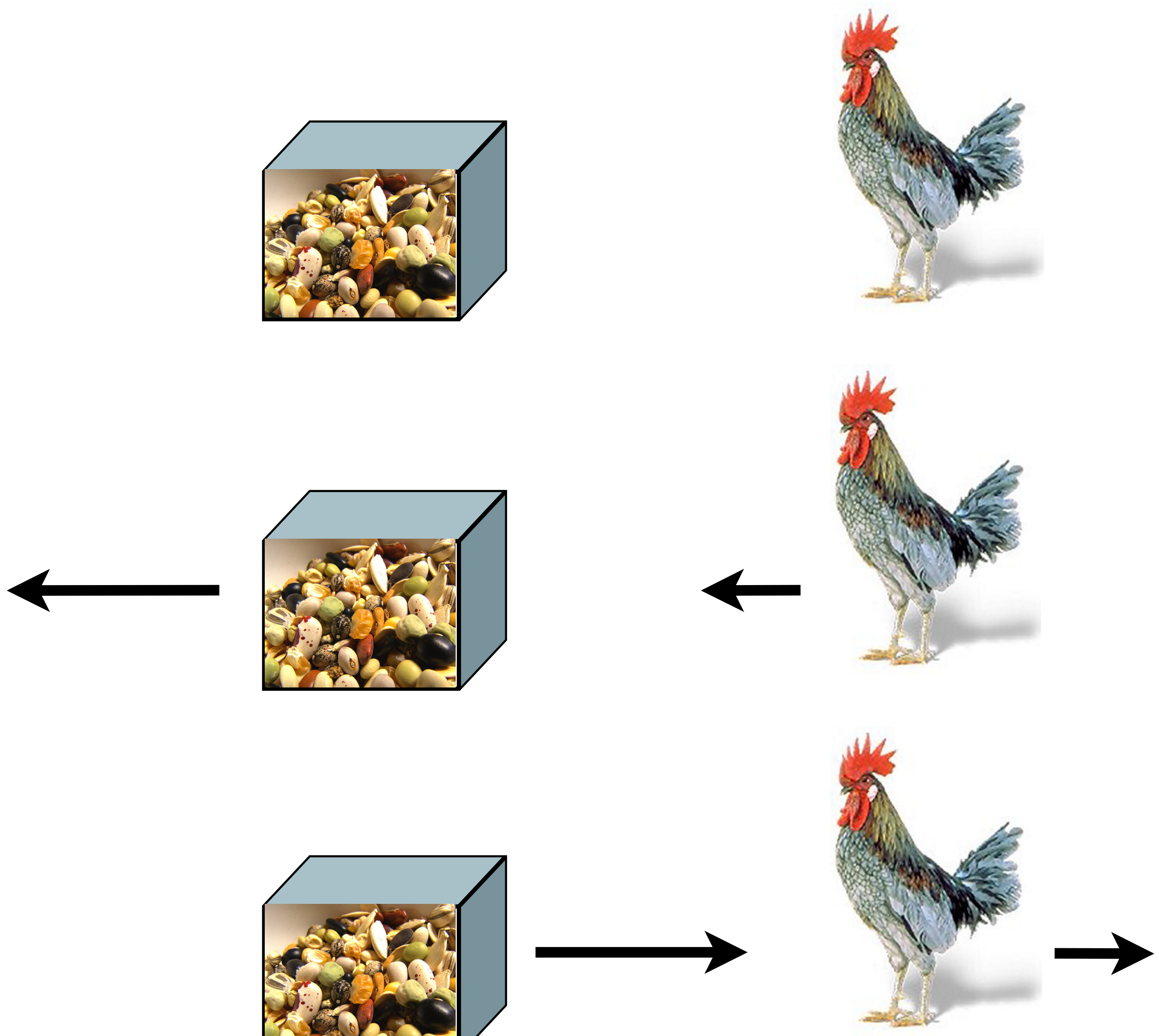
Hershberger 1986

"Pavlovian" unconditioned responses



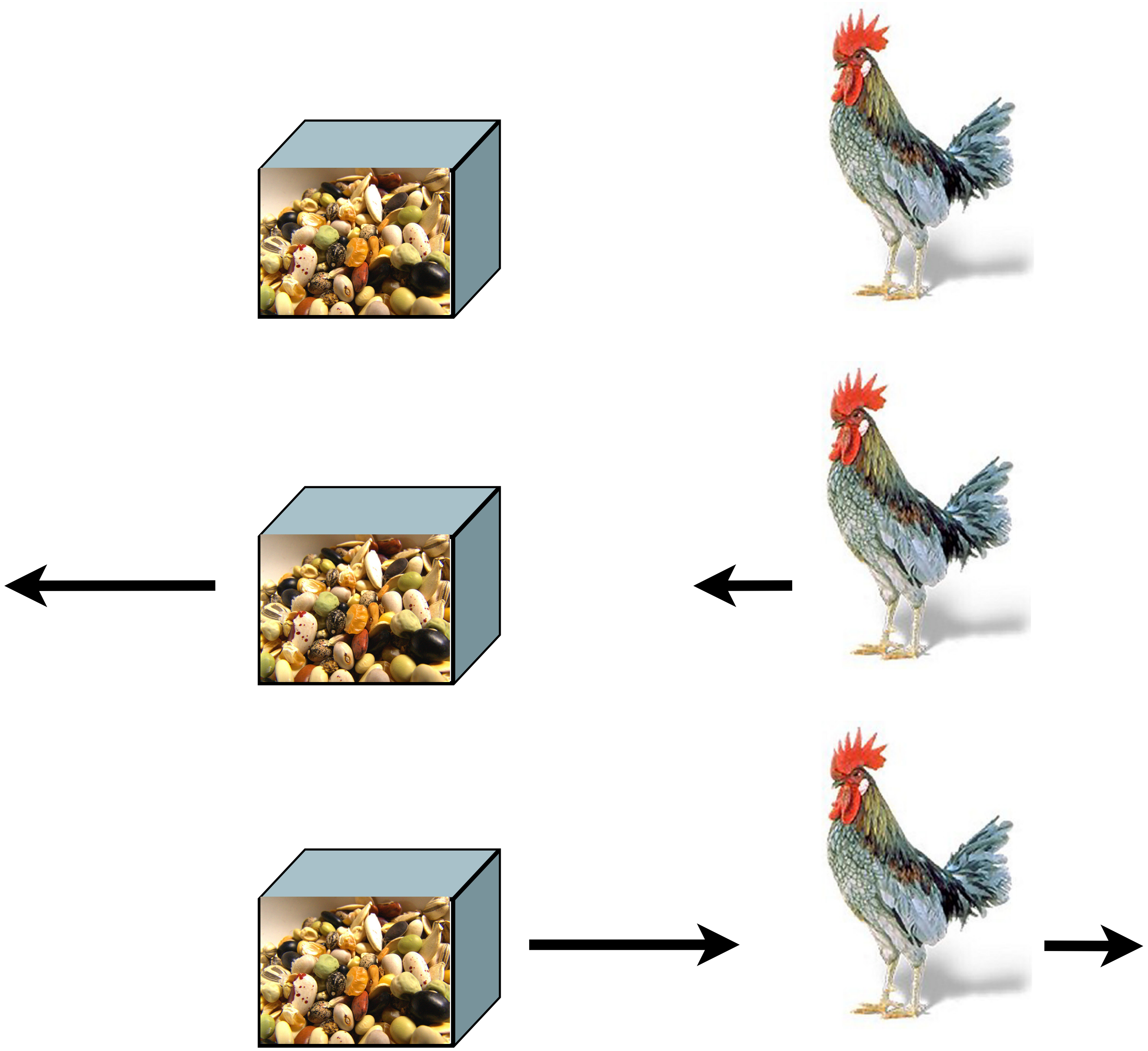
Hershberger 1986

“Pavlovian” unconditioned responses



Hershberger 1986

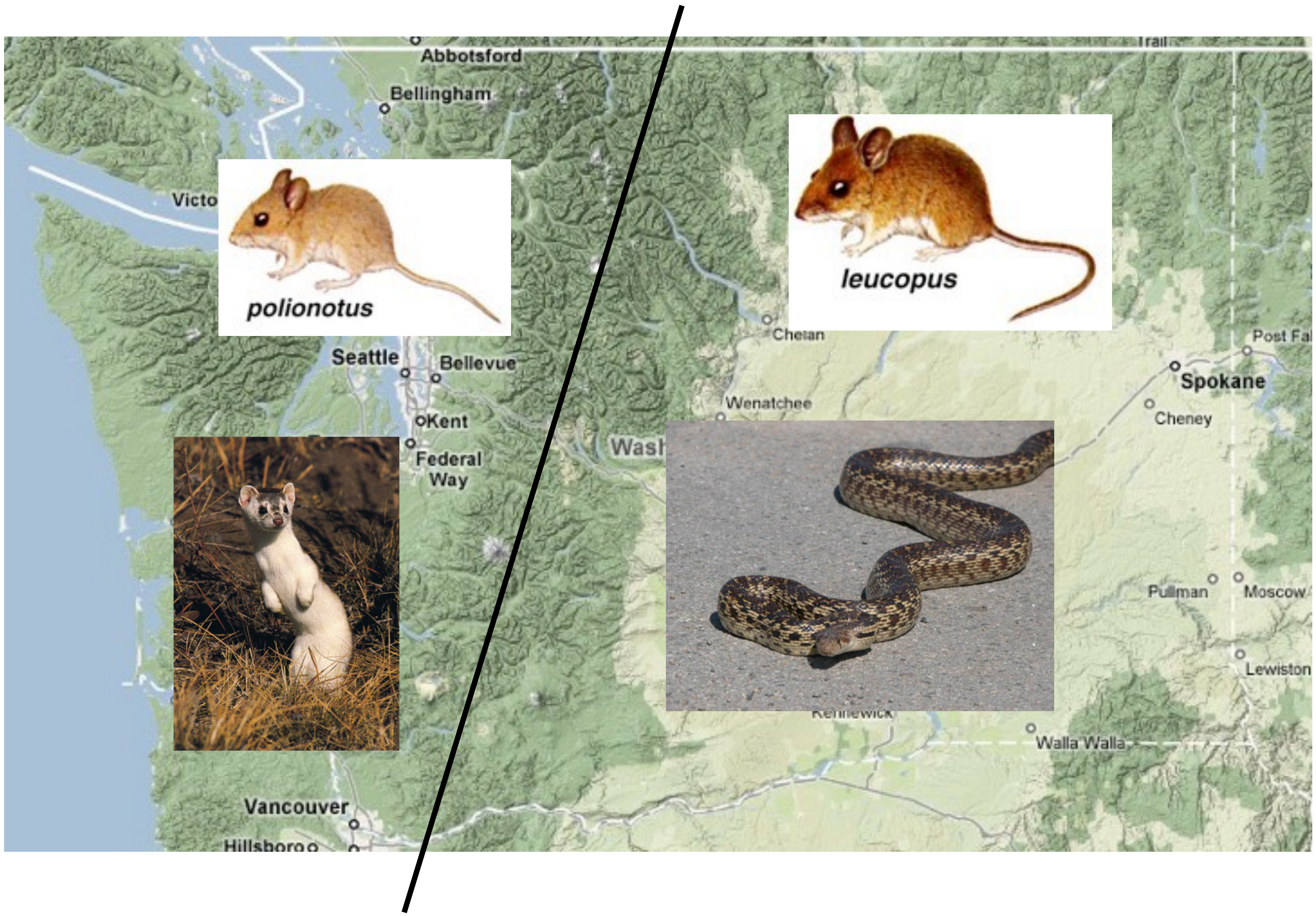
“Pavlovian” unconditioned responses



Hershberger 1986

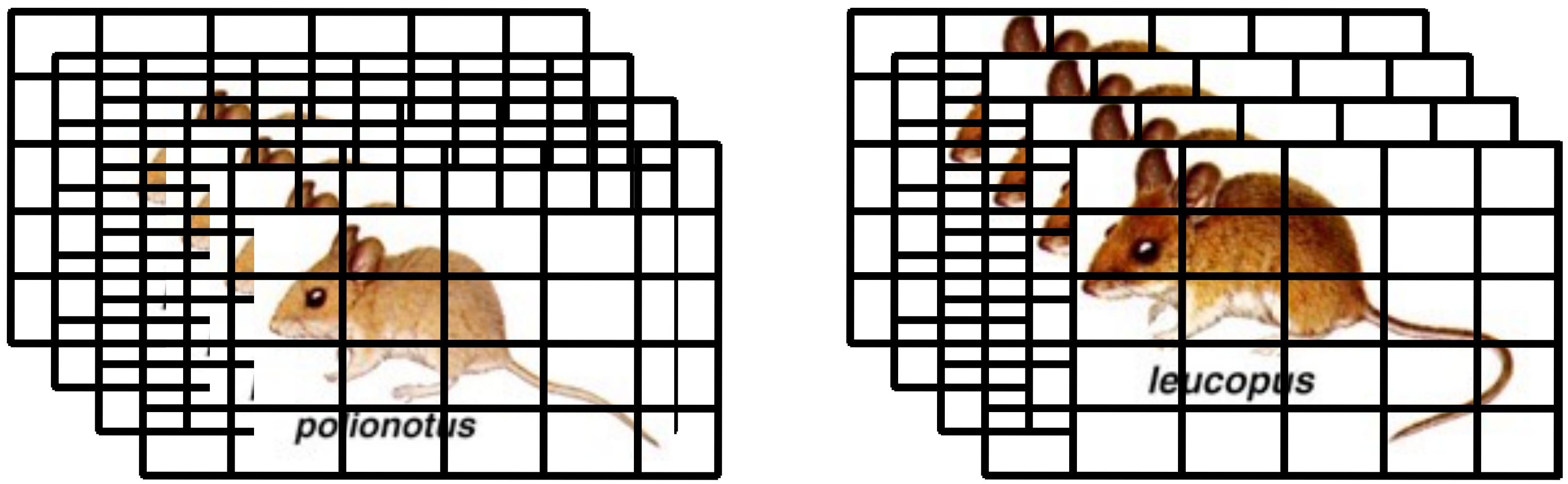
- powerful
- inflexible over short timescale
- adaptive on evolutionary scale

Innate evolutionary strategies



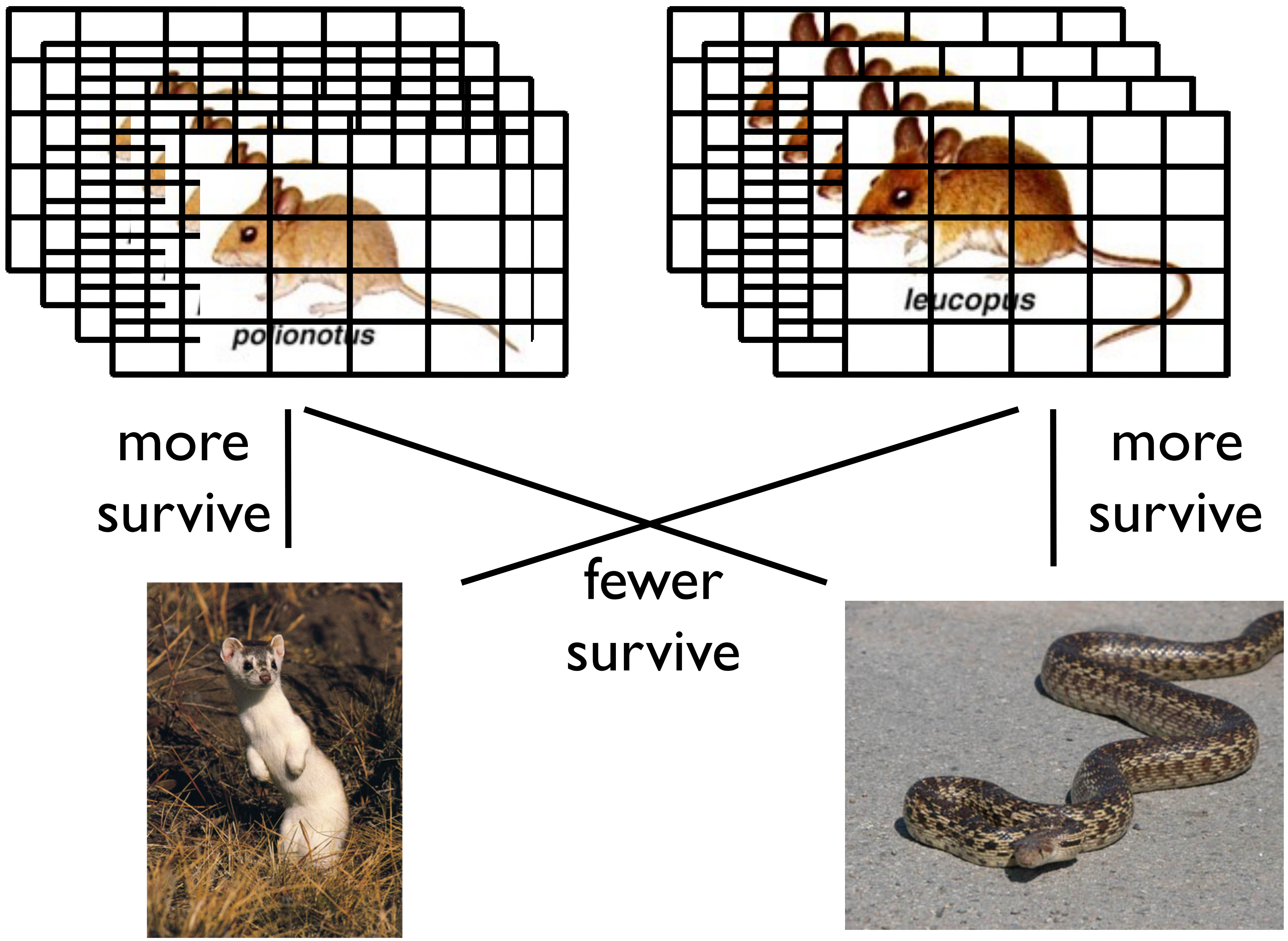
Hirsch and Bolles 1980 Ethology

Innate evolutionary strategies



Hirsch and Bolles 1980 Ethology

Innate evolutionary strategies



Hirsch and Bolles 1980 Ethology

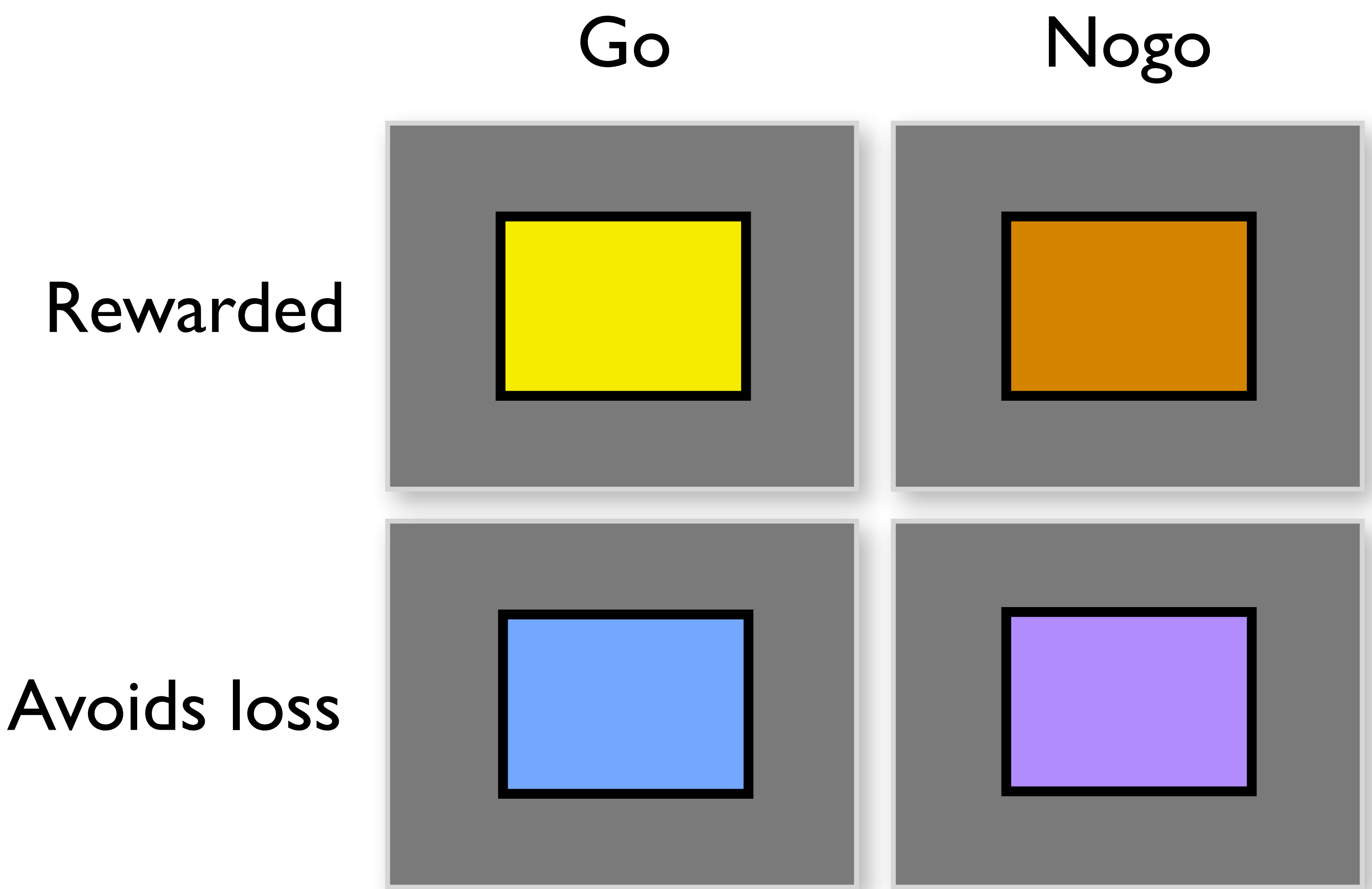
PIT paradigms

- Separate

Pavlovian conditioning → Instrumental conditioning → Instrumental performance in extinction w/ Pavlovian stimuli

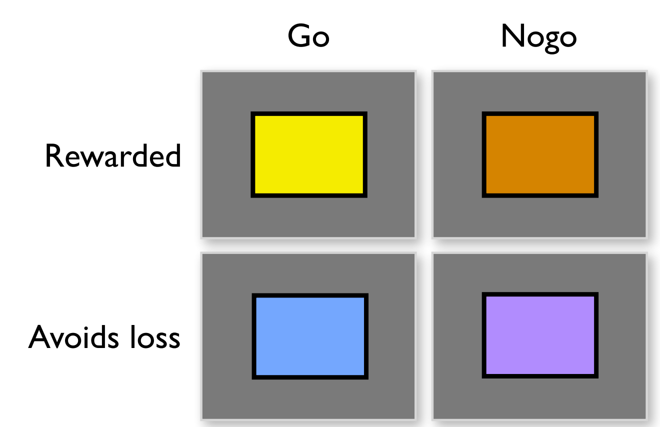
- Joint?

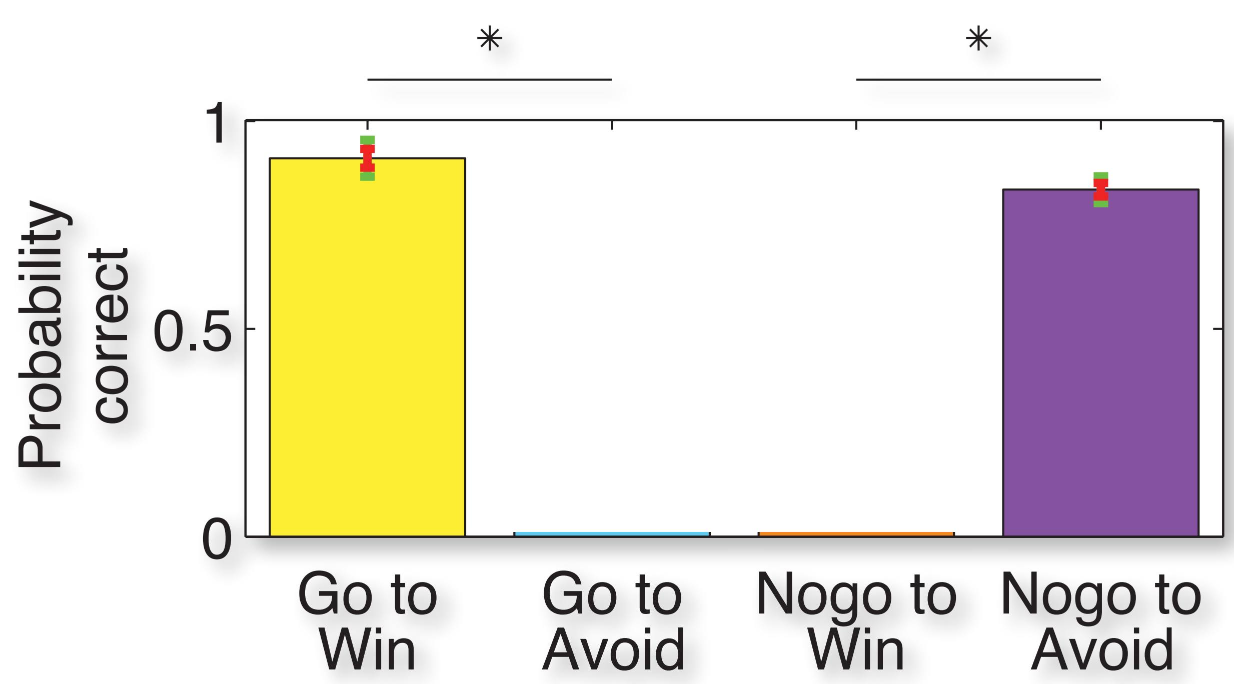
Affective go / nogo task

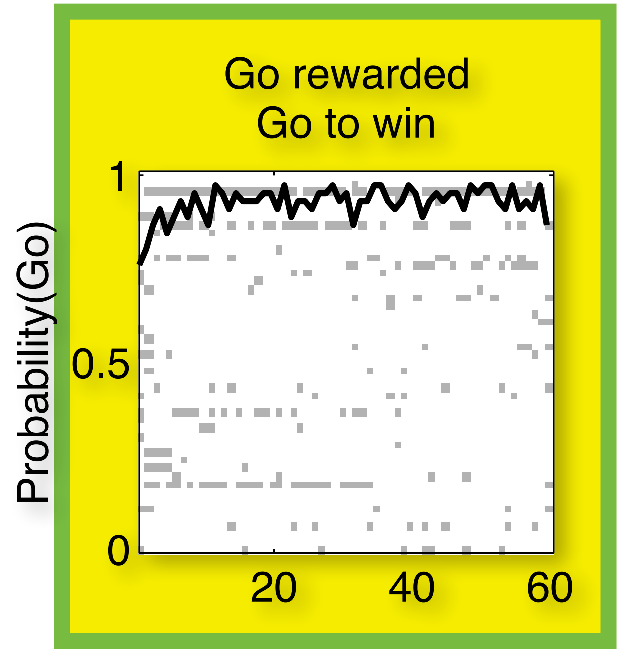


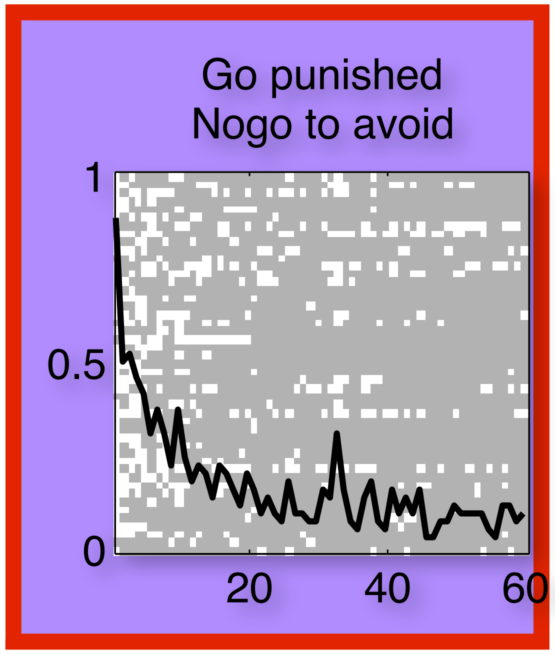
Guitart-Masip, Huys et al. *2012*

Affective go / nogo task



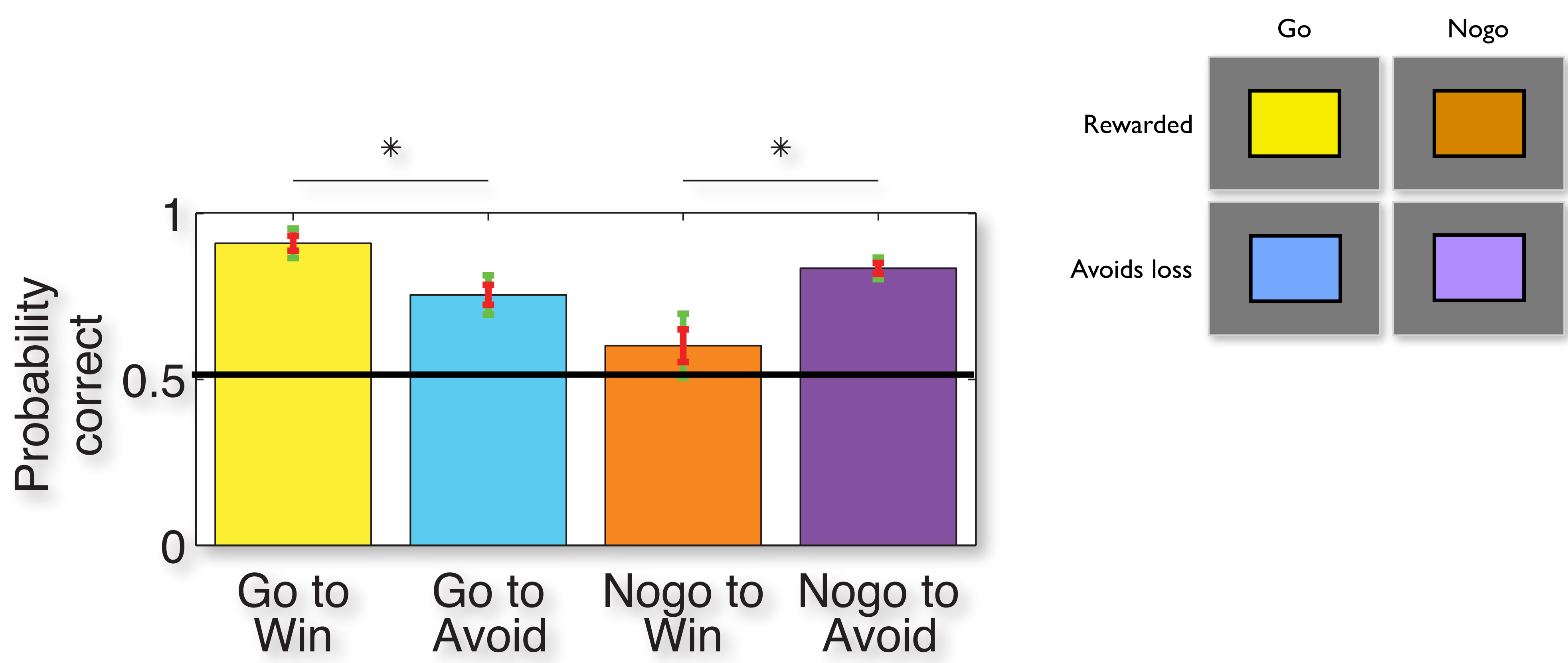


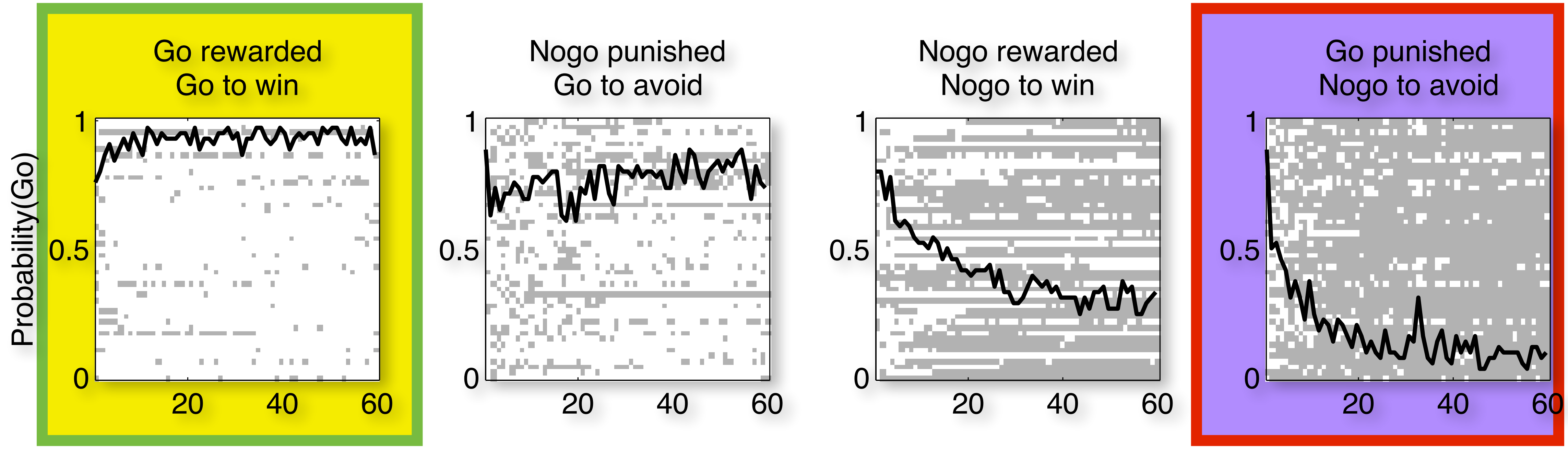




Guitart-Masip, Huys et al. *2012*

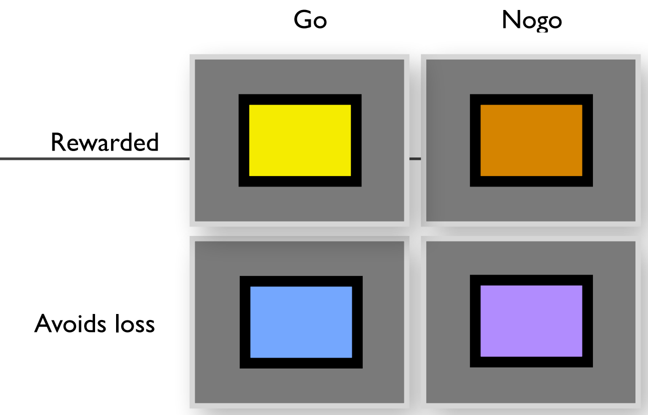
Affective go / nogo task





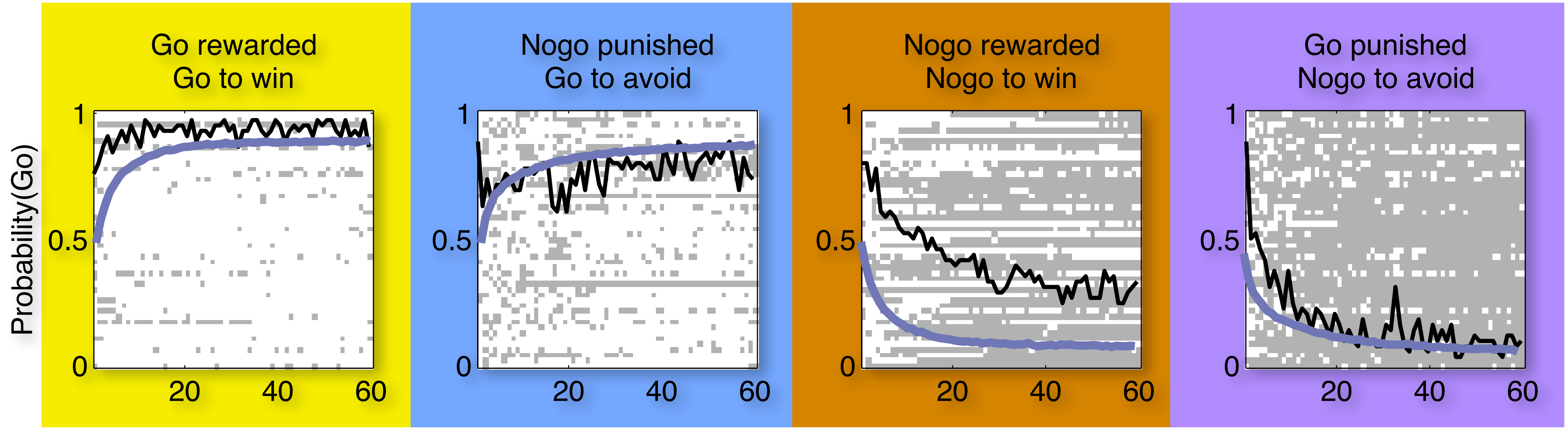
Guitart-Masip, Huys et al. *2012*

Models



- Basic

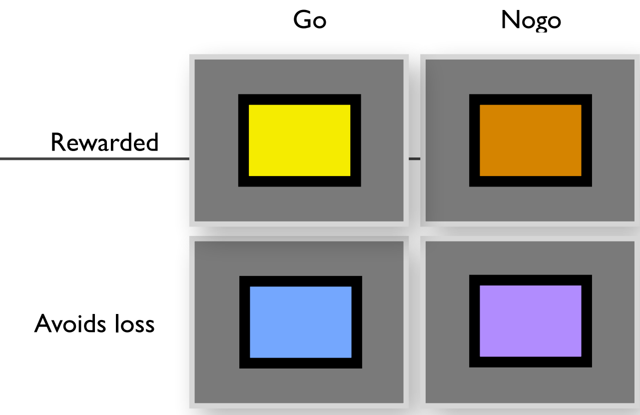
$$p_t(a|s) \propto \mathcal{Q}_t(s,a)$$
$$\mathcal{Q}_{t+1}(s,a) = \mathcal{Q}_t(s,a) + \alpha(r_t - \mathcal{Q}_t(s,a))$$



Guitart et al., 2012 J Neurosci

Models

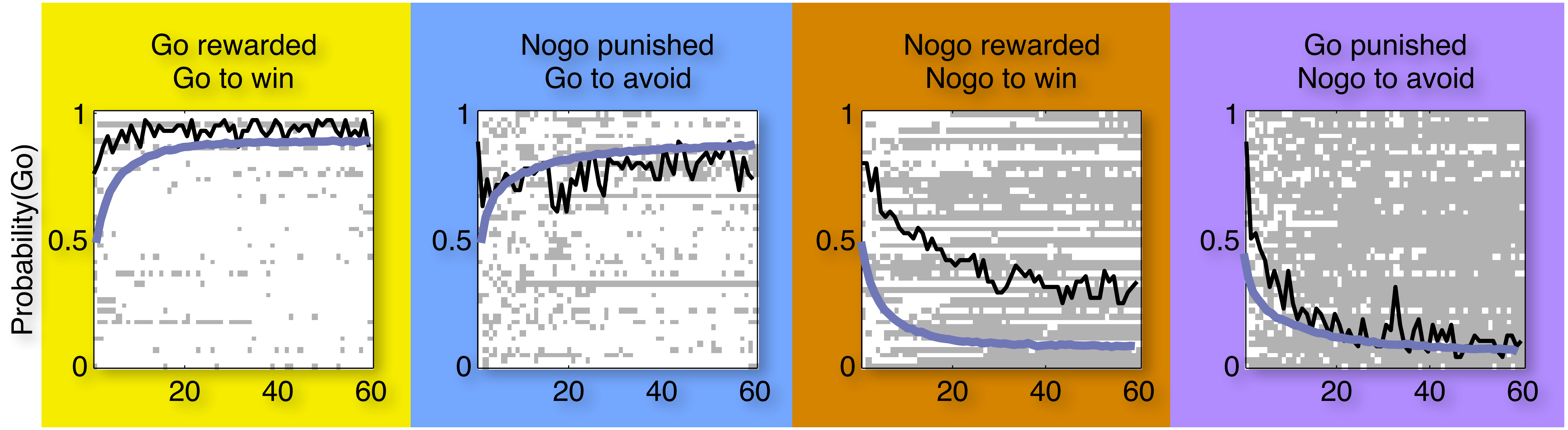
- Basic + bias



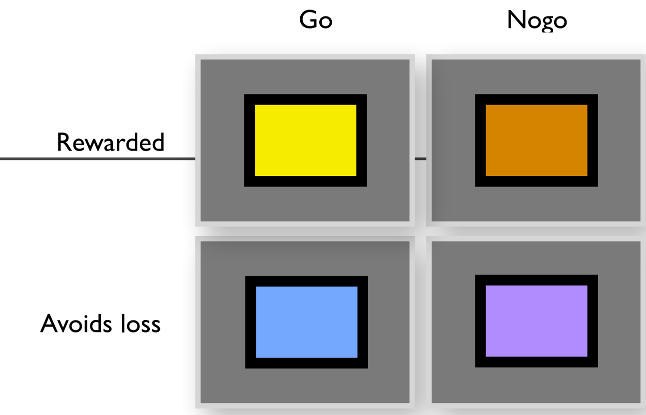
$$p_t(go|s) \propto \mathcal{Q}_t(s, go) + bias(go)$$

$$p_t(nogo|s) \propto \mathcal{Q}_t(s, nogo)$$

$$\mathcal{Q}_{t+1}(s, a) = \mathcal{Q}_t(s, a) + \alpha(r_t - \mathcal{Q}_t(s, a))$$



Models

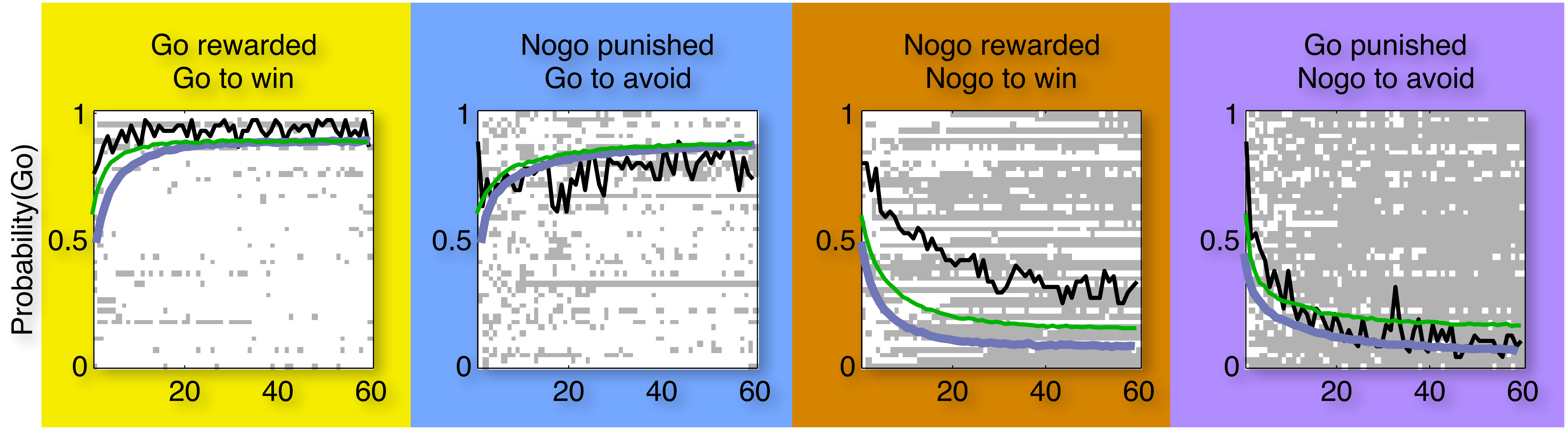


- Basic + bias

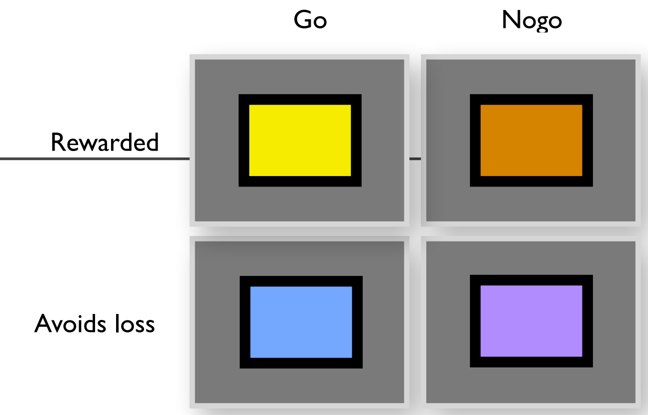
$$p_t(go|s) \propto \mathcal{Q}_t(s, go) + bias(go)$$

$$p_t(nogo|s) \propto \mathcal{Q}_t(s, nogo)$$

$$\mathcal{Q}_{t+1}(s, a) = \mathcal{Q}_t(s, a) + \alpha(r_t - \mathcal{Q}_t(s, a))$$

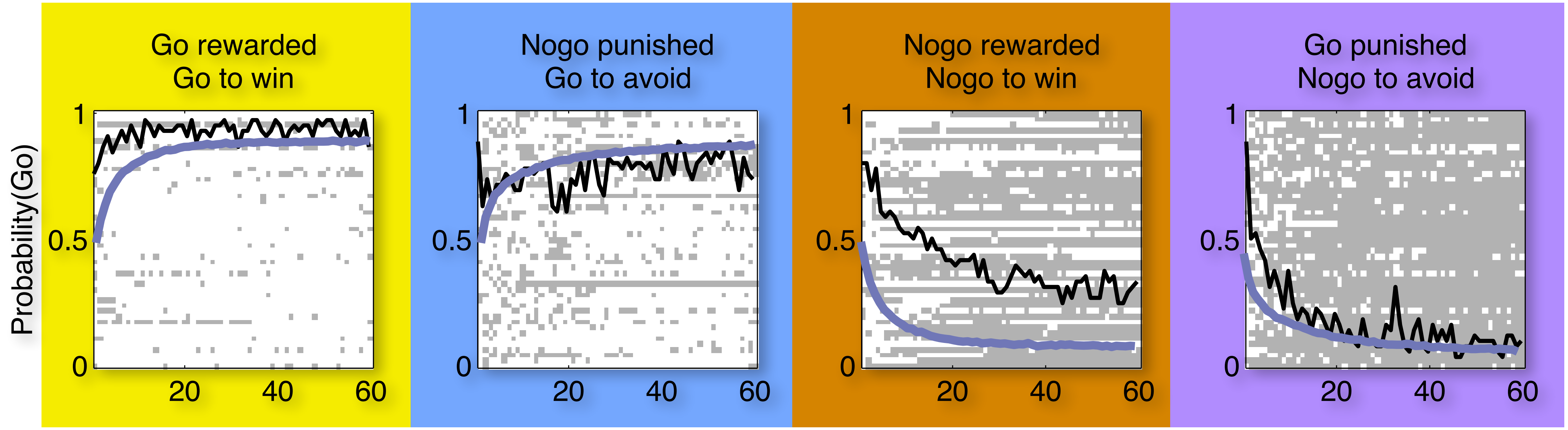


Models

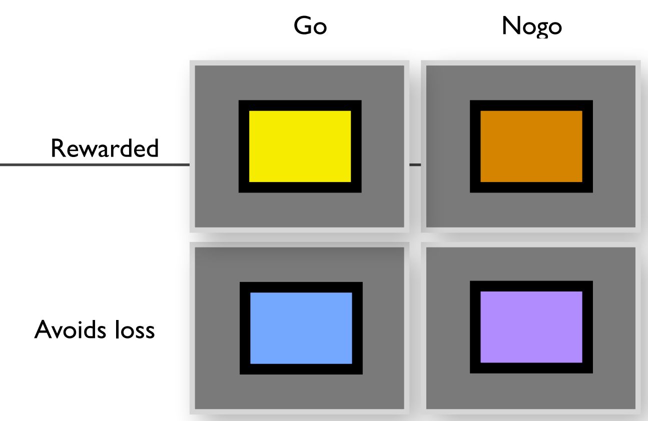


- Basic + bias + Pavlovian influence

$$p_t(go|s) \propto \mathcal{Q}_t(s, go) + bias(go) + \pi \mathcal{V}_t(s)$$
$$p_t(nogo|s) \propto \mathcal{Q}_t(s, nogo)$$
$$\mathcal{Q}_{t+1}(s, a) = \mathcal{Q}_t(s, a) + \alpha(r_t - \mathcal{Q}_t(s, a))$$
$$\mathcal{V}_{t+1}(s) = \mathcal{V}_t(s) + \alpha(r_t - \mathcal{V}_t(s))$$



Models



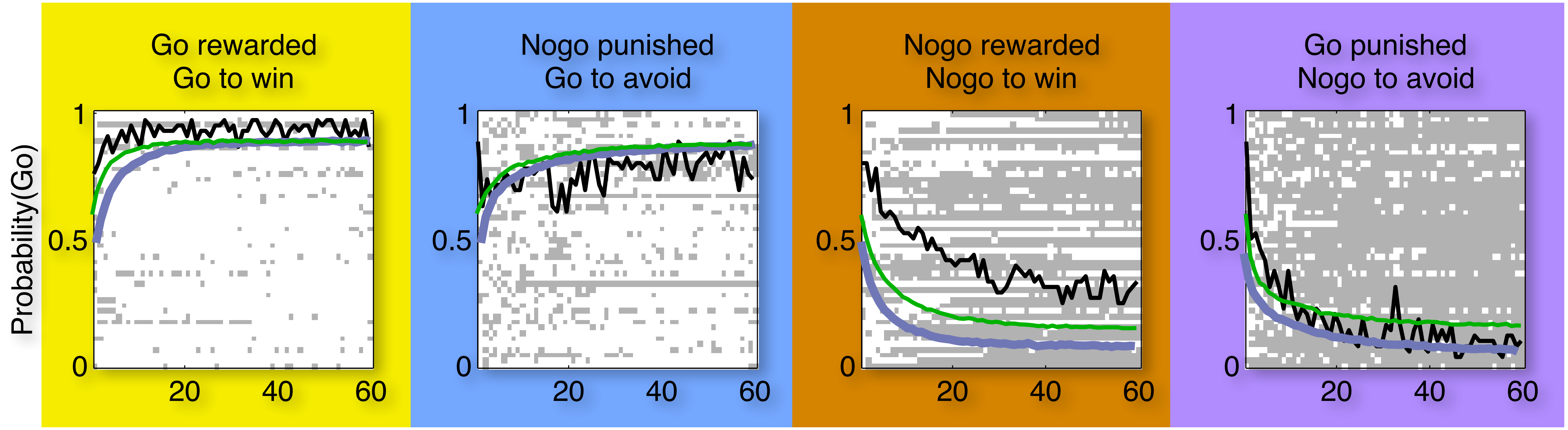
- Basic + bias + Pavlovian influence

$$p_t(go|s) \propto \mathcal{Q}_t(s,go) + bias(go) + \pi \mathcal{V}_t(s)$$

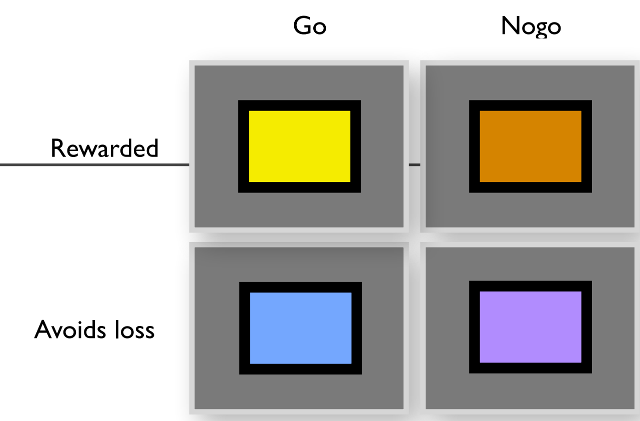
$$p_t(nogo|s) \propto \mathcal{Q}_t(s,nogo)$$

$$\mathcal{Q}_{t+1}(s,a) = \mathcal{Q}_t(s,a) + \alpha(r_t - \mathcal{Q}_t(s,a))$$

$$\mathcal{V}_{t+1}(s) = \mathcal{V}_t(s) + \alpha(r_t - \mathcal{V}_t(s))$$



Models



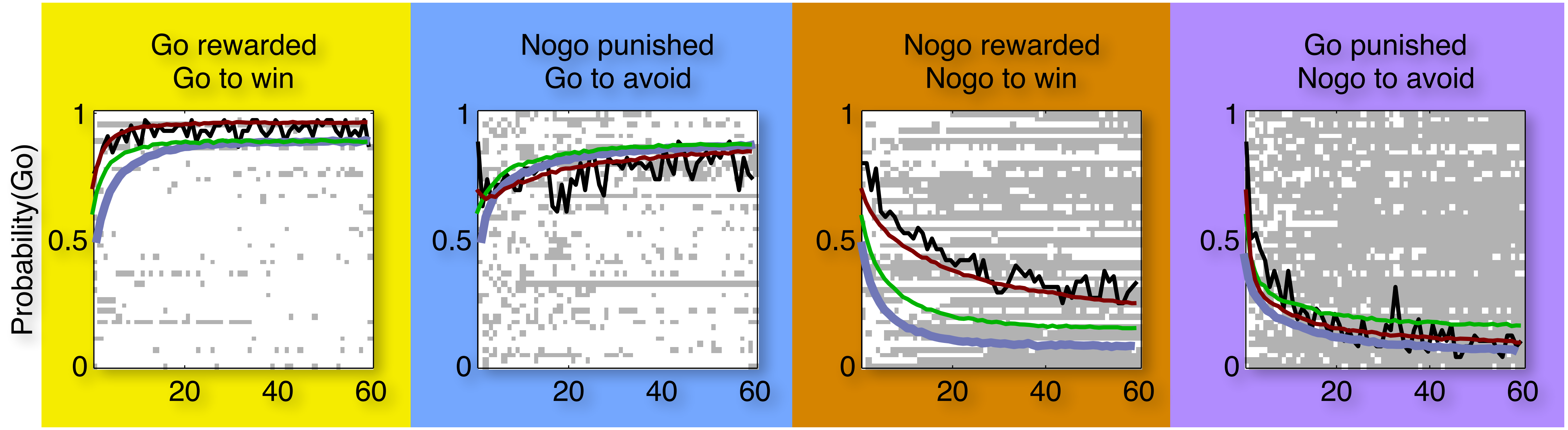
- Basic + bias + Pavlovian influence

$$p_t(go|s) \propto \mathcal{Q}_t(s, go) + bias(go) + \pi \mathcal{V}_t(s)$$

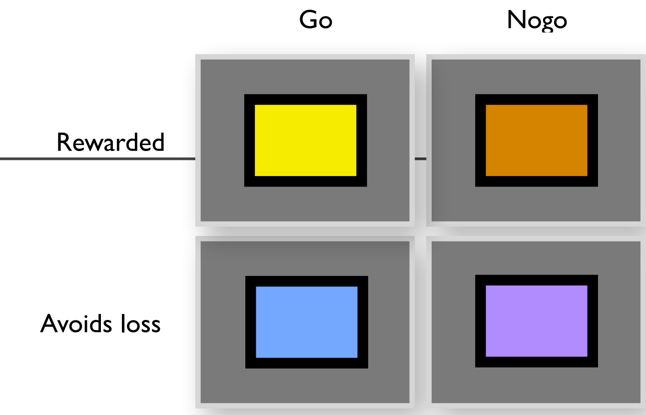
$$p_t(nogo|s) \propto \mathcal{Q}_t(s, nogo)$$

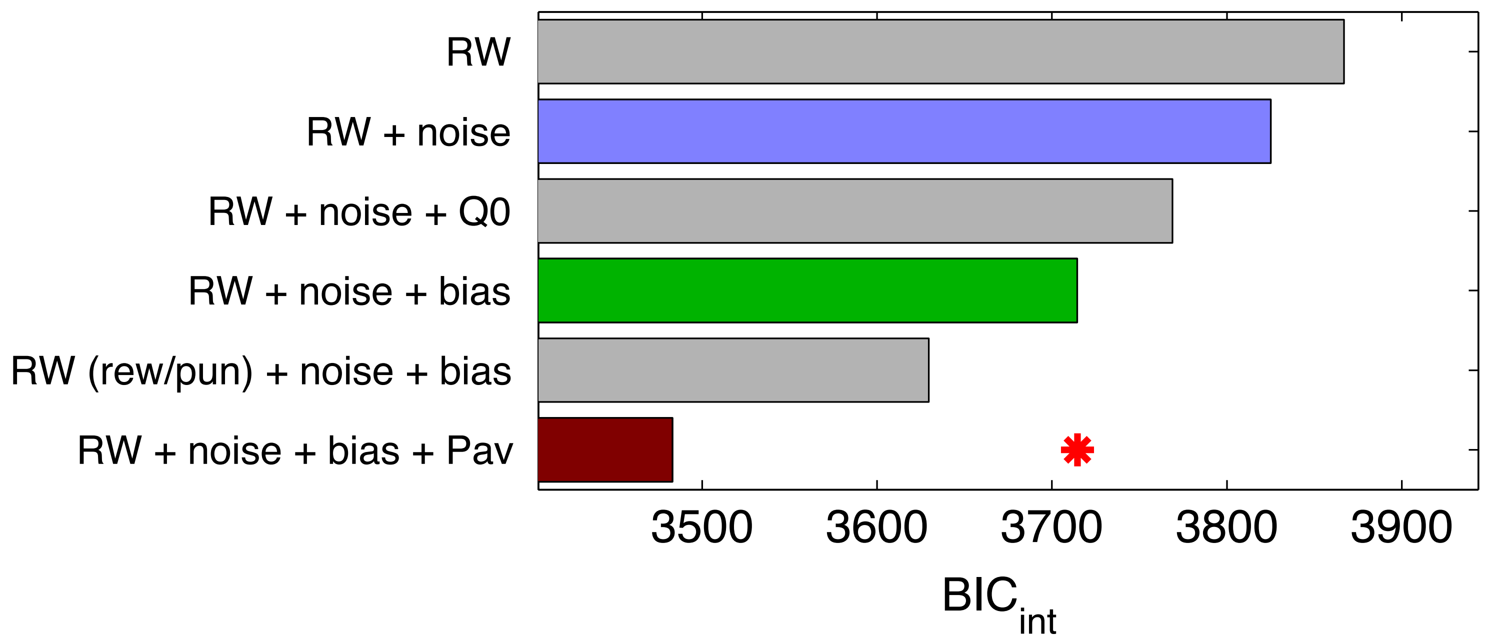
$$\mathcal{Q}_{t+1}(s, a) = \mathcal{Q}_t(s, a) + \alpha(r_t - \mathcal{Q}_t(s, a))$$

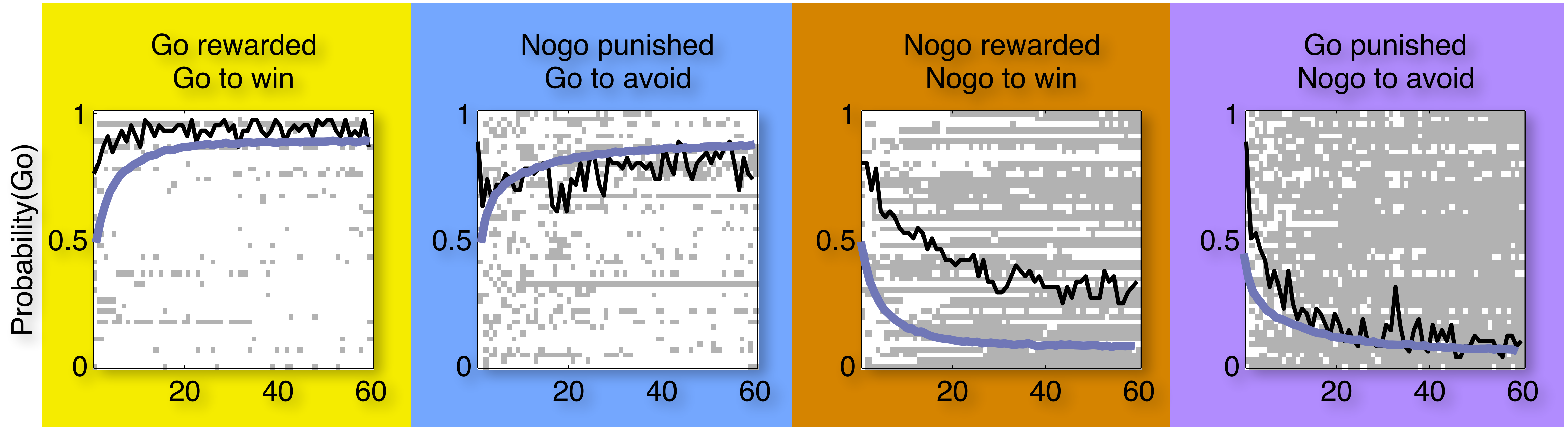
$$\mathcal{V}_{t+1}(s) = \mathcal{V}_t(s) + \alpha(r_t - \mathcal{V}_t(s))$$



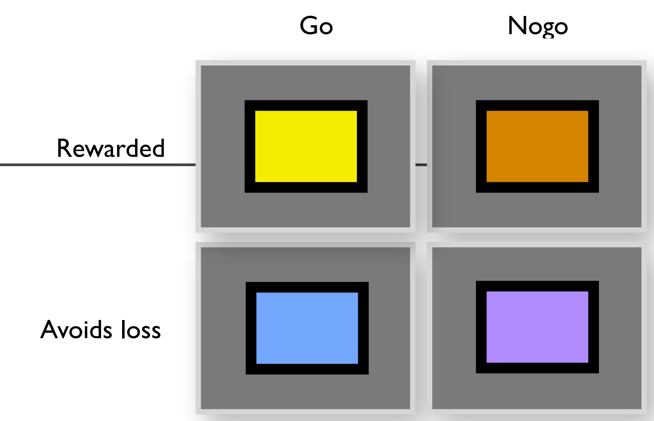
Model comparison: overfitting?

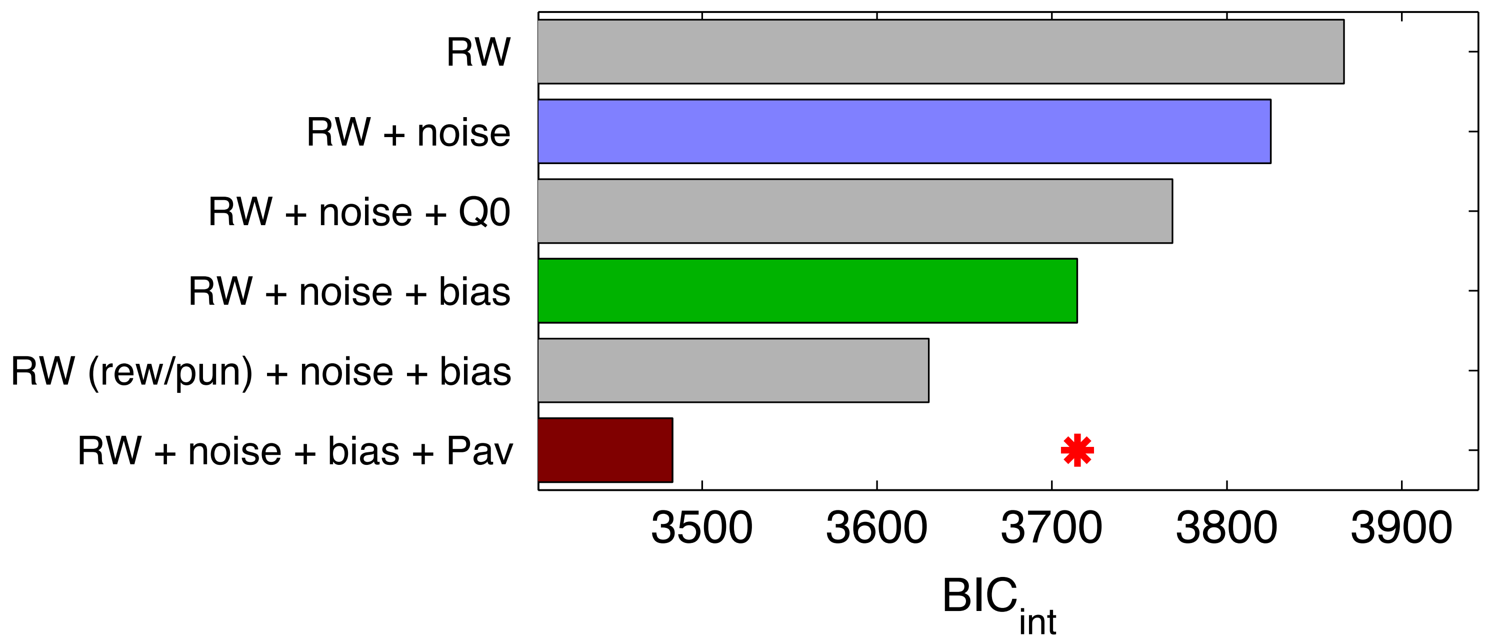


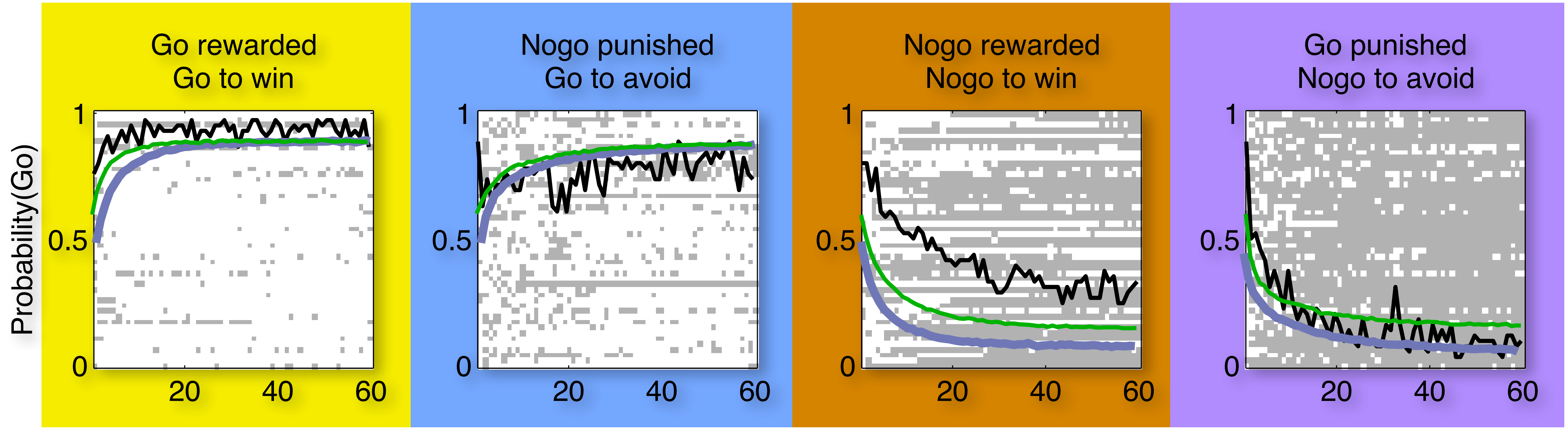




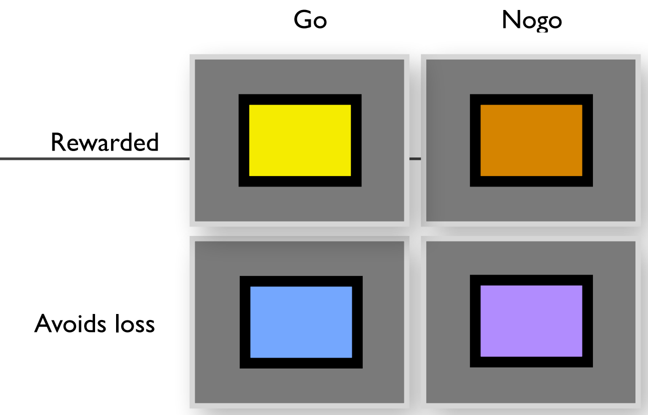
Model comparison: overfitting?

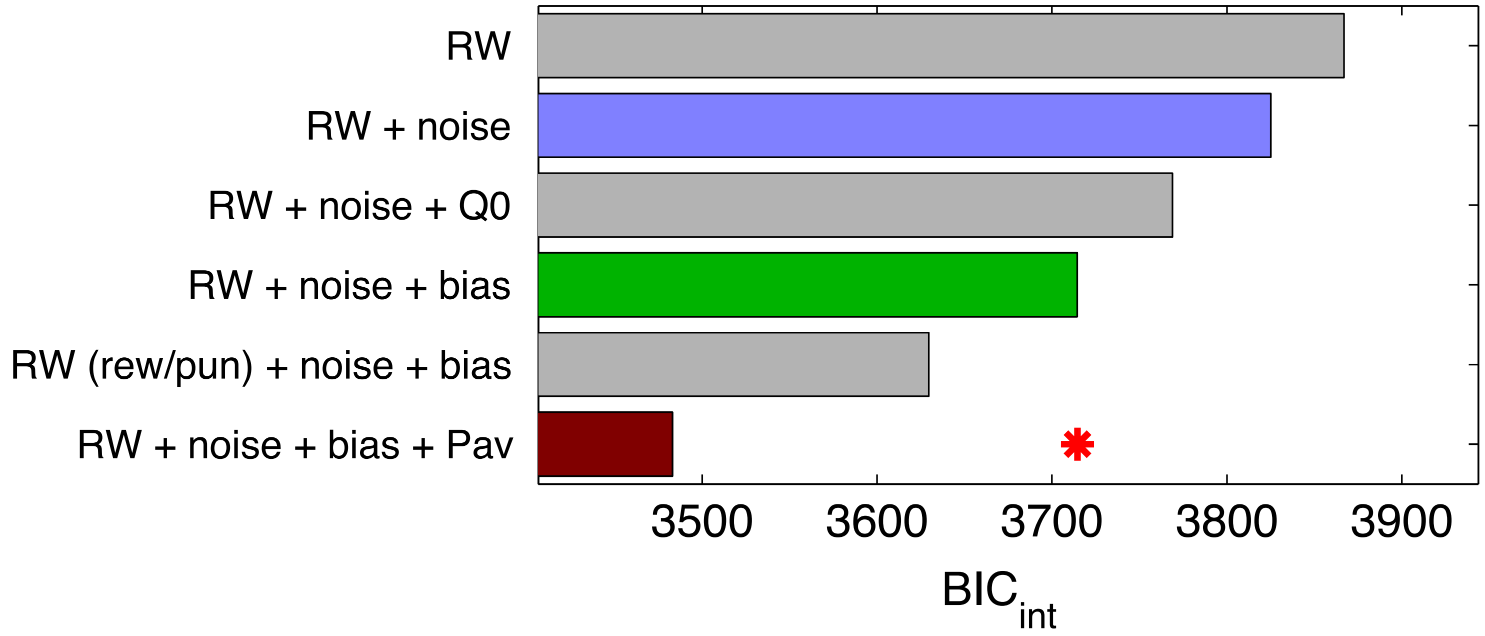


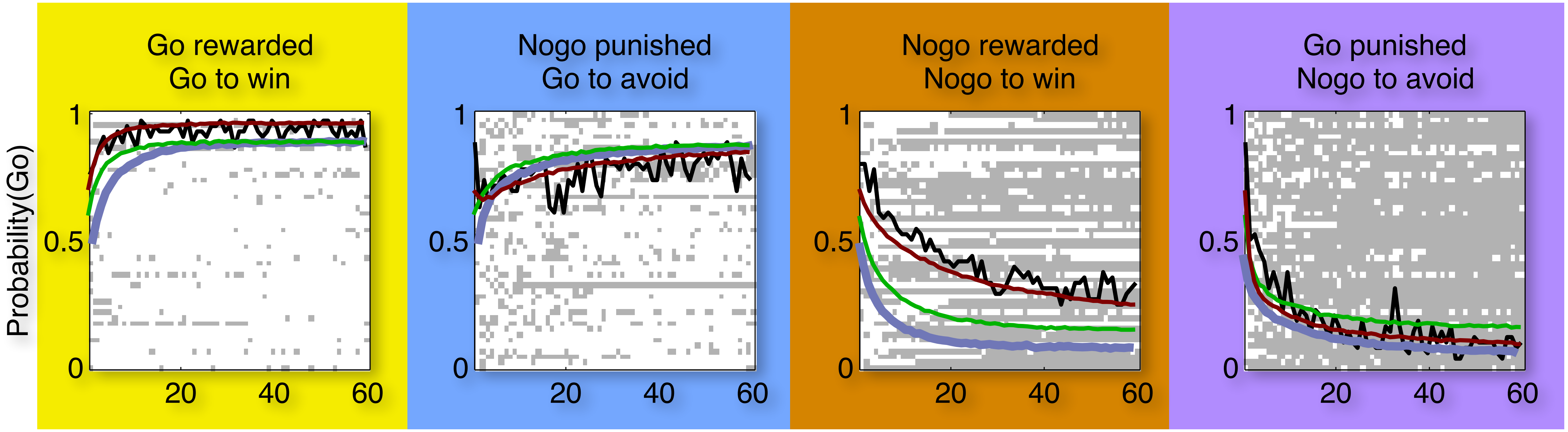




Model comparison: overfitting?



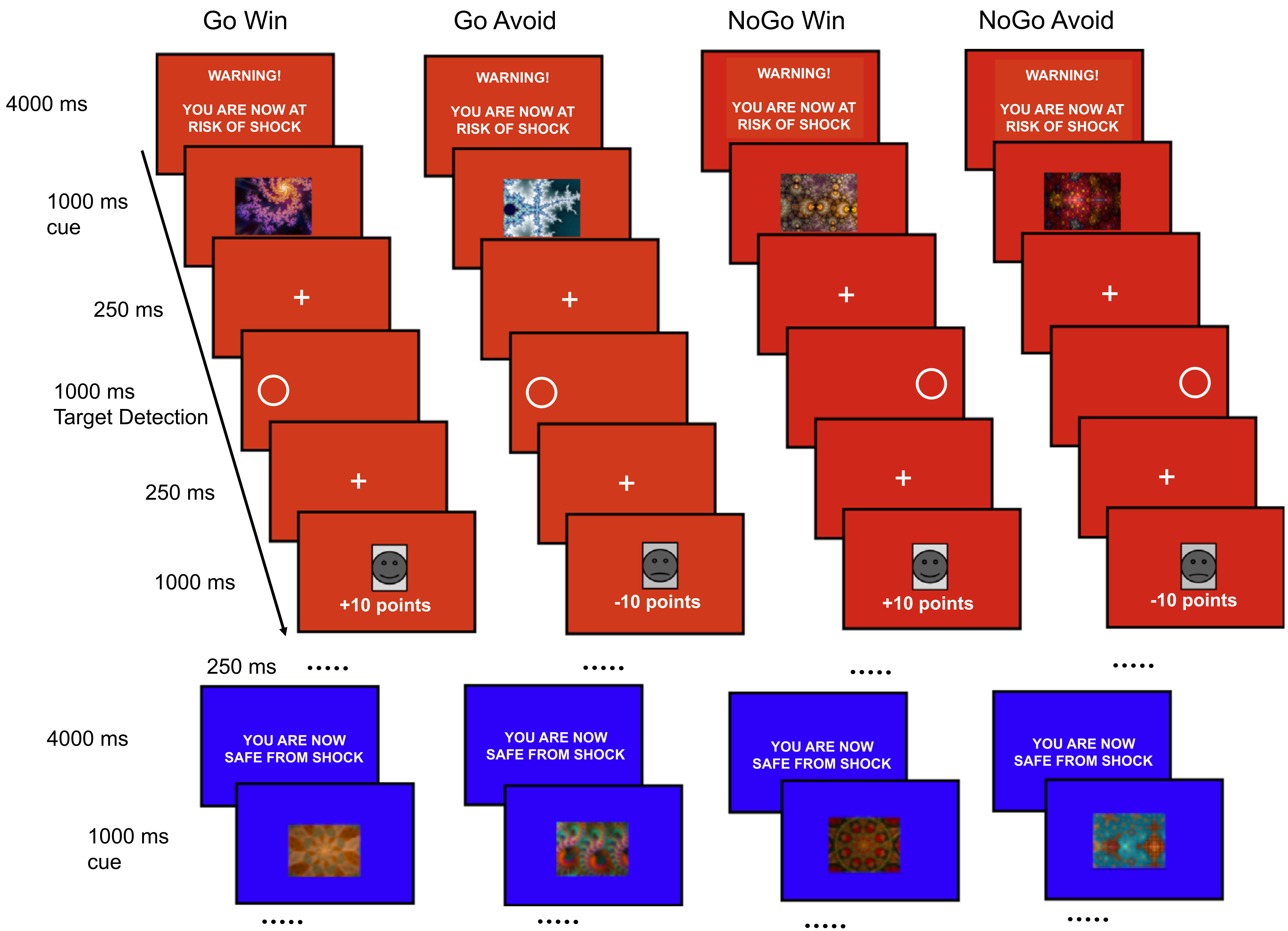




Example code

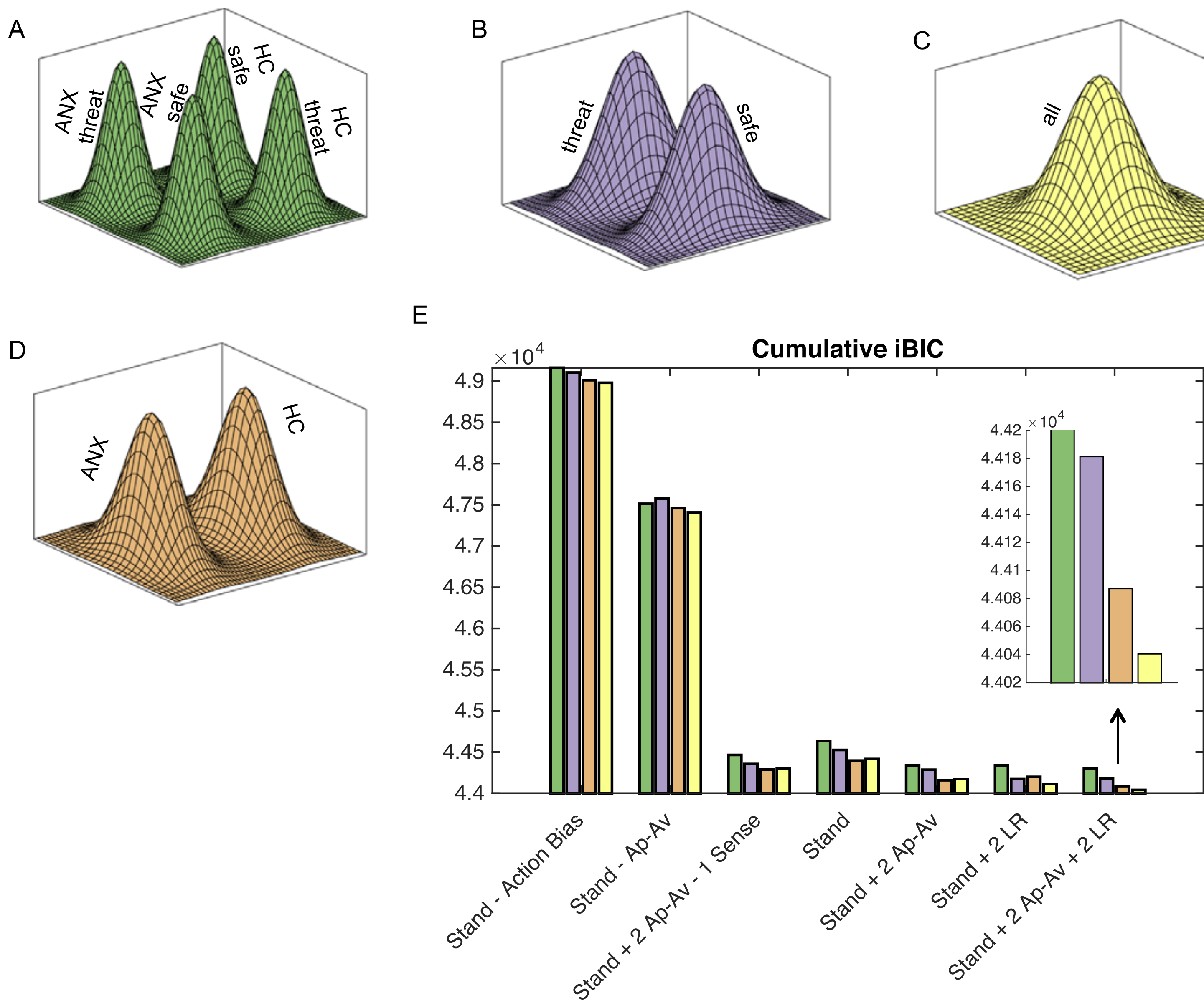
- www.cmod4mh.org/emfit.zip
- batchRunEMfit('mAffectiveGoNogo')
  - will generate example data
  - fit all models in modelList.m
  - perform model comparison
  - generate surrogate data
  - generate plots for basic sanity checks
- final model is llbaepxb.m

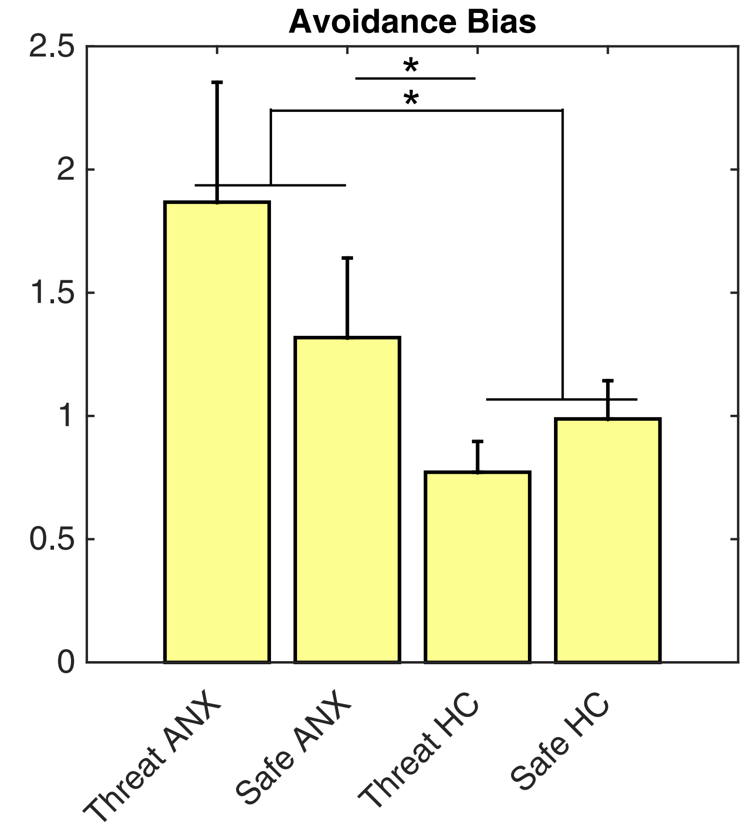
Threat of shock



Mkrtchian et al., 2017 Biol. Psychiatry

Threat potentiates aversive Pavlovian bias in anxious individuals

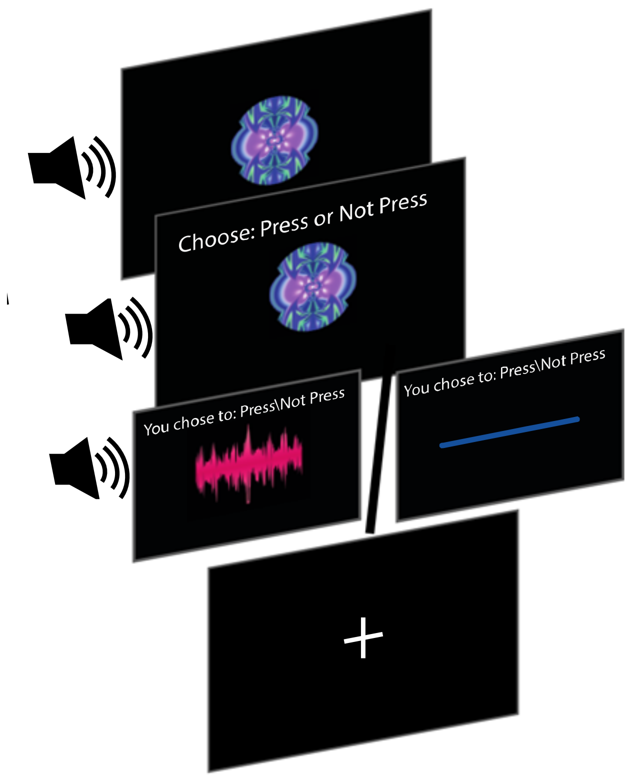




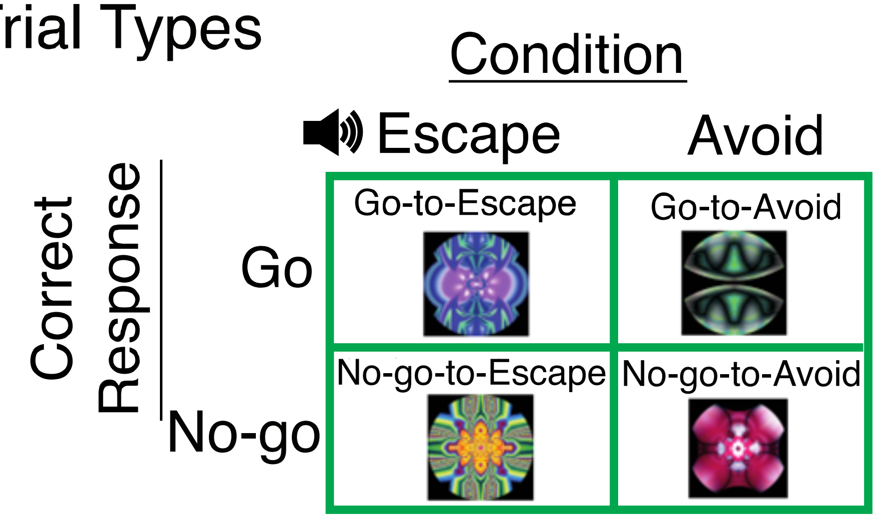
Mkrtchian et al., 2017 Biol. Psychiatry

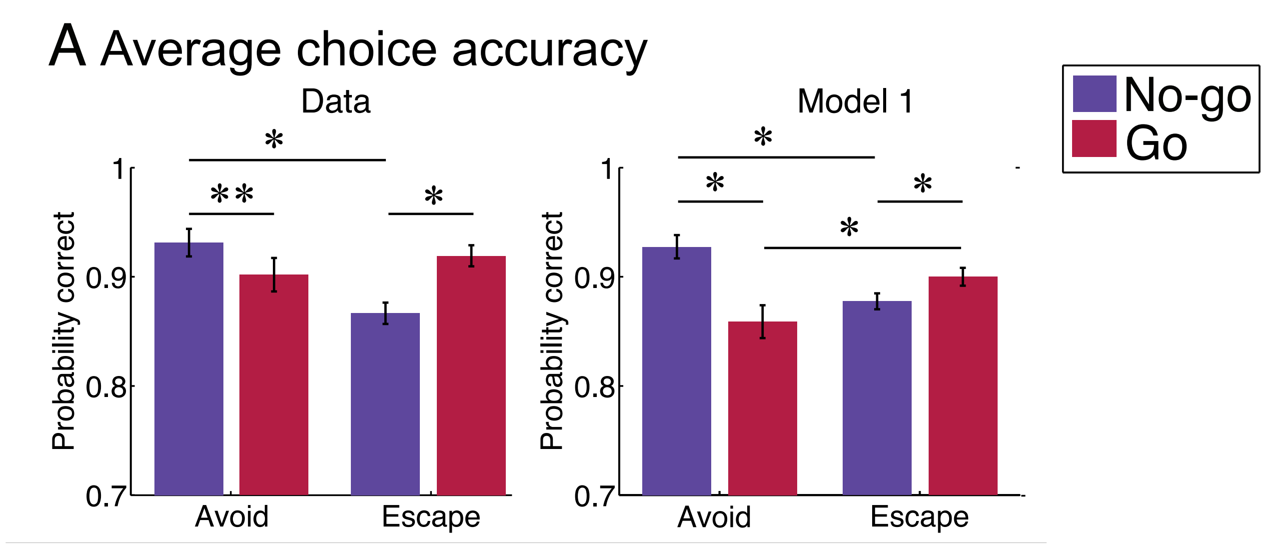
Escape vs avoidance

Go-to-Escape trials



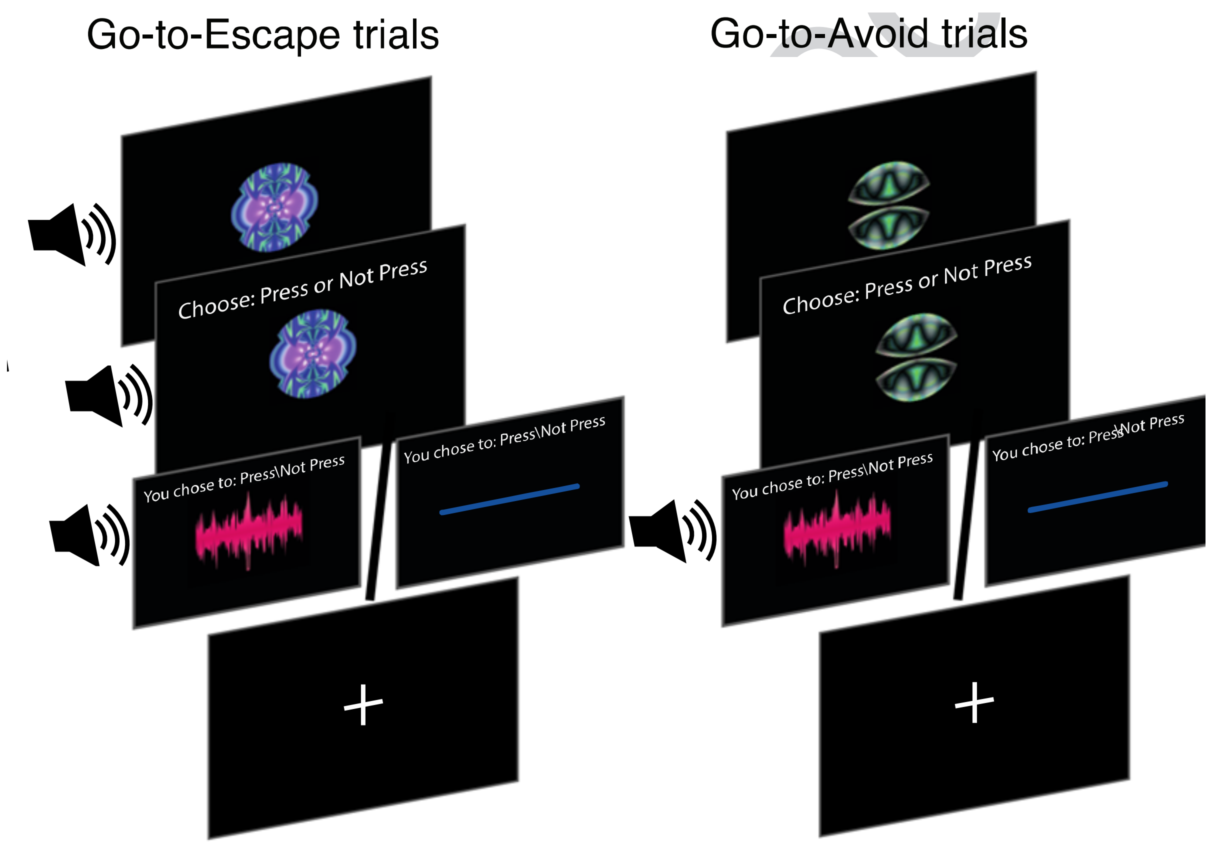
Trial Types

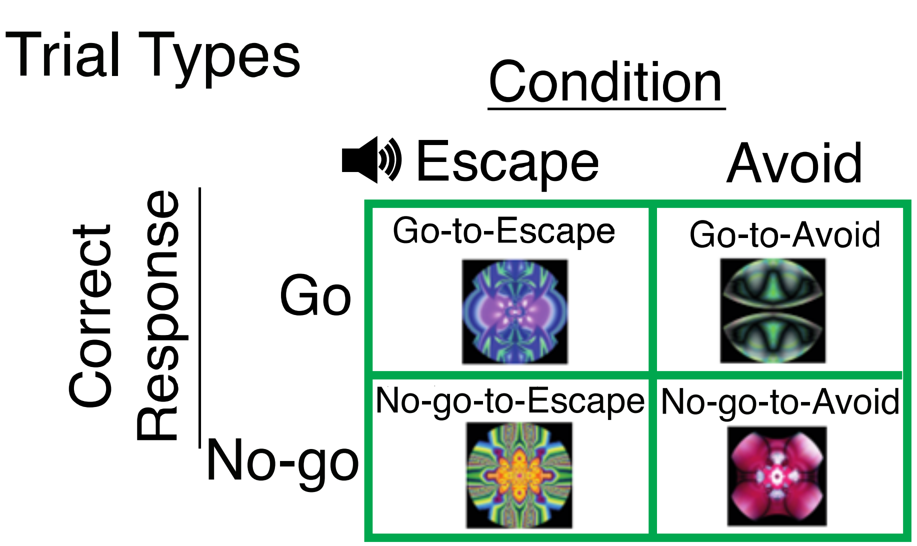


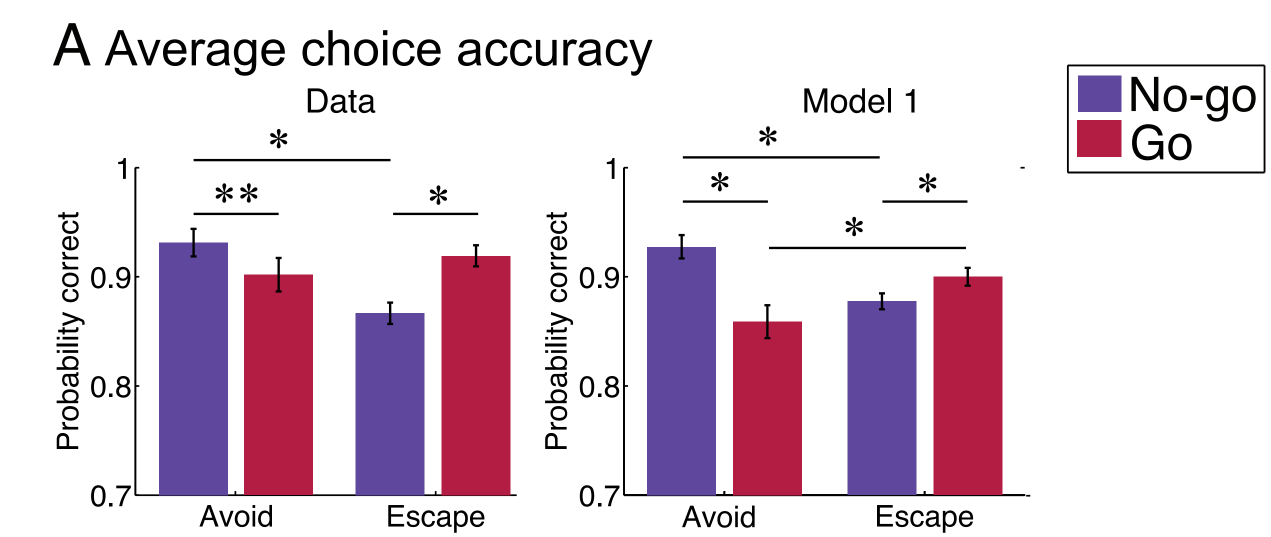


Millner et al., 2018 J Cog Neurosci

Escape vs avoidance

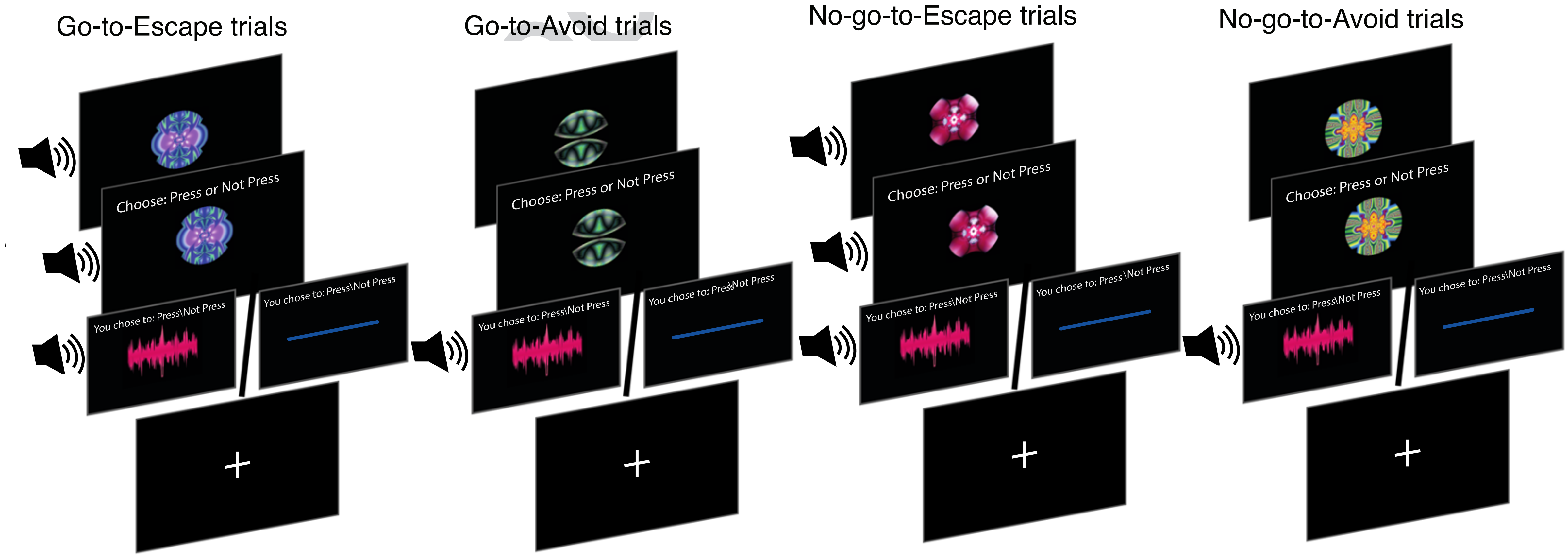


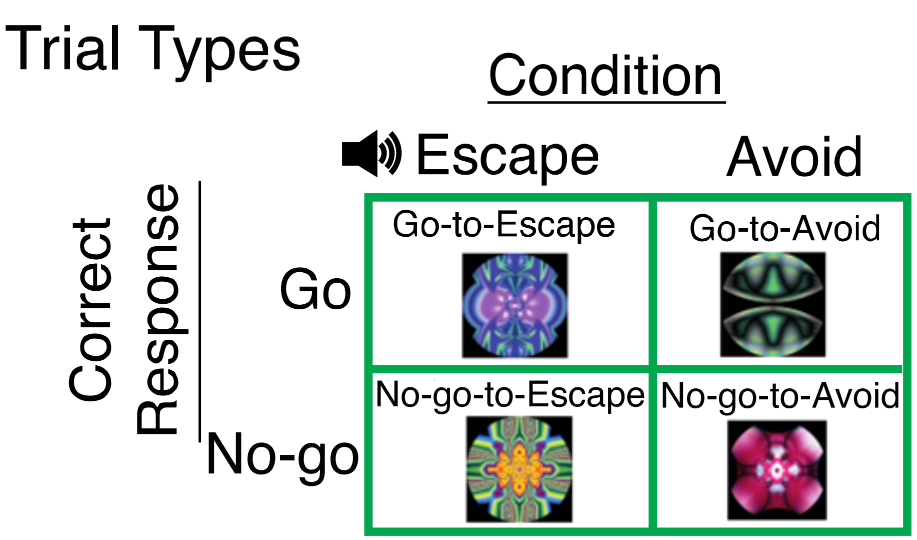


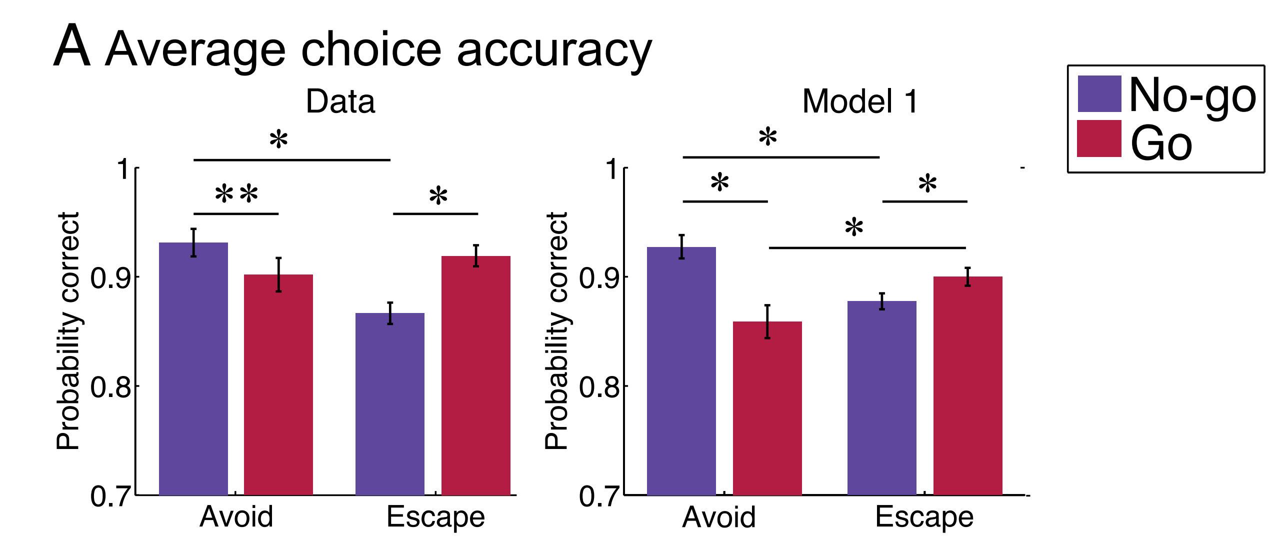


Millner et al., 2018 J Cog Neurosci

Escape vs avoidance

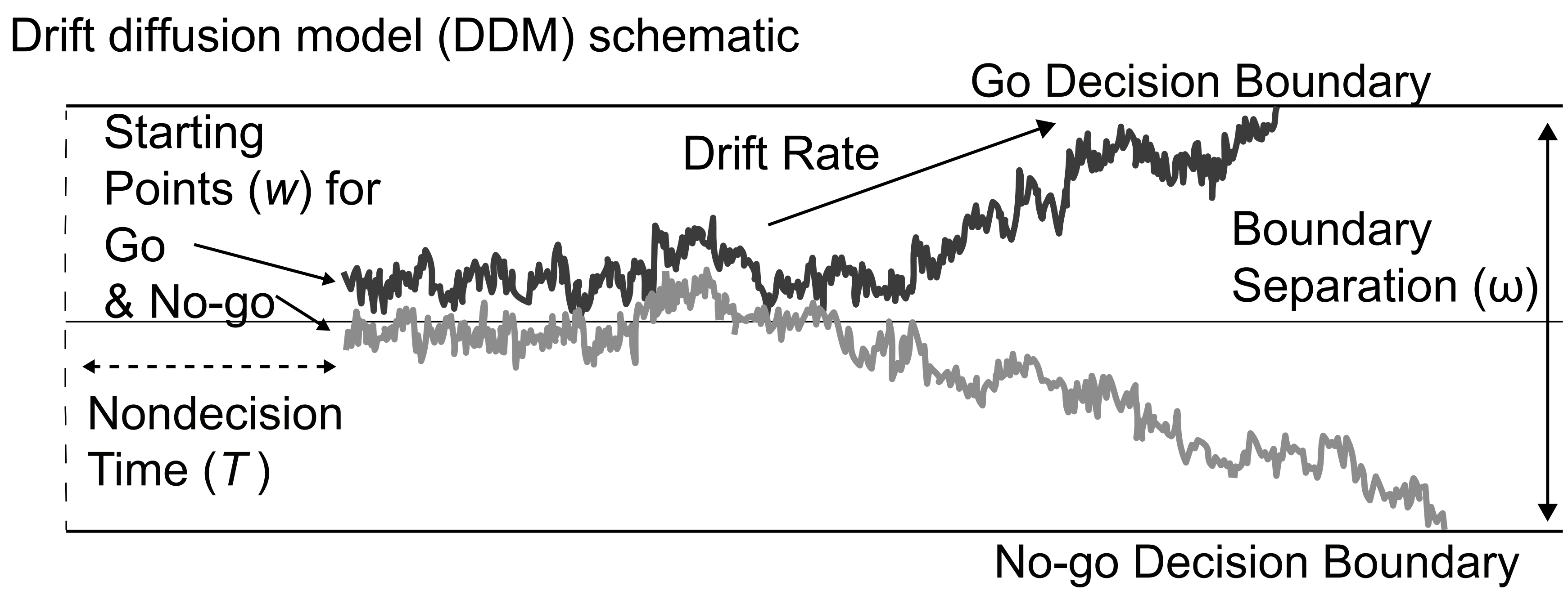






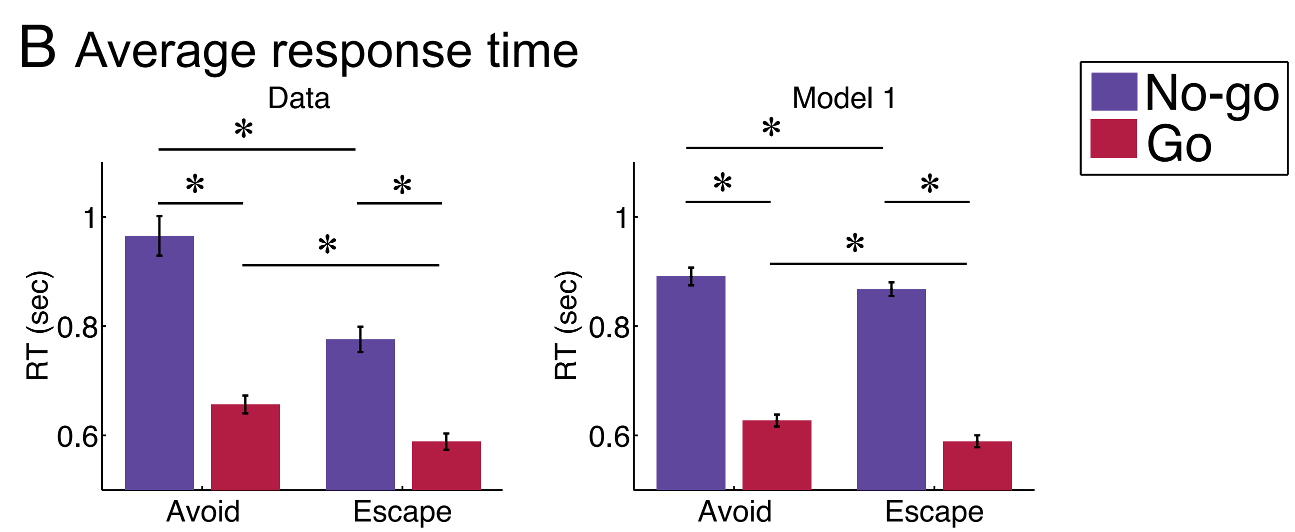
Millner et al., 2018 J Cog Neurosci

Choices and RTs



$$\mu_t = \beta_0 + \beta_1[Q_t(s_t, \text{go}) - Q_t(s_t, \text{no-go})]$$

separate starting points for escape and avoidance



suicidality

Millner et al., 2018

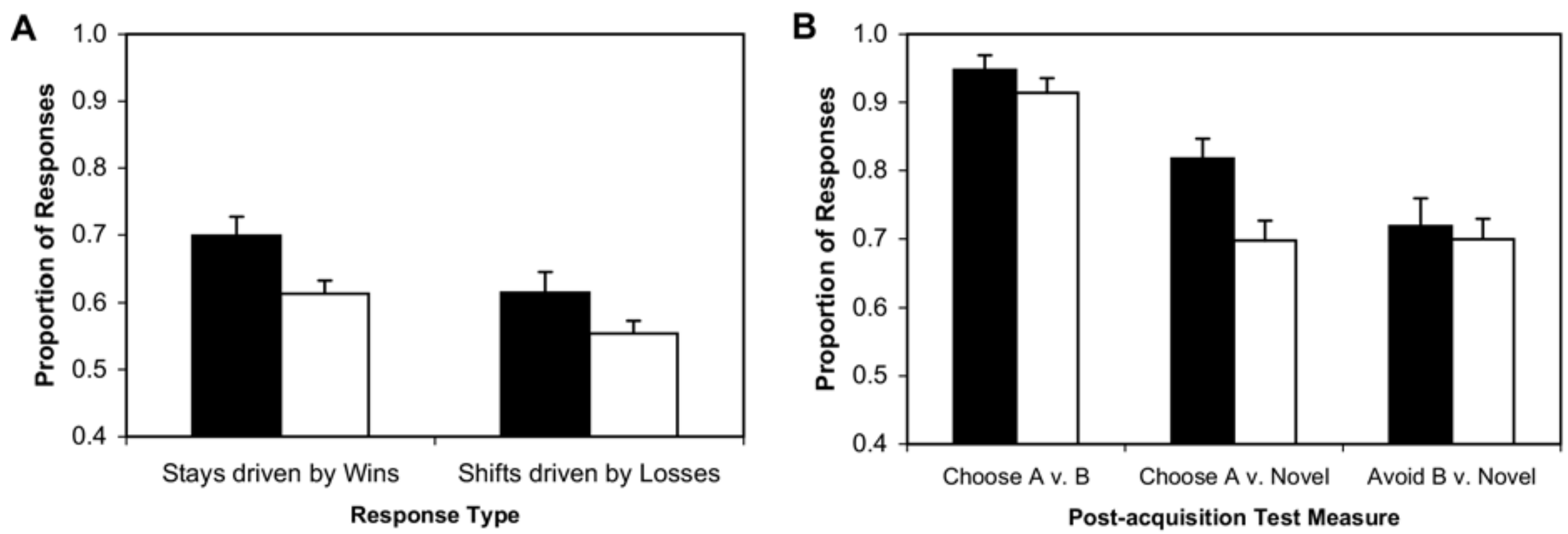
Outline

Depression	Addiction
OCD	Anxiety
Schizophrenia	Parkinson’s
Mood	Metareasoning

Learning from rewards in Sz

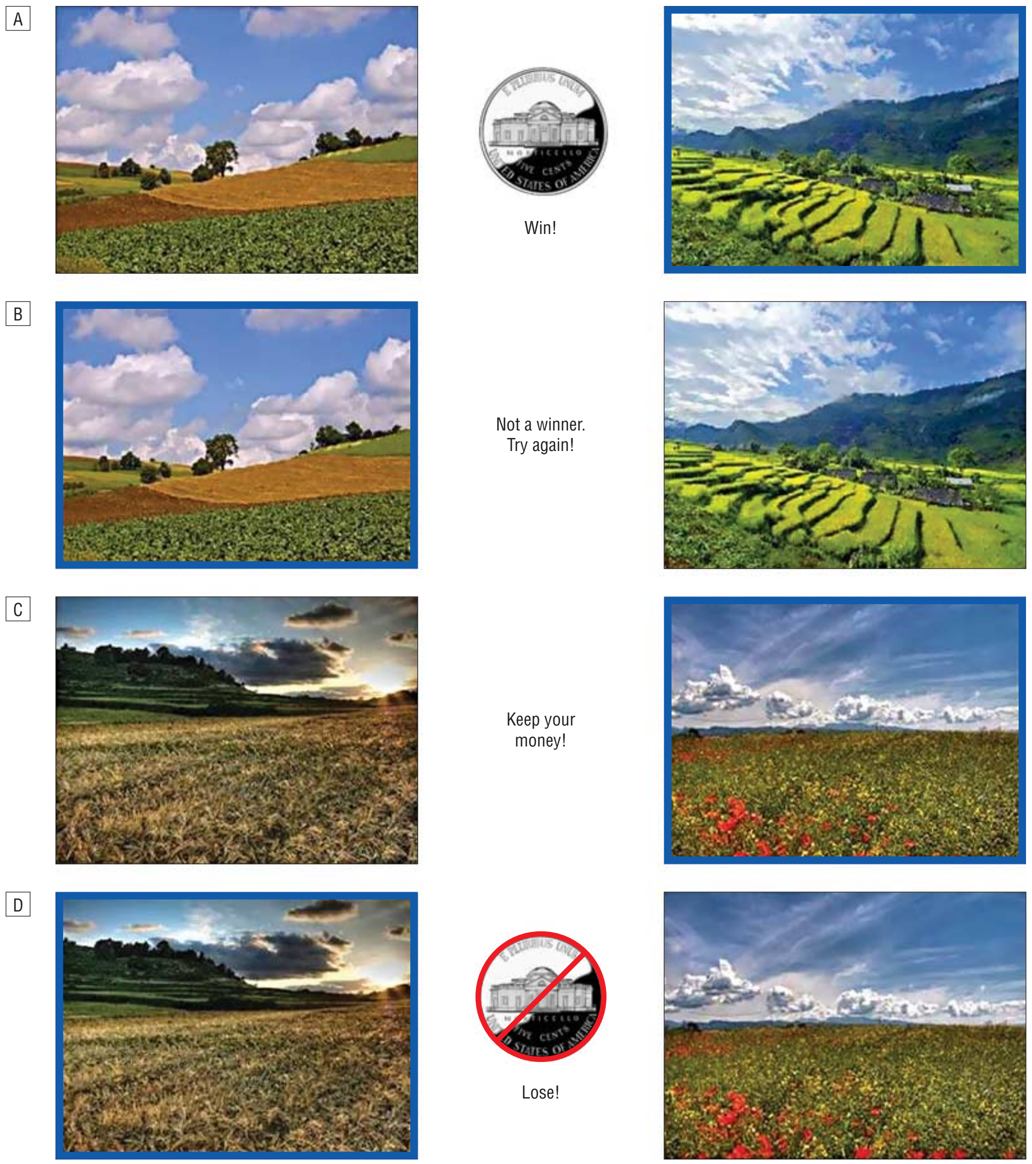
80%	A>>>B	20%
70%	C>>D	30%
60%	E>F	40%

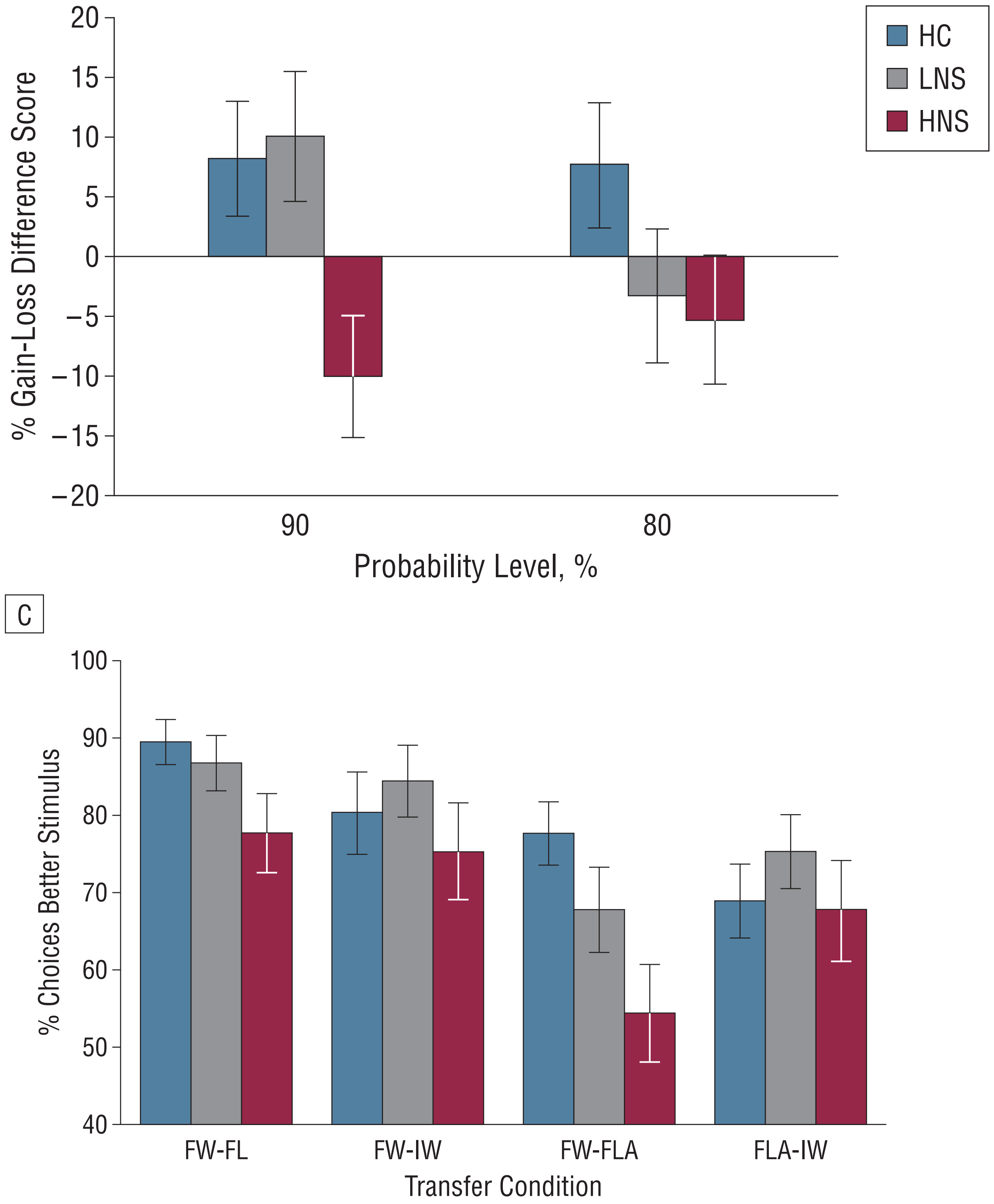
Transfer Pairs	
Go	NoGo
AC	BC
AD	BD
AE	BE
AF	BF



Waltz et al., 2007

Learning from rewards and losses in Sz





Gold et al., 2012

Learning from rewards and losses in Sz

- Q learning to represent value

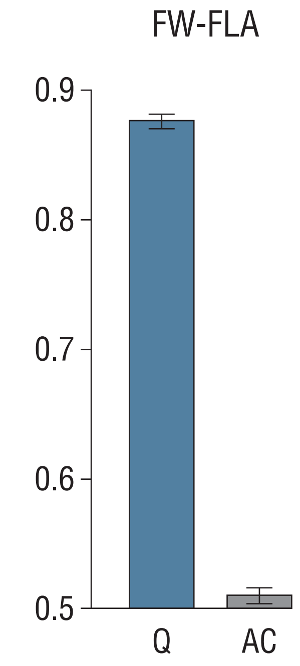
$$\mathcal{Q}_t(s,a) = \mathcal{Q}_{t-1}(s,a) + \alpha(r_t - \mathcal{Q}_{t-1}(s,a))$$

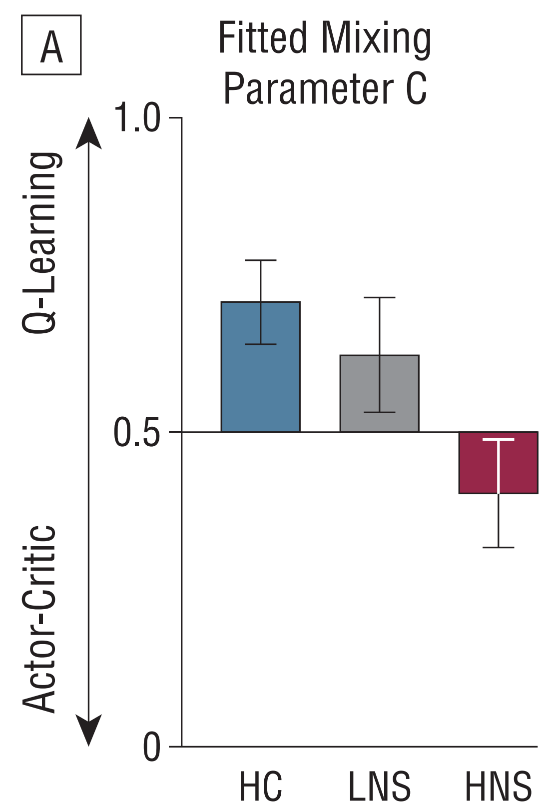
- Actor-critic to represent choice quality independent of value

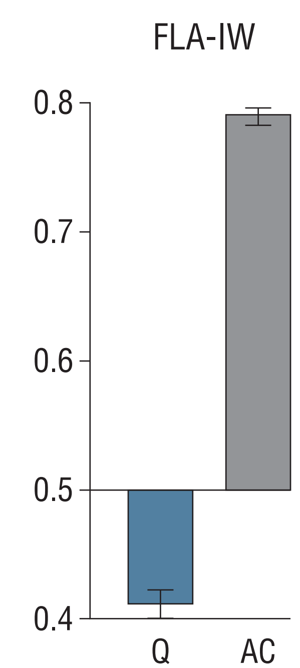
$$\mathcal{V}_t(s) = \mathcal{V}_{t-1}(s) + \alpha\, \delta_t$$

$$\delta_t = r_t - \mathcal{V}_{t-1}(s)$$

$$w_t(a,s) = w_{t-1}(a,s) + \alpha_c\, \delta_t$$

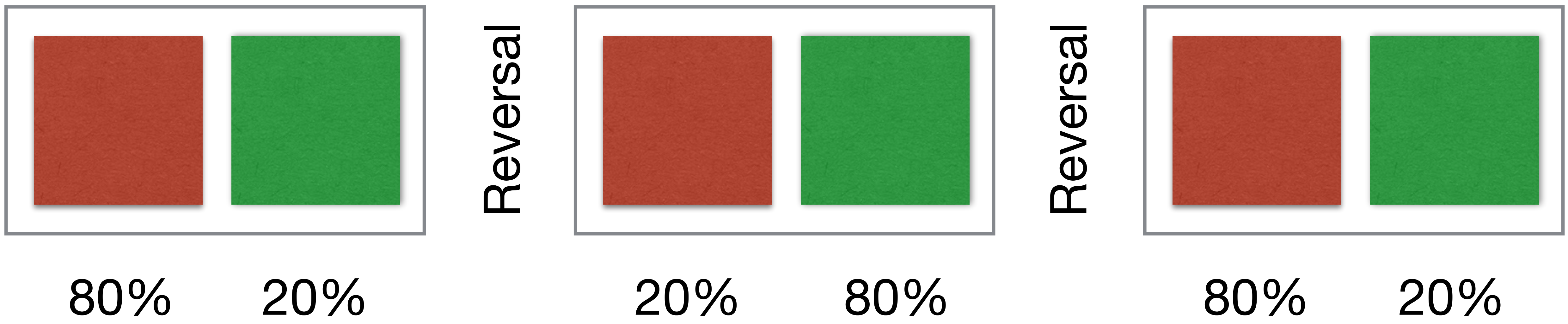


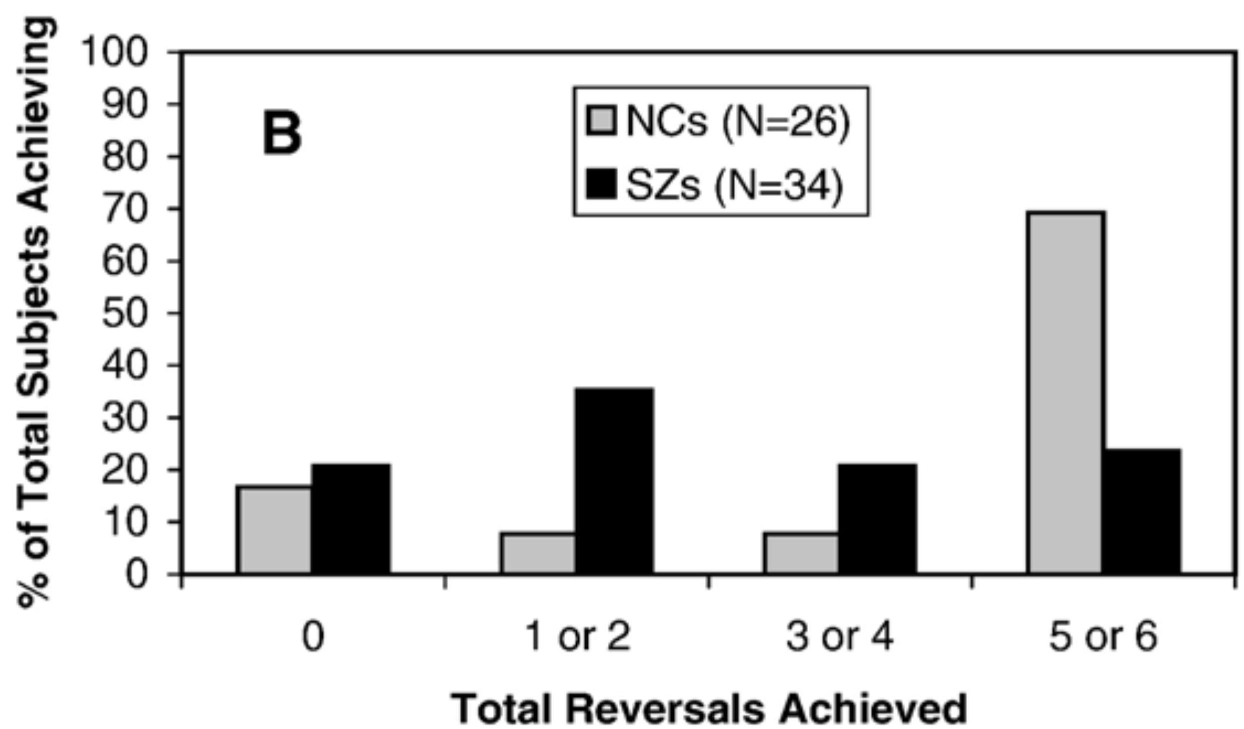




Gold et al., 2012

Reversal learning





Waltz and Gold 2007

Reversal models

- Standard RW Q learning models

$$\mathcal{Q}_t(s,a) = \mathcal{Q}_{t-1}(s,a) + \alpha\,\delta_t$$

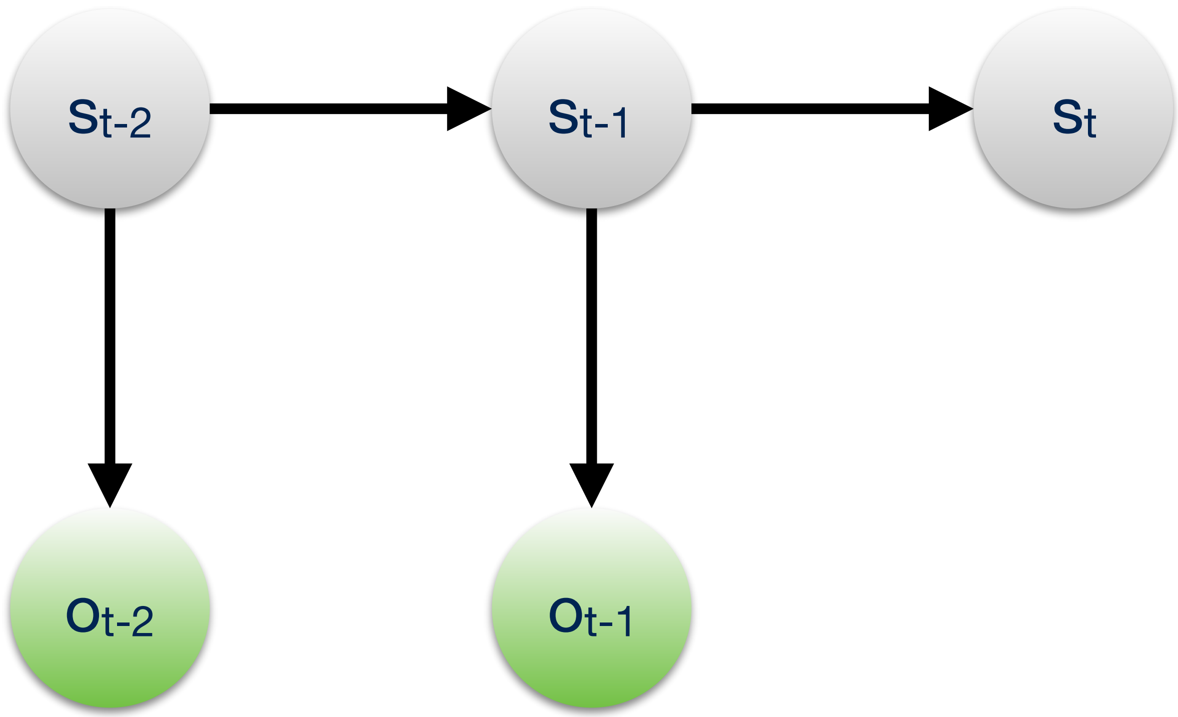
- Double-updated Q learning models

$$\mathcal{Q}_t(s,\bar{a}) = \mathcal{Q}_{t-1}(s,\bar{a}) - \alpha\,\delta_t$$

- Hidden Markov Model
  - captures actual inference
  - allows definition of subjectively informative events

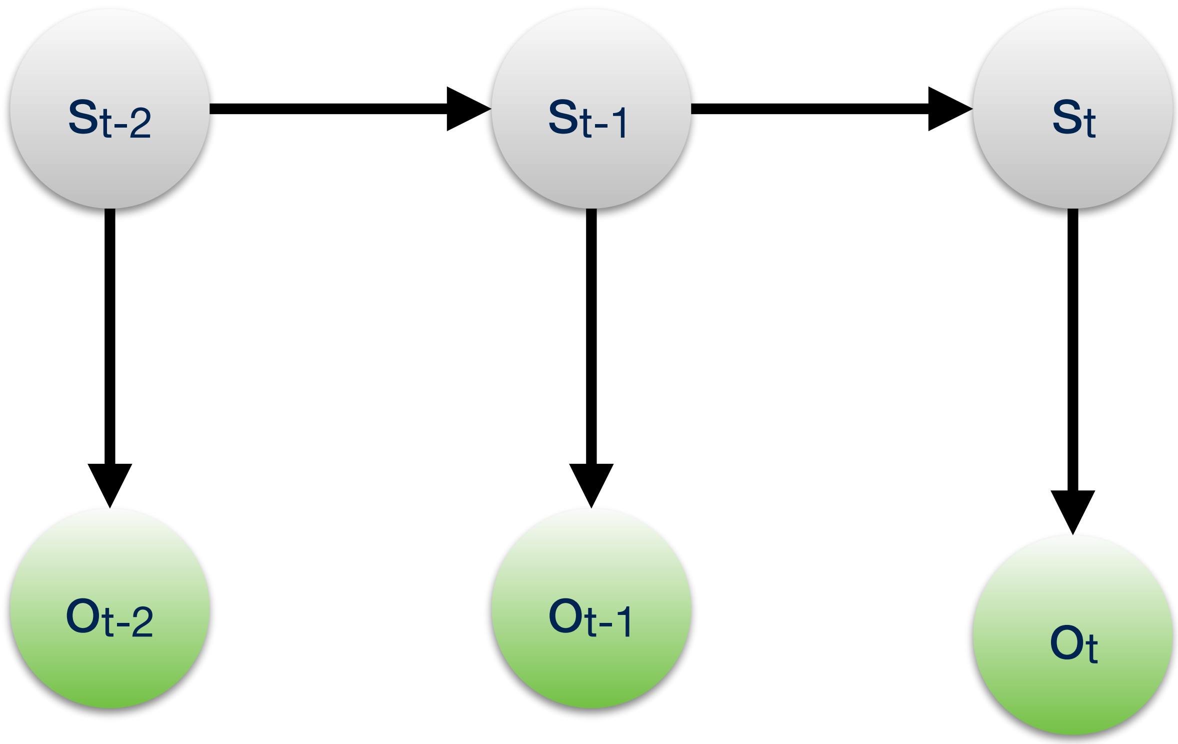
Schlagenhauf et al., 2014

Hidden Markov Model



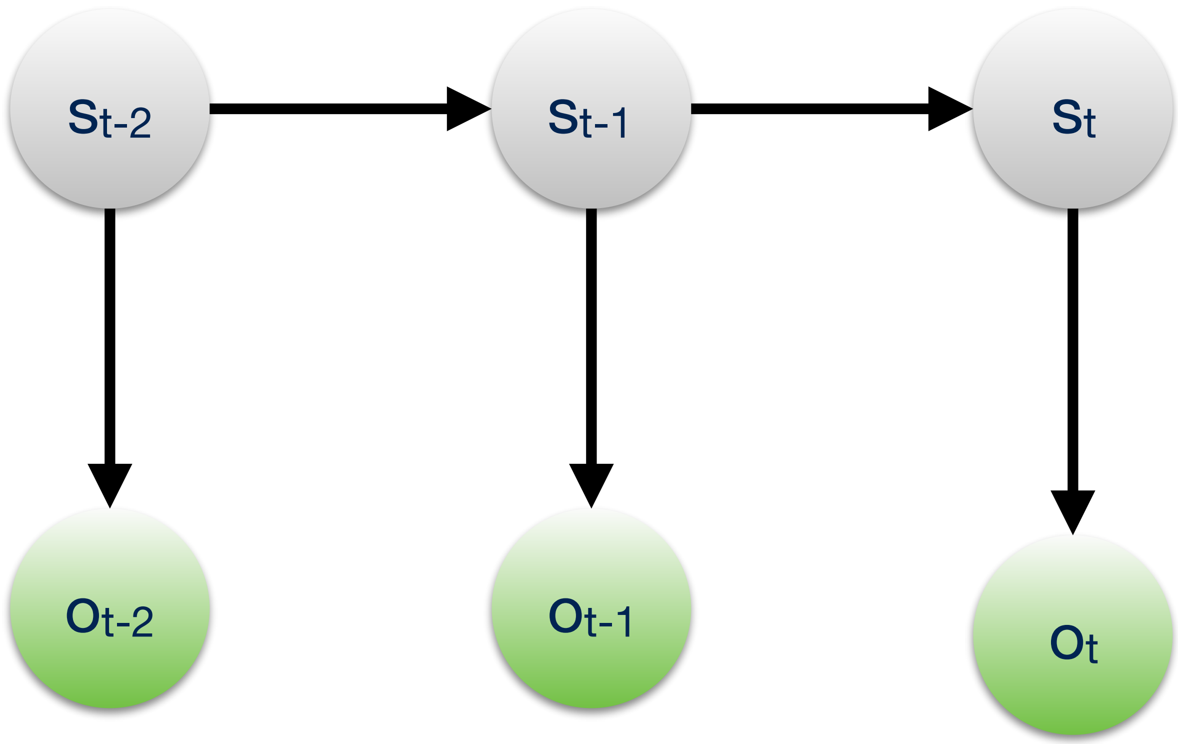
$$p(s_t | o_1, \cdots, o_{t-1})$$

Hidden Markov Model



$$p(s_t | o_1, \cdots, o_{t-1})$$

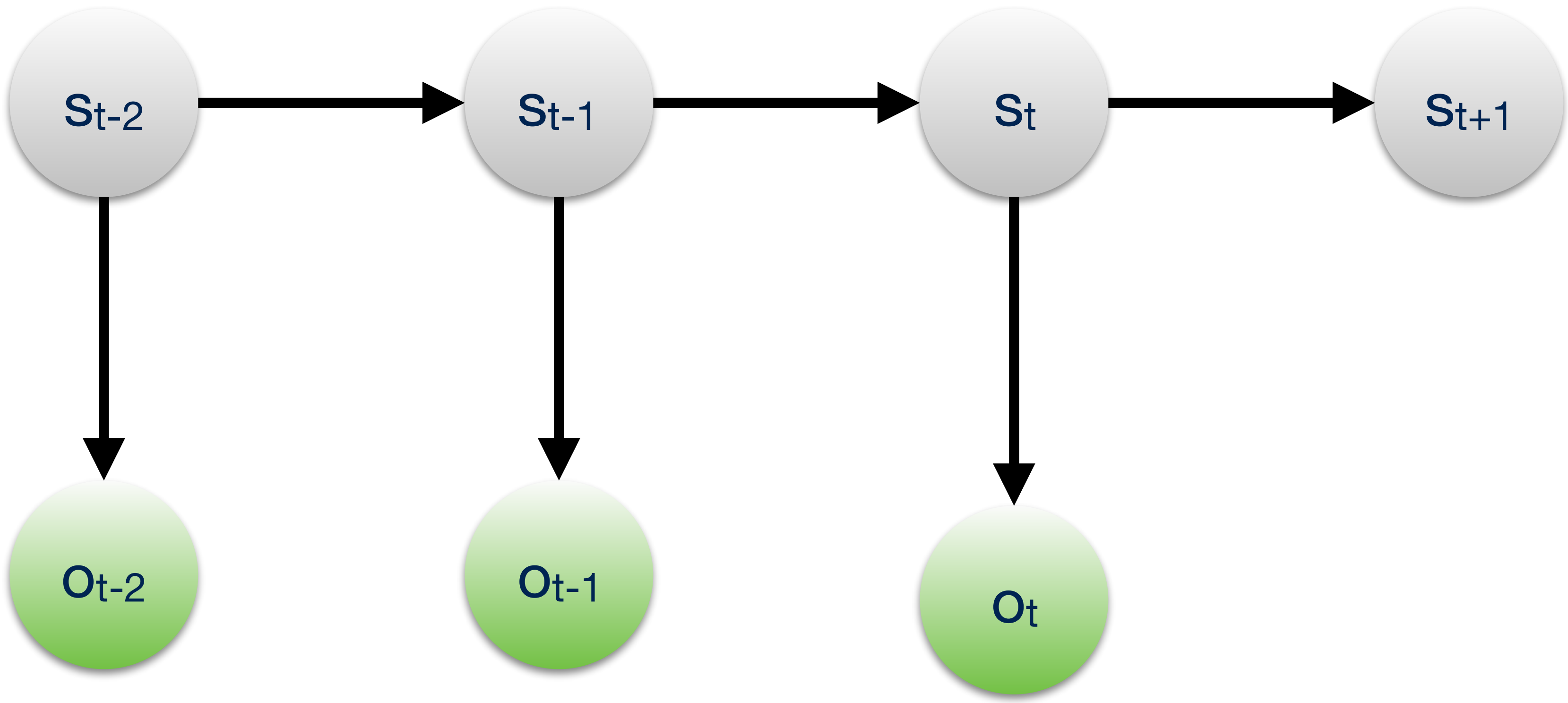
Hidden Markov Model



$$p(s_t|o_1,\cdots,o_{t-1})$$

$$p(s_t|o_1,\cdots,o_t) = \frac{p(o_t|s_t)\,p(s_t|o_1,\cdots,o_{t-1})}{Z}$$

Hidden Markov Model

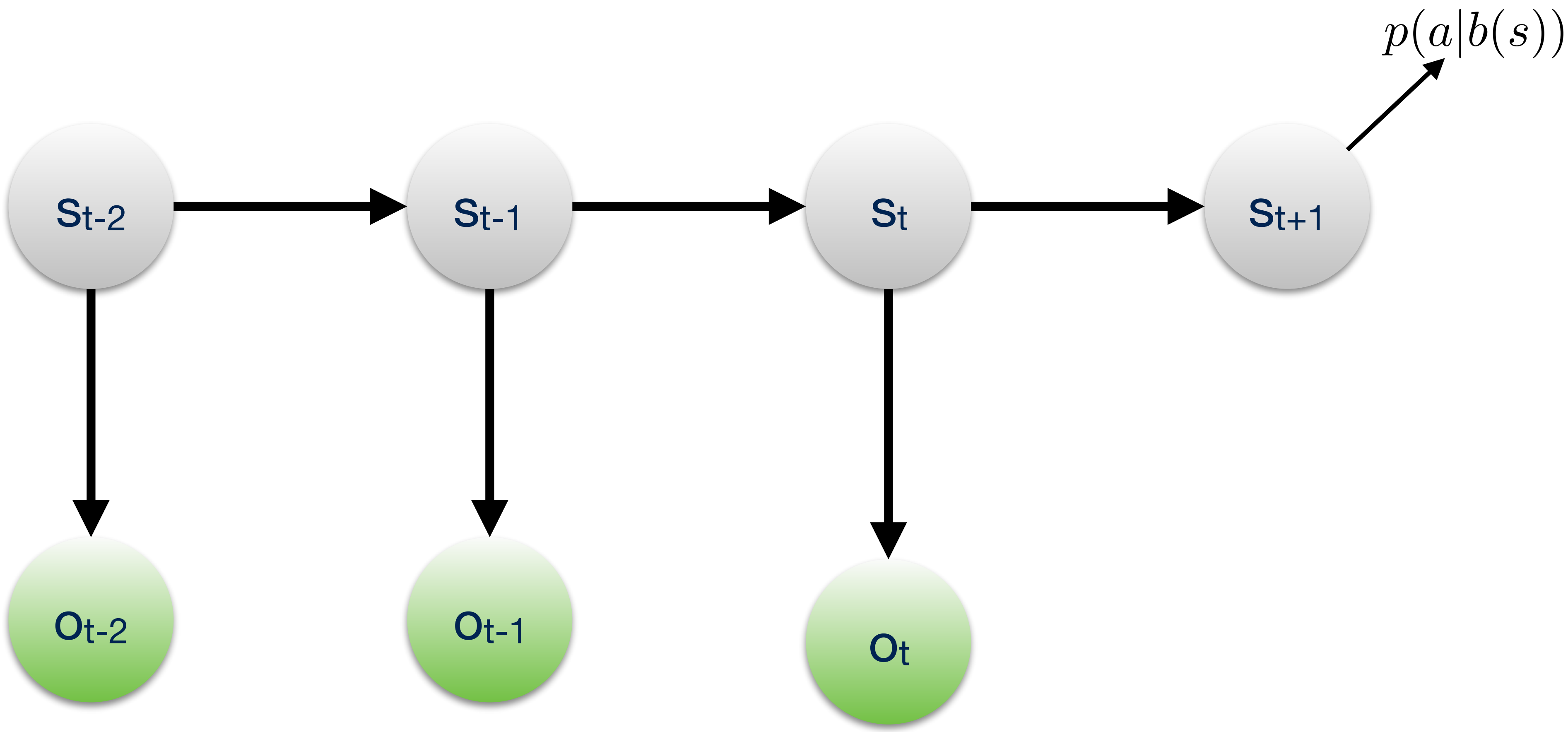


$$p(s_t|o_1,\cdots,o_{t-1})$$

$$p(s_t|o_1,\cdots,o_t) = \frac{p(o_t|s_t)\,p(s_t|o_1,\cdots,o_{t-1})}{Z}$$

$$p(s_{t+1}|o_1,\cdots,o_t) = \sum_s p(s_{t+1}|s)\,p(s|o_1,\cdots,o_t)$$

Hidden Markov Model

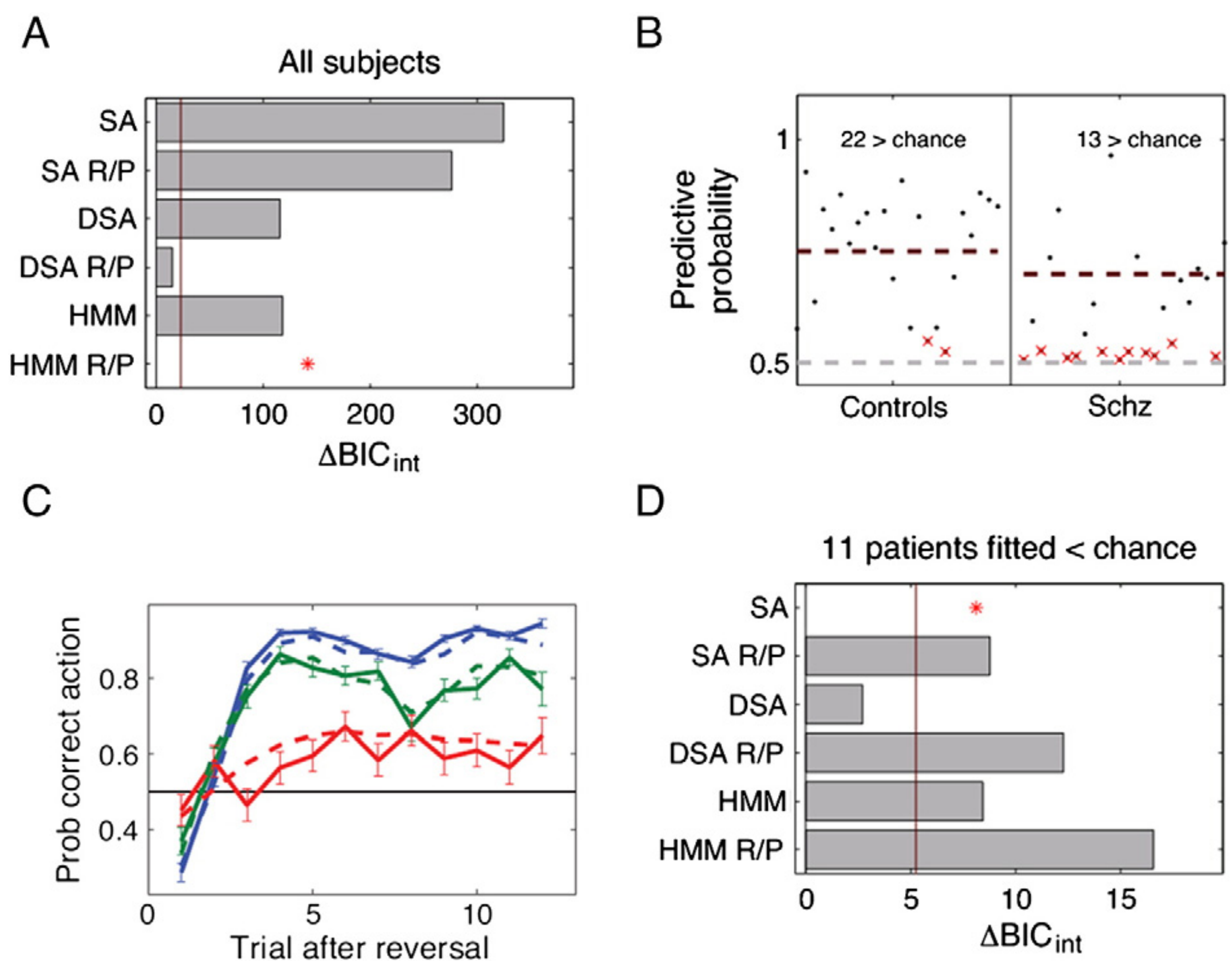


$$p(s_t|o_1,\cdots,o_{t-1})$$

$$p(s_t|o_1,\cdots,o_t) = \frac{p(o_t|s_t)\,p(s_t|o_1,\cdots,o_{t-1})}{Z}$$

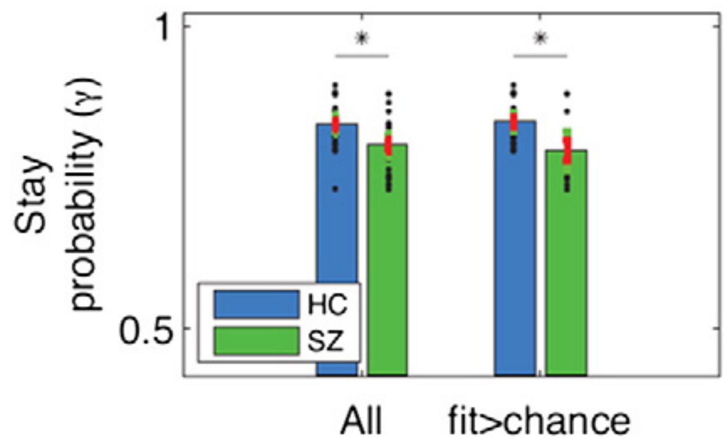
$$p(s_{t+1}|o_1,\cdots,o_t) = \sum_s p(s_{t+1}|s)\,p(s|o_1,\cdots,o_t)$$

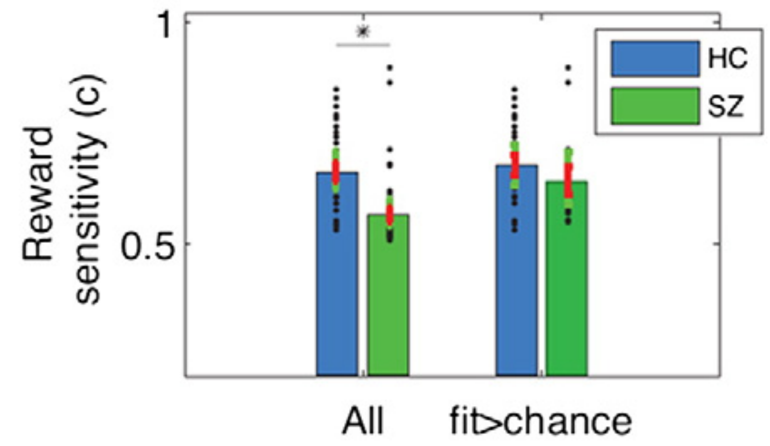
Reversal models



Schlagenhauf et al., 2014

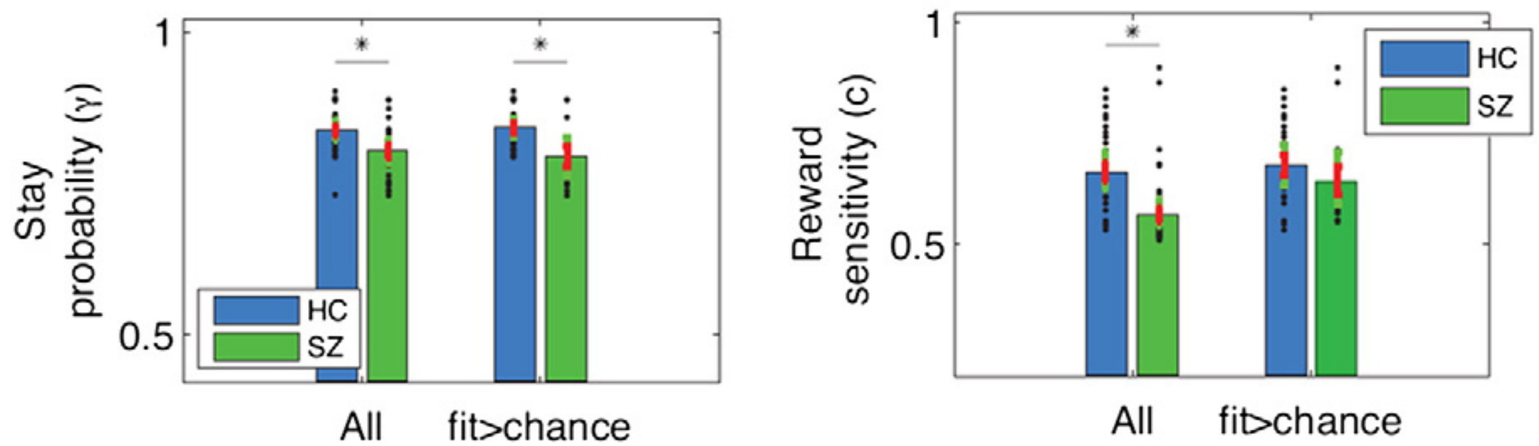
Subjectively informative events

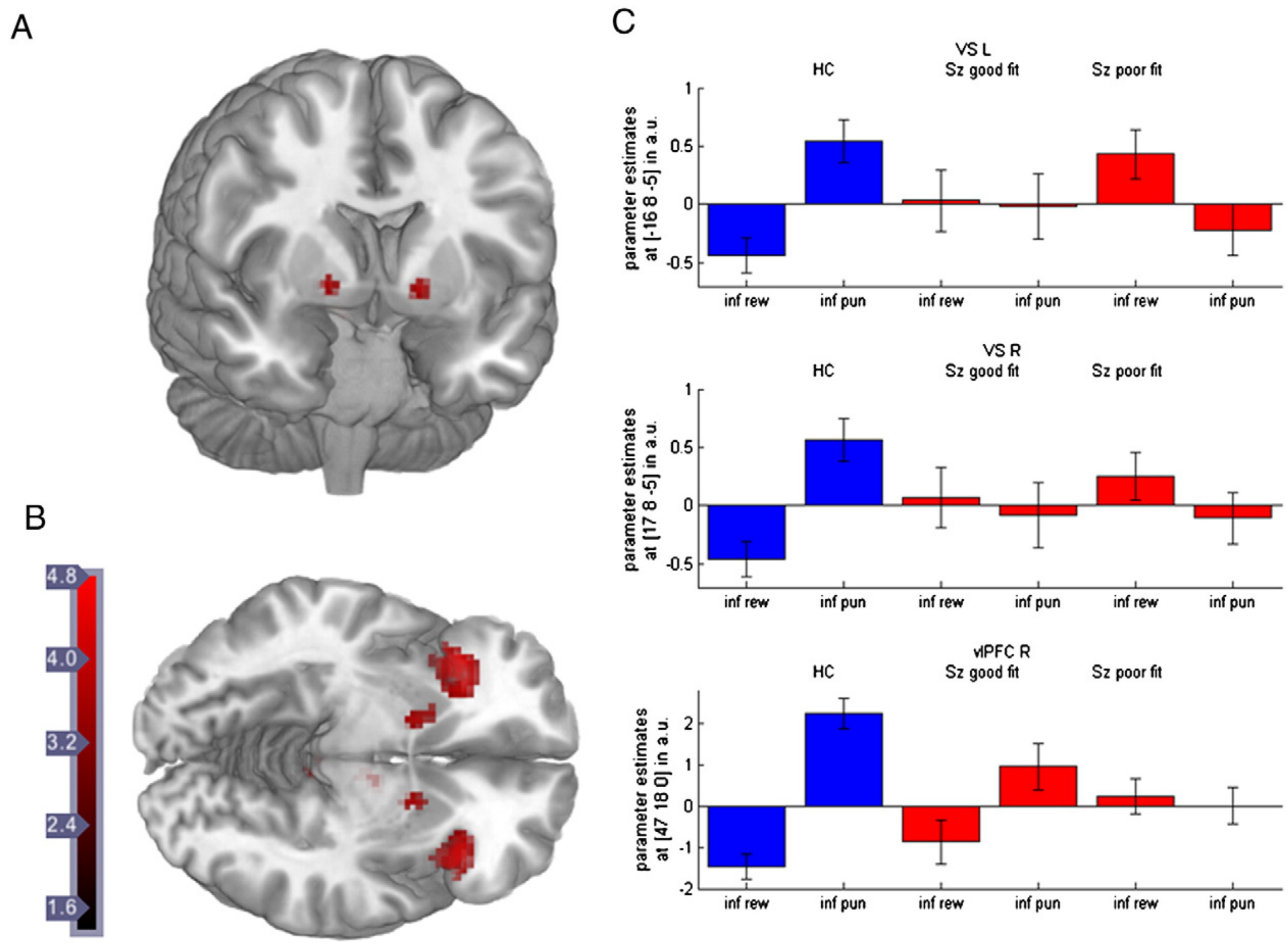




Schlagenhauf et al., 2014

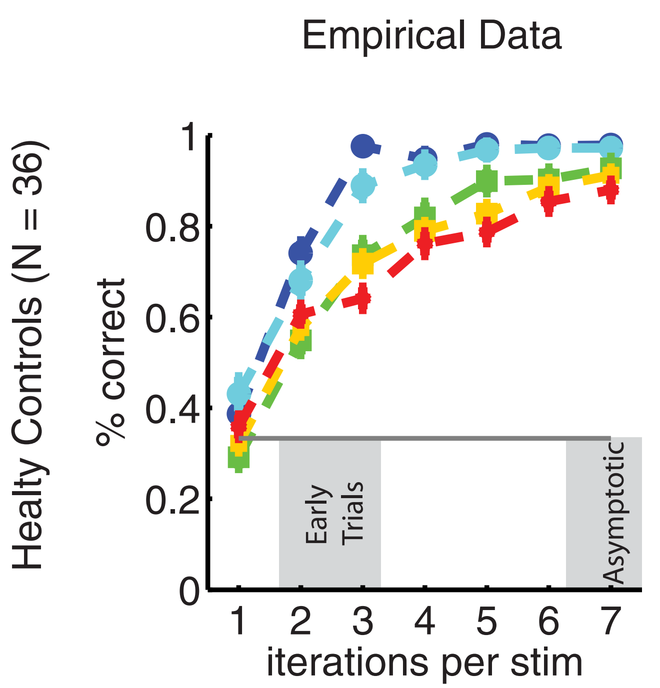
Subjectively informative events

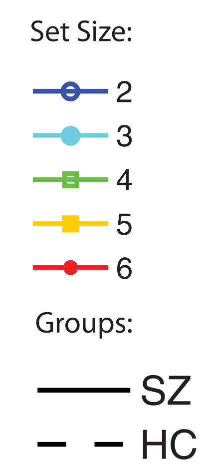




Schlagenhauf et al., 2014

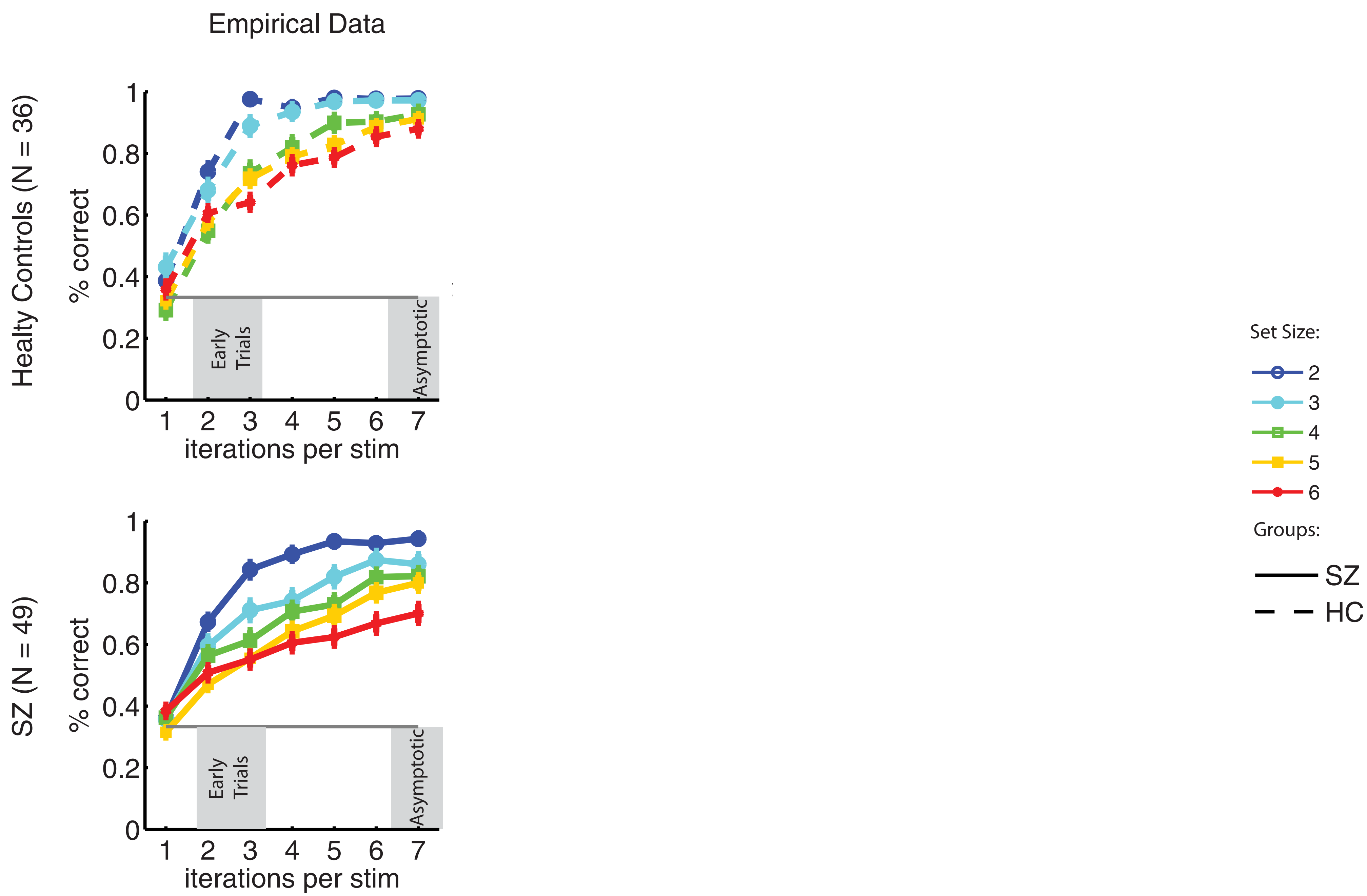
Working memory





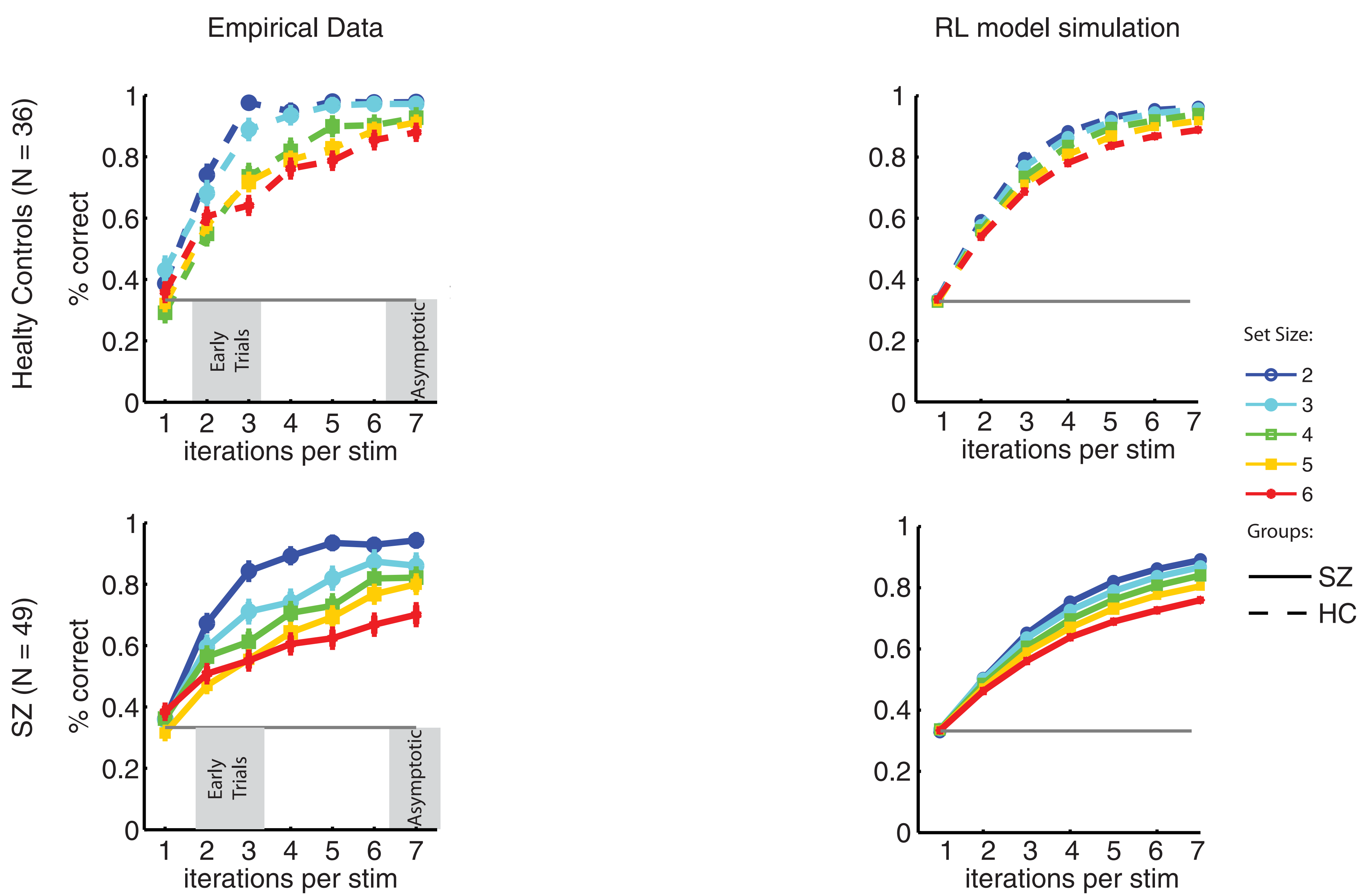
Collins et al., 2014 J Neurosci

Working memory



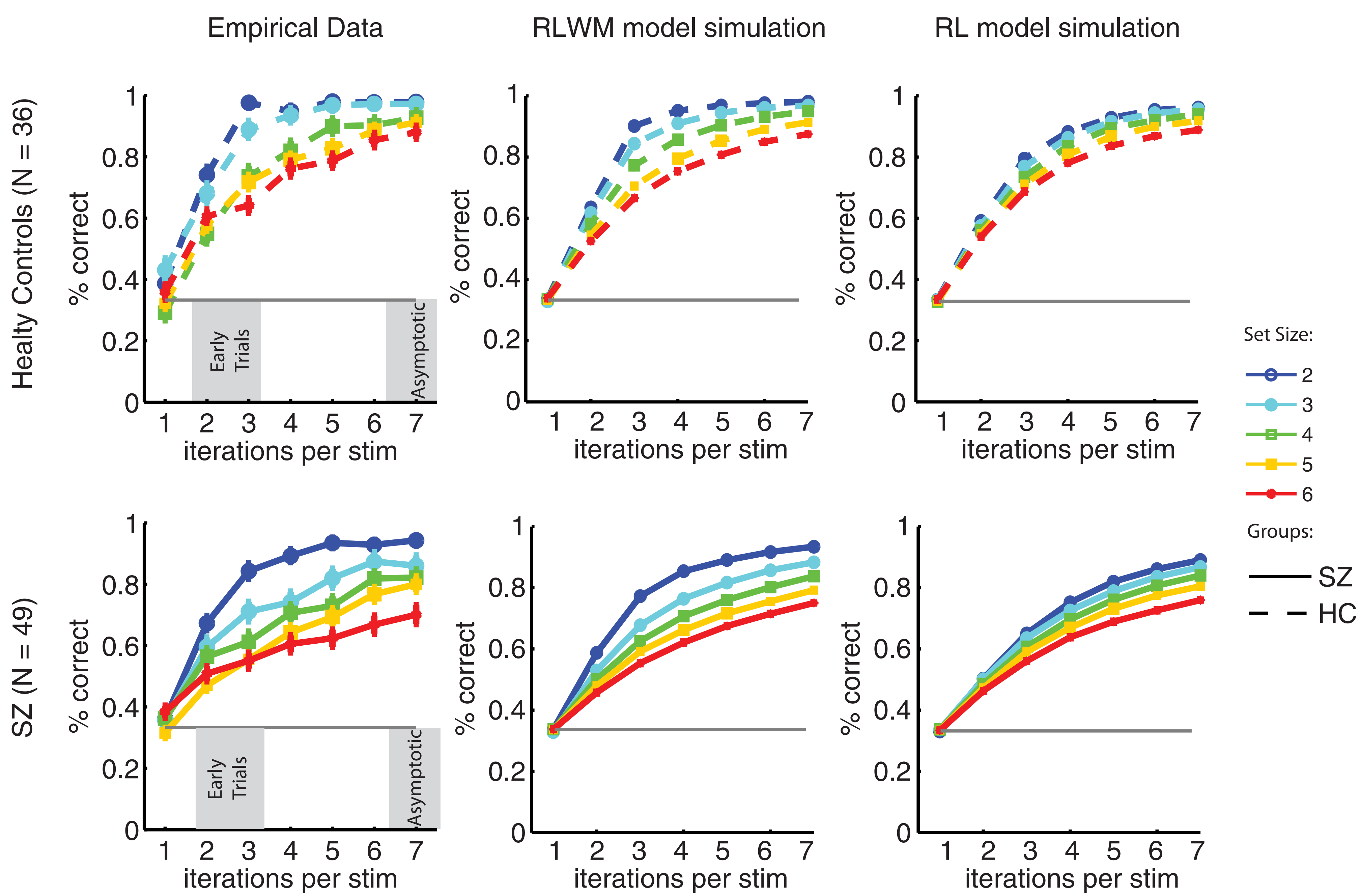
Collins et al., 2014 J Neurosci

Working memory



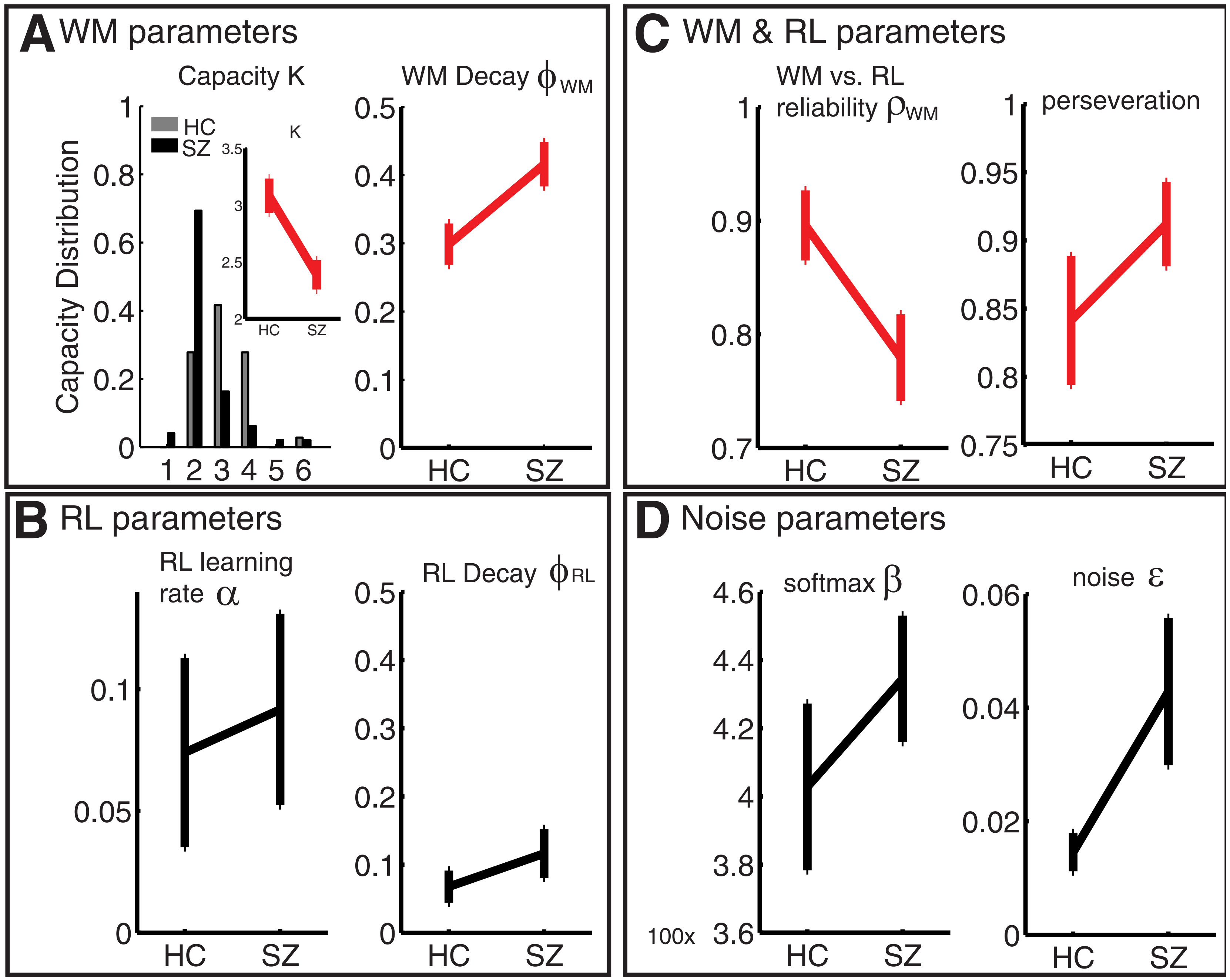
Collins et al., 2014 J Neurosci

Working memory



Collins et al., 2014 J Neurosci

Only working memory is impaired

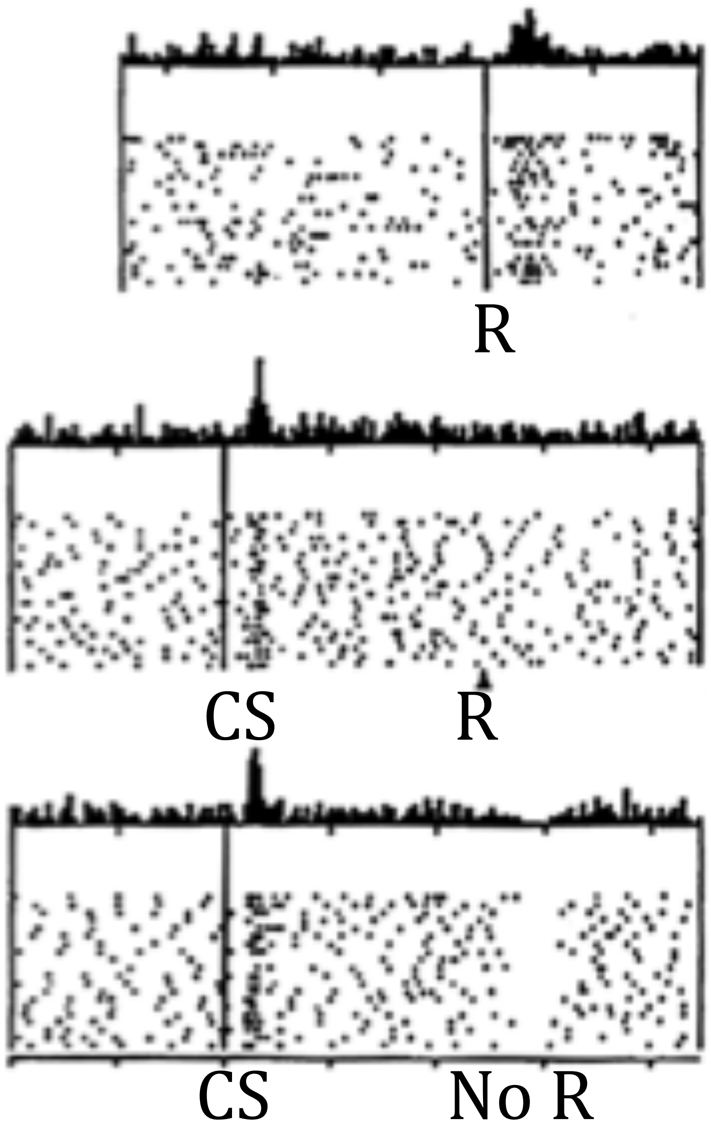


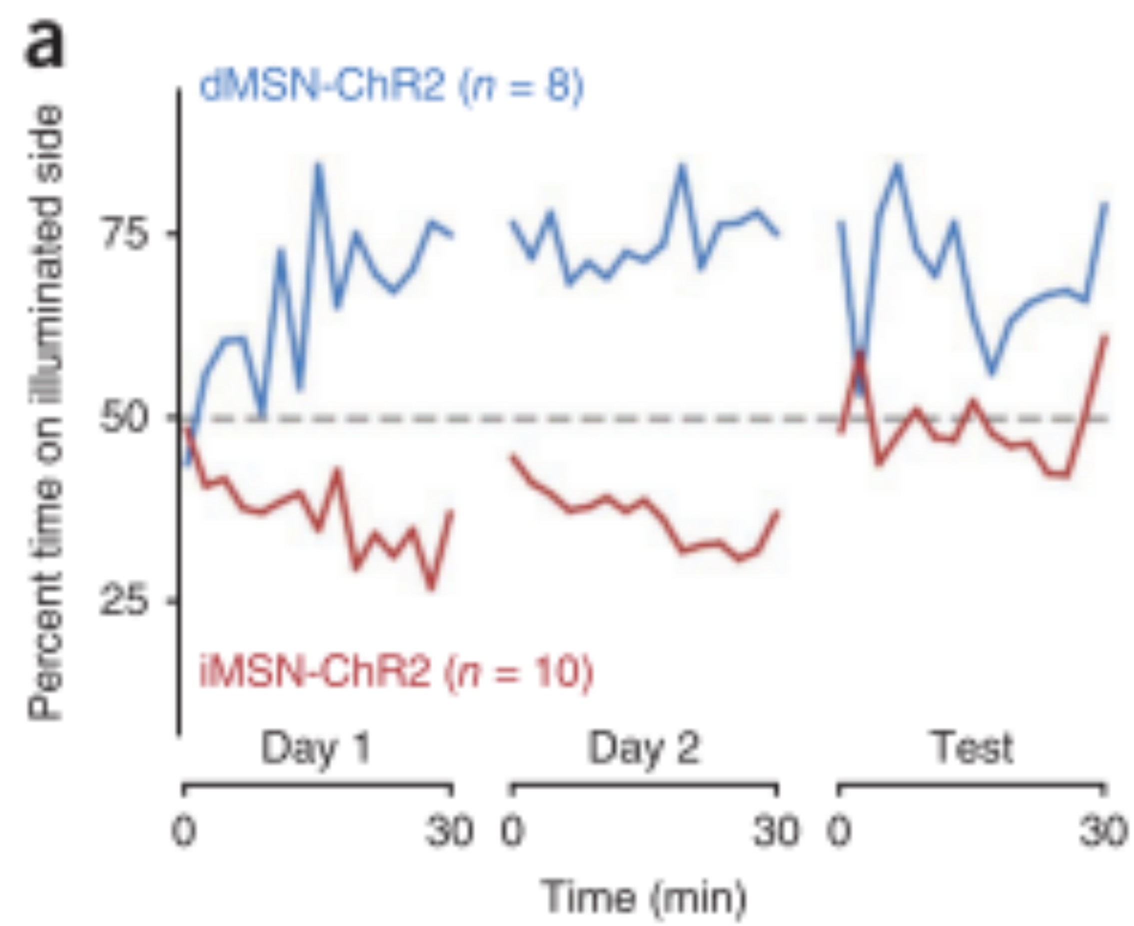
Collins et al., 2014 J Neurosci

Outline

Depression	Addiction
OCD	Anxiety
Schizophrenia	Parkinson’s
Mood	Metareasoning

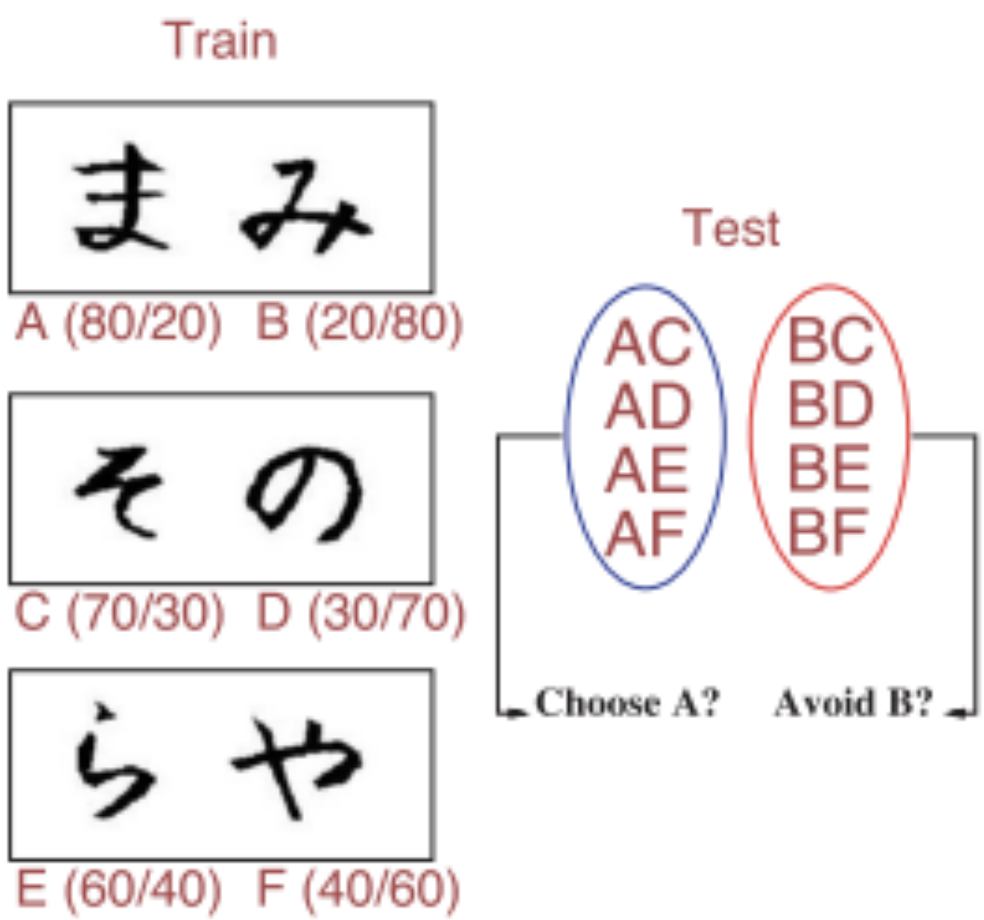
The role of dopamine

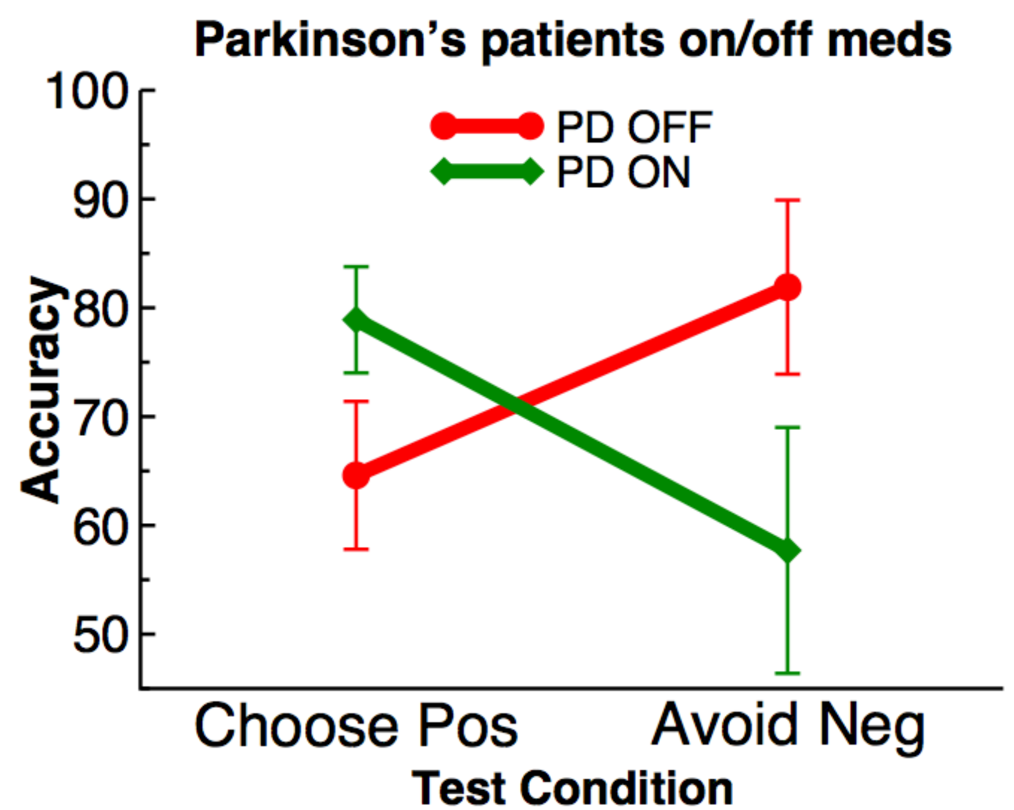




Schultz et al., 1997 Science, Kravitz et al., 2012 Nature

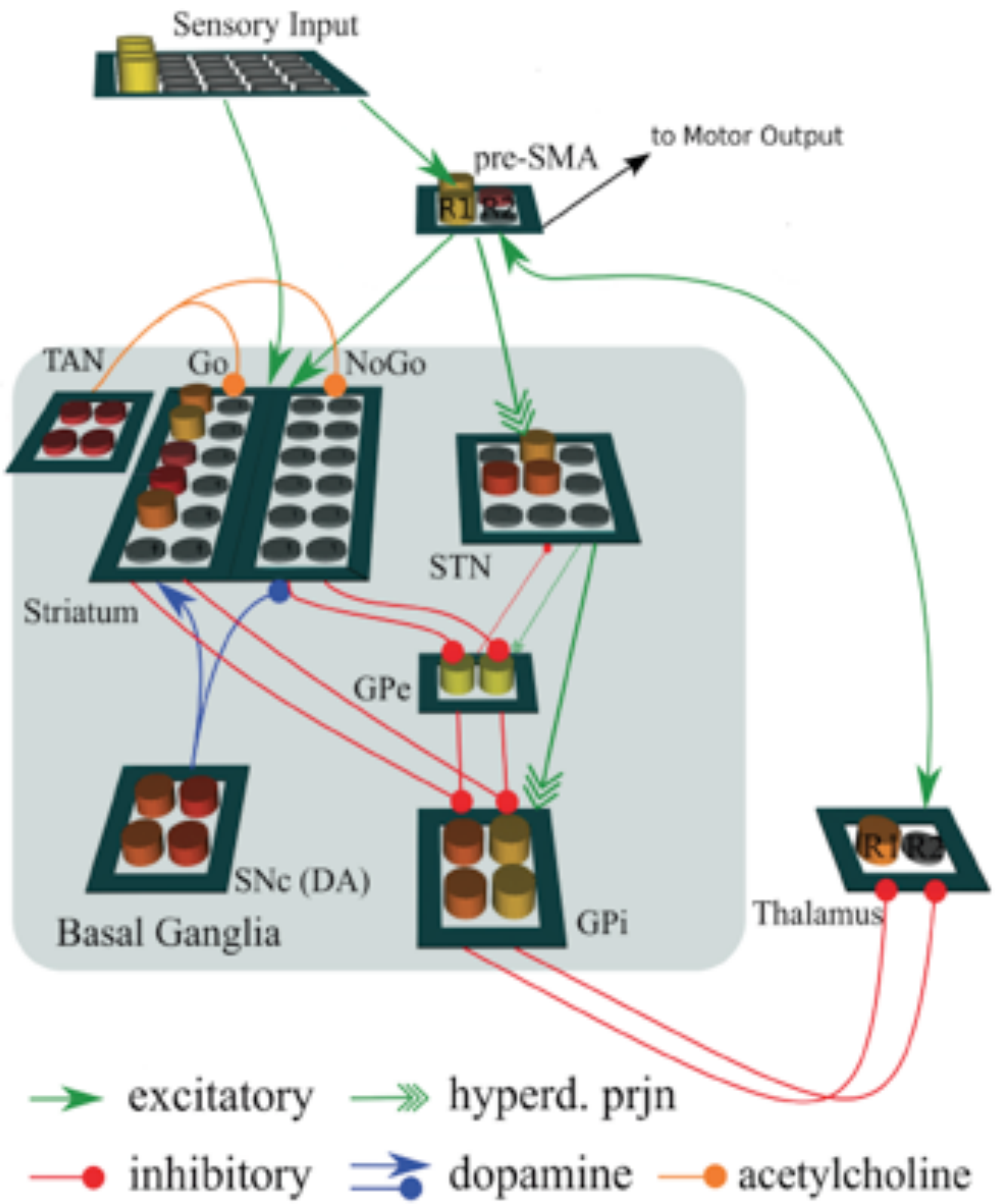
Go and nogo learning





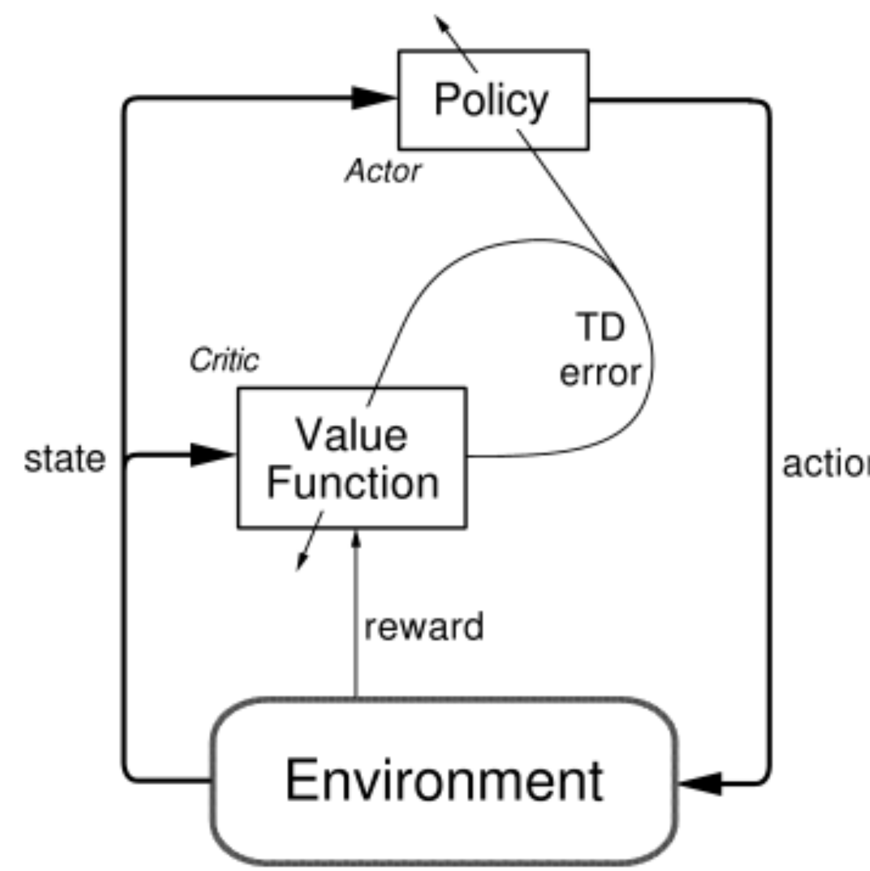
Frank et al., 2004 Science

Neural network model



High DA -> activate Go
Low DA -> release Nogo
from inhibition

RL?



Frank 2005 J Cog Neurosci

OpAL

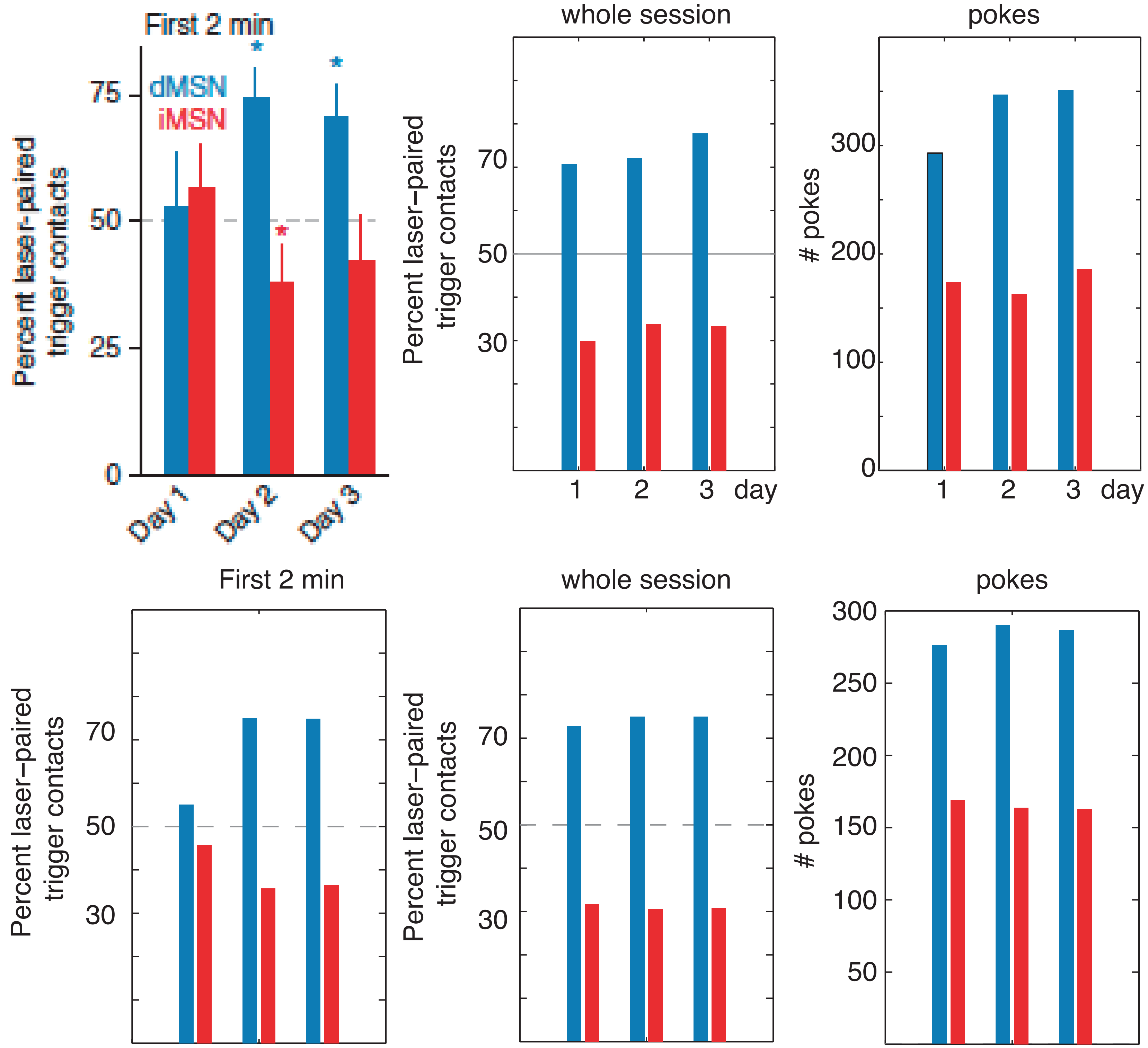
- Critic update:
  - $\delta_t = r_t - Q_t(s, a)$
  - $Q_{t+1}(s,a) = Q_t\,(s,a) + \alpha_C\,\delta_t$
- Actor update:
  - $G_{t+1}(s,a) = G_t(s,a) + \alpha_G \times (+\,\delta) \times G_t(s,a)$
  - $N_{t+1}(s,a) = N_t(s,a) + \alpha_N \times (-\,\delta) \times N_t\,(s,a)$
- Actor choice
  - $Act(s,a) = \beta_G\,G(s,a) \;-\; \beta_N\,N(s, a)$
  - $P(a \mid s) = \quad softmax(Act(s,a))$

Collins and Frank Psych Review 2014

OpAL

Experimental Results

OpAL Simulations



Collins and Frank Psych Review 2014

Effects OpAL captures

- Learning
- Performance
- Vigor
- Interactions

Outline

Depression

Addiction

OCD

Anxiety

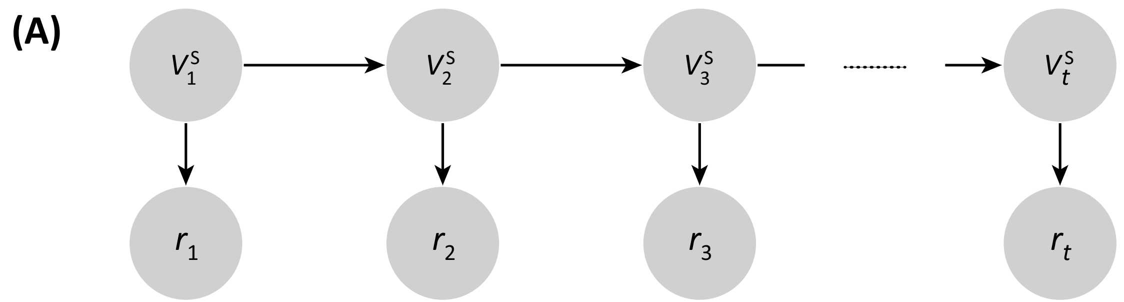
Schizophrenia

Parkinson's

Mood

Metareasoning

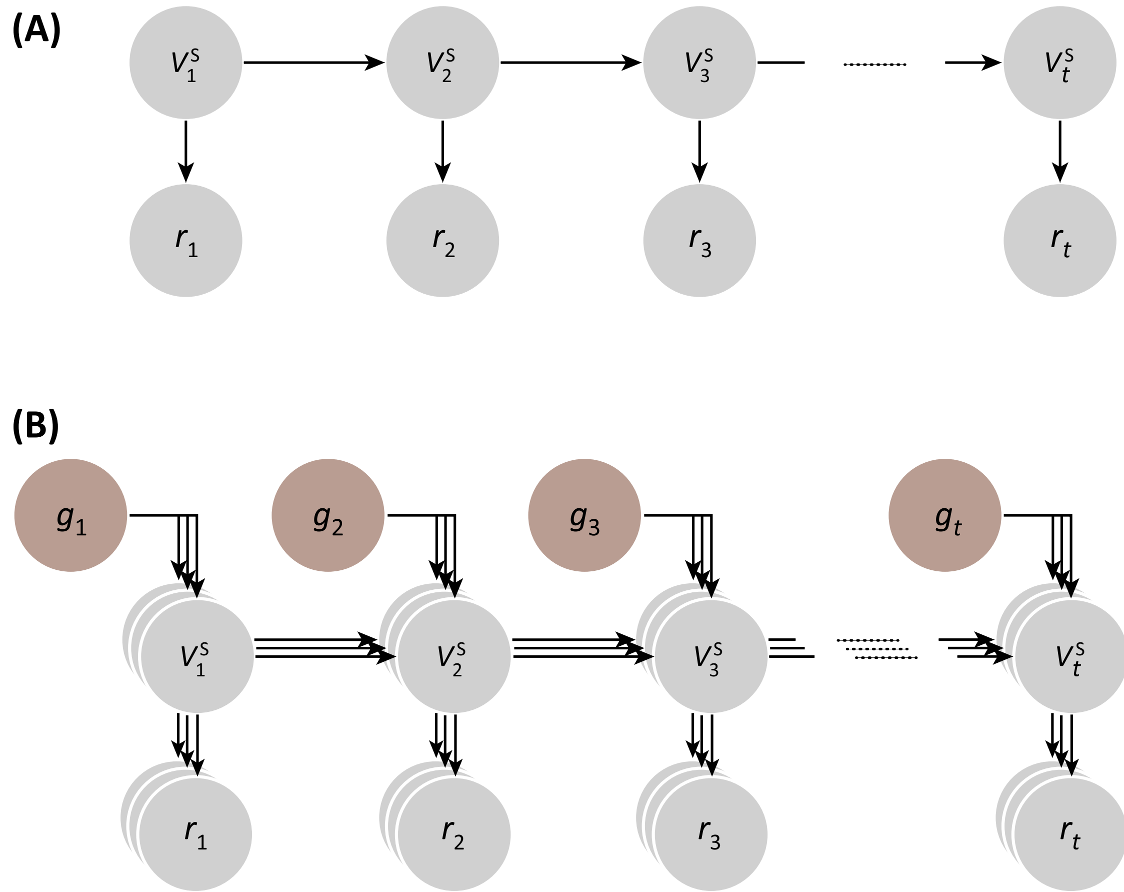
Mood as generalization / momentum



$$\mathcal{V}_t(s) = \mathcal{V}_{t-1}(s) + \alpha(r_t - \mathcal{V}_{t-1}(s))$$

Eldar et al., 2016 TICS

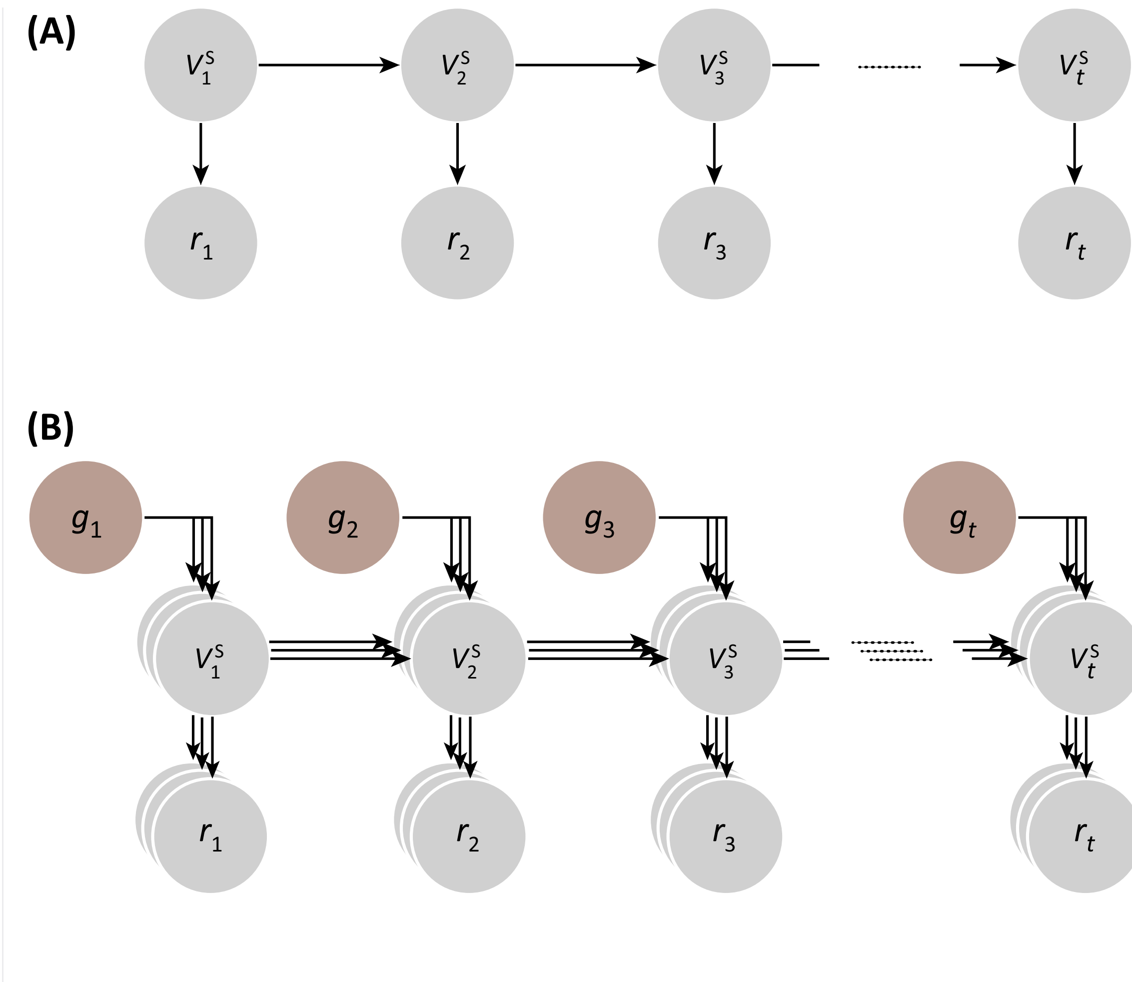
Mood as generalization / momentum



$$\mathcal{V}_t(s) = \mathcal{V}_{t-1}(s) + \alpha(r_t - \mathcal{V}_{t-1}(s))$$

Eldar et al., 2016 TICS

Mood as generalization / momentum

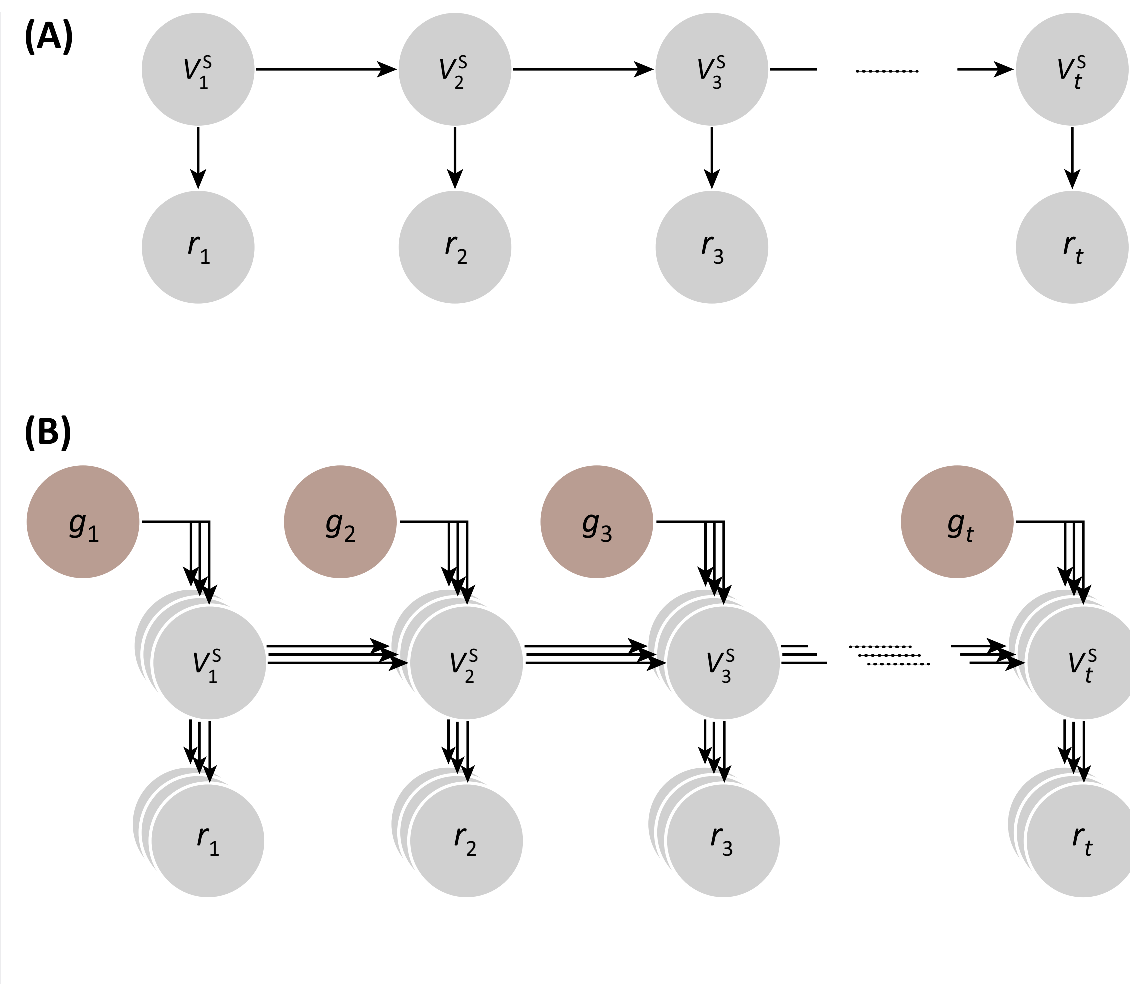


$$\mathcal{V}_t(s) = \mathcal{V}_{t-1}(s) + \alpha(r_t - \mathcal{V}_{t-1}(s))$$

$$m_{t=1} = m_t + \alpha'_t((r_t - \mathcal{V}_t(s)) - m_t)$$

Eldar et al., 2016 TICS

Mood as generalization / momentum



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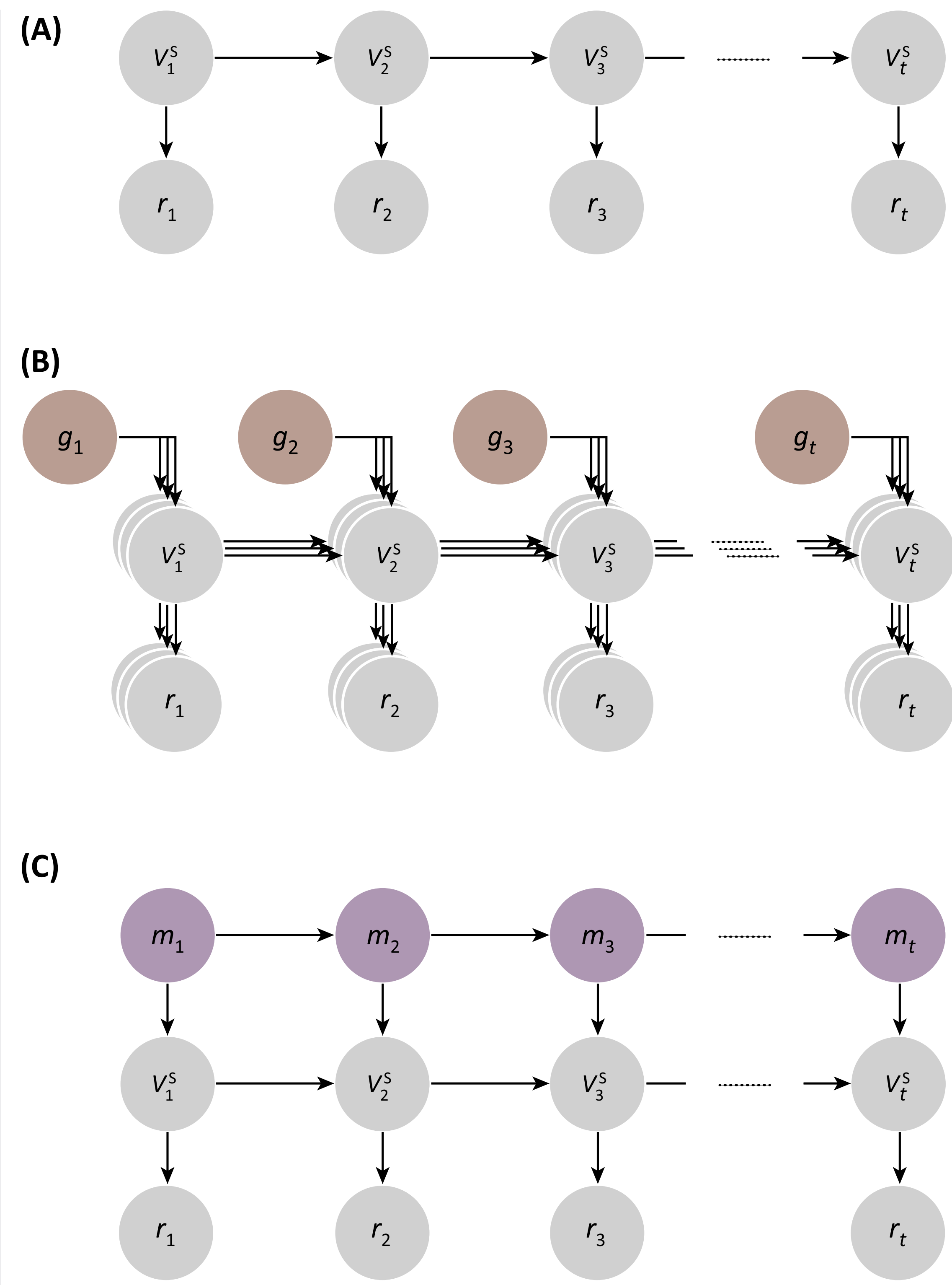
$$m_{t=1} = m_t + \alpha'_t((r_t - \mathcal{V}_t(s)) - m_t)$$

$$\mathcal{V}_t(s) = \mathcal{V}_{t-1}(s) + \alpha(f * m_{t-1} + r_t - \mathcal{V}_{t-1}(s))$$

Eldar et al., 2016 TICS

Mood as generalization / momentum



$$\mathcal{V}_t(s) = \mathcal{V}_{t-1}(s) + \alpha(r_t - \mathcal{V}_{t-1}(s))$$

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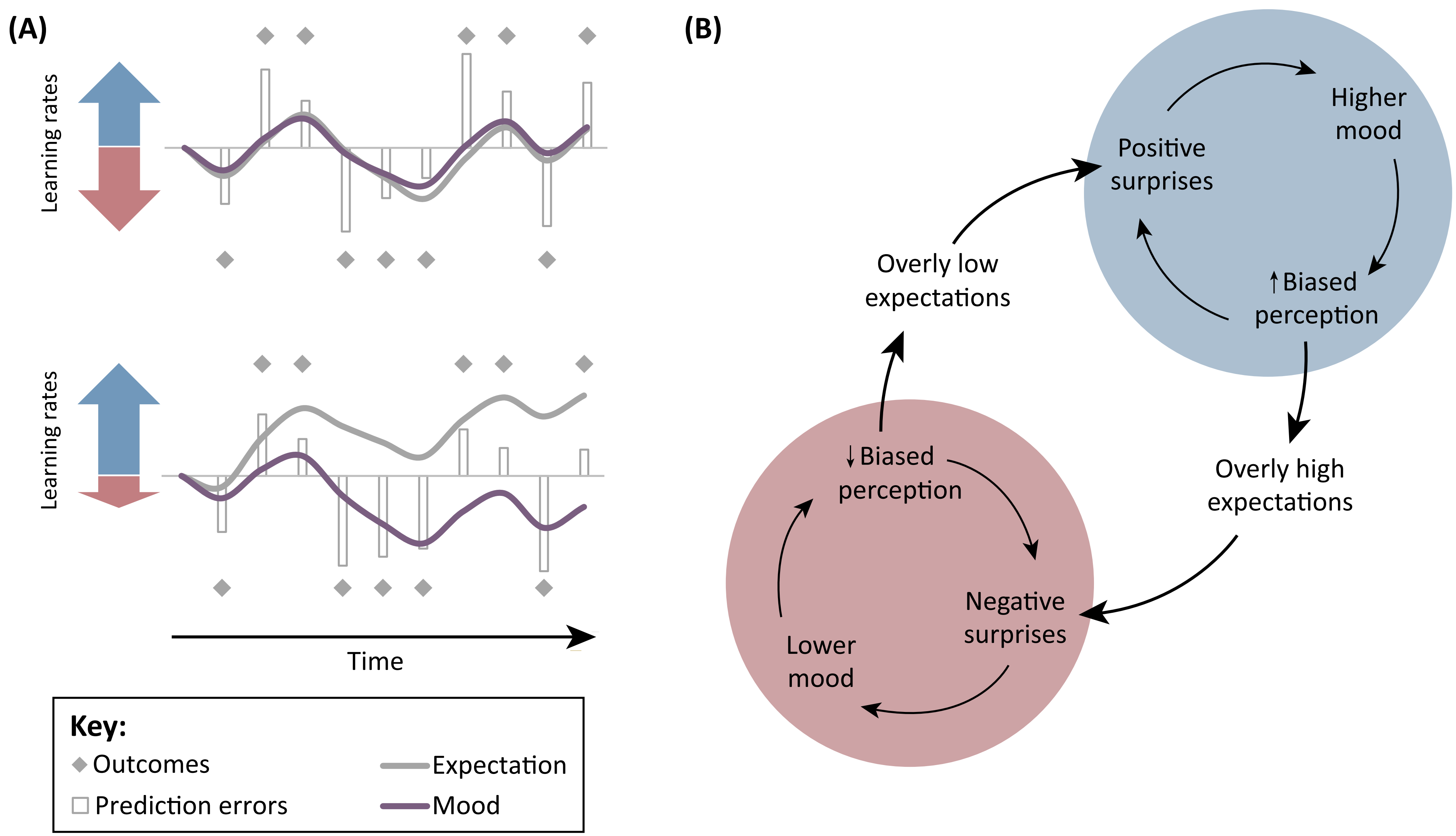
$$\mathcal{V}_t(s) = \mathcal{V}_{t-1}(s) + \alpha(f * m_{t-1} + r_t - \mathcal{V}_{t-1}(s))$$

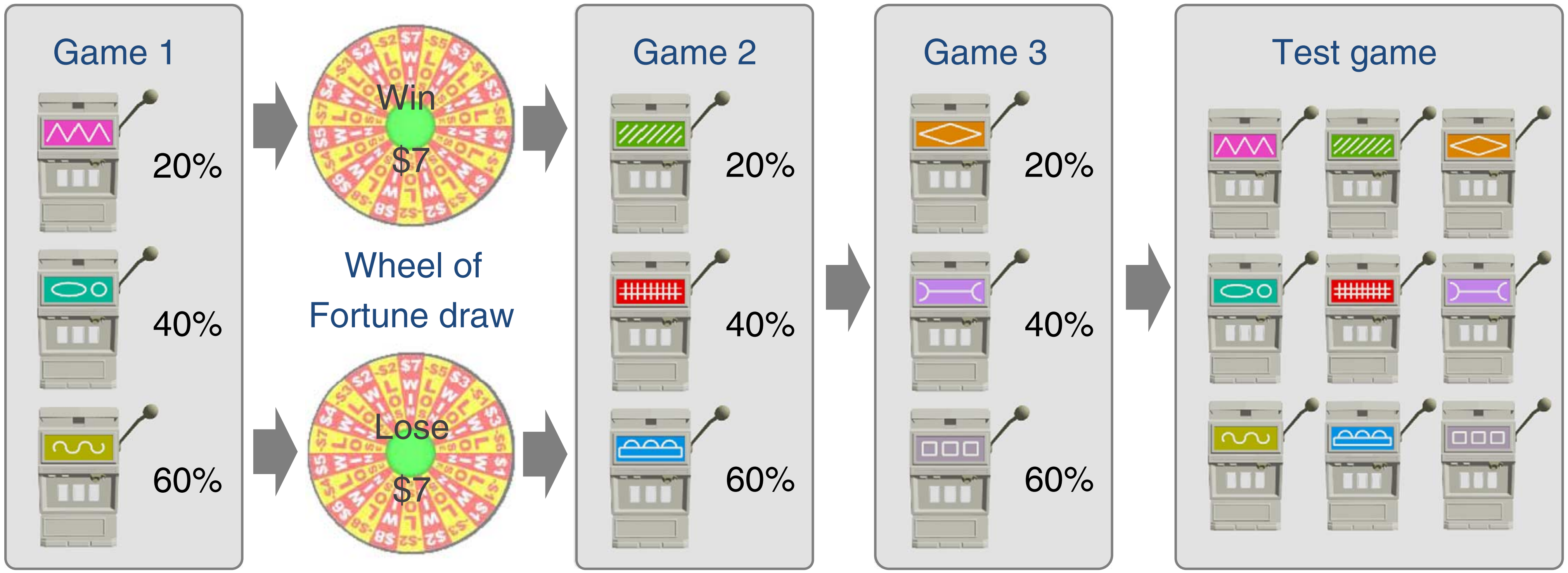
Eldar et al., 2016 TICS

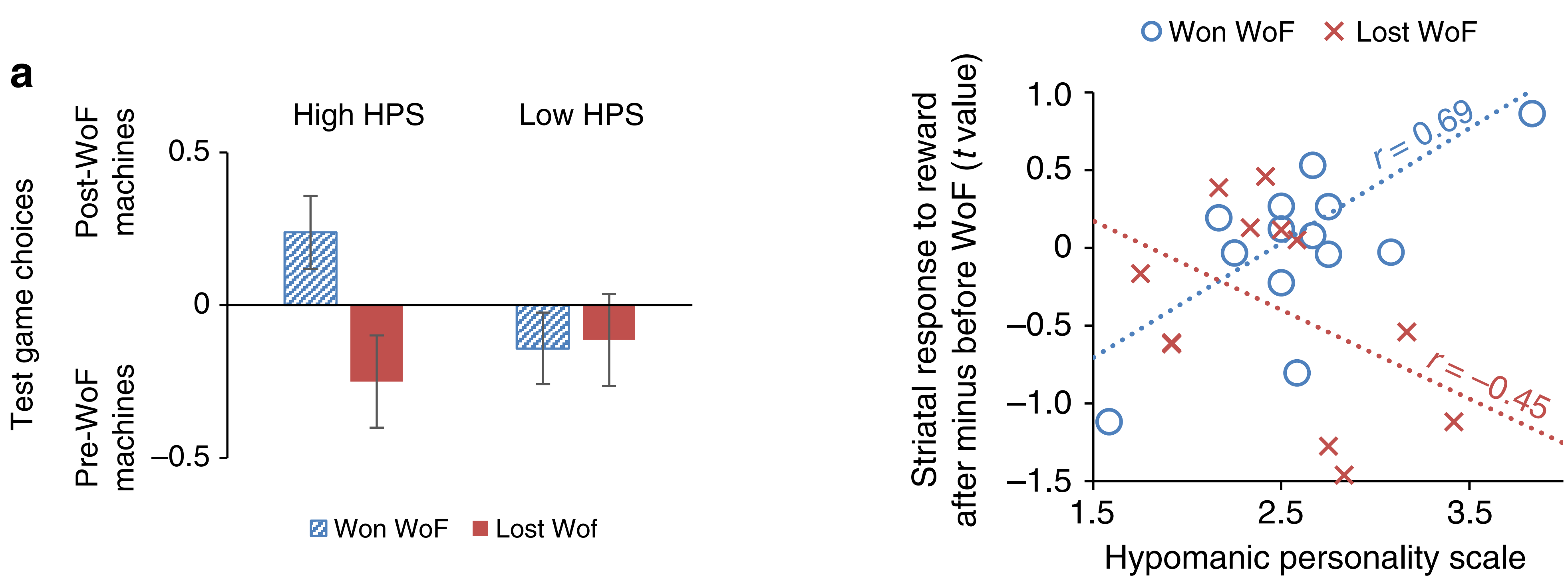
Mood fluctuations



Eldar et al., 2016 TICS

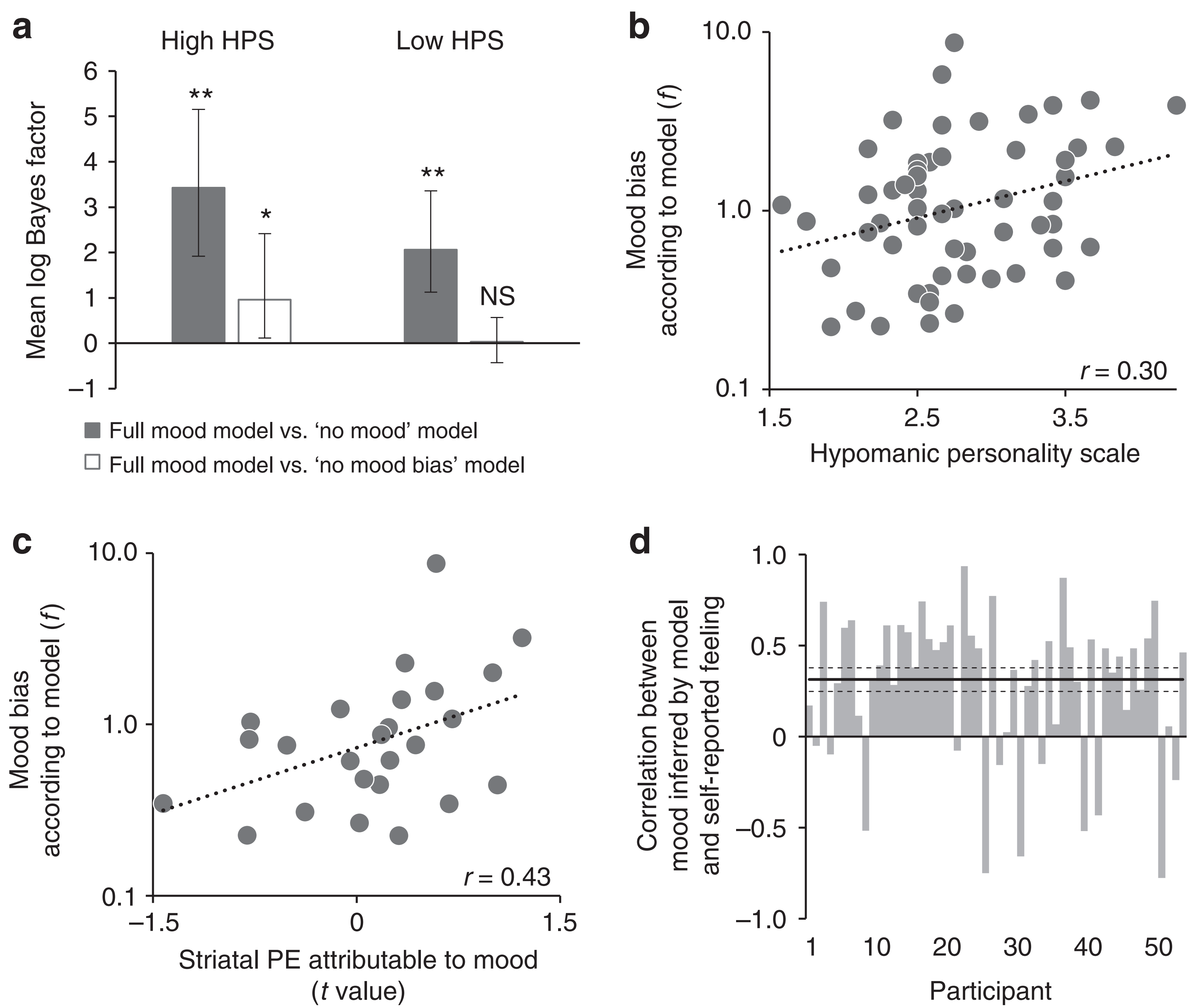
Reinforcer interaction





Eldar et al., 2015 Nat. Comm.

Momentum captures changes in reward



Eldar et al., 2015 Nat. Comm.

Outline

Depression

Addiction

OCD

Anxiety

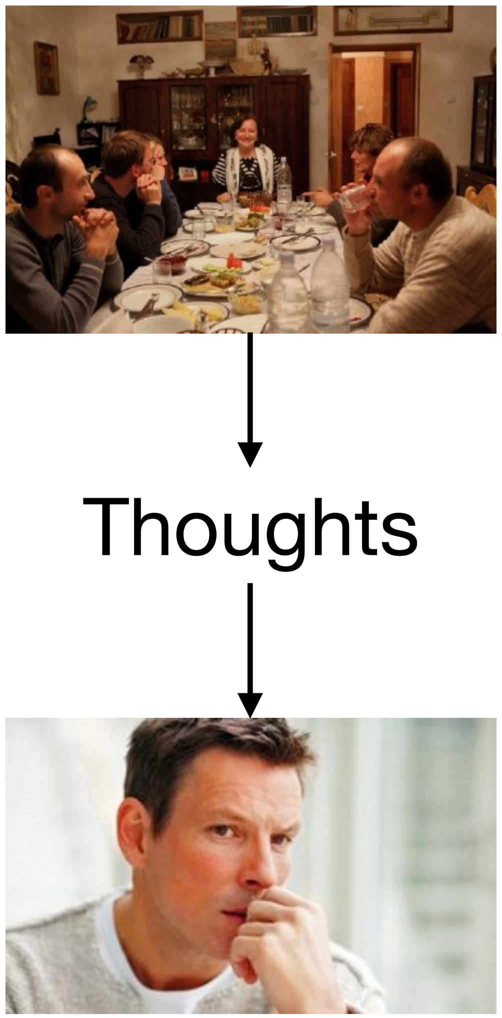
Schizophrenia

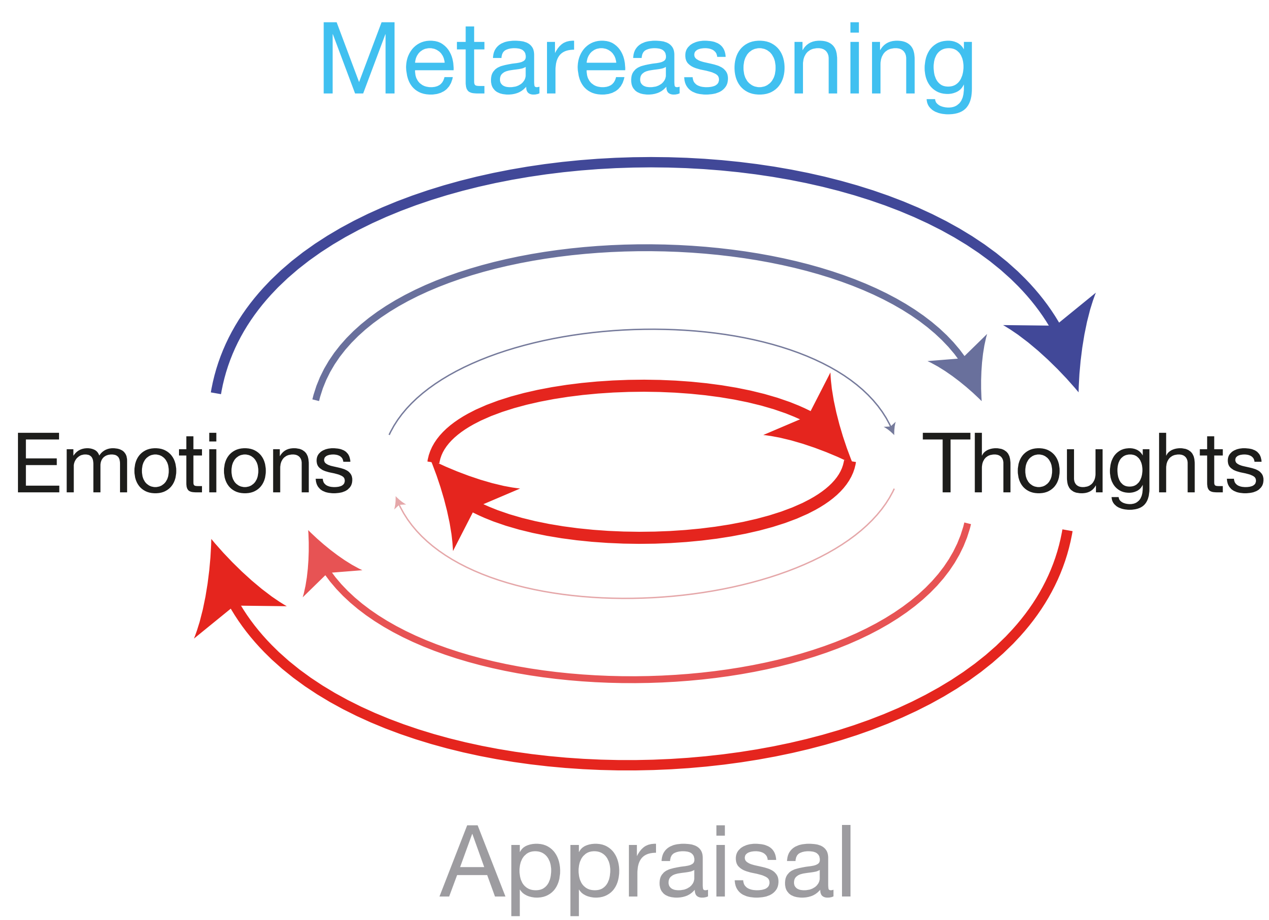
Parkinson’s

Mood

Metareasoning

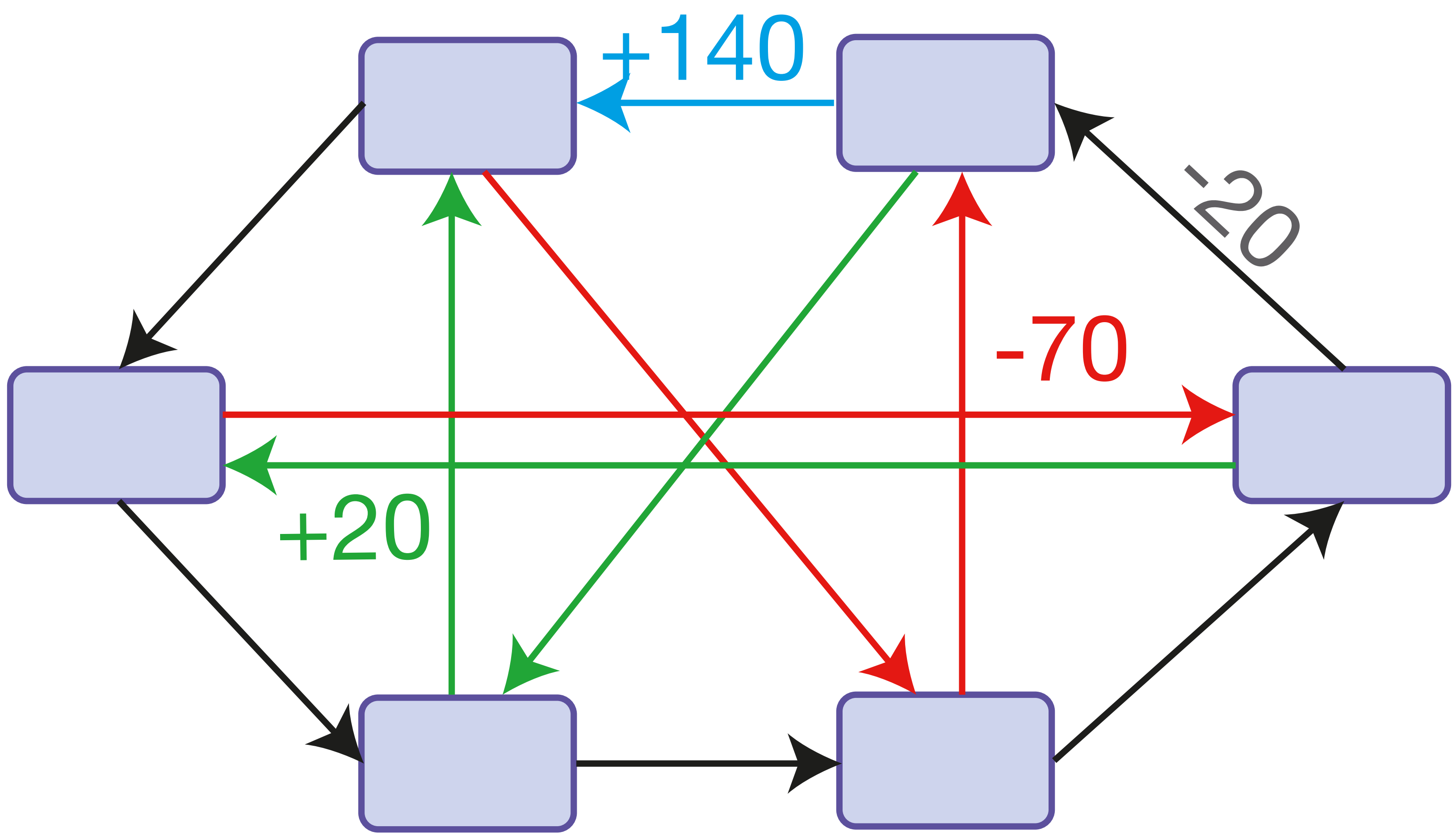
The cognitive model of depression

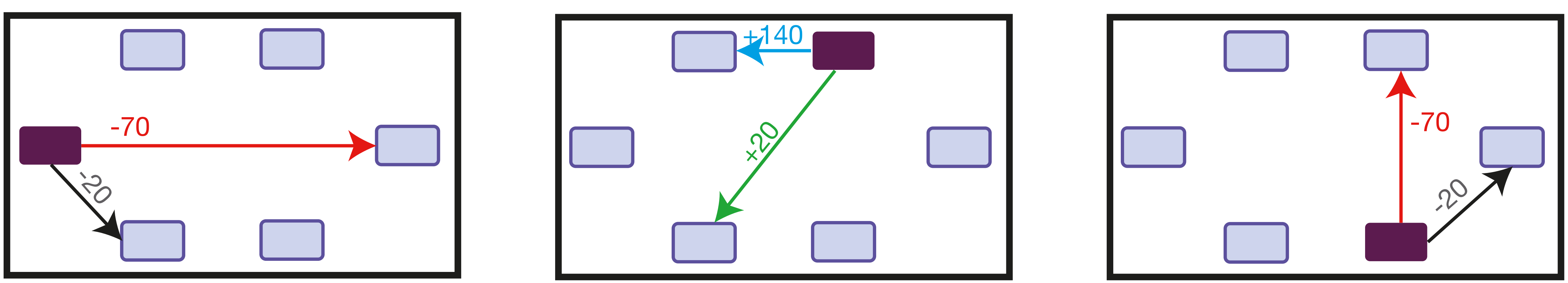




Metareasoning is the internal process by which we choose what to think about.

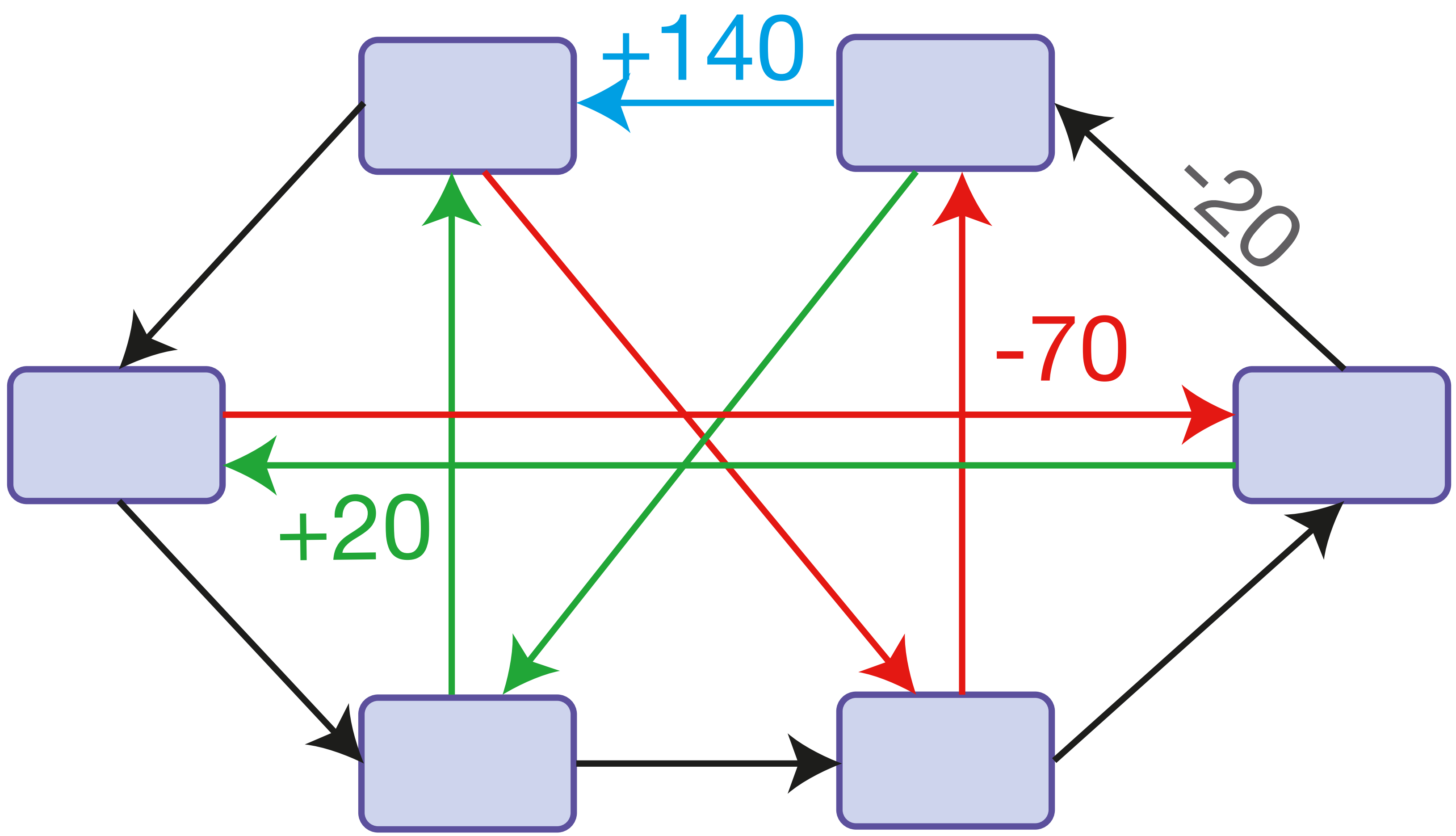
Studying metareasoning

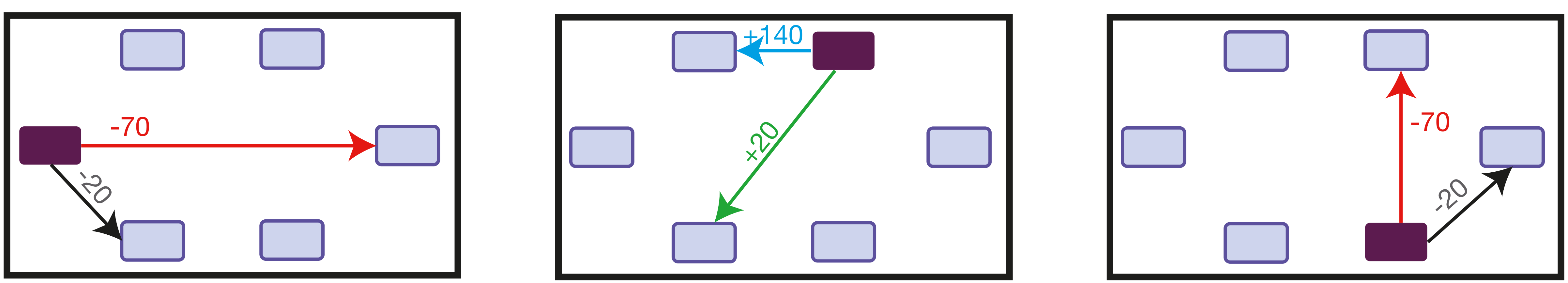




Huys et al., 2012 PLoS CB, Huys et al., 2015 PNAS, Lally*, Huys* et al., 2017 J. Neurosci

Studying metareasoning





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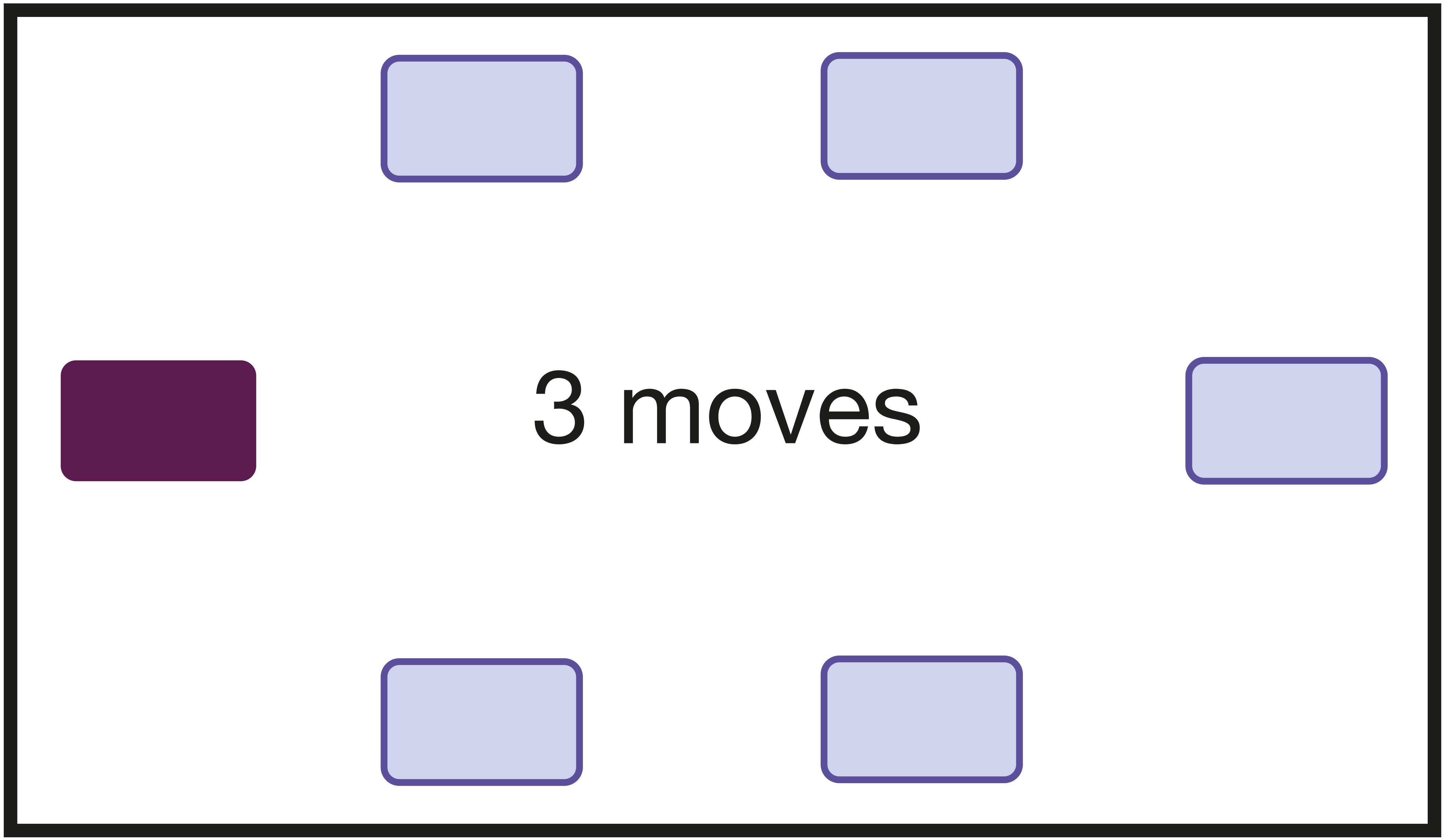
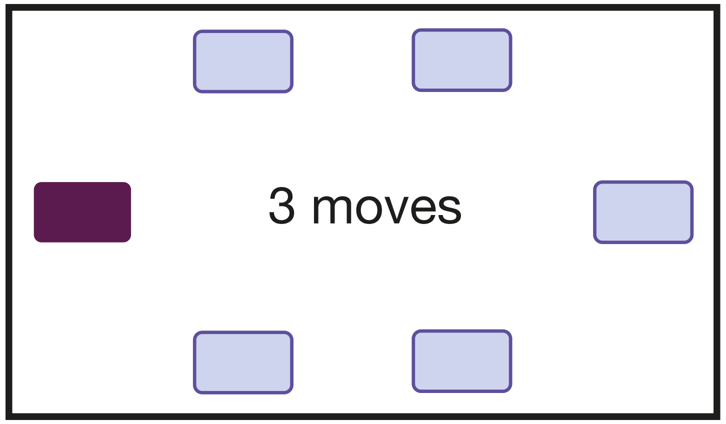
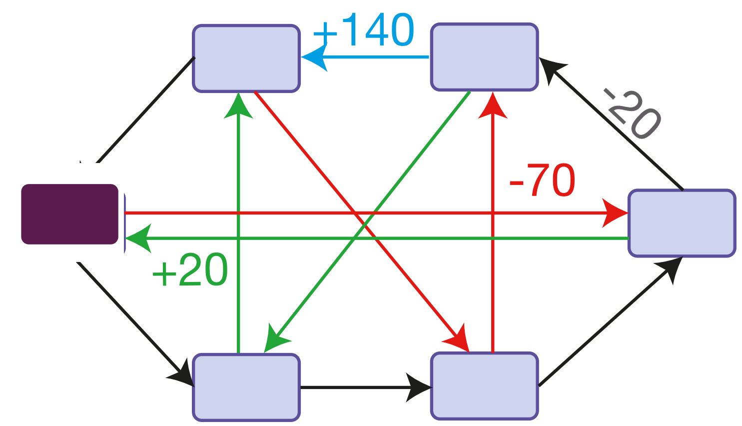
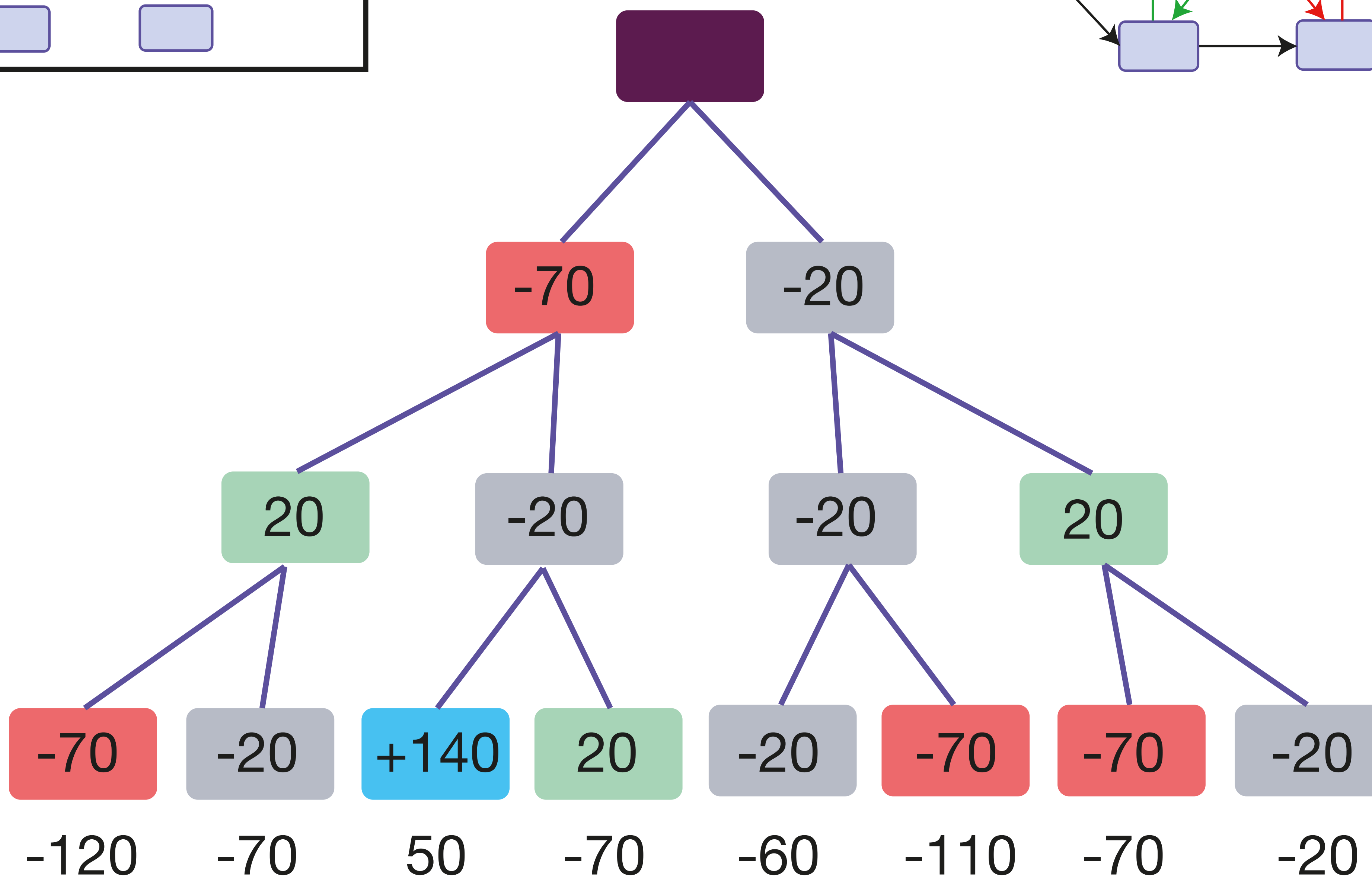
Psychochess



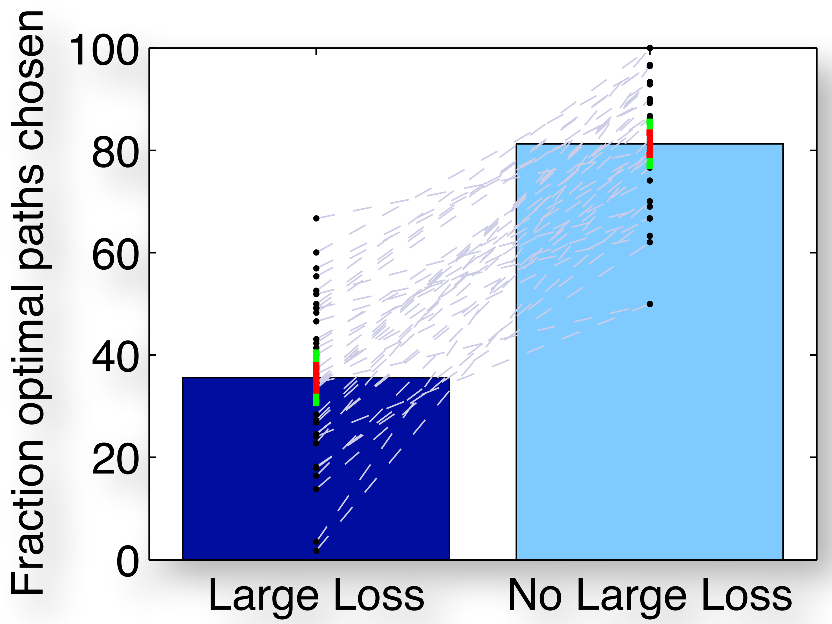
Solving a binary decision-tree

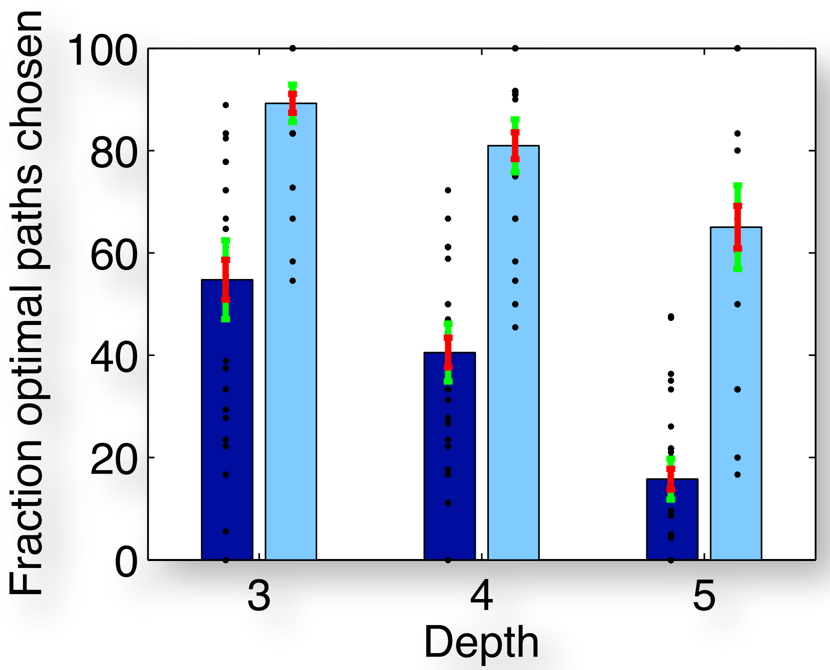






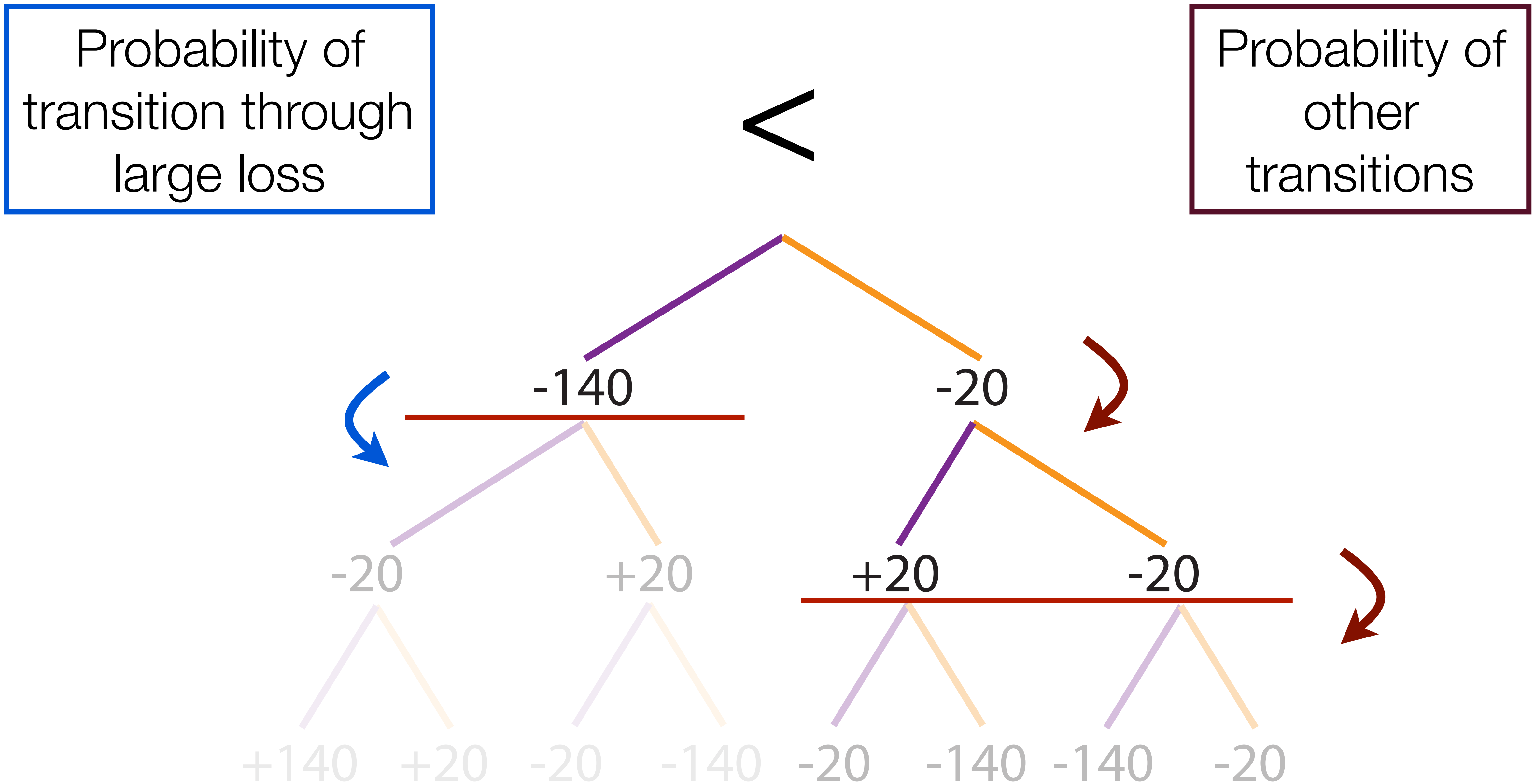
Optimal sequences containing losses





Huys et al., 2012 PLoS CB, Huys et al., 2015 PNAS, Lally*, Huys* et al., 2017 J. Neurosci

Adaptive pruning model



Measuring metareasoning

- If evaluated all branches fully

$$Q^{lo}(\mathbf{a}) = \sum_{j=1}^{d} r_j(\mathbf{a})$$

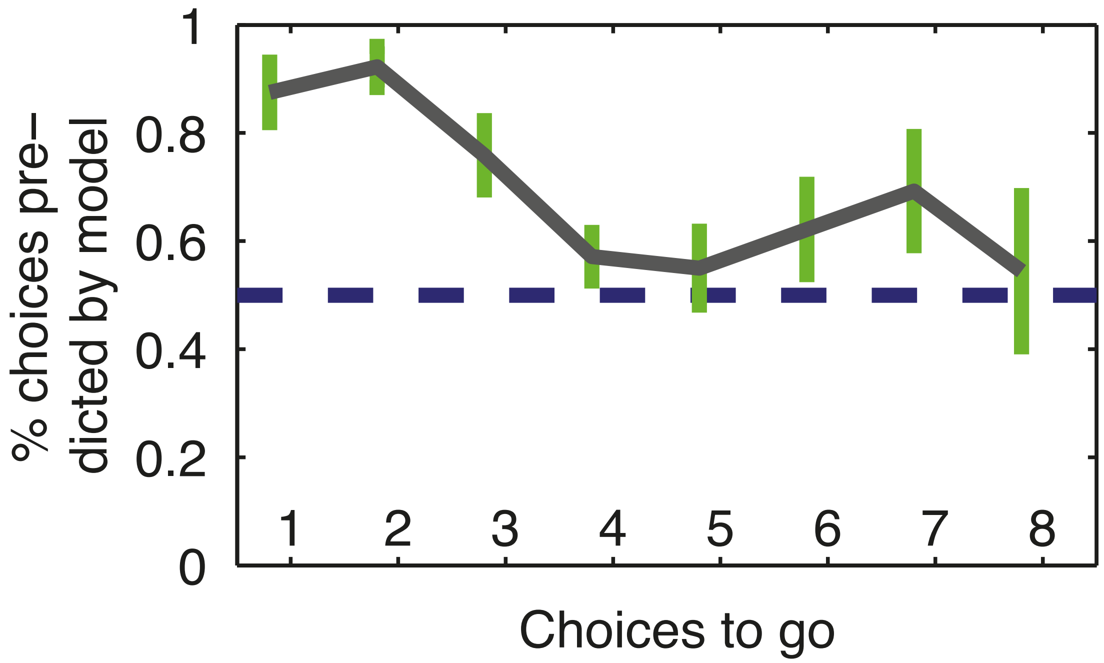
- If stopped with probability p at every evaluation

$$Q^{d}(\mathbf{a}) = \sum_{j=1}^{d} (1-\gamma)^{j-1} r_j(\mathbf{a})$$

- If stopped with different probabilities

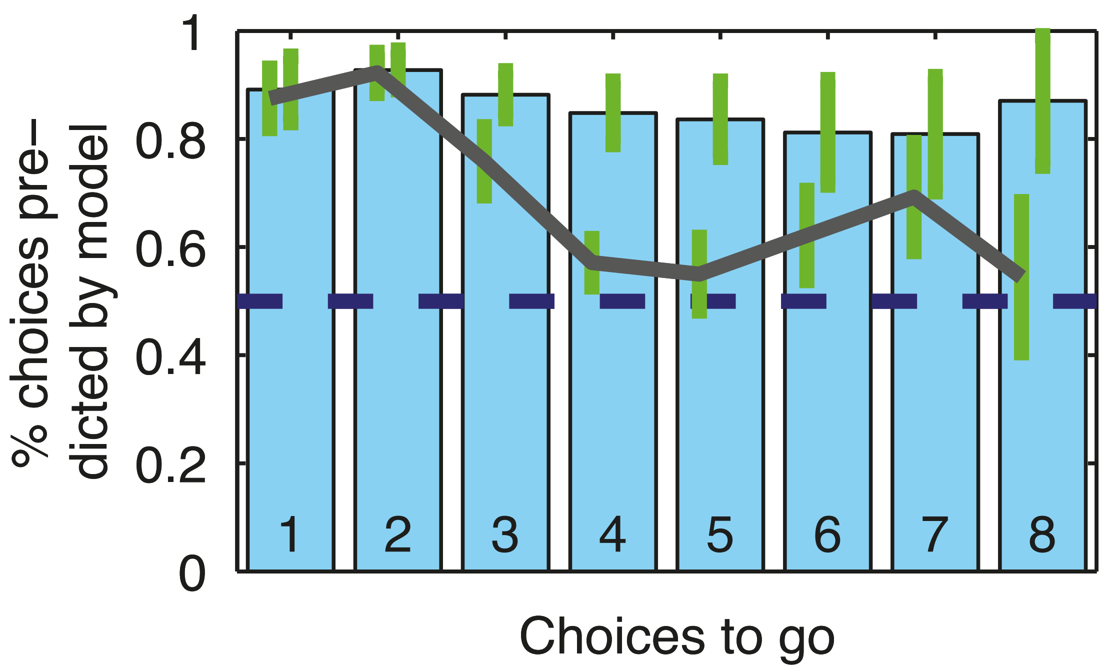
$$Q^{p}(\mathbf{a}) = \sum_{j=1}^{d} (1-\gamma_G)^{x-1}(1-\gamma_S)^{y-1} r_j(\mathbf{a})$$

Pruning explains choice behaviour



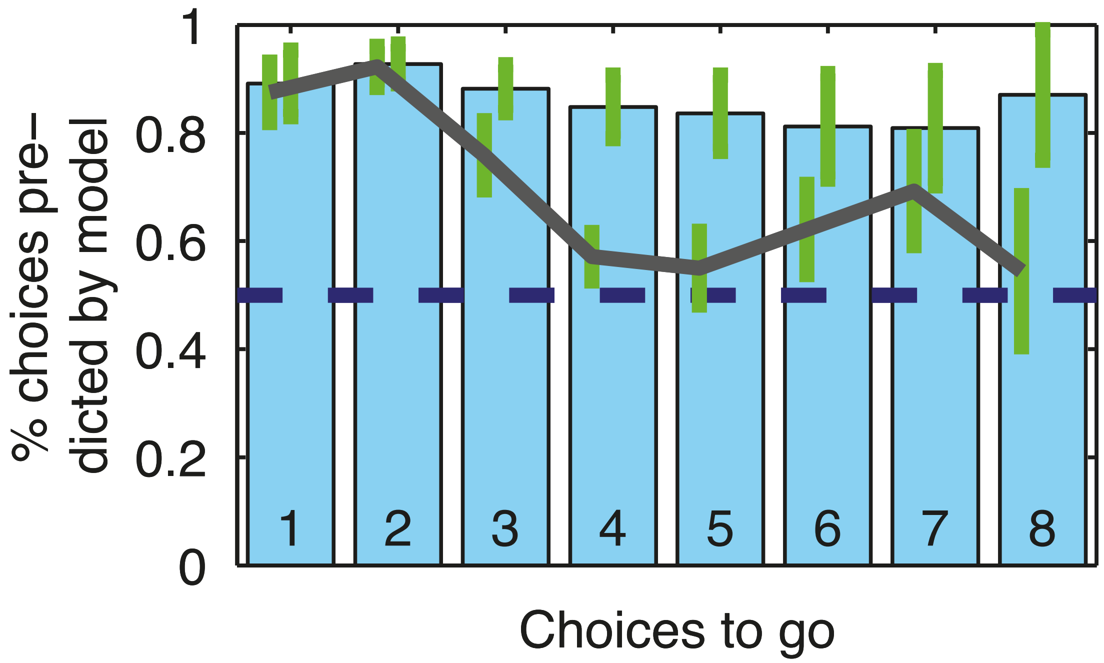
Huys et al., 2012, PLoS CB

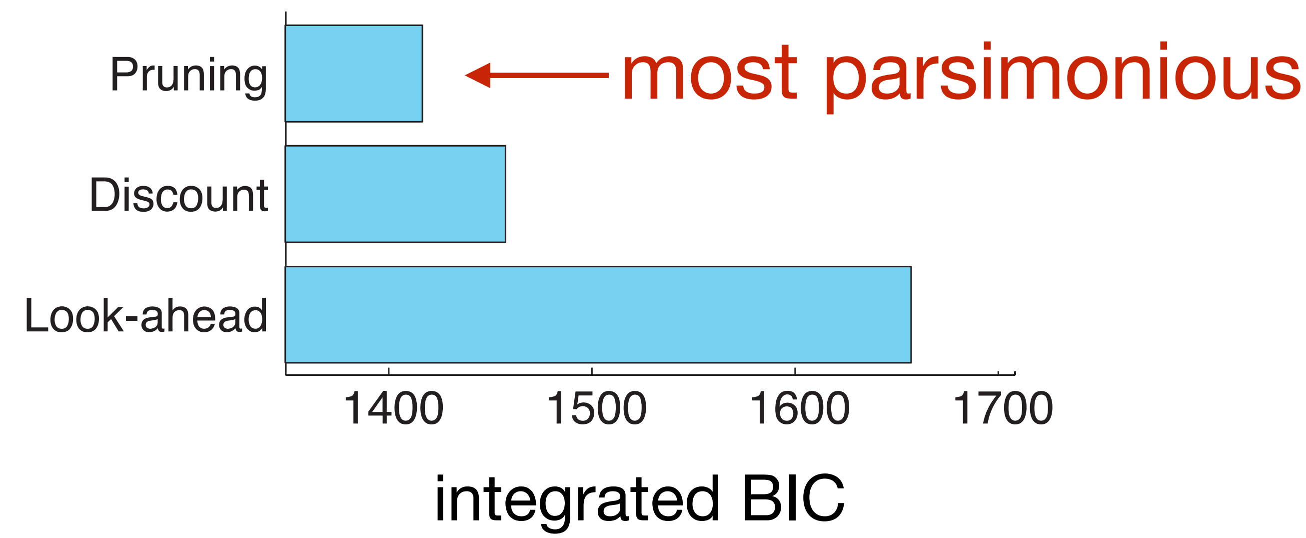
Pruning explains choice behaviour



Huys et al., 2012, PLoS CB

Pruning explains choice behaviour





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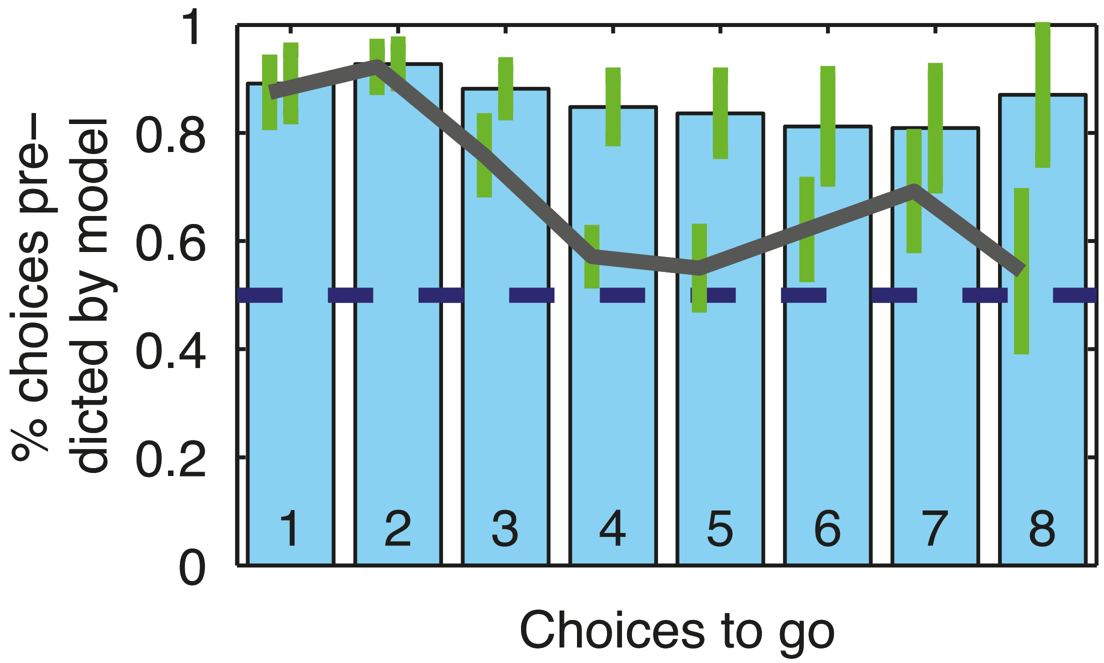
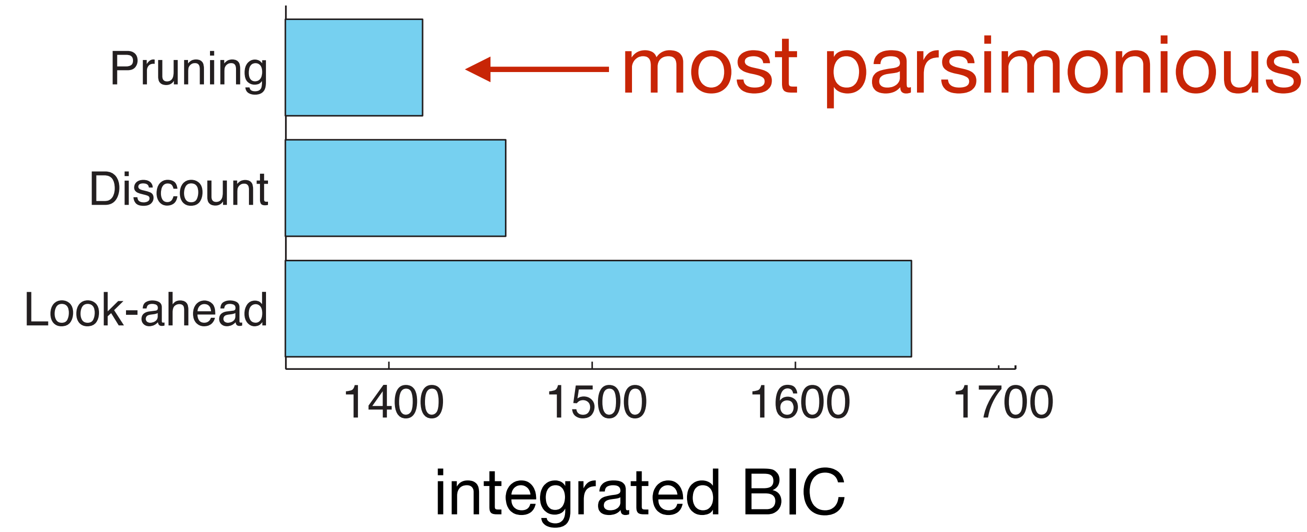
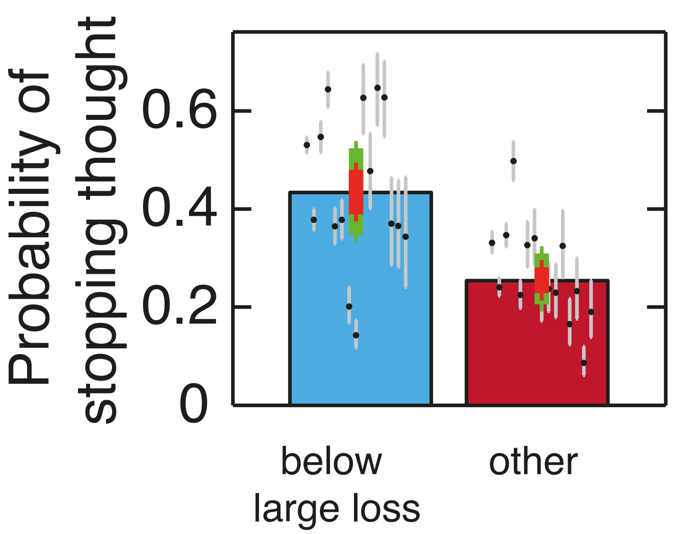
Pruning explains choice behaviour



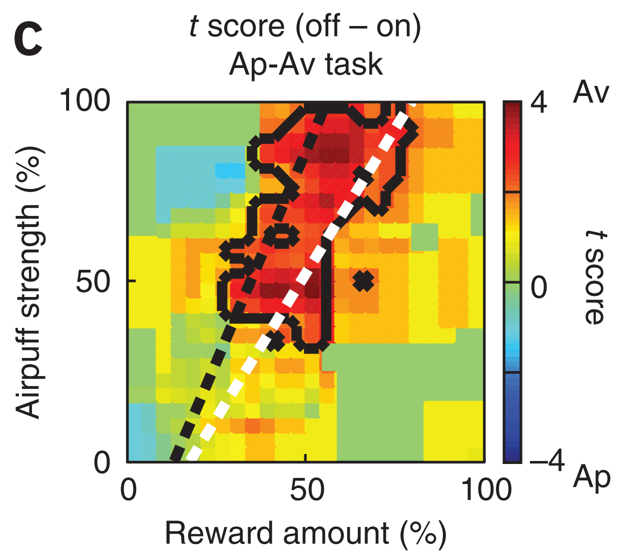




Huys et al., 2012, PLoS CB

Subgenual anterior cingulate

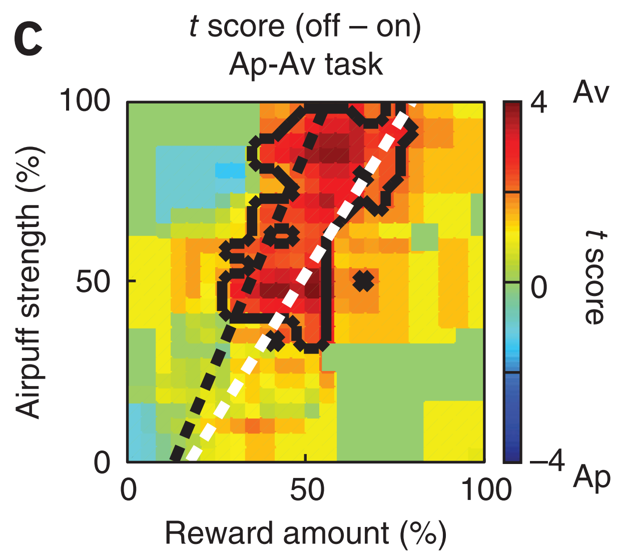
Impact of aversive events



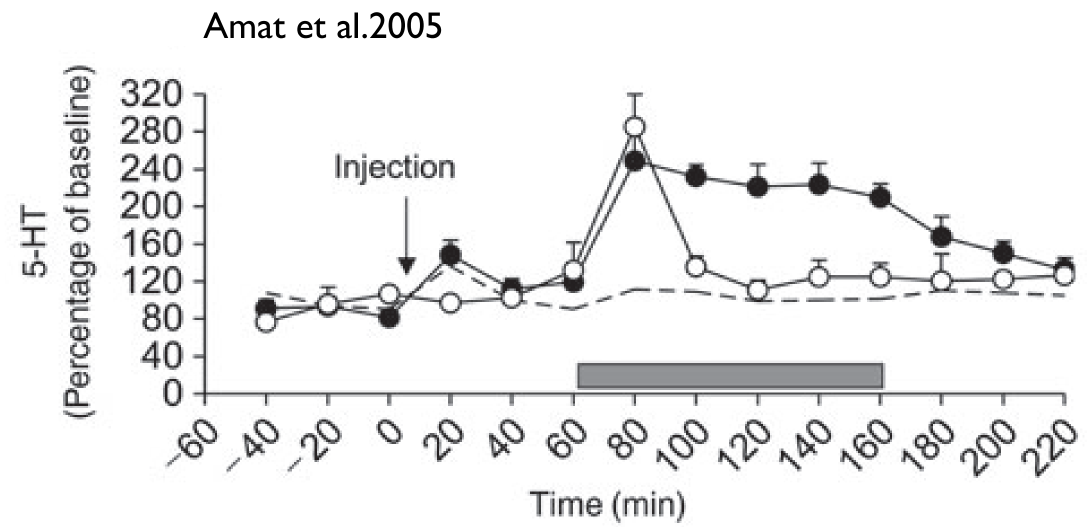
Amemory and Graybiel 2012, Amat et al., 2005; Siegle et al., 2012; Cooney et al. 2010

Subgenual anterior cingulate

Impact of aversive events



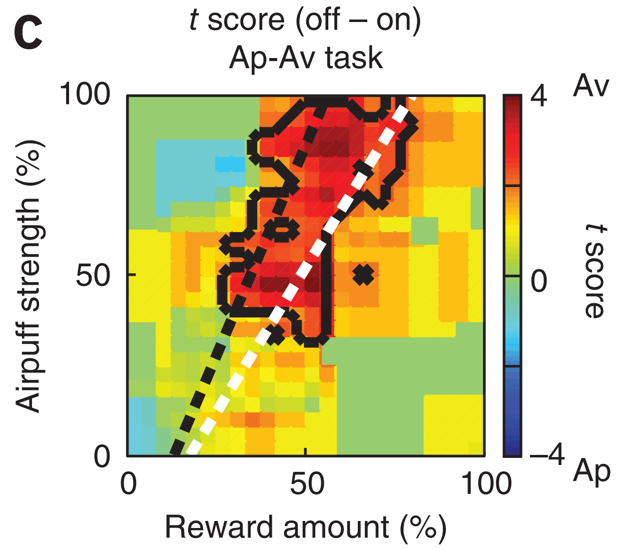
Necessary for helplessness



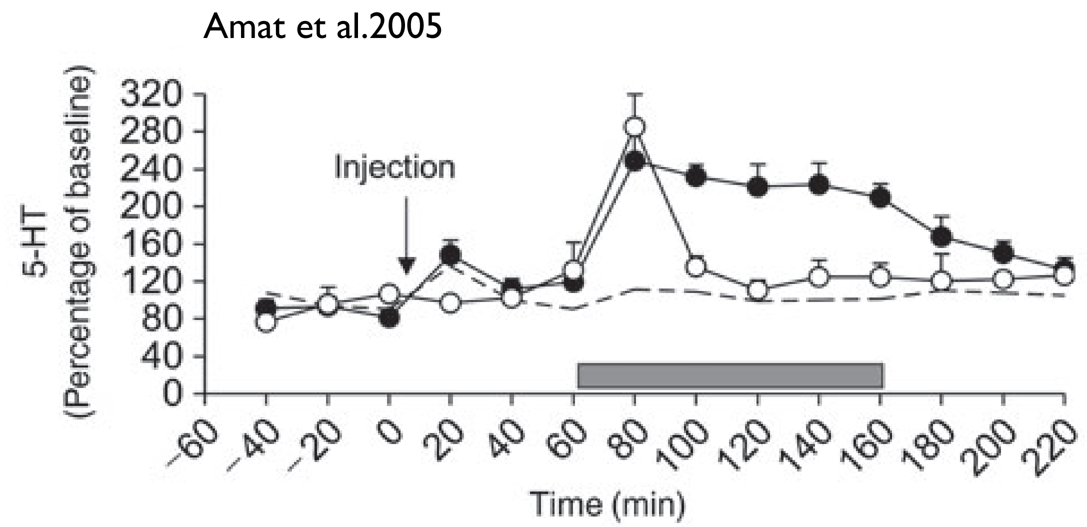
Amemory and Graybiel 2012, Amat et al., 2005; Siegle et al., 2012; Cooney et al. 2010

Subgenual anterior cingulate

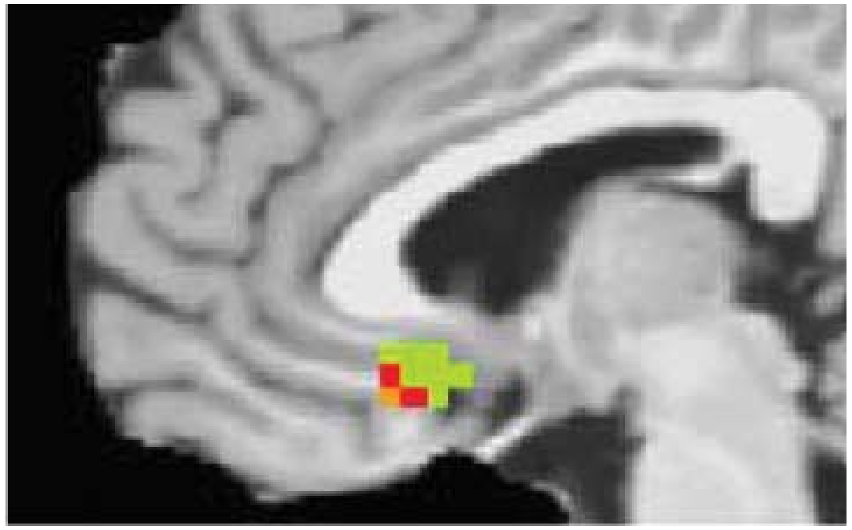
Impact of aversive events



Necessary for helplessness



Predicts treatment response



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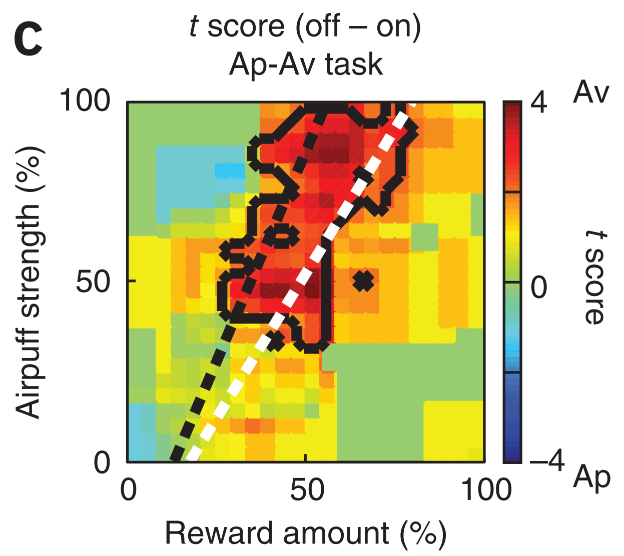
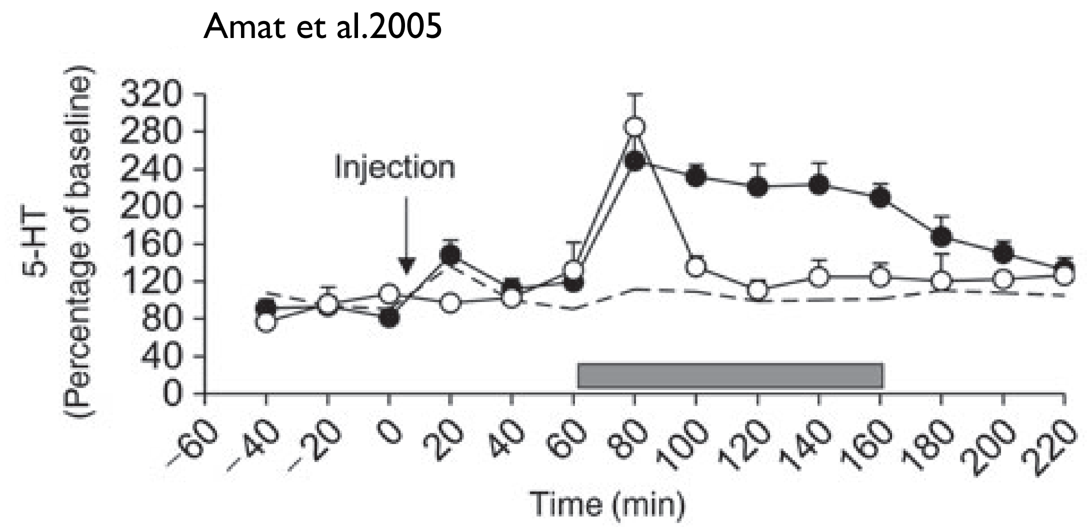
Subgenual anterior cingulate

Impact of aversive events



Necessary for helplessness



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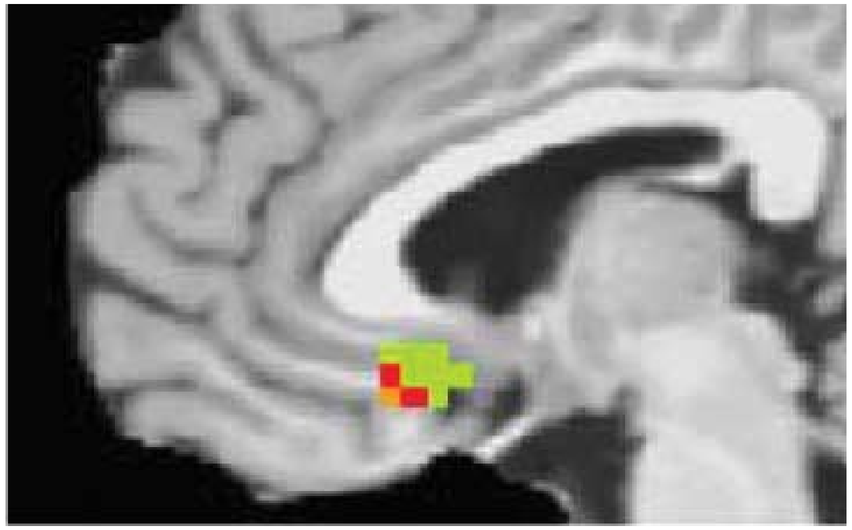
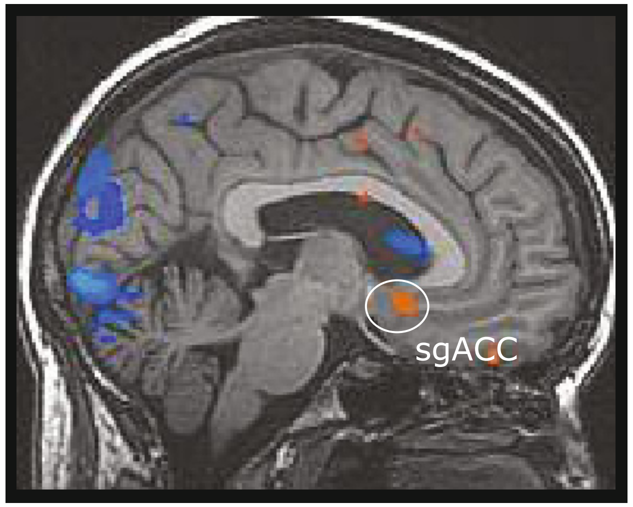


Correlates with rumination

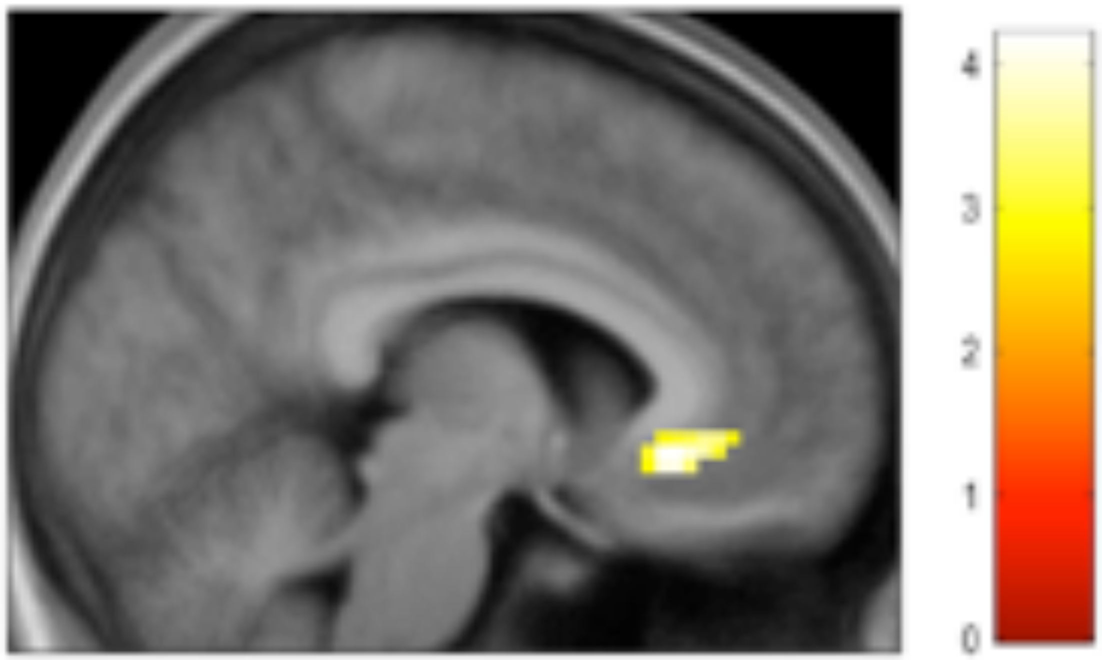


Amemory and Graybiel 2012, Amat et al., 2005; Siegle et al., 2012; Cooney et al. 2010

Pruning - sgACC and rumination

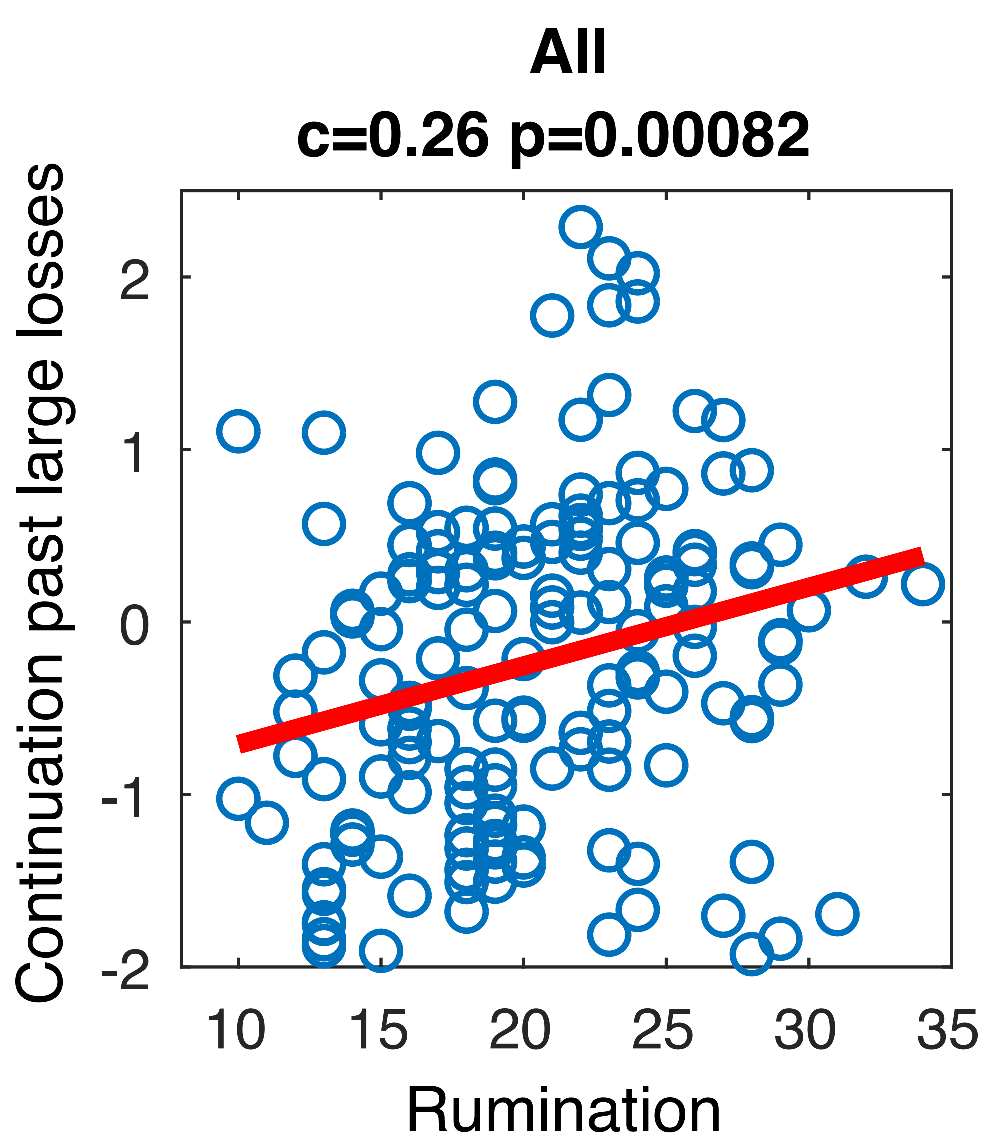
- fMRI too slow to pinpoint pruning events
- trial by trial measure of “pruning urge”

$$p_t = D_{KL}\left(p(\mathbf{a}_t|\mathcal{Q},\gamma_S=\gamma_G)||p(\mathbf{a}_t|\mathcal{Q},\gamma_S,\gamma_G)\right)$$



Lally*, Huys* et al., 2017 J. Neurosci.

Pruning and rumination



Outline

Depression

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OCD

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Schizophrenia

Parkinson’s

Mood

Metareasoning

Acknowledgements

SOCIETY OF BIOLOGICAL PSYCHIATRY

- Zurich
  - Isabel Berwian
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  - Martin Goelzer
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  - Peter Dayan
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  - Jon Roiser
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- US
  - Anne Collins
  - Michael Frank
  - Martin Paulus
  - Diego Pizzagalli

FNSNF

minz
Molecular Imaging Network Zurich

DFG Deutsche Forschungsgemeinschaft

TCPW

TCPW

Transcontinental Computational Psychiatry Workgroup

Home   Meetings schedule   Participate   Resources   Login

The **Transcontinental Computational Psychiatry Workgroup (TCPW)** organizes a monthly web-based meeting and a computational psychiatry satellite meeting with the Society of Biological Psychiatry. We hope to foster discussion and exchange between those involved in computational psychiatry—a rapidly growing, highly multidisciplinary field.

Videos of past meetings are here.

Next workgroup meeting

Network Analysis Tutorial

Eiko Fried

Tuesday, June 12th 2018 at 14:30 - 16:30 **UTC** (Other timezones)
General participation info | Participate online | + Phone-in

TBC

Eiko Fried, PhD
Postdoctoral research fellow
Psychological Methods
University of Amsterdam

News

- Postdoc @ UNIST & Seoul National University
- EBPS Workshop: Using Computational Approaches to Build a Two-way Bridge Between Animals And Humans
- Computational Psychiatry postdoc @ TU Dresden / Smolka lab
- Computational psychiatry postdocs @ UCL
- Zurich Computational Psychiatry Course Sep 10-14
- London Computational Psychiatry Course 2018
- Postdoc @ NIH in machine learning applied to MRI data
- RL for mental health – Computational Psychiatry Satellite @ SOBP
- Computational Psychiatry postdoc @ Oxford
- Postdoctoral position in computational psychiatry @ UiT The Arctic University of Norway

Meetings

- Title TBC - Sam Gershman *Sep 12th 2018*
- Title TBC - Yael Niv *Aug 13th 2018*
- Title TBC - Leanne Williams *Jul 24th 2018*
- Network Analysis Tutorial - Eiko Fried *Jun 12th 2018*
- Pavlovian control of escape: General effects and relevance to suicidal behaviors - Alexander Millner *May 03rd 2018*

www.cmod4mh.org

On the computational structure of mood and anxiety disorders

Algorithms for survival: characterising anxiety-like behavioural inhibition
Dominik Bach

Computational models of effort-based choice in patients with major depression and schizophrenia
Jessica Cooper

The interaction between mood and reward learning
Yael Niv

A Computational Approach to Understanding Motivational Symptoms in Depression
Jonathan Roiser

Feedback please!

https://tnusurvey.ethz.ch/index.php/472246