

Decision-making in depression

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DSM IV Major Depressive Disorder

- ▶ depressed mood
 - ▶ anhedonia
 - ▶ oversleeping / *undersleeping
 - ▶ weight gain / weight loss
 - ▶ psychomotor retardation
 - ▶ fatigue
 - ▶ guilt / worthlessness / helplessness
 - ▶ indecisiveness, concentration difficulties
 - ▶ suicidality
-
- ▶ duration & impairment

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TABLE 1. Sensitivity, Specificity, OR, PPV and NPV of Alternative Symptom Criteria for Major Depressive Disorder ($N = 1523$)^a

Symptom	Sensitivity %	Specificity %	OR	PPV %	NPV %
Depressed mood	92.9	82.4	61.2	86.3	90.6
Diminished interest/pleasure	80.6	87.8	29.7	88.7	79.1

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Depressed mood	92.9	82.4	61.2	86.3	90.6
Loss of energy or diminished drive	97.6	55.3	50.1	72.3	95.0
Loss of energy	87.2	68.4	14.8	76.8	81.8
Diminished drive	88.2	69.9	17.3	77.8	83.2
Diminished interest/pleasure or diminished drive	94.2	66.4	32.2	77.0	90.6
Diminished interest/pleasure	80.6	87.8	29.7	88.7	79.1

Table 5

Prevalences of lifetime interference, help seeking, and use of medication for minor depression and major depression

	Interference ^a		Saw MD ^a		Saw other ^a		Took medication ^a		Any of the four		(n)
	%	(S.E.)	%	(S.E.)	%	(S.E.)	%	(S.E.)	%	(S.E.)	
Minor depression	18.1	(1.1)	24.5	(1.3)	12.1	(1.0)	10.0	(0.9)	42.0	(1.5)	(810)
Major depression 5–6	29.7 ^b	(1.4)	27.8	(1.4)	18.0 ^b	(1.2)	15.8 ^b	(1.1)	49.7 ^b	(1.5)	(664)
Major depression 7–9	52.3 ^b	(1.7)	35.3 ^b	(1.6)	21.5 ^b	(1.4)	20.3 ^b	(1.4)	68.2 ^b	(1.6)	(606)

Average (mean) number of 30-day work loss and work cutback days associated with 12-month minor depression and major depression

	Employed					Homemakers				
	Work loss days		Work cutback days		(n)	Work loss days		Work cutback days		(n)
	\bar{x}	(S.E.)	\bar{x}	(S.E.)		\bar{x}	(S.E.)	\bar{x}	(S.E.)	
Minor depression	0.17	(0.11)	0.79	(0.23)	(242)	0.10	(0.10)	1.15	(0.78)	(40)
Major depression 5–6	0.17	(0.04)	0.99	(0.20)	(227)	0.36	(0.35)	1.20	(0.46)	(30)
Major depression 7–9	0.48 ^a	(0.13)	2.75 ^a	(0.34)	(222)	1.70 ^a	(0.59)	4.27 ^a	(1.08)	(49)

The course of depression

Table 5.—Adjusted and Unadjusted Attributable Risks for First-Onset Major Depression at Wave II		
Psychiatric Disorder	Unadjusted Attributable Risk	Adjusted Attributable Risk
Dysthymia	0.050	0.077
Panic disorder	0.039	0.007
Somatization	0.017	0.006
Alcohol abuse	0.057	0.020
Other drug abuse	0.030	0.000
Obsessive-compulsive disorder	0.049	0.011
Schizophrenia	0.040	0.013
Depressive symptoms	0.581	0.553

Horwath et al., 1992 - ECA

The course of depression

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Horwath et al., 1992 - ECA

Table 3

Frequency of Symptom Presentation in the Prodromal and Residual Phases (N = 331 Episodes)

Symptom	Prodromal frequency	Residual frequency
Depressed mood	95	79
Decreased appetite	42	40
Weight loss	13	12
Increased appetite	10	12
Weight gain	20	17
Initial insomnia	29	30
Middle insomnia	13	10
Early waking	11	14
Hypersomnia	23	22
Decreased energy	38	35
Decreased interest or pleasure	82	75
Self-blame	51	55
Decreased concentration	78	75
Indecision	6	8
Suicidality	6	5
Psychomotor agitation	6	5
Psychomotor retardation	10	7
Crying more frequently	34	31
Inability to cry	4	2
Hopelessness	195	201
Worrying/Brooding	104	118
Decreased self-esteem	195	199
Irritability	85	72
Dependency	45	46
Self-pity	24	28
Somatic complaints	5	4
Decreased effectiveness	38	37
Helplessness	35	28
Decreased initiation of voluntary responses	19	23

The course of depression

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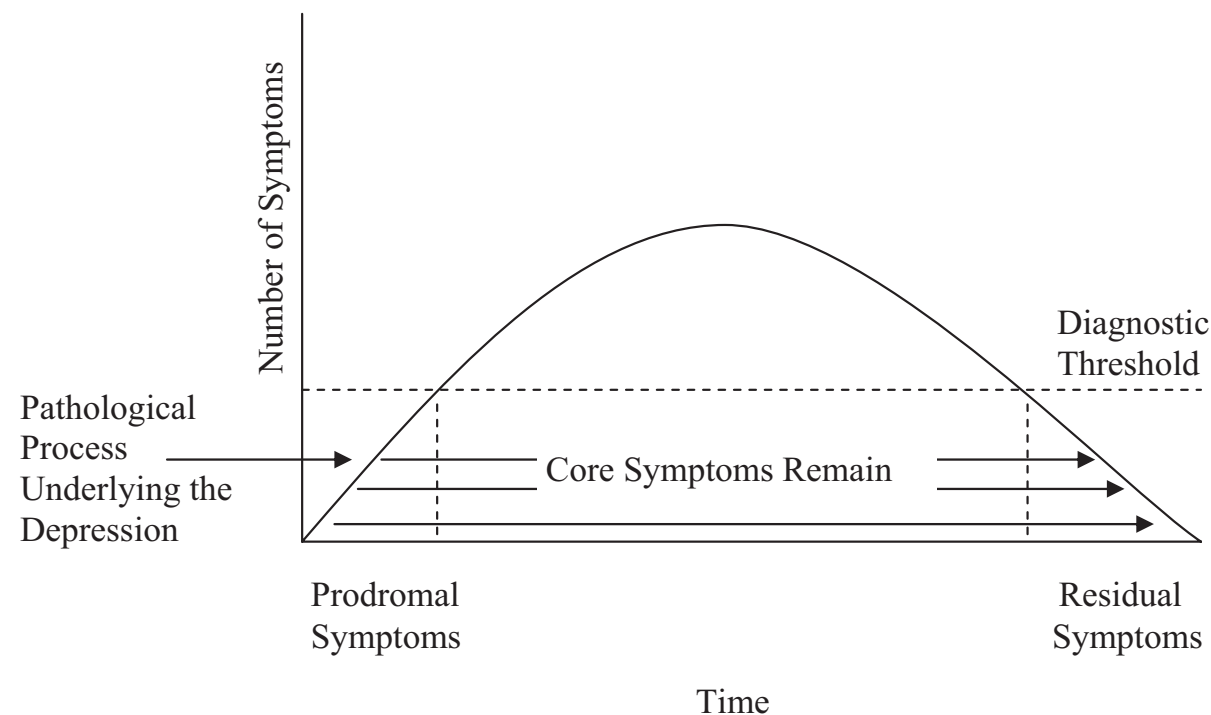


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Iacoviello et al., 2010

Types

- ▶ Carney et al. 1965
 - endogenous vs neurotic
 - ECT response
- ▶ Kendler et al., 1992
 - atypical
 - mild typical
 - severe typical
 - in terms of vegetative symptoms
- ▶ Parker et al., 1994
 - Melancholia
- ▶ Lamers et al., 2010
 - Severe melancholic
 - Severe atypical
 - Moderate severity

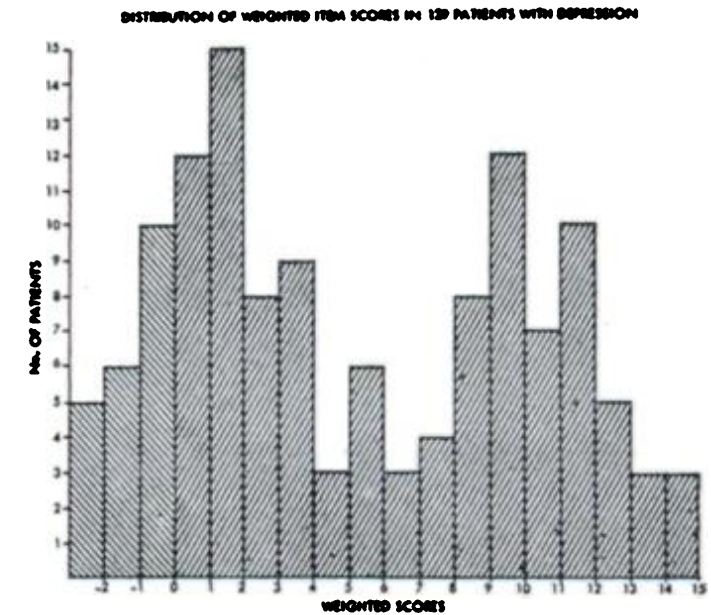


FIG. 1.

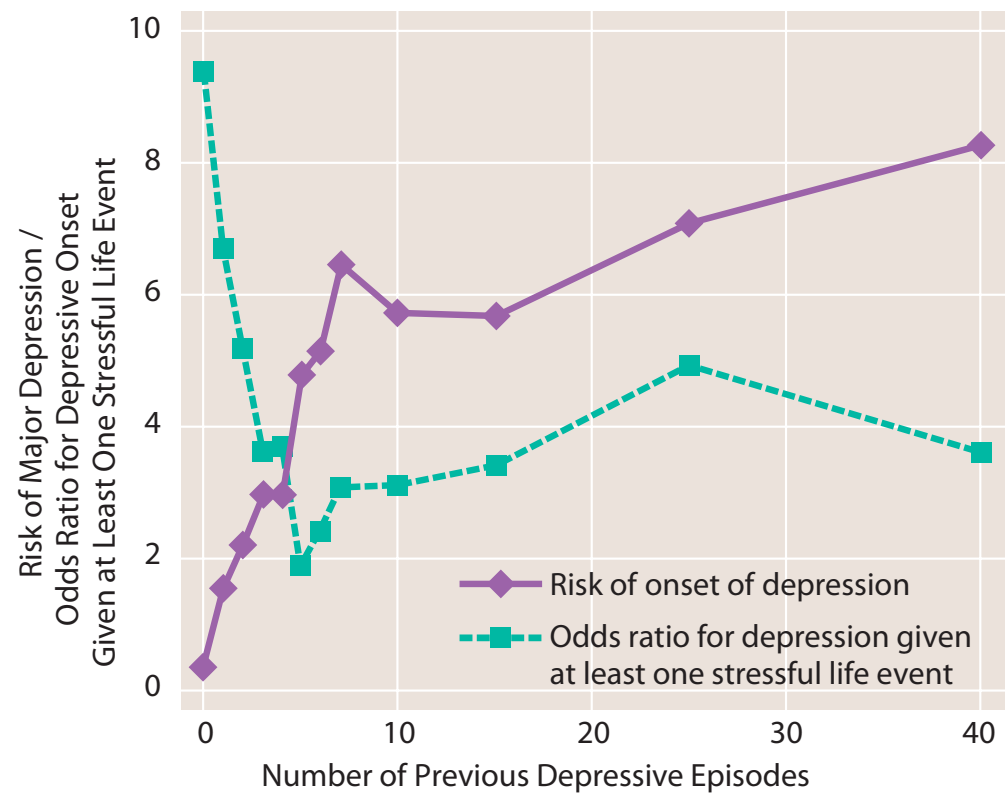
Table 1. Observed Class Membership and Endorsement Frequencies of 14 Depressive Symptoms in the Best Fitting Latent Class Model

		Prevalence by Class						
	DSM-III-R*	1	2	3	4	5	6	7
Symptom								
Felt depressed	A1	0.15	0.28	0.61	0.53	0.99	0.97	1.00
Loss of interest and/or pleasure	A2	0.00	0.06	0.42	0.16	0.82	0.80	1.00
Decreased appetite	A3	0.00	0.00	0.00	0.91	0.58	0.05	0.69
Increased appetite	A3	0.00	1.00	0.00	0.02	0.01	0.64	0.19
Weight loss	A3	0.01	0.00	0.00	0.47	0.42	0.00	0.43
Weight gain	A3	0.06	0.44	0.04	0.01	0.00	0.60	0.14
Insomnia	A4	0.04	0.14	0.24	0.27	0.60	0.27	1.00
Hypersomnia	A4	0.00	0.00	0.08	0.02	0.12	0.41	0.24
Psychomotor agitation	A5	0.03	0.08	0.23	0.16	0.57	0.36	1.00
Psychomotor retardation	A5	0.00	0.05	0.11	0.04	0.28	0.30	0.73
Tired	A6	0.06	0.15	0.33	0.24	0.59	0.69	1.00
Guilt	A7	0.00	0.03	0.19	0.08	0.46	0.36	0.83
Trouble concentrating	A8	0.00	0.04	0.16	0.12	0.48	0.23	0.86
Suicide	A9	0.00	0.01	0.04	0.05	0.18	0.14	0.38
Observed class membership, %		52.2	4.6	21.6	7.2	8.9	3.9	1.6
N		1075	95	445	148	183	86	32
% Diagnosed MD by DSM-III-R		0.0	0.0	3.8	2.0	66.1	46.3	96.9
No. of symptoms, mean		0.4	2.3	2.8	3.1	6.3	6.2	9.9
No. of symptoms, ±SD		0.5	1.0	1.0	1.3	1.3	1.5	1.2

What is depression?

- ▶ **Low expected reward**
 - depressed mood
 - anhedonia
 - guilt / worthlessness / helplessness
 - suicidality
- ▶ **Low energy**
 - fatigue
 - psychomotor retardation
 - oversleeping / *undersleeping
 - weight gain / weight loss
- ▶ **Cognition**
 - indecisiveness, concentration difficulties
- ▶ **Duration & Impairment**

External causes



Kendler et al., 2000

- ▶ Loss events
 - ▶ Severe stress
 - ▶ Chronic stress
 - ▶ Social defeat
-
- ▶ But: 30% acausal

Kendler et al., 1999,2000

Decision-making in psychiatry

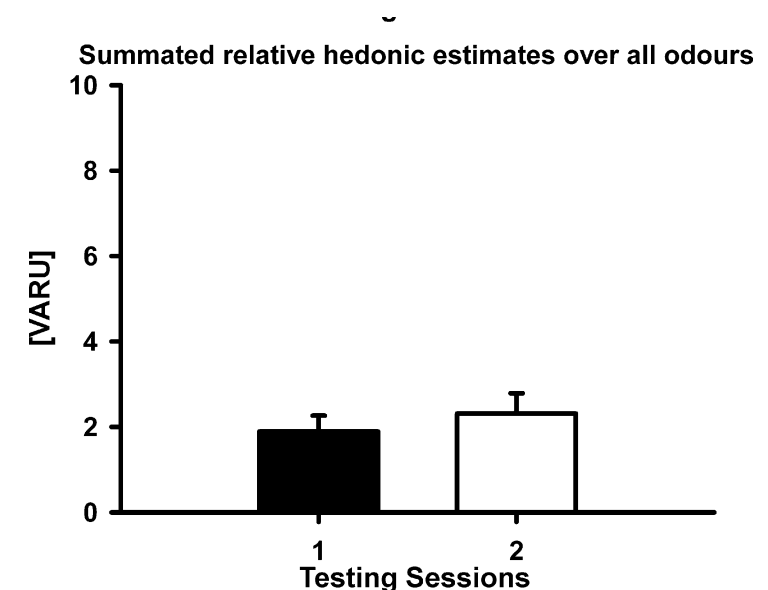
- ▶ Gaining prominence
- ▶ Applied broadly
- ▶ Central concepts: valuation
- ▶ What explanations do these models afford?
 - Wrong problem
 - Wrong inference
 - Wrong data

Decision-making in depression

- ▶ Emotional components
- ▶ Cognitive components
- ▶ Neuromodulatory components

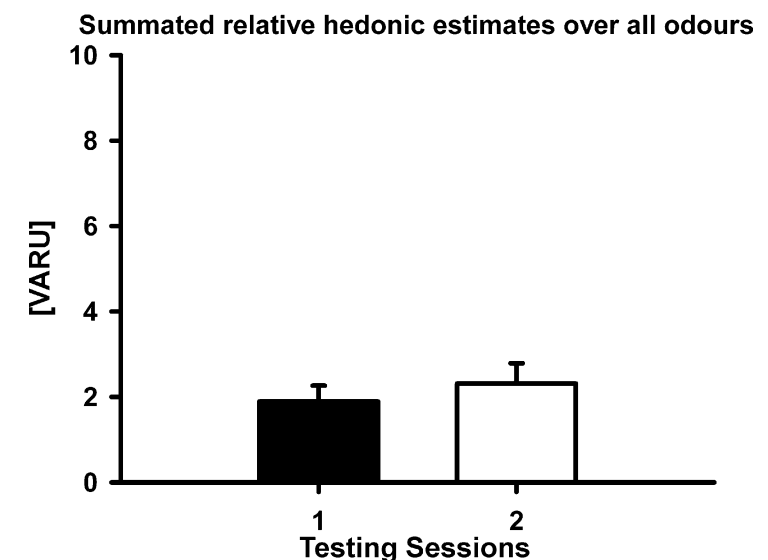
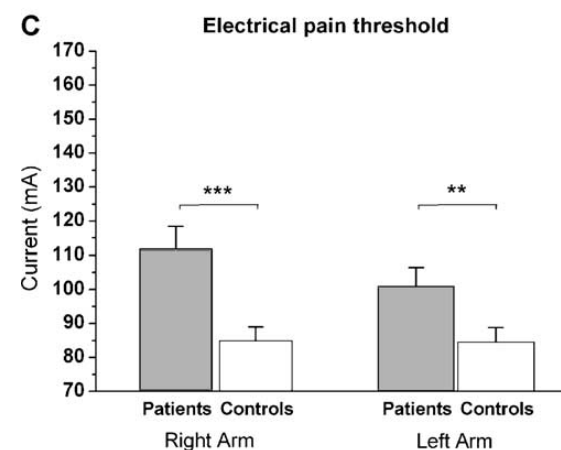
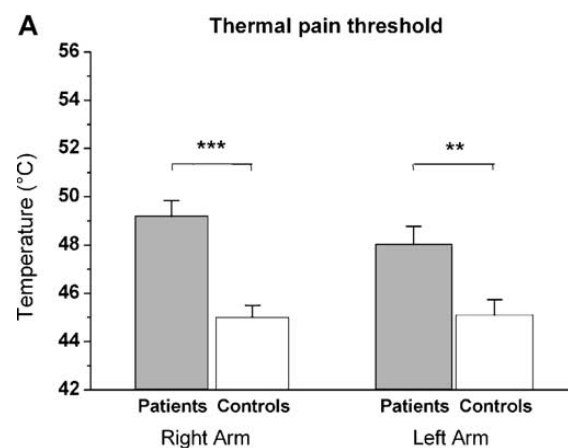
No primary impairment

- ▶ diminished interest or pleasure in response to stimuli that were previously perceived as rewarding
- ▶ What is “stimuli”?
 - sucrose preference test
 - standard animal assessment of anhedonia, Willner 1997
 - Dichter et al., 2010
 - no difference between MDD & HC
 - no effect of psychotherapy (BA)
 - Olfaction (Klepce et al., 2010)
 - Pain (e.g. Baer et al., 2005)



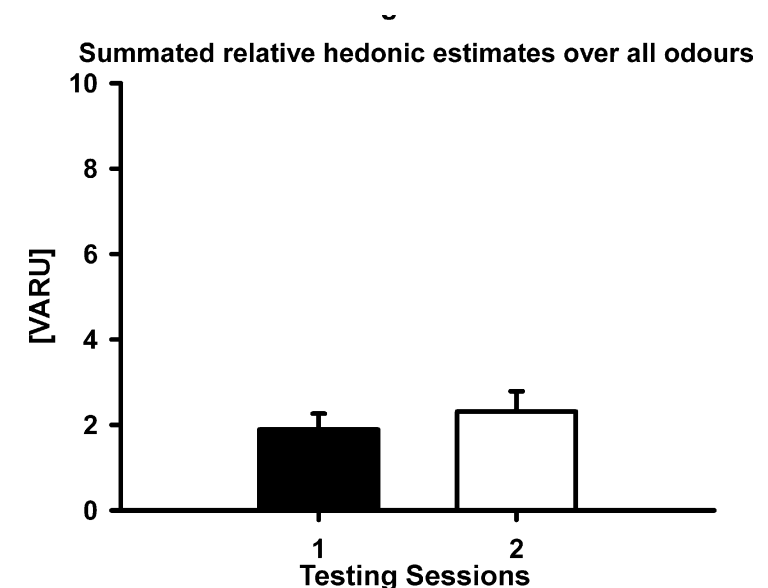
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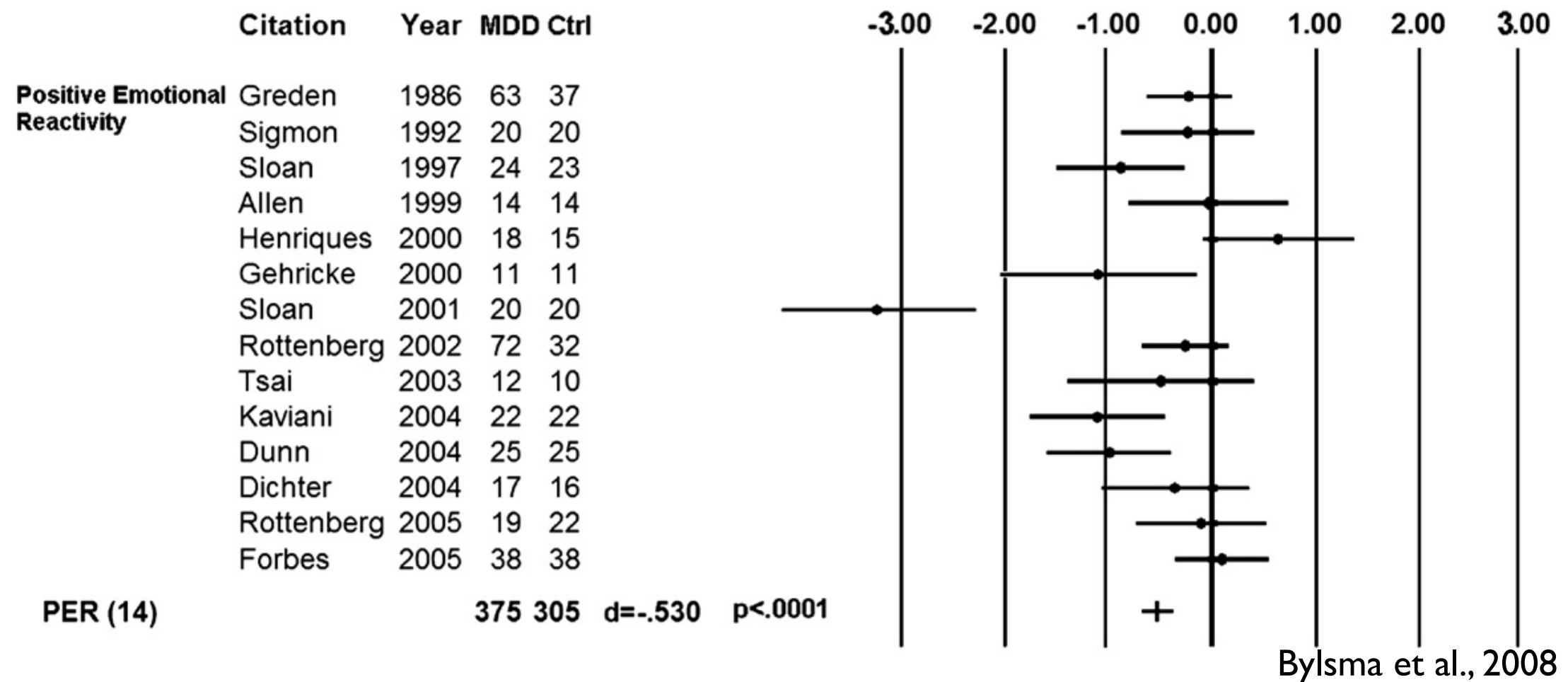


Or is there?

- ▶ Reduced “emotional” responses to more complex “affective” stimuli

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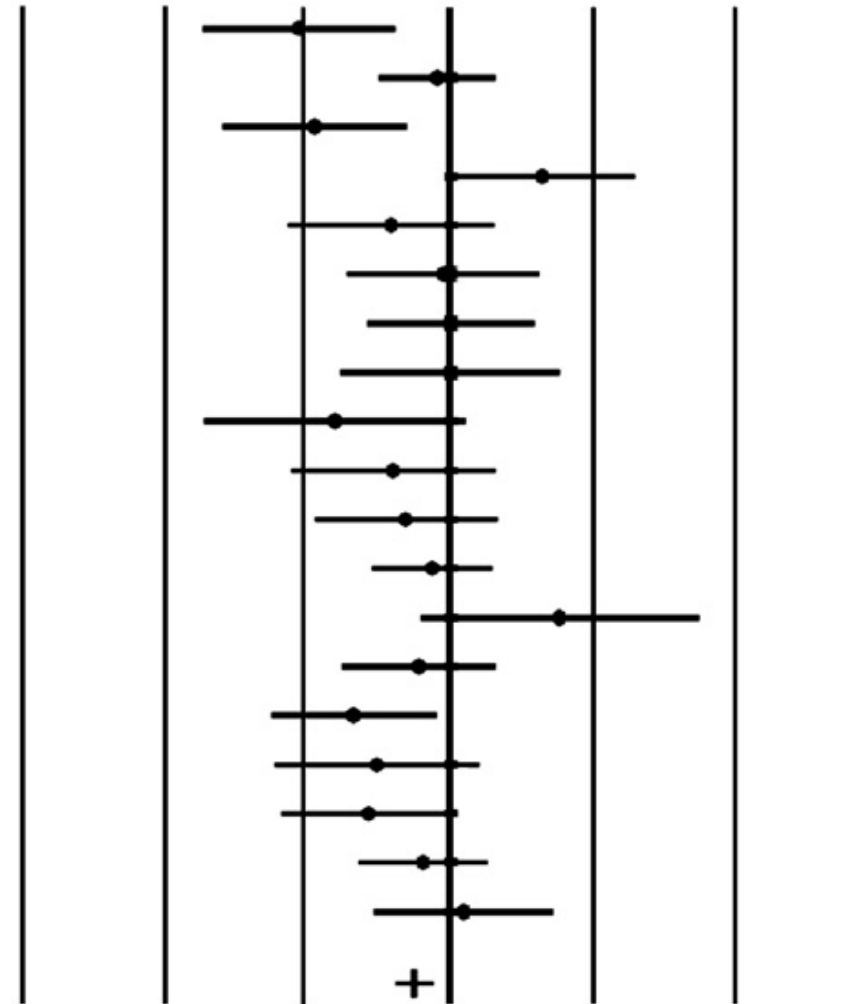


How about negative stimuli?

Negative Emotional Reactivity	Dawson	1977	20	20
	Greden	1986	63	37
	Albus	1987	12	63
	Sigmon	1992	20	20
	Persad	1993	16	16
	Guinjoan	1995	18	18
	Sloan	1997	24	23
	Allen	1999	14	14
	Gehricke	2000	11	11
	Henriques	2000	18	15
	Sloan	2001	20	20
	Rottenberg	2002	72	32
	Tsai	2003	11	9
	Rottenberg	2003	25	31
	Dunn	2004	25	25
	Dichter	2004	17	16
	Kaviani	2004	22	22
	Forbes	2005	38	38
	Rottenberg	2005	19	22

NER (19)

465 452 $d = -.251$ $p < .0001$

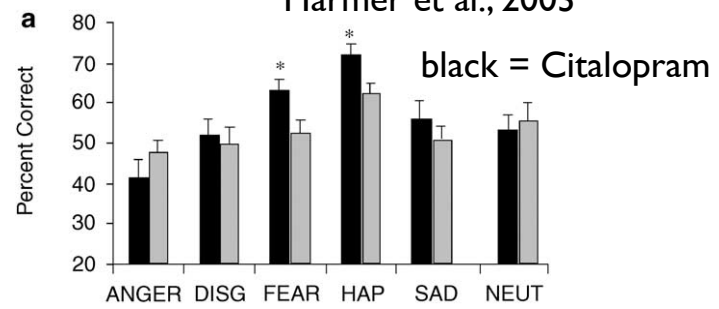


Face processing

Face processing

Citalopram, acute

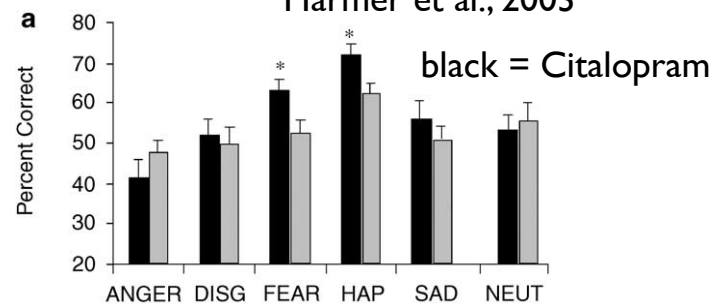
Harmer et al., 2003



Face processing

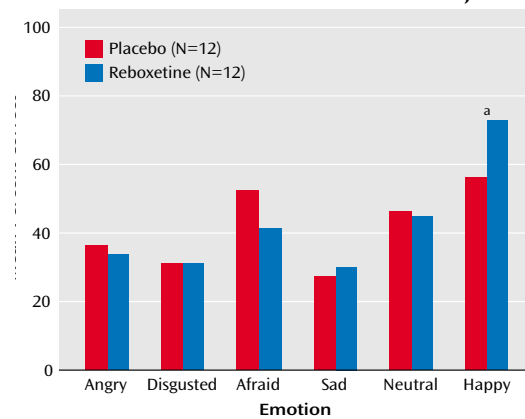
Citalopram, acute

Harmer et al., 2003



Reboxetine, acute

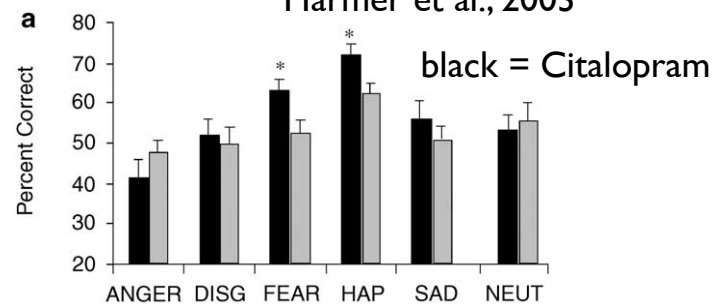
Harmer et al., 2003b



Face processing

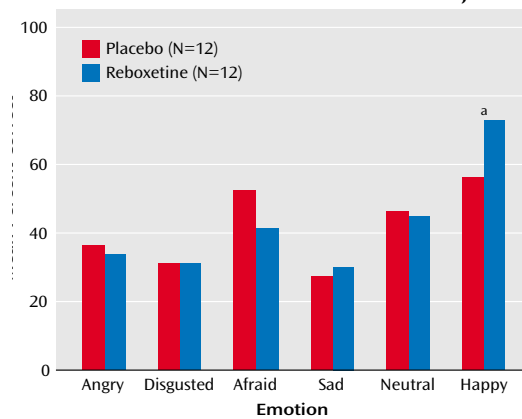
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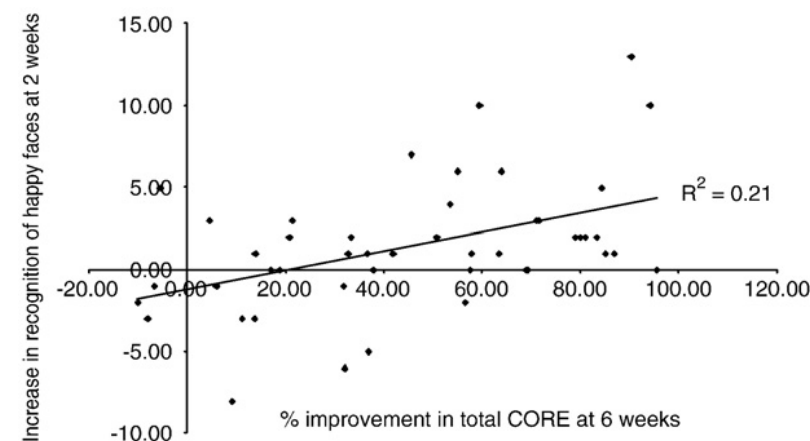
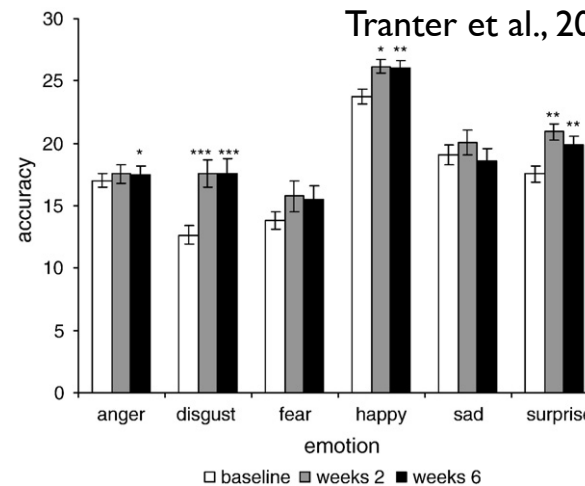
Reboxetine, acute

Harmer et al., 2003b



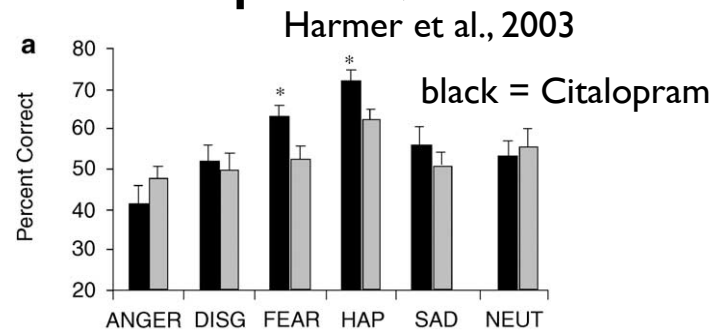
Cit/Reb, chronic, MDD

Tranter et al., 2009

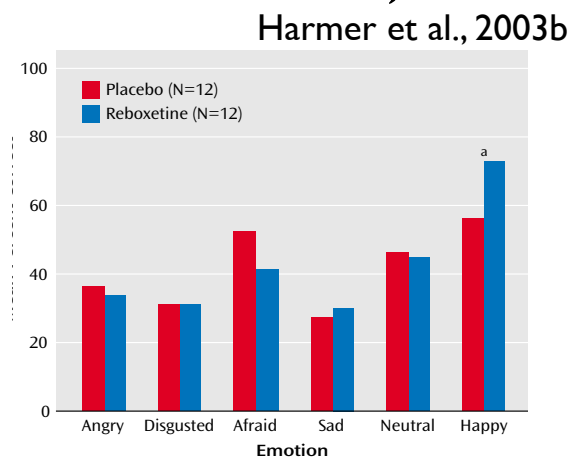


Face processing

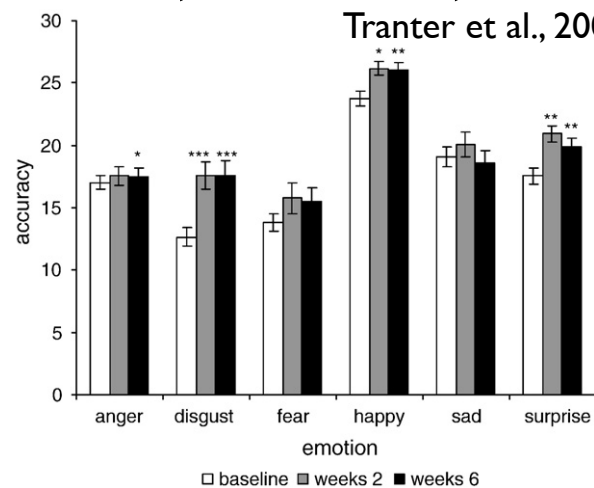
Citalopram, acute



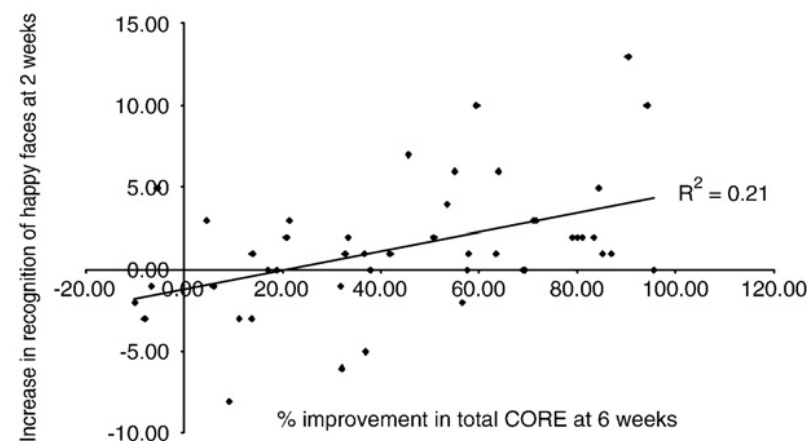
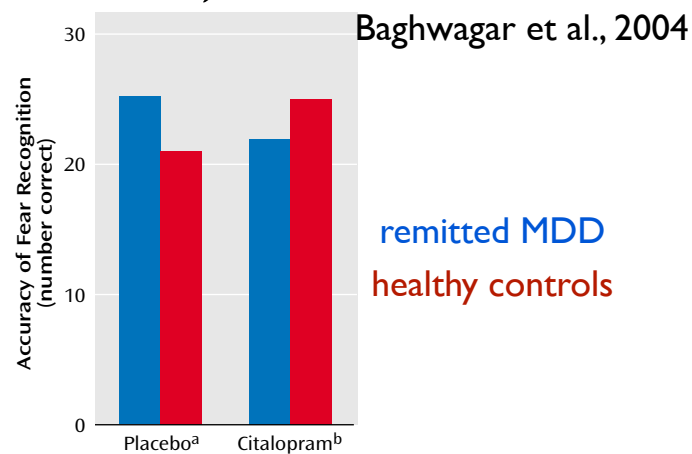
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Cit/Reb, chronic, MDD



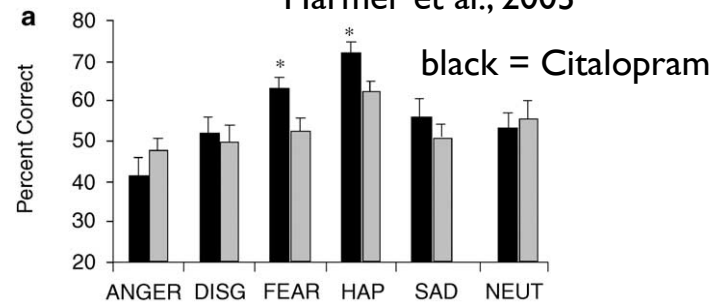
Cit, rem MDD



Face processing

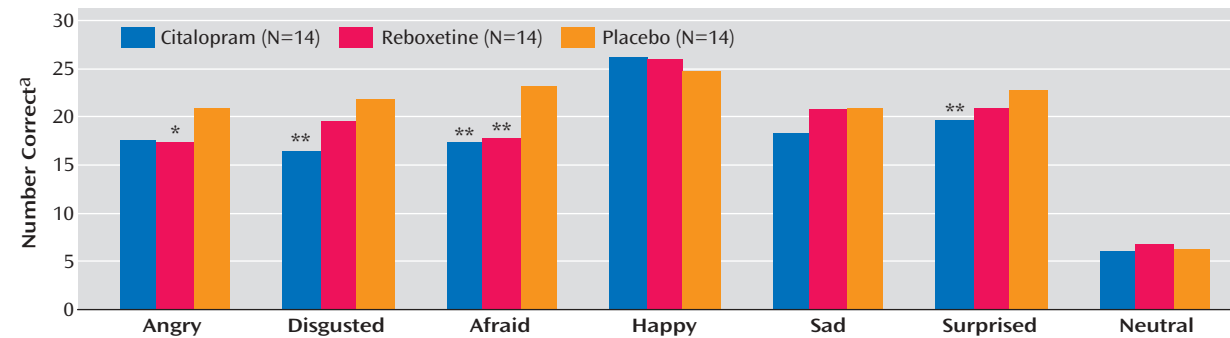
Citalopram, acute

Harmer et al., 2003



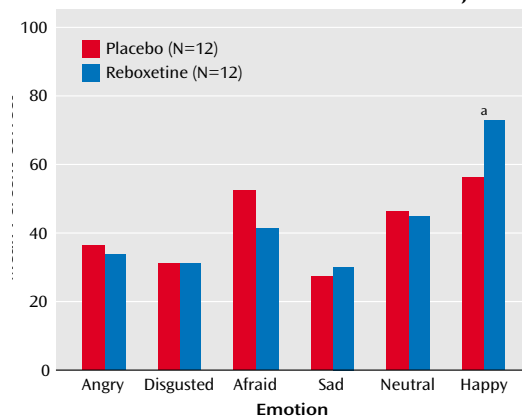
Cit/Reb, chronic, HC

Harmer et al., 2004



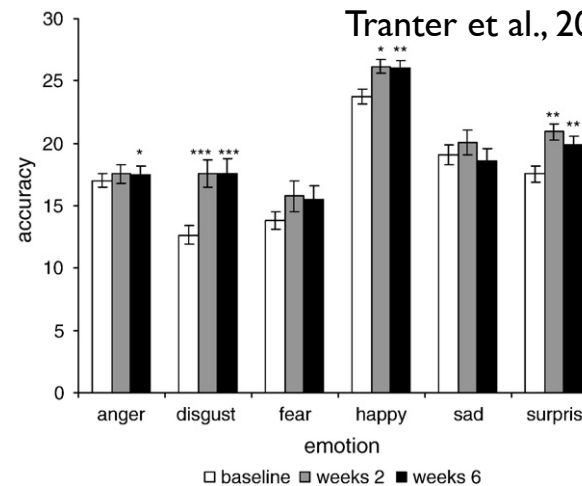
Reboxetine, acute

Harmer et al., 2003b



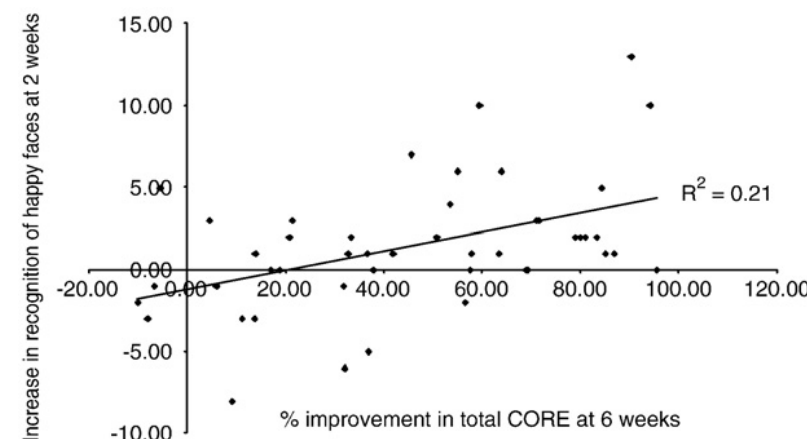
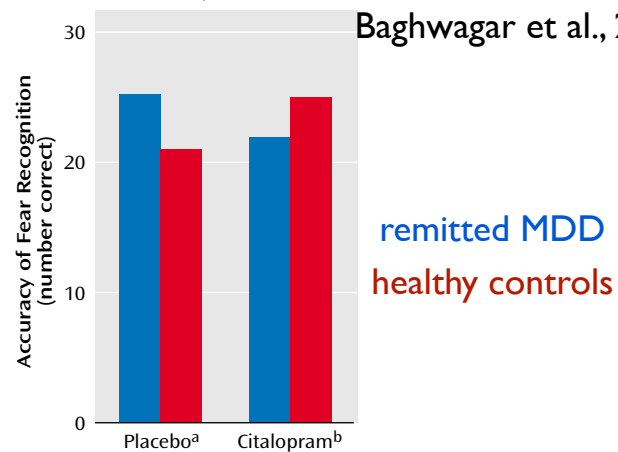
Cit/Reb, chronic, MDD

Tranter et al., 2009



Cit, rem MDD

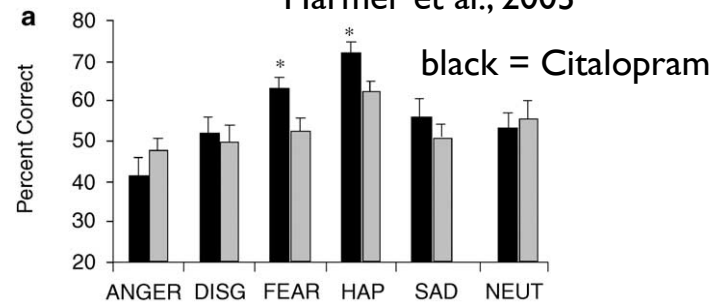
Baghwagar et al., 2004



Face processing

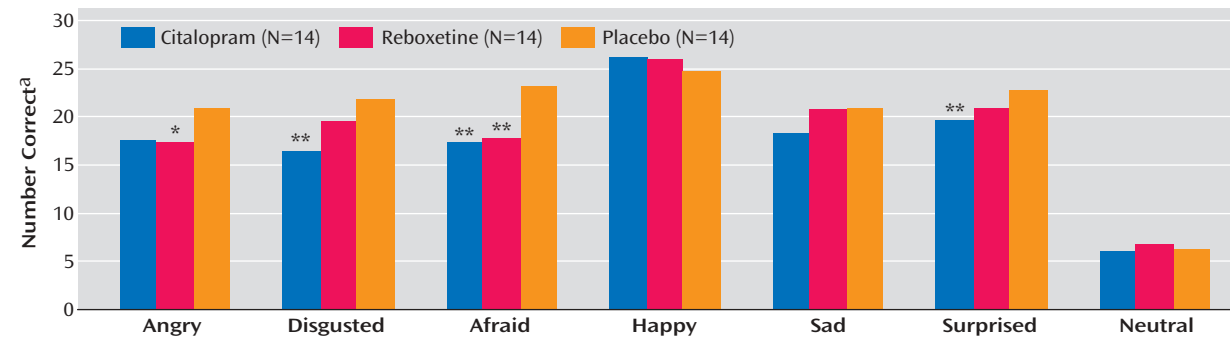
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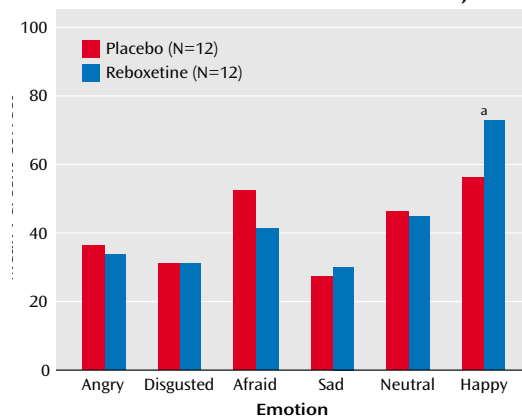
Cit/Reb, chronic, HC

Harmer et al., 2004



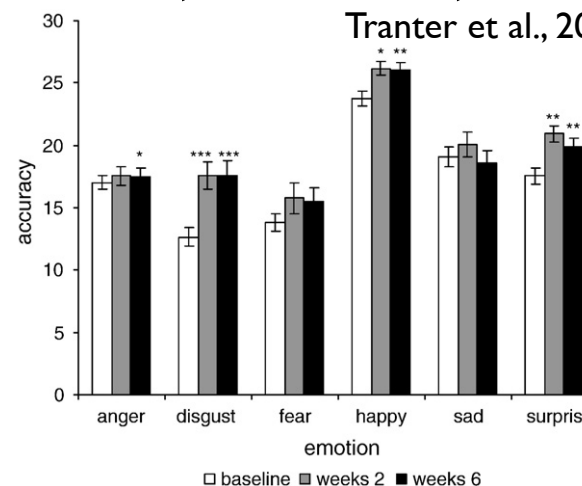
Reboxetine, acute

Harmer et al., 2003b



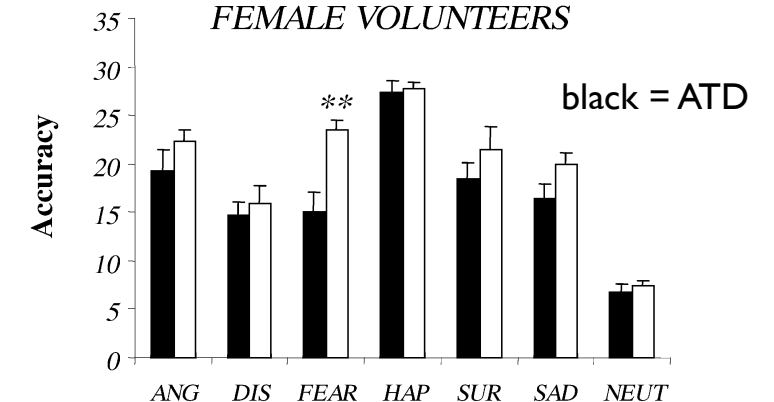
Cit/Reb, chronic, MDD

Tranter et al., 2009



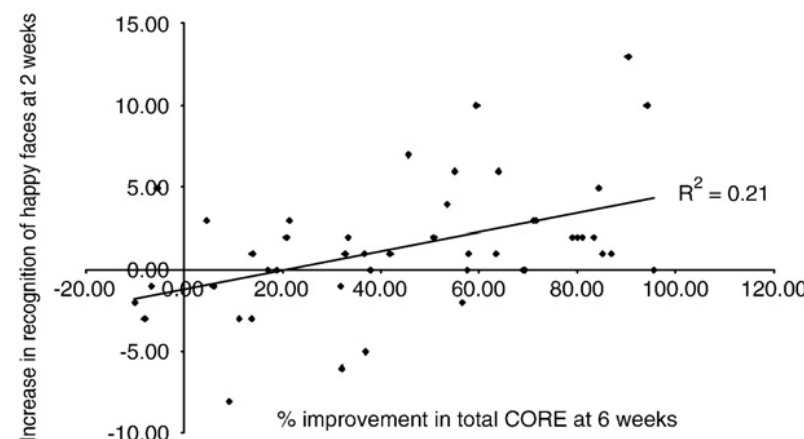
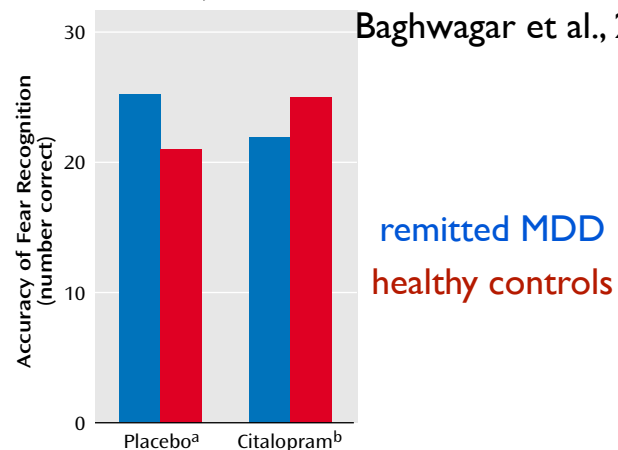
ATD, acute, HC never depr

Harmer et al., 2003c



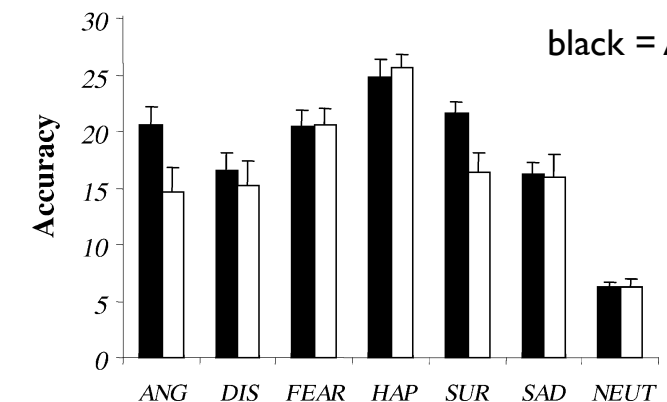
Cit, rem MDD

Baghwagar et al., 2004



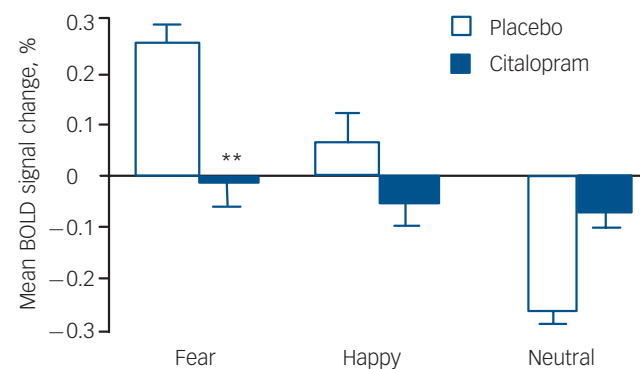
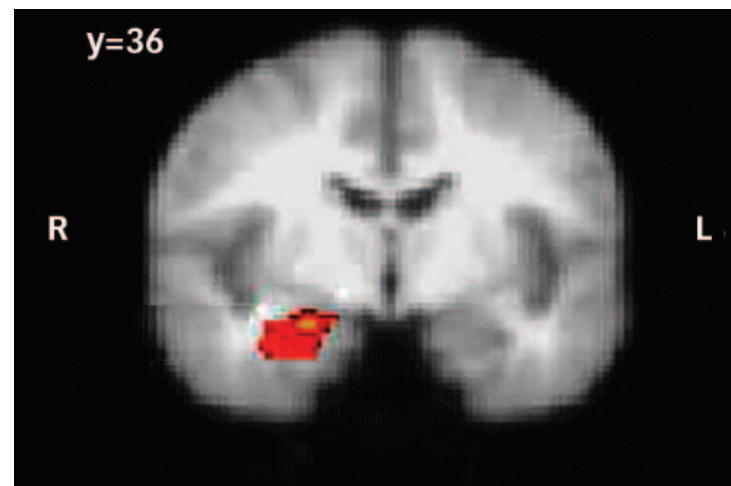
MALE VOLUNTEERS

black = ATD

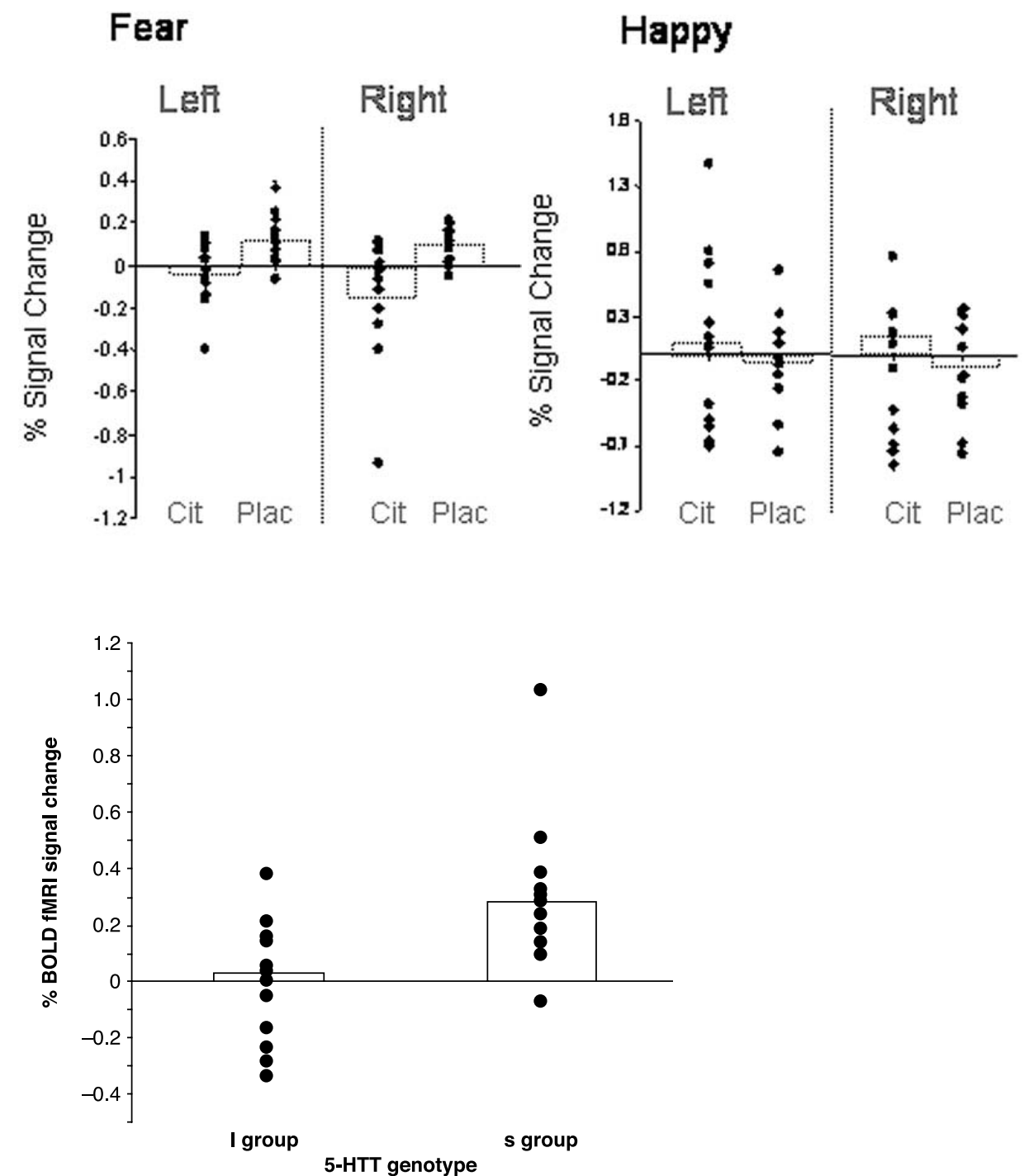


Face reactivity in the amygdala

Single dose citalopram



7 days citalopram



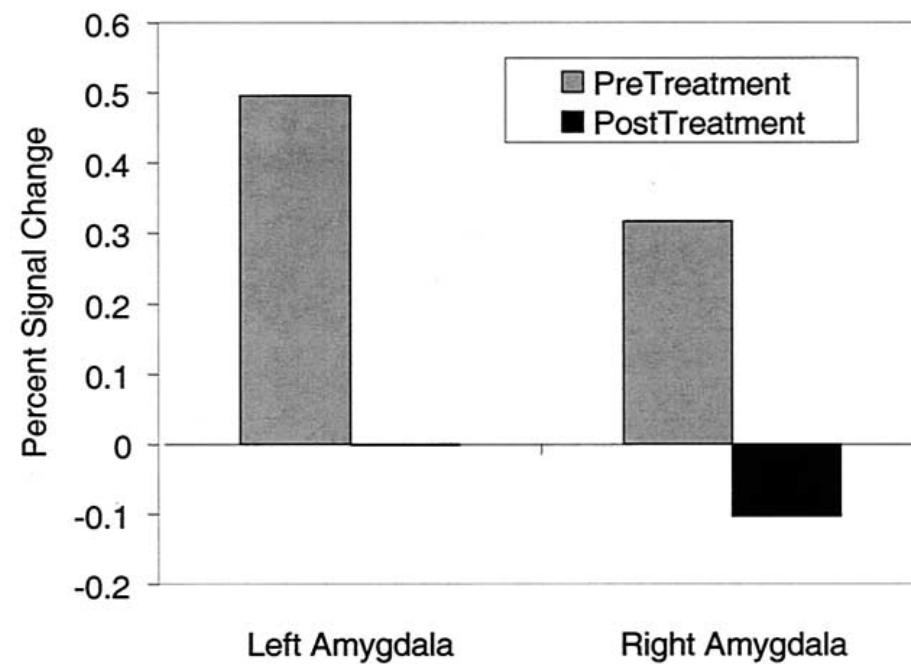
Hariri et al., 2002, Murphy et al., 2009, Harmer et al., 2006, see also Murphy et al., 2013

Treatment

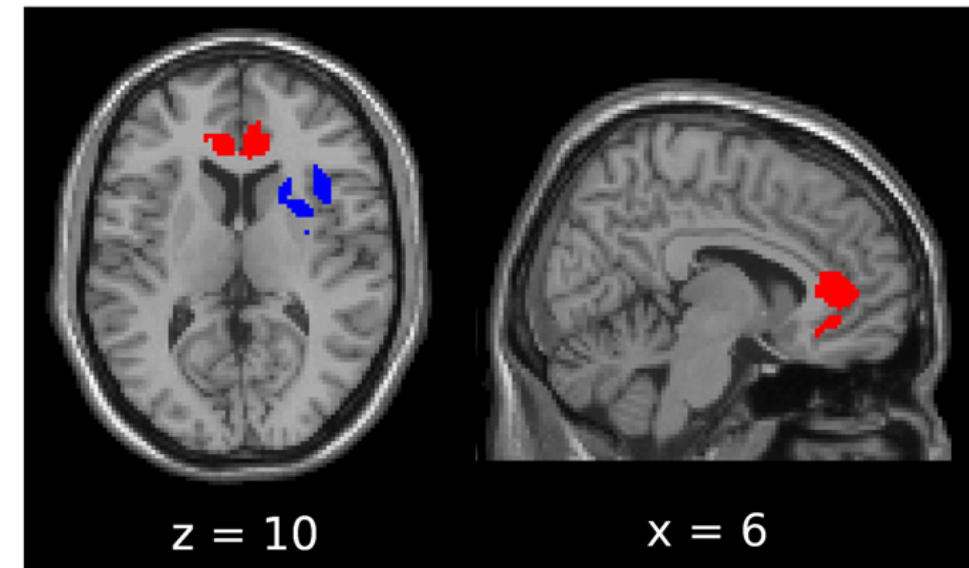
Hyperreactivity recovers with treatment

Sheline et al., 2001

Sertraline, 8 weeks, ca 100mg



ACC and amygdala response (to faces)
predicts treatment response

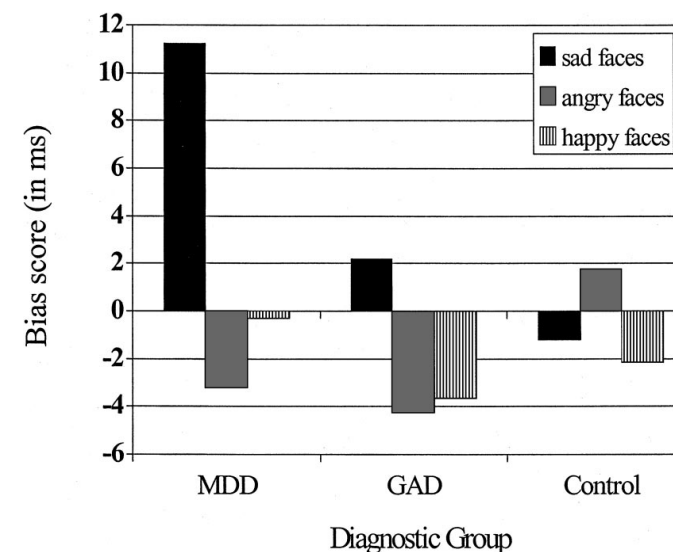
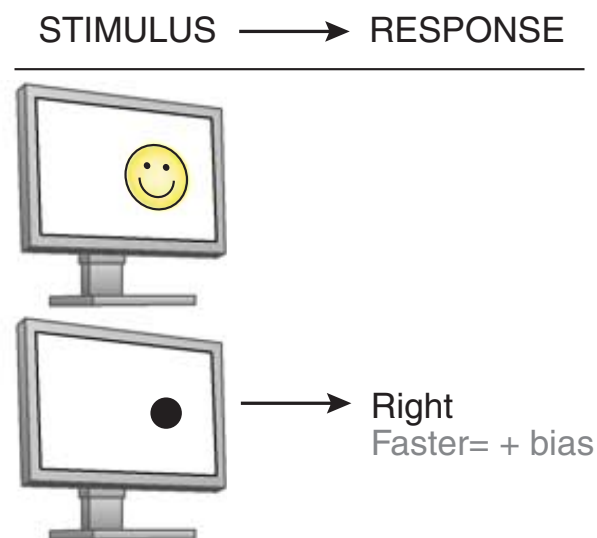


Sheline et al., 2001, Fu et al., 2013

Attentional bias

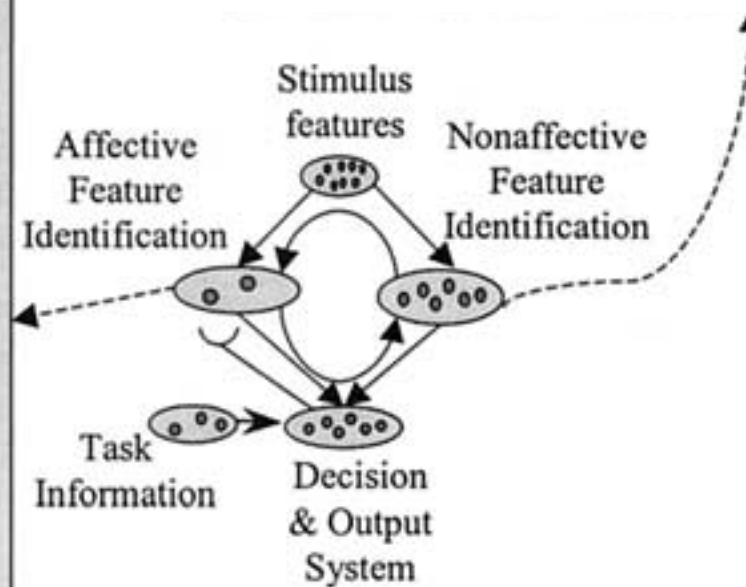
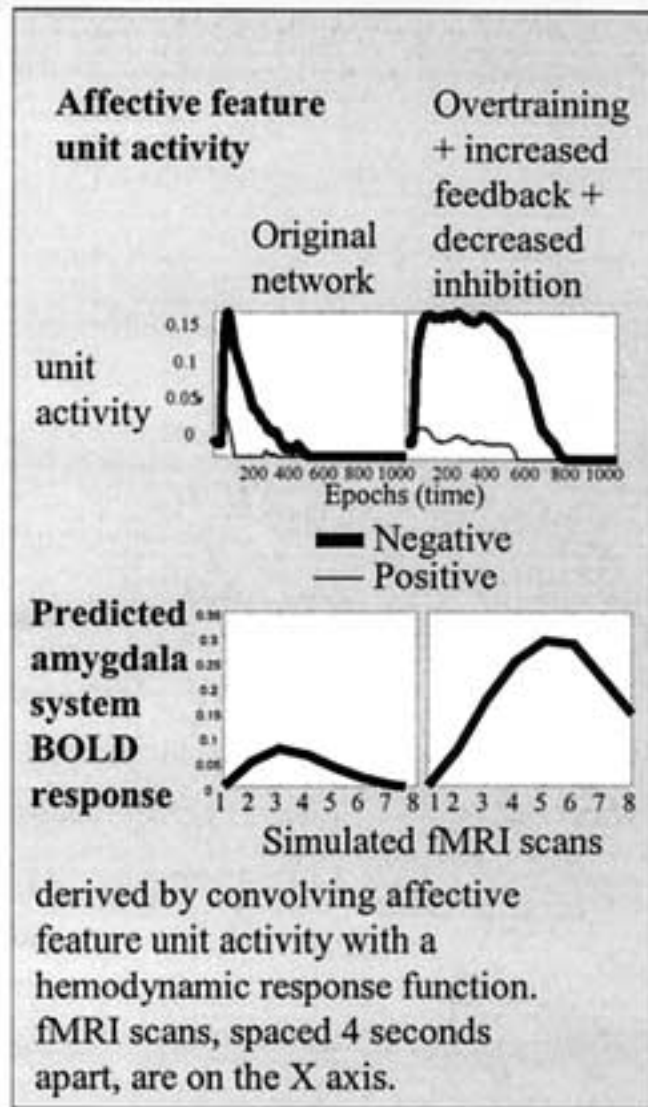
Table 1
Group Means and Standard Deviations on Color-Naming Response Latencies to the Stimulus Words

Subject group	Word type					
	Depressed		Neutral		Manic	
	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>
Nondepressed	694.67	76.88	699.67	82.82	692.47	70.53
Depressed	762.40	94.94	739.00	77.44	746.80	77.09

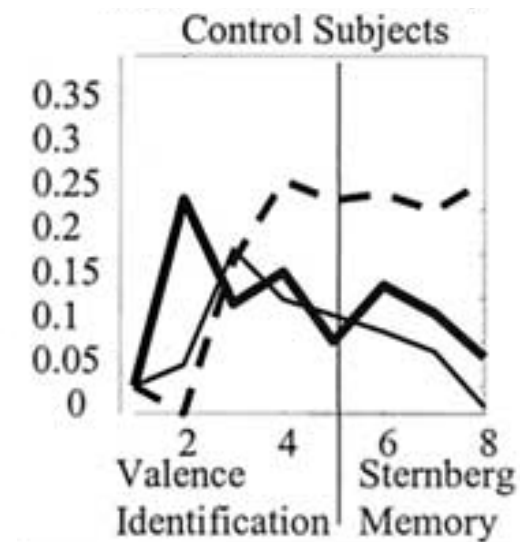
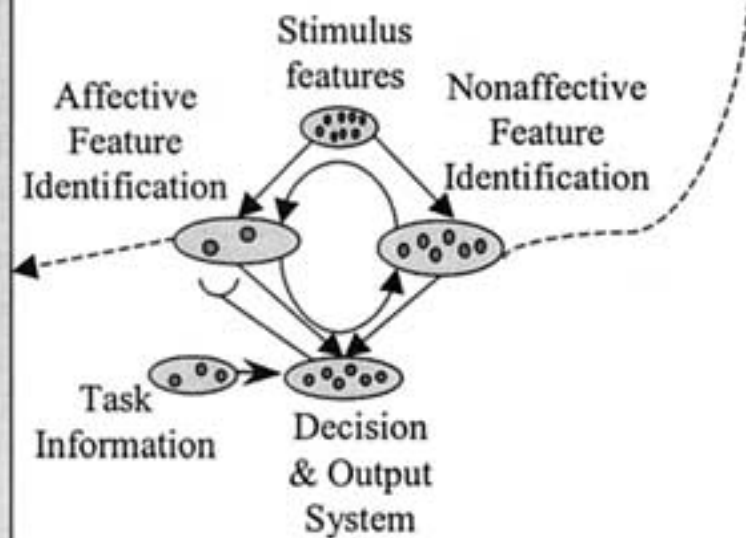
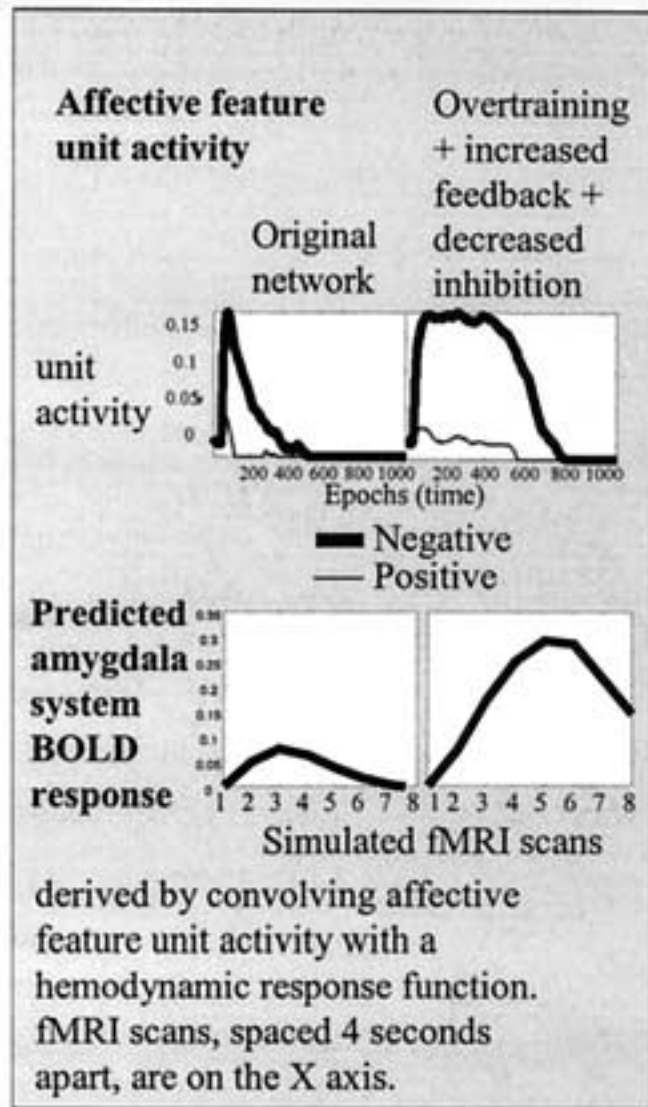


- ▶ In panic/phobia: fast (50ms stimulus presentation)
- ▶ In GAD/MDD: slow (only at longer, 500ms)
- ▶ High-level + need time for elaboration

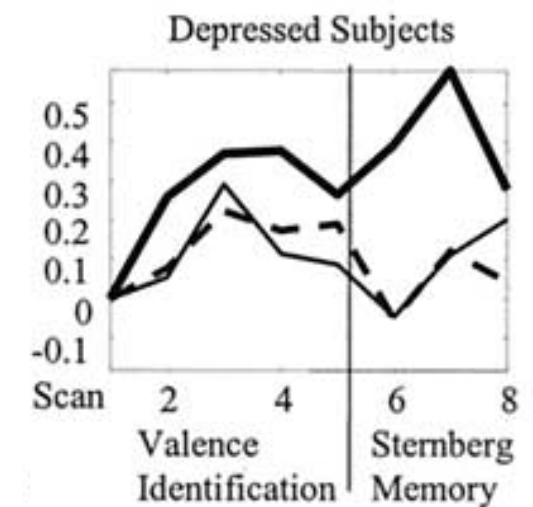
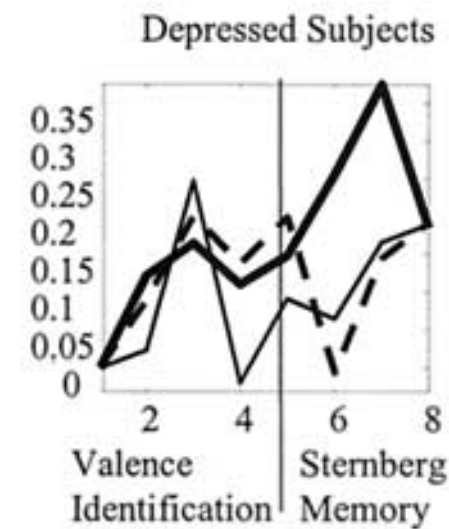
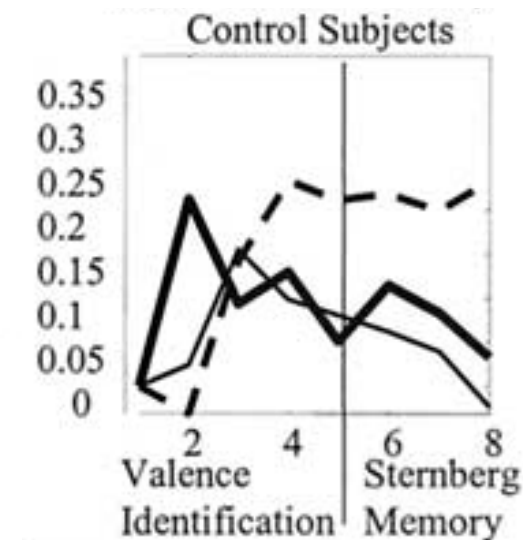
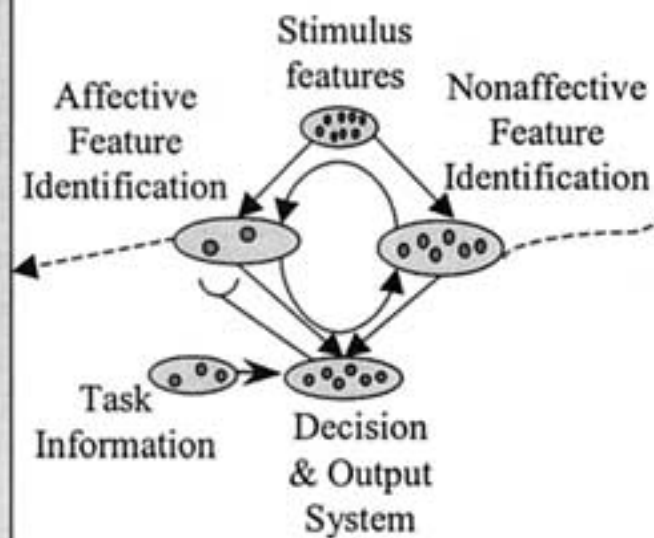
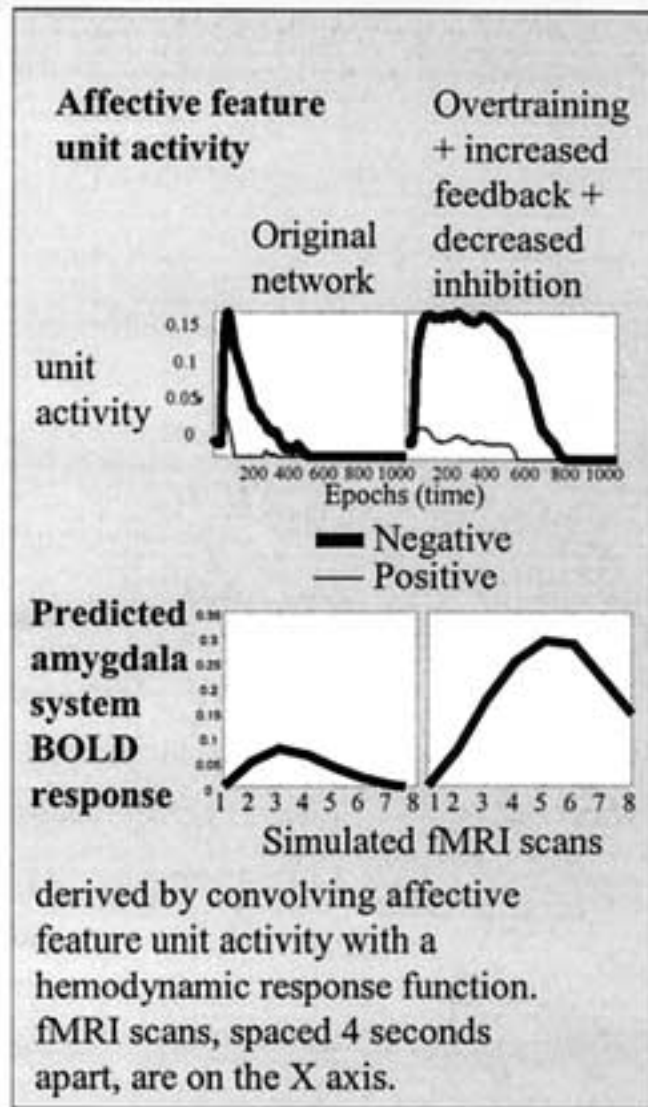
Sticky aversive info



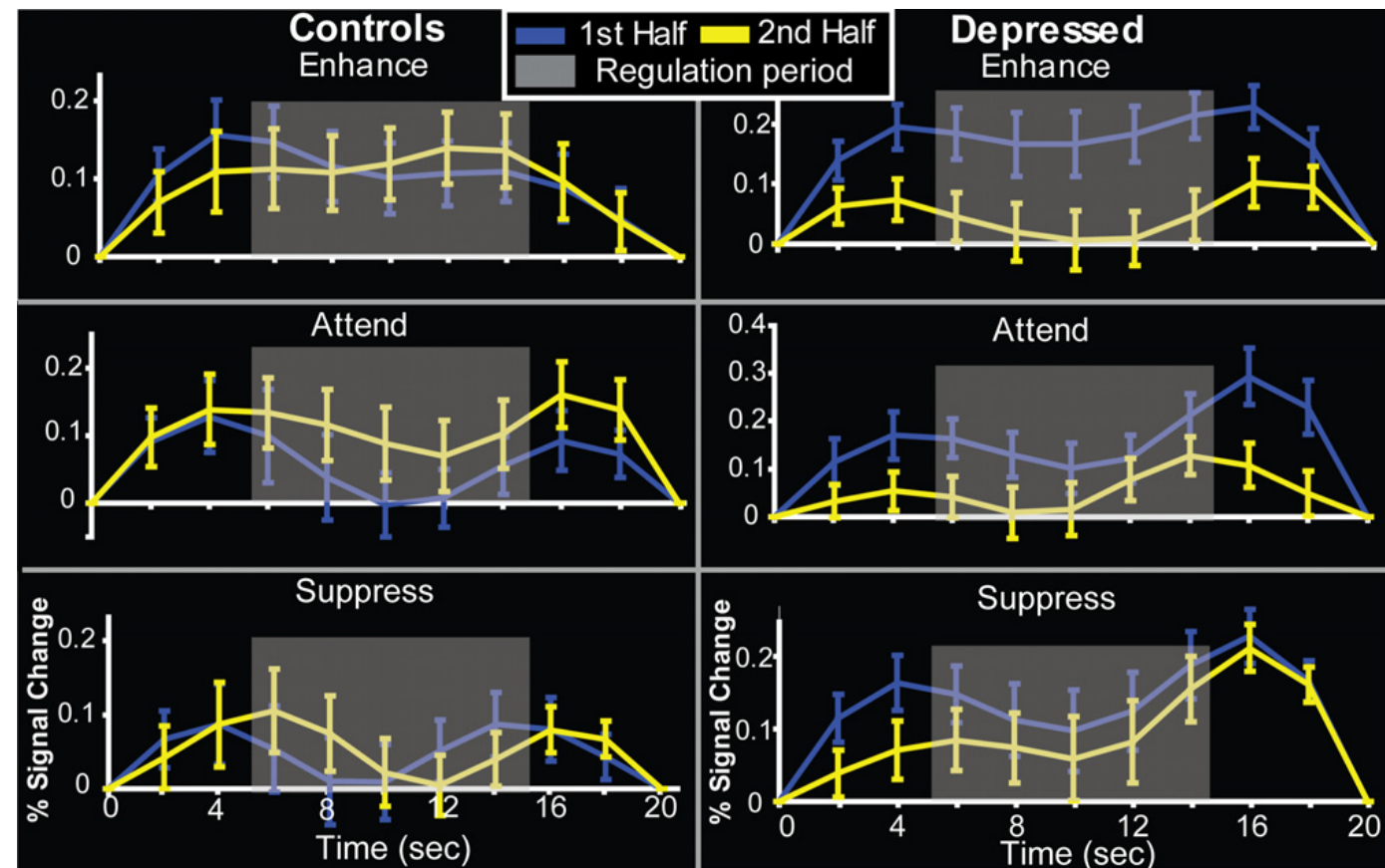
Sticky aversive info



Sticky aversive info

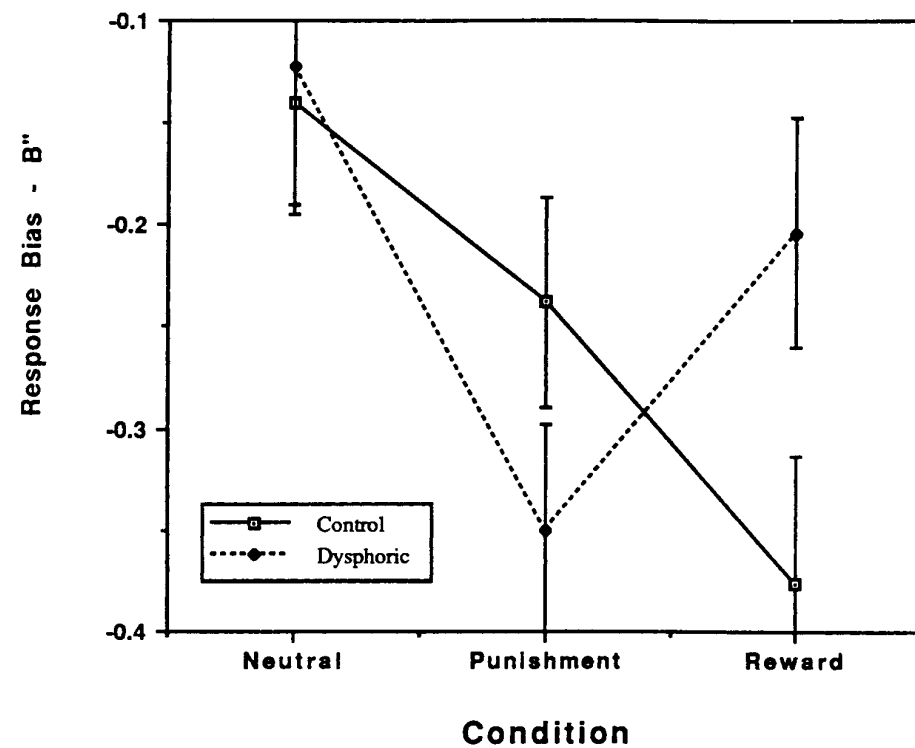


Maintaining positive affect

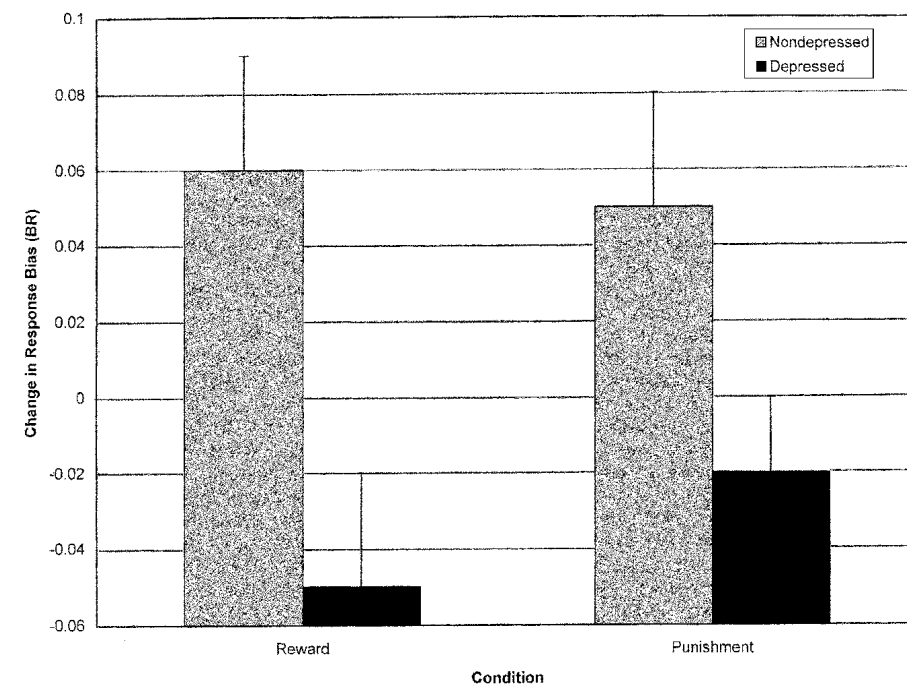


- ▶ No primary changes (pain, hedonic taste, sucrose)
- ▶ Reduced emotional responses +<-
- ▶ Attention & memory biased towards negative
 - at conceptual level
 - if allow for elaboration
 - negative conceptual information sticks around longer, positive dissipates away
- ▶ Cognitive biases:
 - Negative information is more 'important'
- ▶ Next: learning from reinforcement
 - learning impaired, or outcome insensitive?

Learning & choice

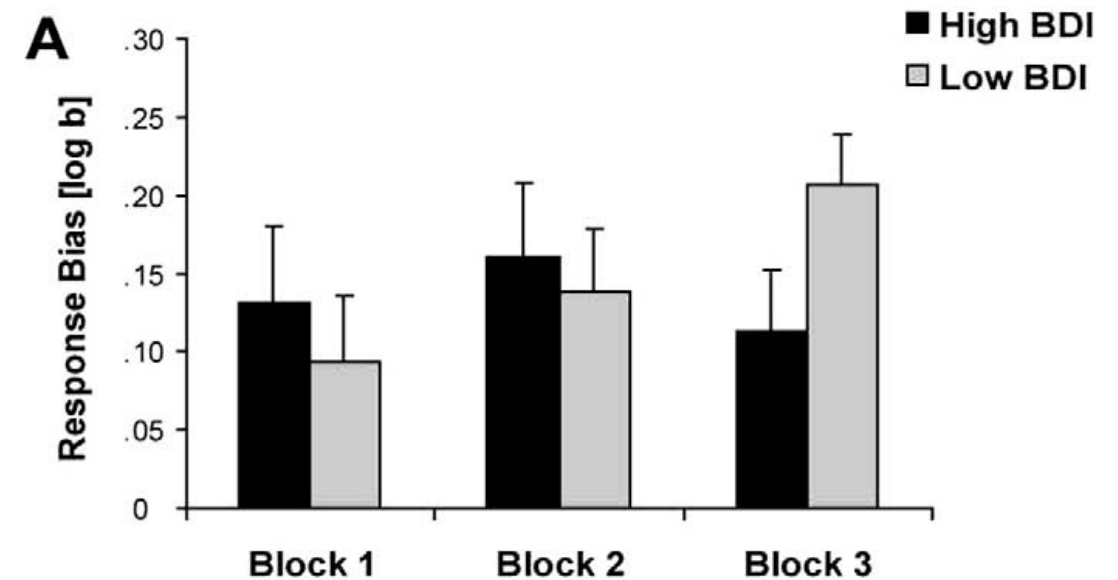
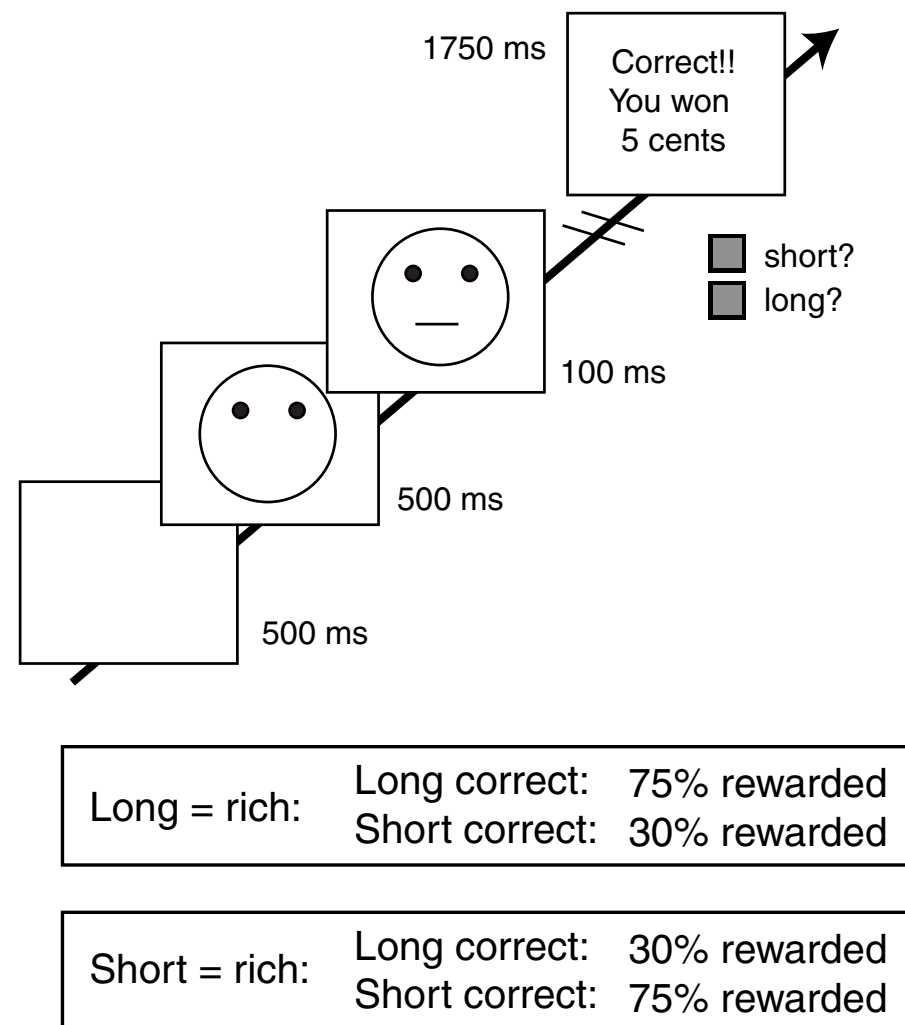


Henriques et al., 1994



Henriques and Davidson, 2000

Learning & choice cont'd



Learning or sensitivity?

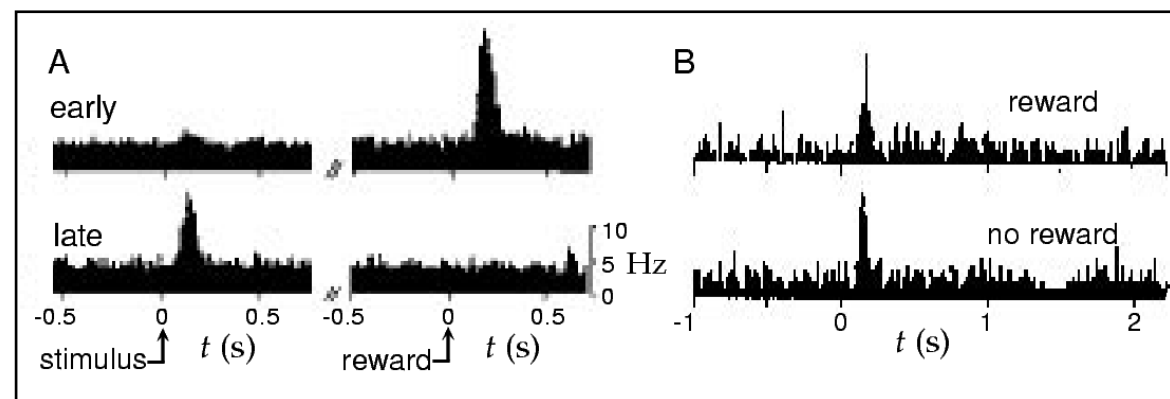
$$Q_t(a, s) = Q_{t-1}(a, s) + \epsilon(r_t - Q_{t-1}(a, s))$$

Kapur and Mann 1992, Muscat et al. 1992, Papp et al. 1994, Willner et al. 1997, Dunlop and Nemeroff 2007, Gershon et al. 2007, Martin-Soelch 2009
Text

Learning or sensitivity?

$$Q_t(a, s) = Q_{t-1}(a, s) + \epsilon(r_t - Q_{t-1}(a, s))$$

Dopamine



Montague et al. 1996, Schultz et al. 1997

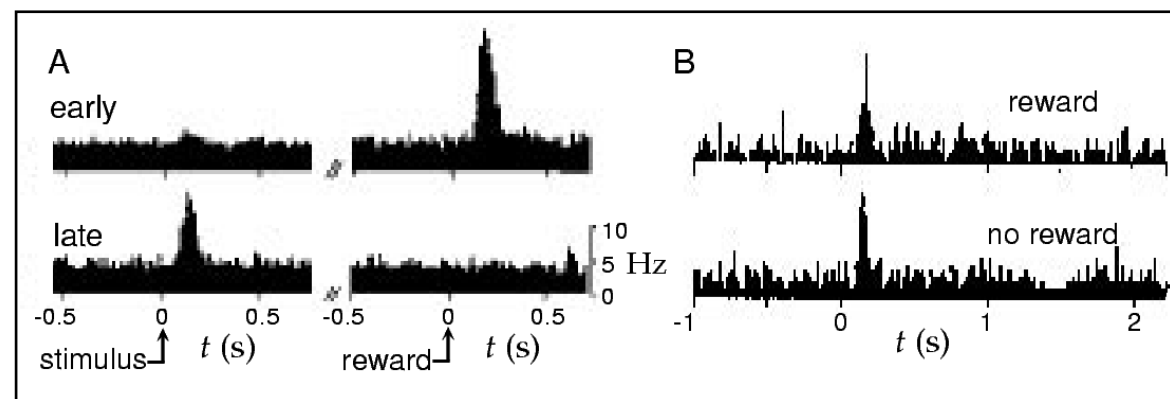
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Learning or sensitivity?

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Anhedonia

Dopamine



Montague et al. 1996, Schultz et al. 1997

Kapur and Mann 1992, Muscat et al. 1992, Papp et al. 1994, Willner et al. 1997, Dunlop and Nemeroff 2007, Gershon et al. 2007, Martin-Soelch 2009

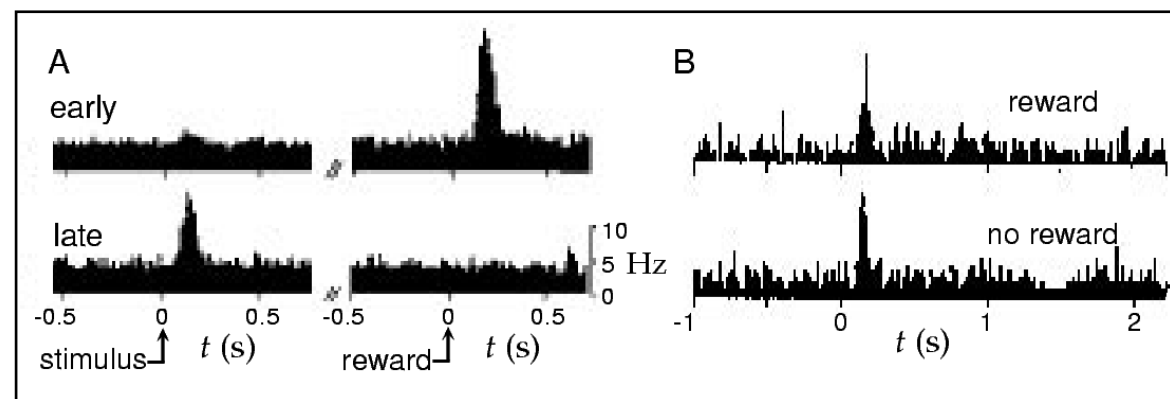
Text

Learning or sensitivity?

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Anhedonia β

Dopamine

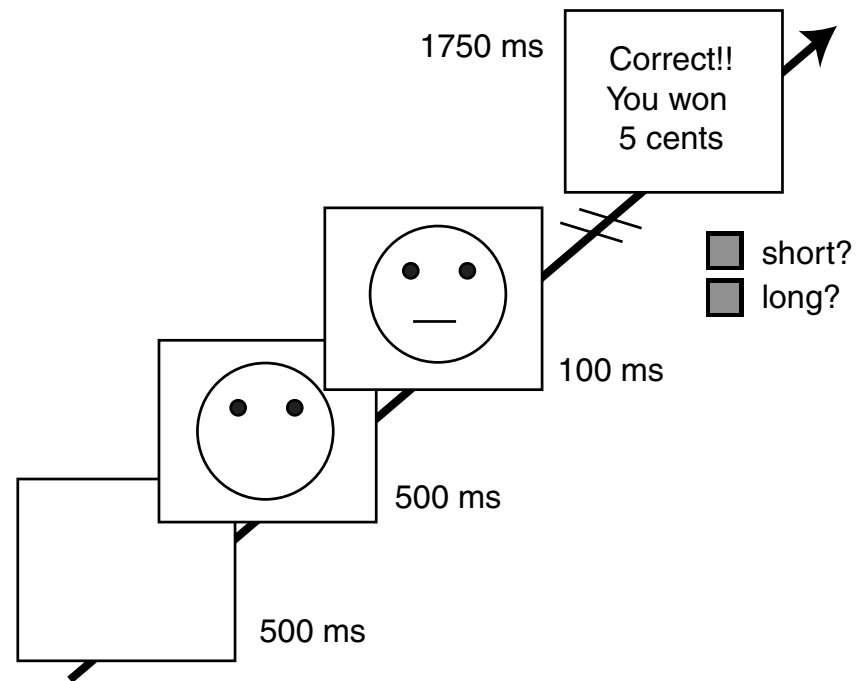


Montague et al. 1996, Schultz et al. 1997

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Text

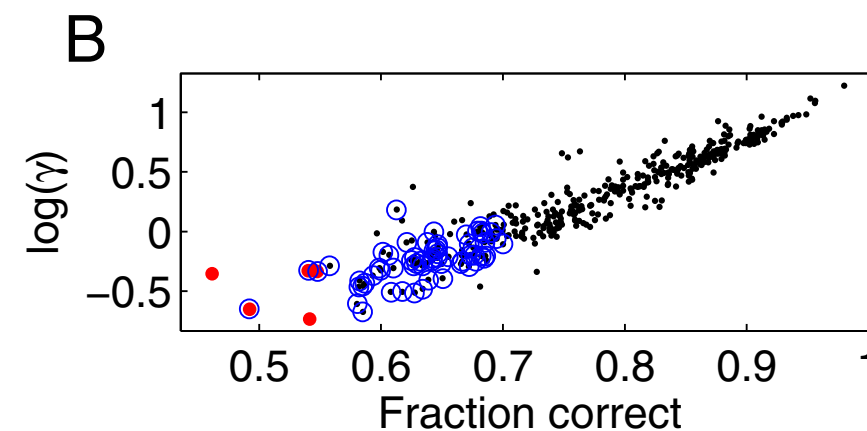
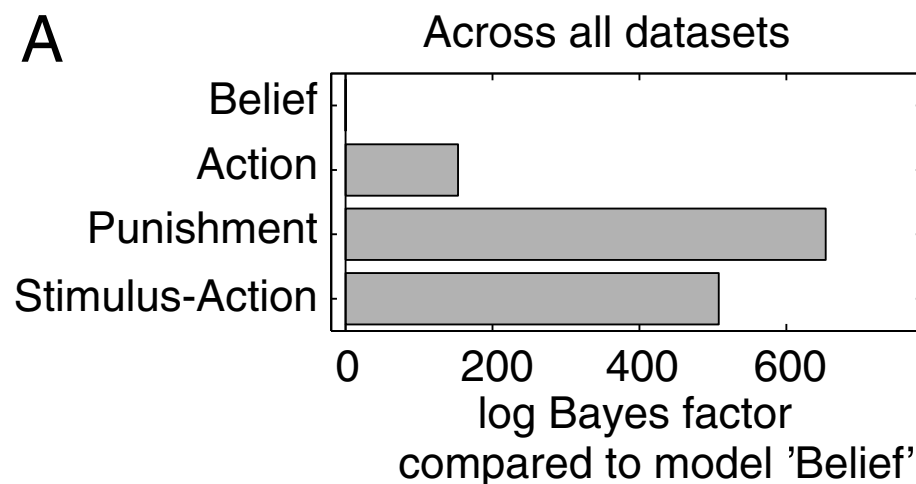
Modelling: first get the task



$$p(a_t|s_t) = \frac{1}{1 + \exp [-(\mathcal{W}_t(a_t, s_t) - \mathcal{W}_t(\bar{a}_t, s_t))]}$$

$$\mathcal{W}_t(a_t, s_t) = \gamma \mathcal{I}(a_t, s_t) + \zeta \mathcal{Q}_t(a_t, s_t) + (1 - \zeta) \mathcal{Q}_t(a_t, \bar{s}_t)$$

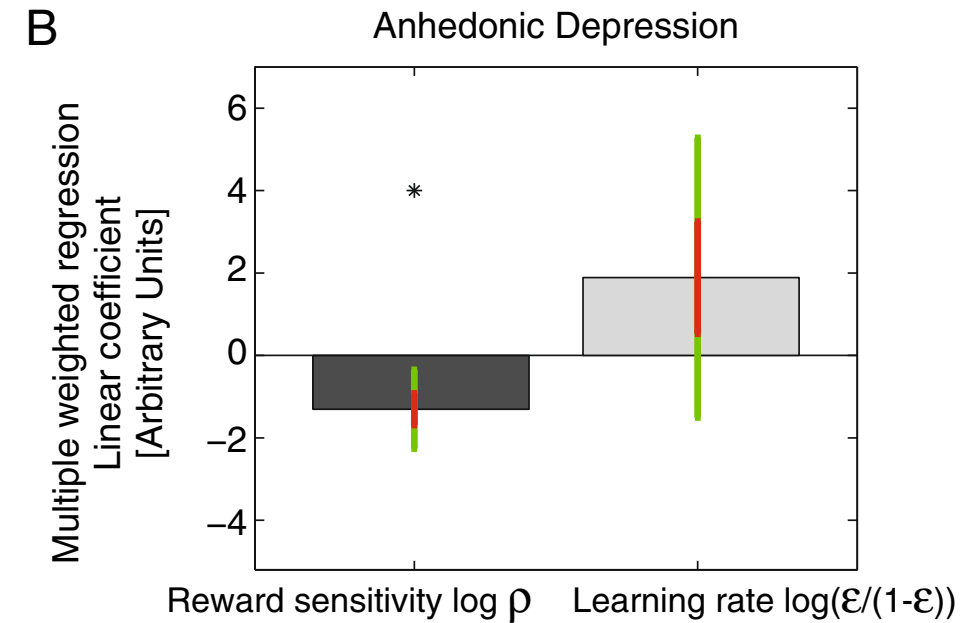
Instruction Reward/bias component



Learning or sensitivity?

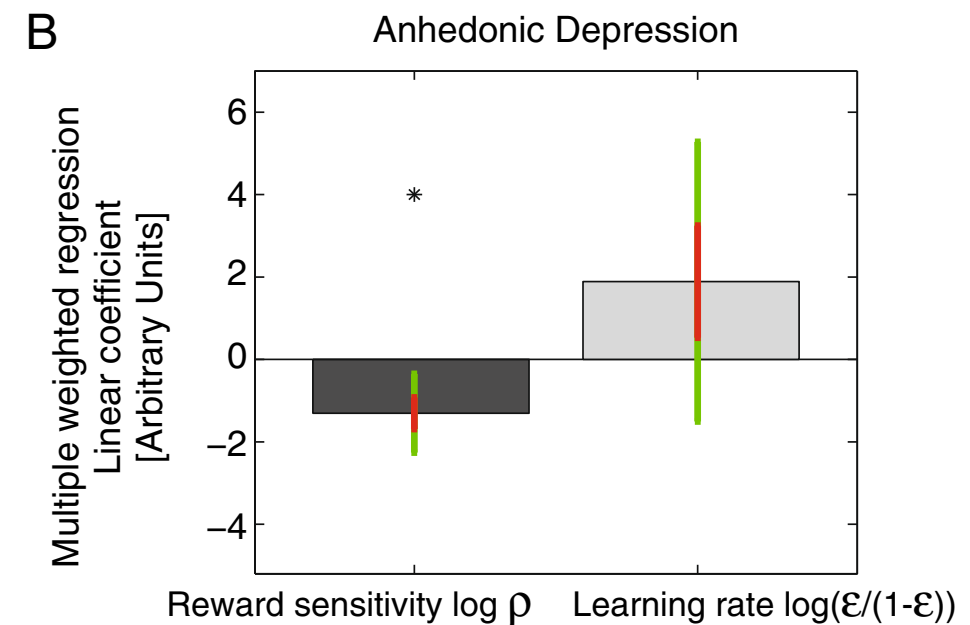
Learning or sensitivity?

- Correlation of anhedonia is with reward sensitivity, not learning rate



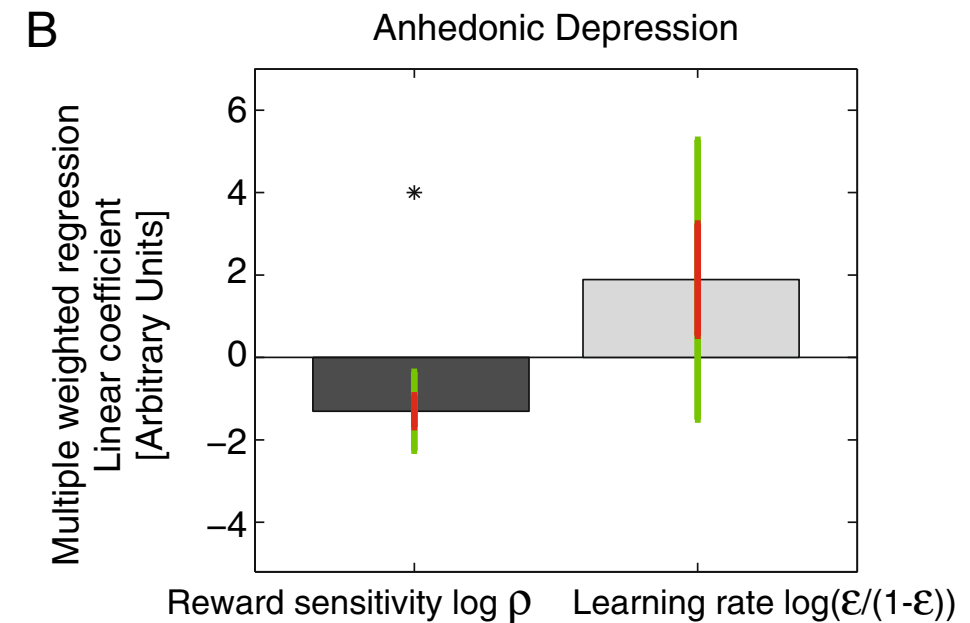
Learning or sensitivity?

- ▶ Correlation of anhedonia is with reward sensitivity, not learning rate
- ▶ But: correlations



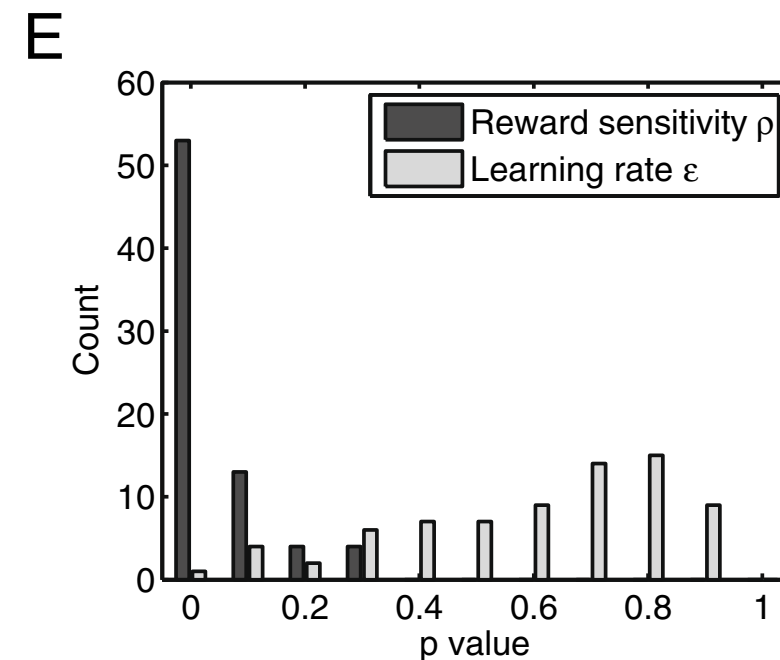
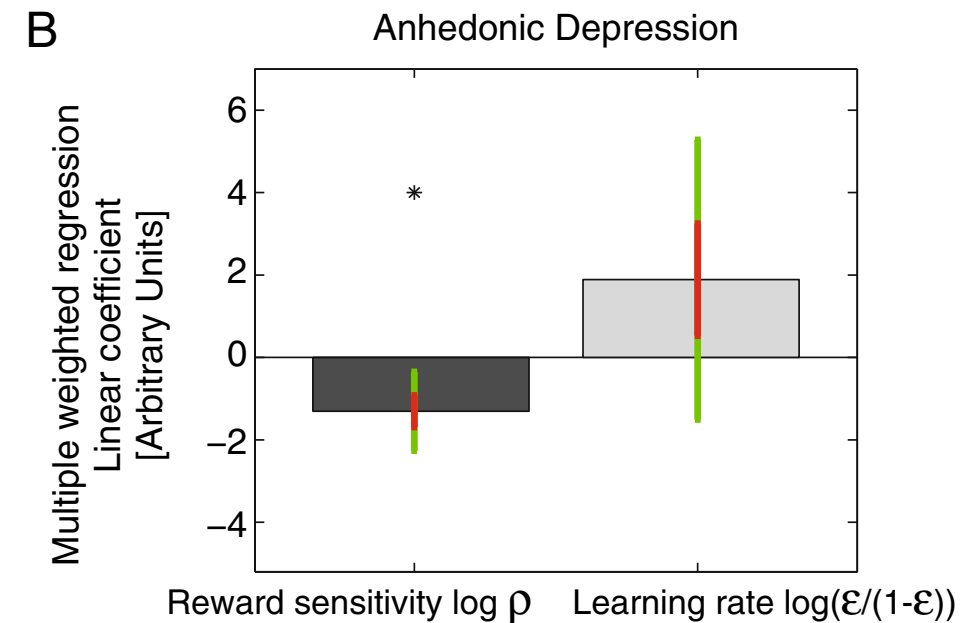
Learning or sensitivity?

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- ▶ But: correlations
- ▶ Fit, generate surrogate data, examine correlations - has the model really captured something about the data?



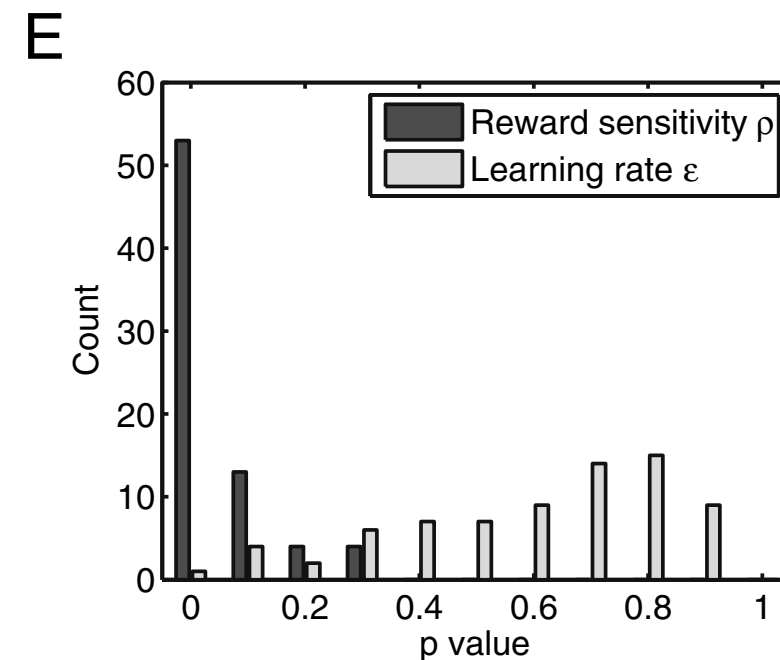
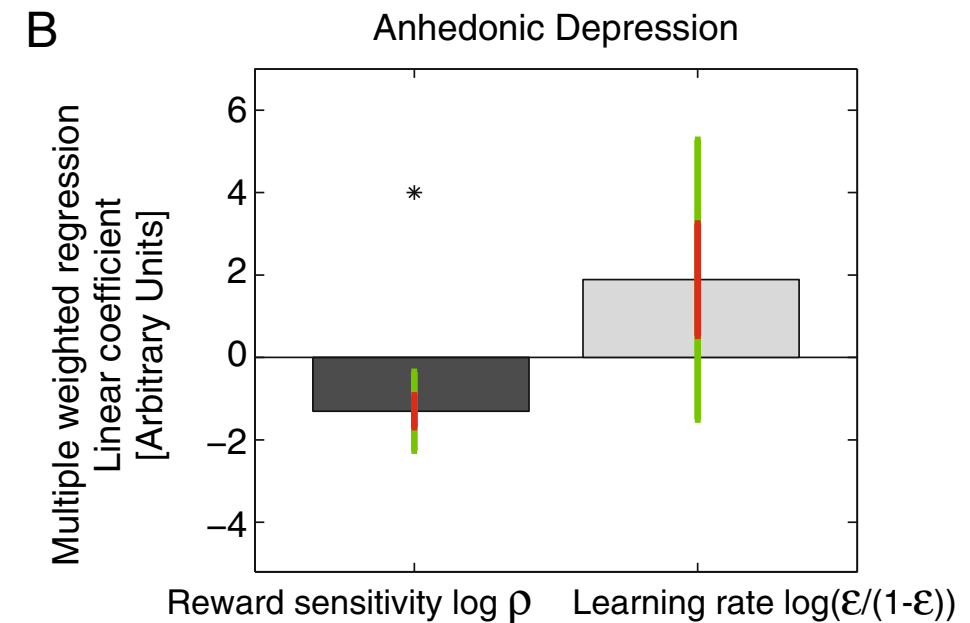
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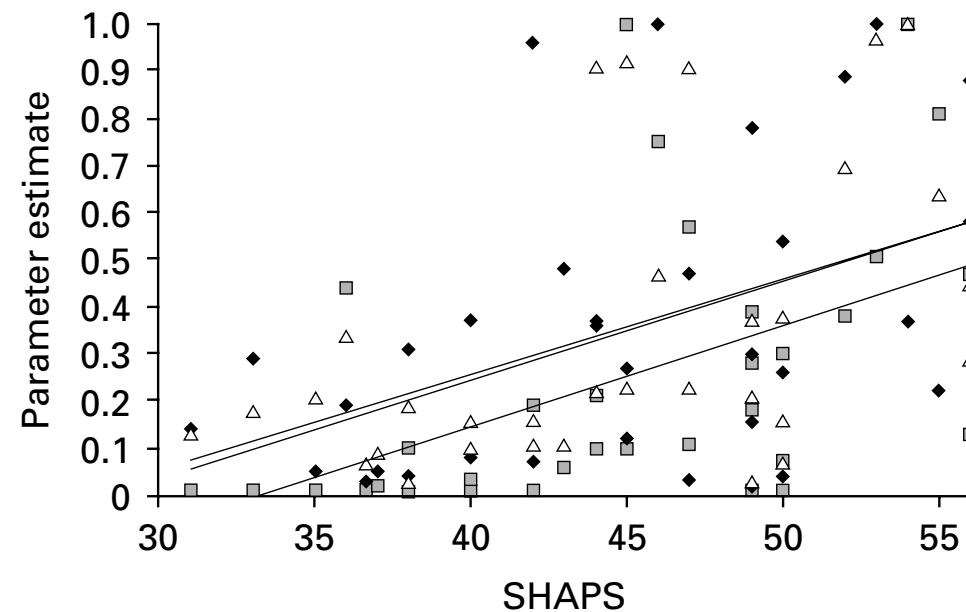
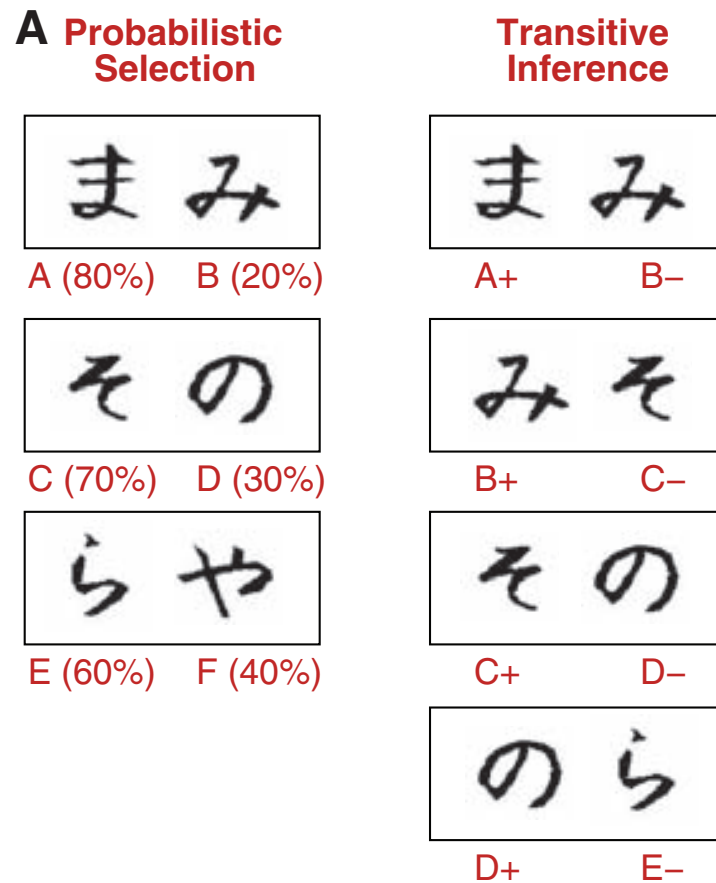
Learning or sensitivity?

- ▶ Correlation of anhedonia is with reward sensitivity, not learning rate
- ▶ But: correlations
- ▶ Fit, generate surrogate data, examine correlations - has the model really captured something about the data?
- ▶ Not that they can't learn, but don't care.



But...

► Chase et al., 2009



- slower learning rates from rewards & losses, and less sensitive to outcomes overall
- even when partial out BDI score

But...

► Chase et al., 2009

A Probabilistic Selection

ま み

A (80%) B (20%)

そ の

C (70%) D (30%)

ら や

E (60%) F (40%)

Transitive Inference

ま み

A+ B-

み そ

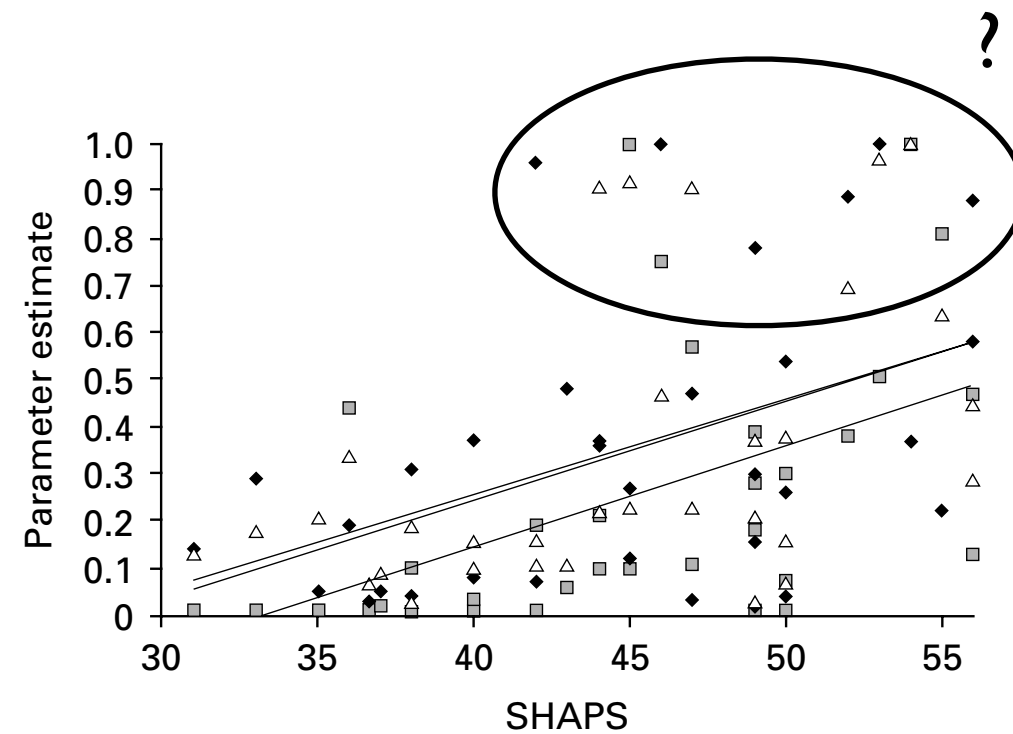
B+ C-

そ の

C+ D-

の ら

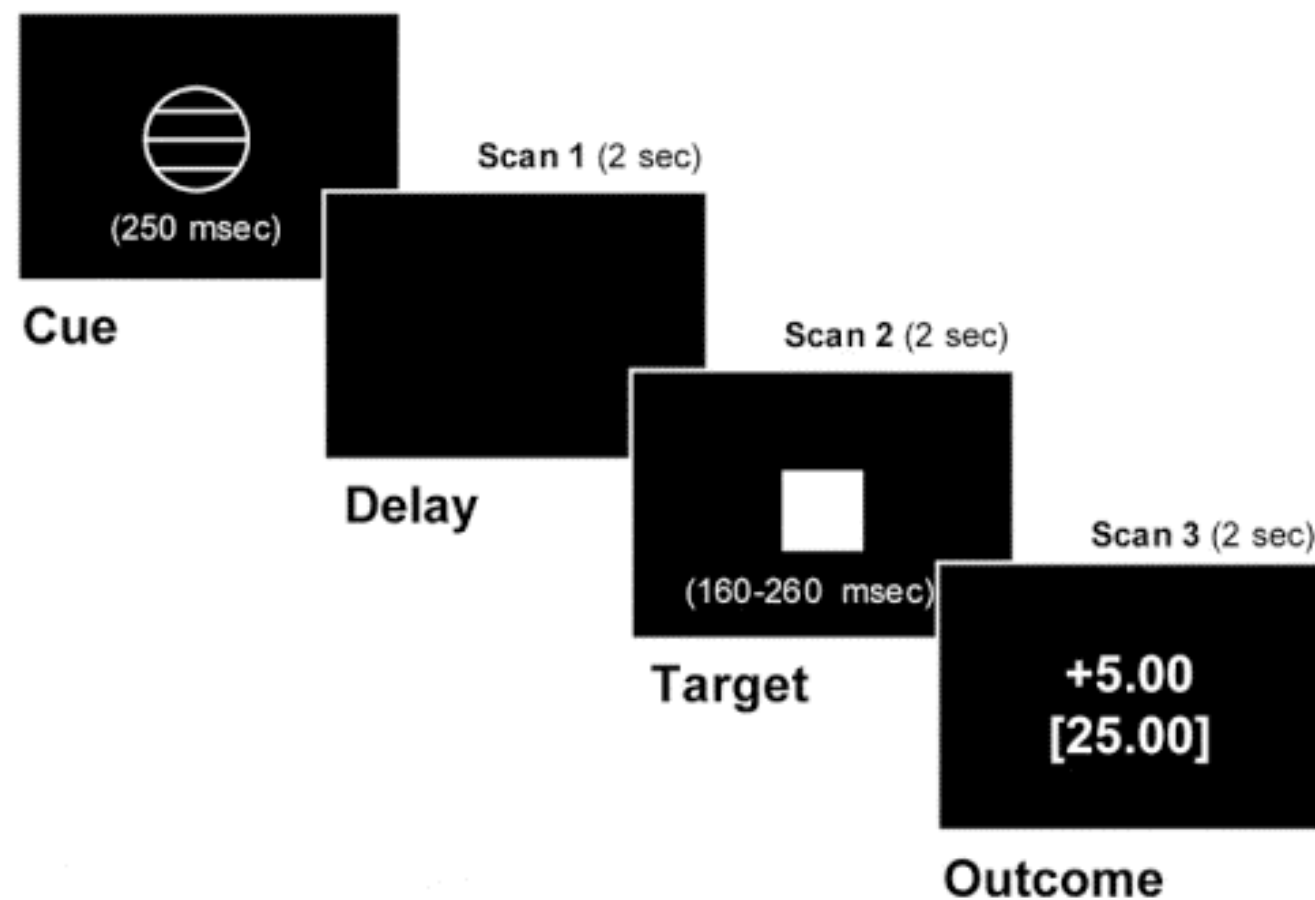
D+ E-



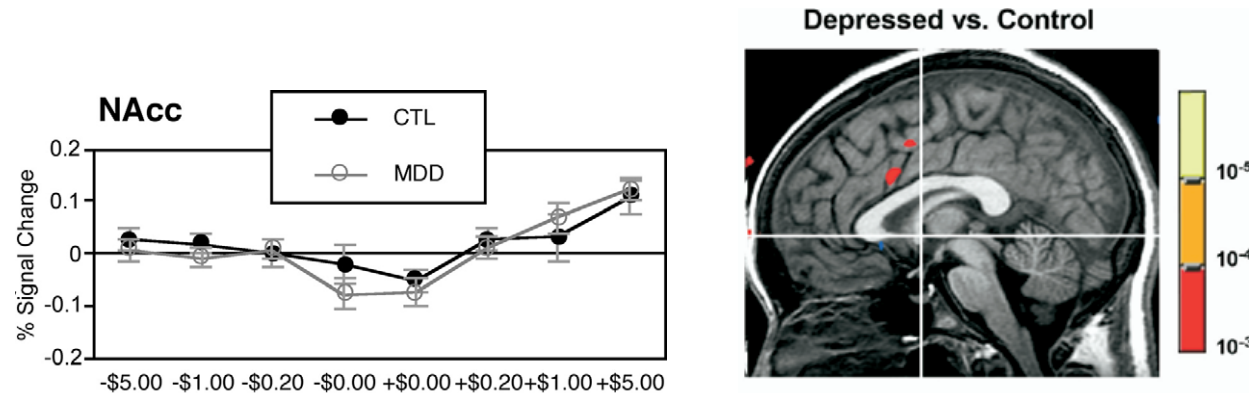
- slower learning rates from rewards & losses, and less sensitive to outcomes overall
- even when partial out BDI score

fMRI - learning or reward?

► MID task (Knutson, Schiff...)



► Anticipation



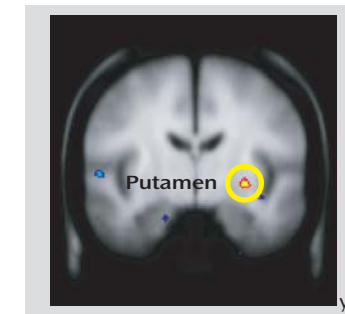
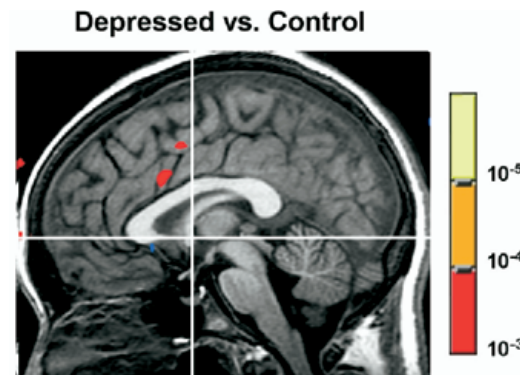
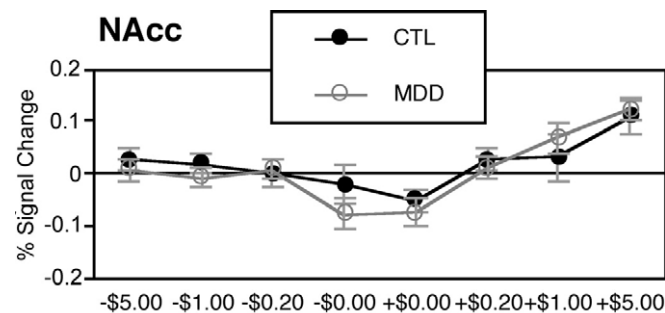
► Outcome

- No NAcc

- R MPFC (BA 32)
- L Insula (BA 47)
- R Putamen
- L Putamen
- L Superior Frontal Gyrus (BA 6)
- L Insula (BA 13)
- L Postcentral Gyrus (BA 3)
- L Inferior Parietal Lobe (BA 40)

Knutson et al., 2008

► Anticipation

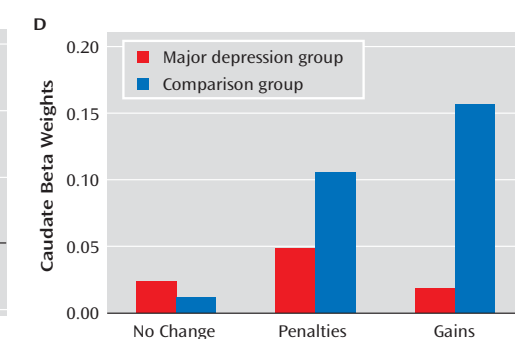
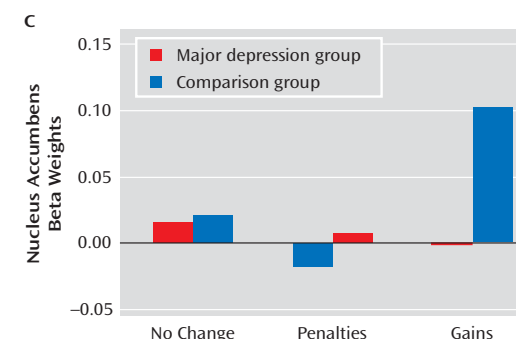
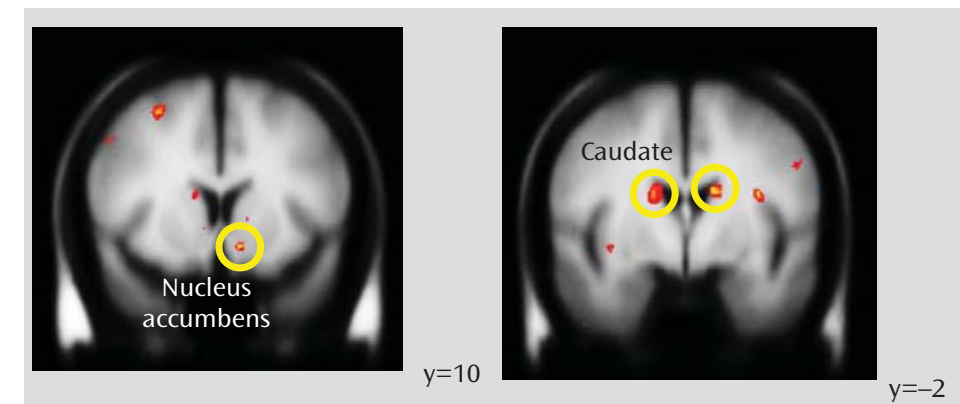


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Knutson et al., 2008

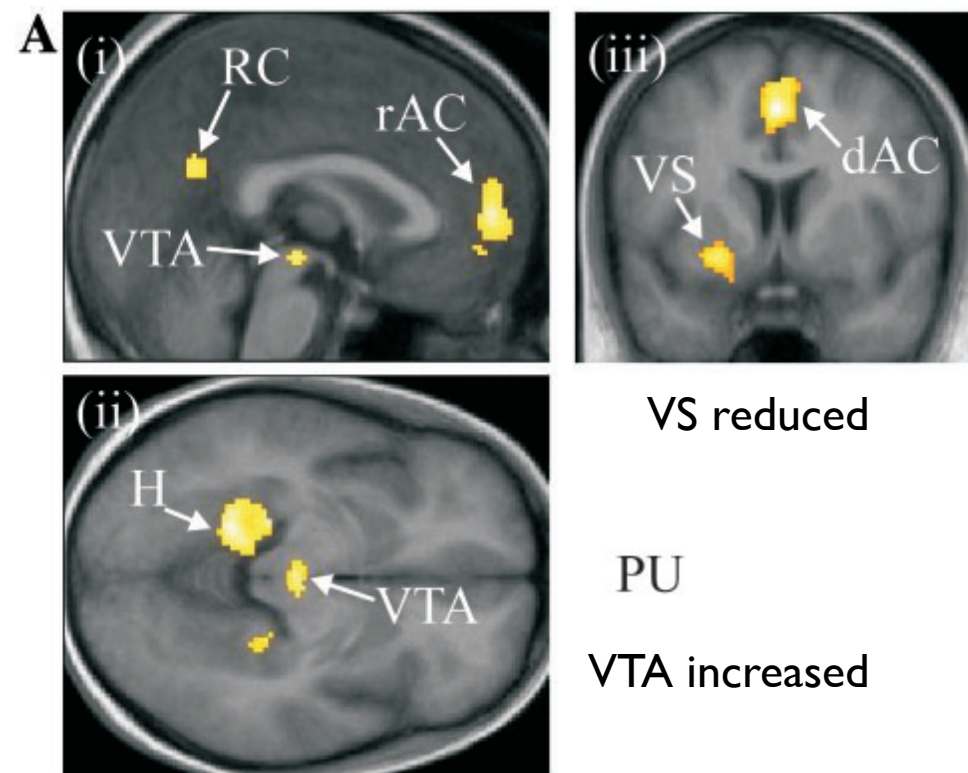


Pizzagalli et al., 2009

Model-based fMRI - TD learning

► Pavlovian task

- correlate of reward PE, water outcome

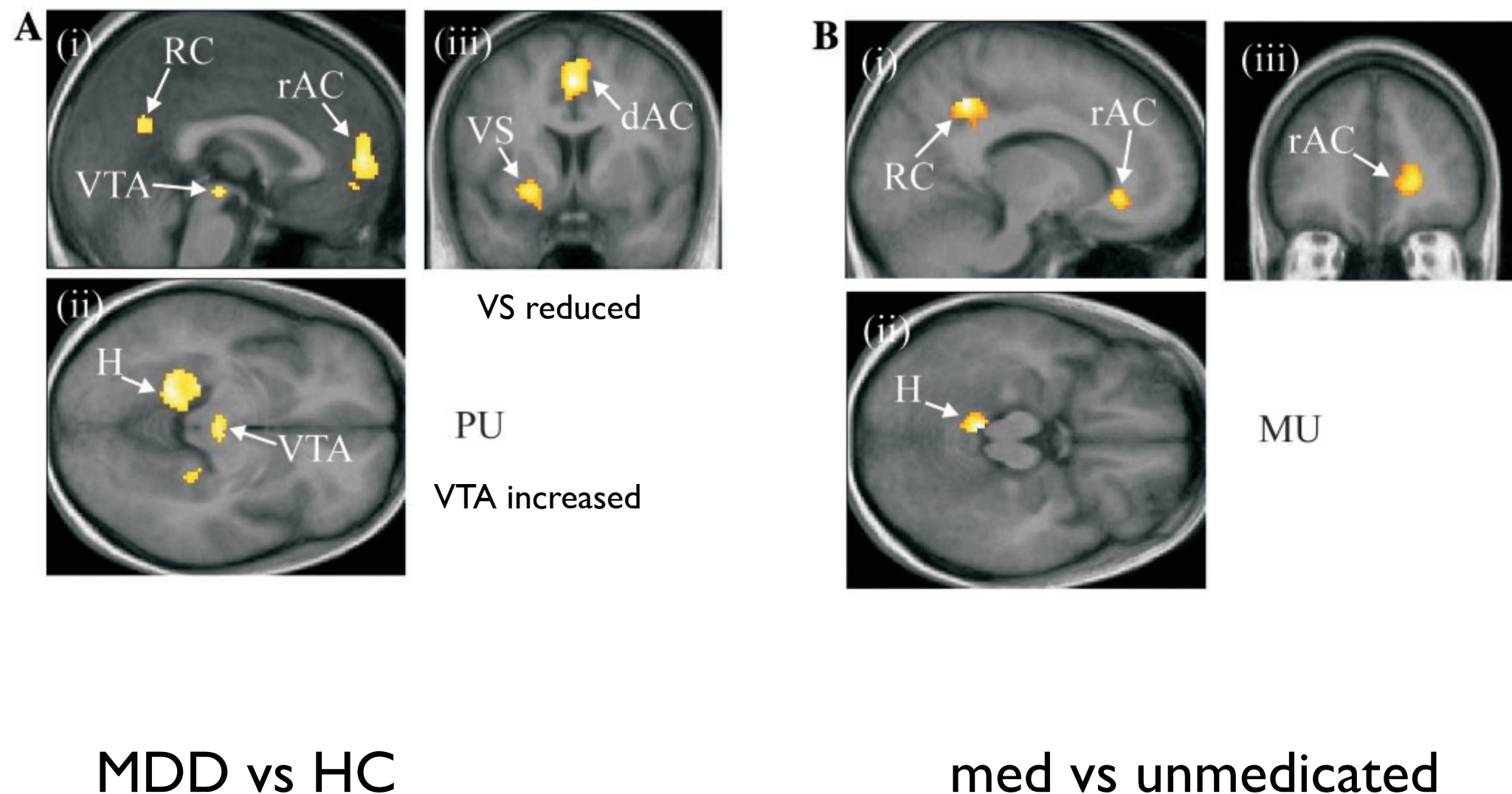


MDD vs HC

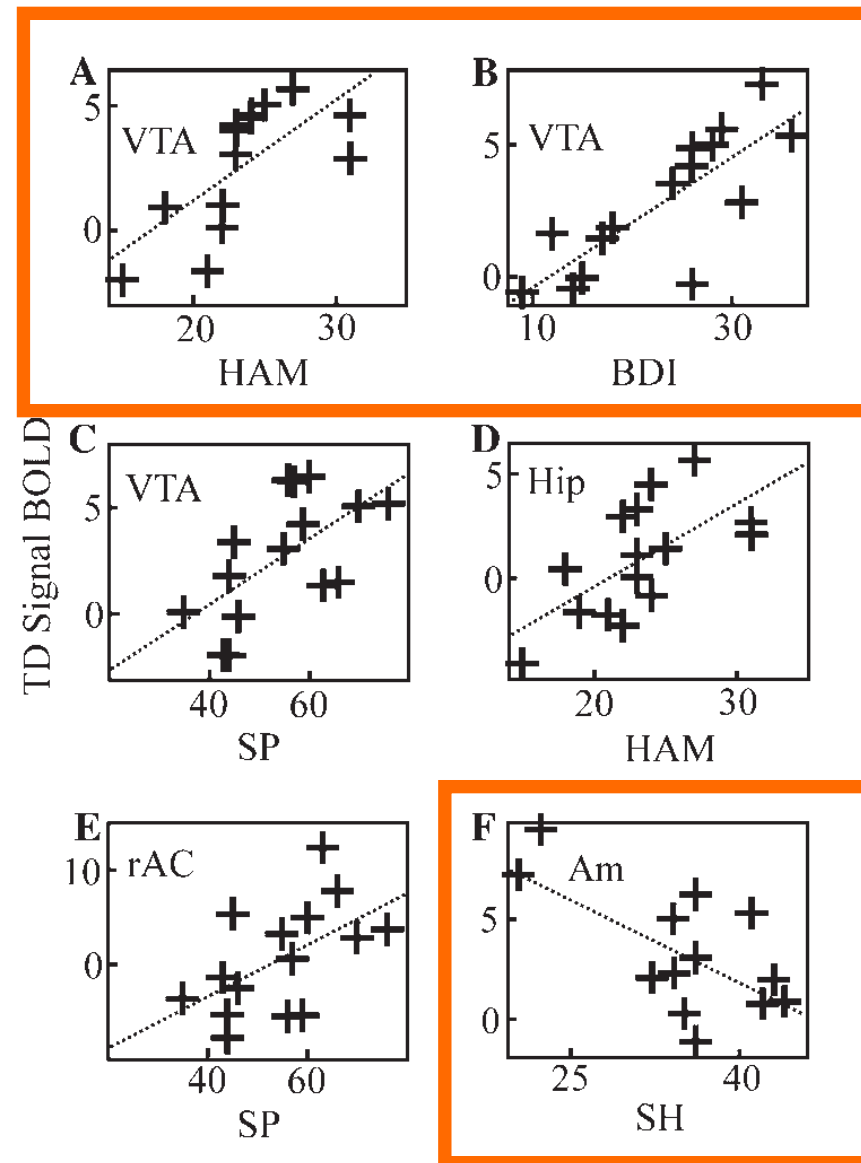
Model-based fMRI - TD learning

► Pavlovian task

- correlate of reward PE, water outcome



Correlates with anhedonia?



Reward tasks in MDD

Reward tasks in MDD

- ▶ Meta-analysis of reward processing tasks in fMRI w/ MDD

Reward tasks in MDD

► Meta-analysis of reward processing tasks in fMRI w/ MDD

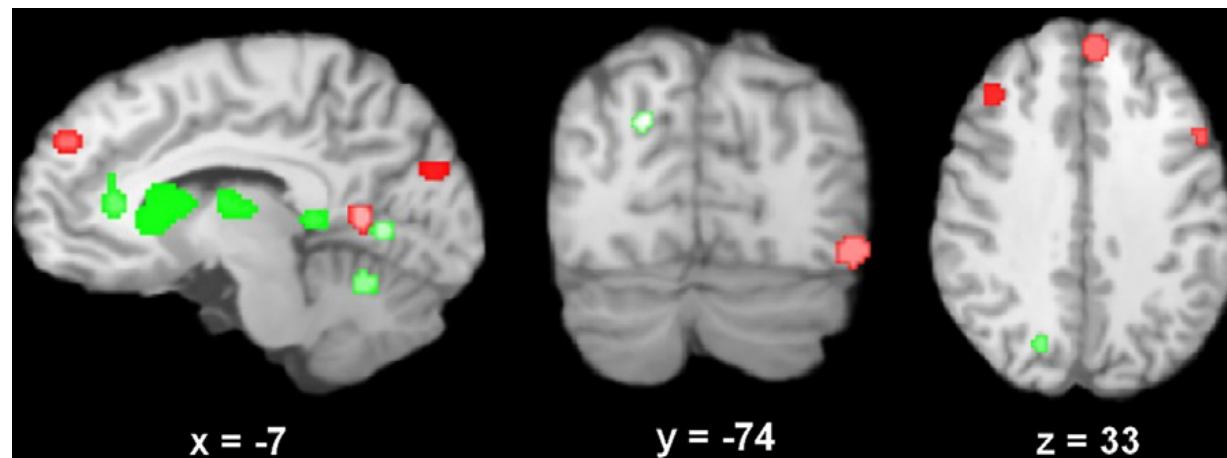


Table 3

Results from the global ALE analyses of reward-related processing in MDD (results from 22 studies, FDR corrected $p < 0.05$).

Brain Region	Side	BA	Site of maximum ALE			Volume (mm ³)	Maximum ALE value
			x	y	z		
Areas of decreased activation (178 foci from 30 experimental contrasts)							
Caudate	L		-6	18	4	1800	0.017
Caudate	L		-8	8	10		0.014
Thalamus	L		-10	-12	8	1192	0.013
Thalamus	L		-14	-14	16		0.013
Caudate	L		-12	-4	20		0.010
Cerebellum	R		4	-36	-4	1144	0.015
Cerebellum	L		-4	-42	4		0.014
Putamen	R		14	8	2	904	0.012
Caudate	R		14	14	10		0.012
Anterior Cingulate	L	24	-8	30	10	584	0.013
Insula	R	13	34	-4	16	400	0.016
Cerebellum	L		-6	-60	-20	304	0.014
Areas of increased activation (118 foci from 20 experimental contrasts)							
Cuneus	R	18	4	-86	18	1104	0.014
Cuneus	L	18	-6	-86	22		0.012
Frontal Lobe	R	47	20	30	-6	912	0.013
Middle Frontal Gyrus	R	8	40	28	38	744	0.016
Superior Frontal Gyrus	L	9	-4	48	32	480	0.015
Fusiform Gyrus	L	19	-48	-74	-12	440	0.014
Middle Frontal Gyrus	L	9	-48	14	30	344	0.011
Lingual Gyrus	R	18	12	-52	4	288	0.010
Lingual Gyrus	R	19	14	-54	0		0.010

ALE, activation likelihood estimation; BA, Brodmann area; L, left; R, right; (x y z), Talairach coordinate.

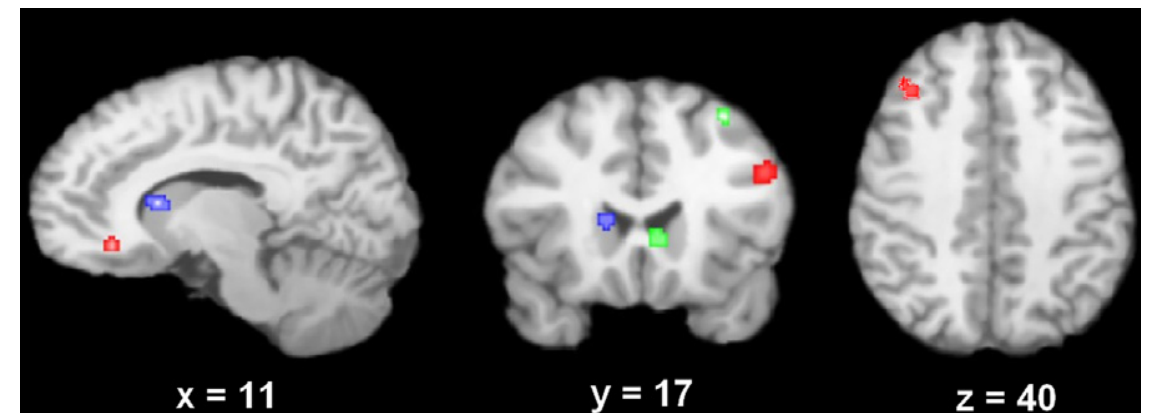
Reward tasks in MDD

► Meta-analysis of reward processing tasks in fMRI w/ MDD

Table 6

ALE results of monetary reward anticipation from 6 studies and outcome from 5 studies in MDD (FDR corrected $p < 0.05$).

Brain region	Side	BA	Site of maximum ALE			Volume (mm ³)	Maximum ALE value
			<i>x</i>	<i>y</i>	<i>z</i>		
Areas of decreased activation during reward anticipation (37 foci from 6 experimental contrasts)							
Caudate	L		−16	16	4	288	0.009
Areas of increased activation during reward anticipation (34 foci from 5 experimental contrasts)							
Middle Frontal Gyrus	L	9	−48	14	30	352	0.011
Anterior Cingulate	R	32	12	32	−8	242	0.009
Frontal Lobe	R	47	18	30	−4		0.008
Middle Frontal Gyrus	R	8	36	24	40	242	0.009
Areas of decreased activation during reward outcome (52 foci from 5 experimental contrasts)							
Caudate	R		14	14	10	328	0.011
Areas of increased activation during reward outcome (18 foci from 5 experimental contrasts)							
No significant ALE clusters have been identified							



Reward tasks in MDD

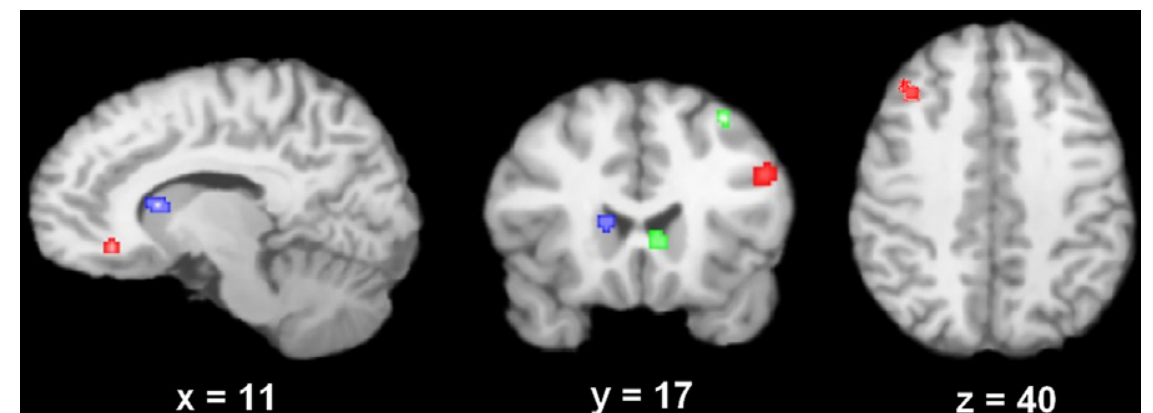
► Meta-analysis of reward processing tasks in fMRI w/ MDD

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- no NAcc, no VTA



Reward tasks in MDD

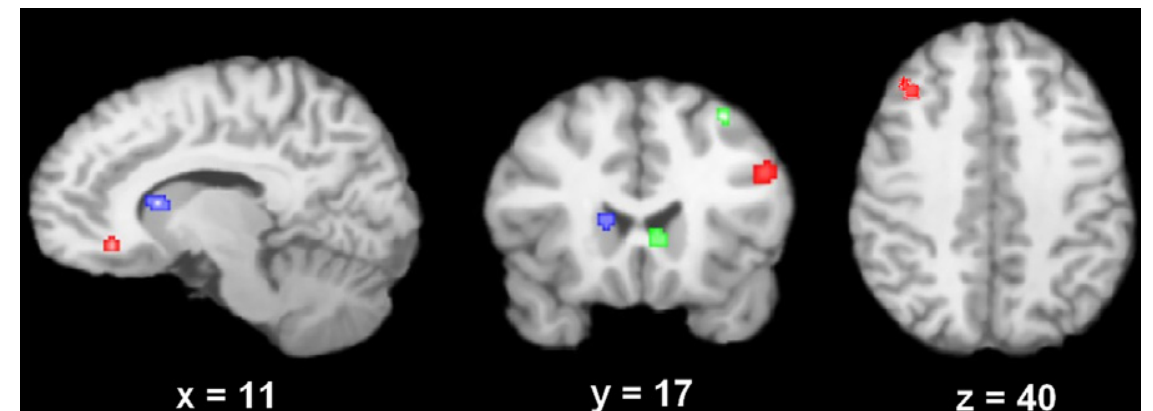
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- no NAcc, no VTA
- partial overlap with PET



Reward tasks in MDD

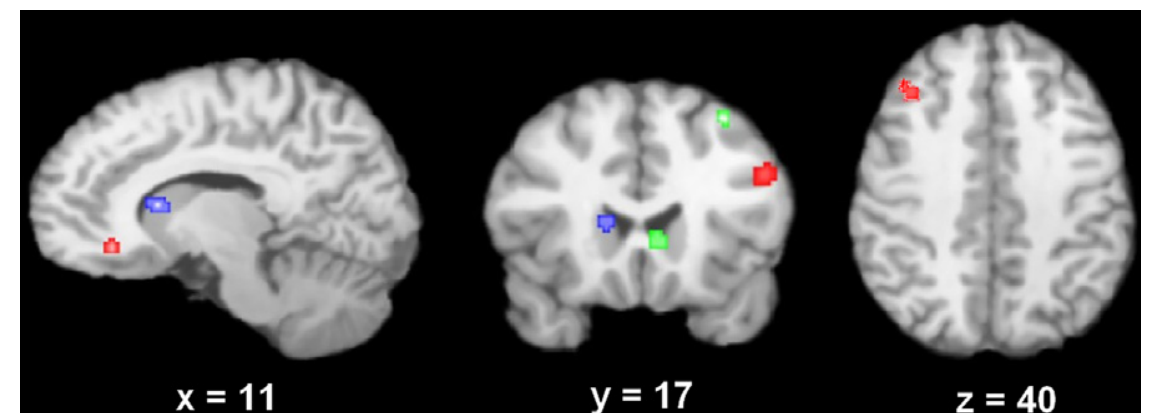
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- partial overlap with PET
 - Thal



Reward tasks in MDD

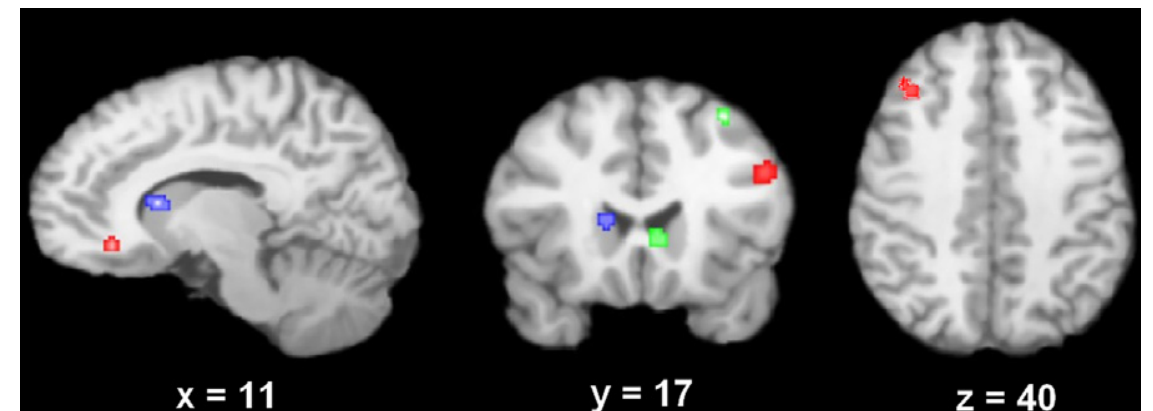
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- no NAcc, no VTA
- partial overlap with PET
 - Thal
 - Caudate



Reward tasks in MDD

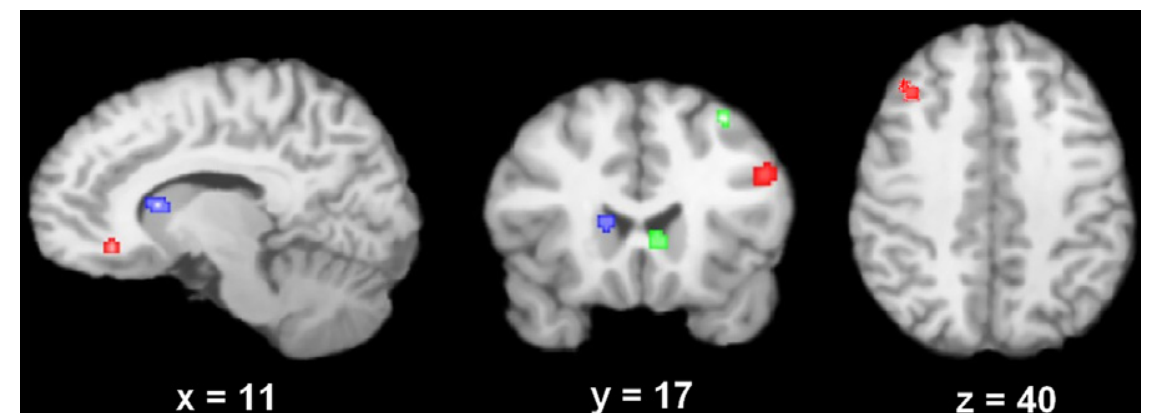
► Meta-analysis of reward processing tasks in fMRI w/ MDD

Table 6

ALE results of monetary reward anticipation from 6 studies and outcome from 5 studies in MDD (FDR corrected $p < 0.05$).

Brain region	Side	BA	Site of maximum ALE			Volume (mm ³)	Maximum ALE value
			<i>x</i>	<i>y</i>	<i>z</i>		
Areas of decreased activation during reward anticipation (37 foci from 6 experimental contrasts)							
Caudate	L		−16	16	4	288	0.009
Areas of increased activation during reward anticipation (34 foci from 5 experimental contrasts)							
Middle Frontal Gyrus	L	9	−48	14	30	352	0.011
Anterior Cingulate	R	32	12	32	−8	242	0.009
Frontal Lobe	R	47	18	30	−4		0.008
Middle Frontal Gyrus	R	8	36	24	40	242	0.009
Areas of decreased activation during reward outcome (52 foci from 5 experimental contrasts)							
Caudate	R		14	14	10	328	0.011
Areas of increased activation during reward outcome (18 foci from 5 experimental contrasts)							
No significant ALE clusters have been identified							

- no NAcc, no VTA
- partial overlap with PET
 - Thal
 - Caudate
 - pgACC variable - response



Reward tasks in MDD

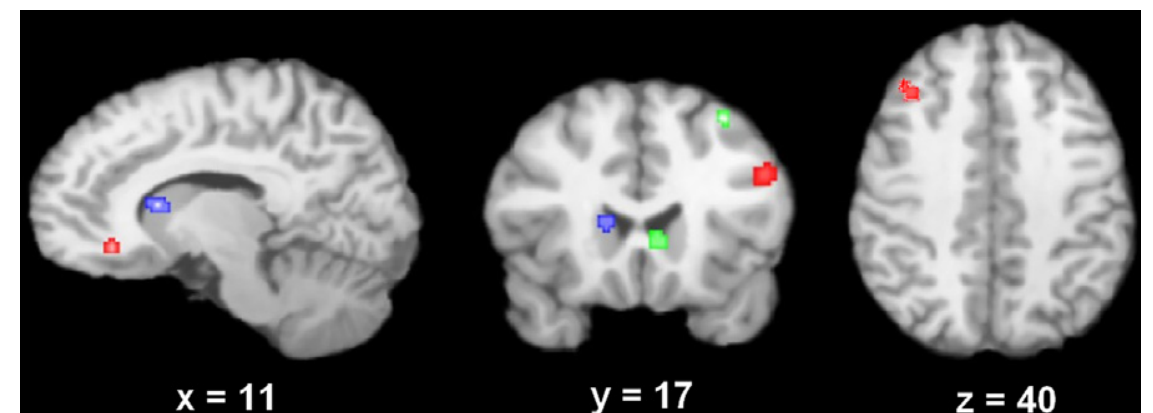
► Meta-analysis of reward processing tasks in fMRI w/ MDD

Table 6

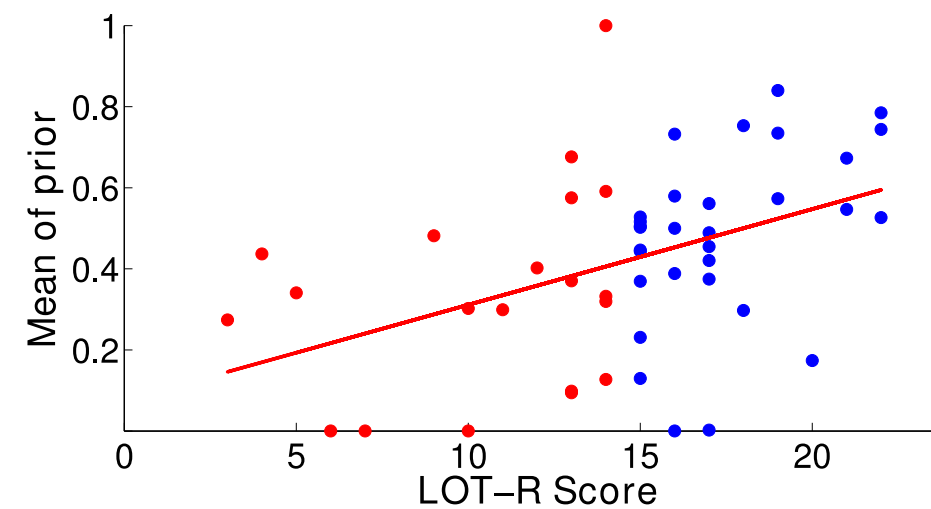
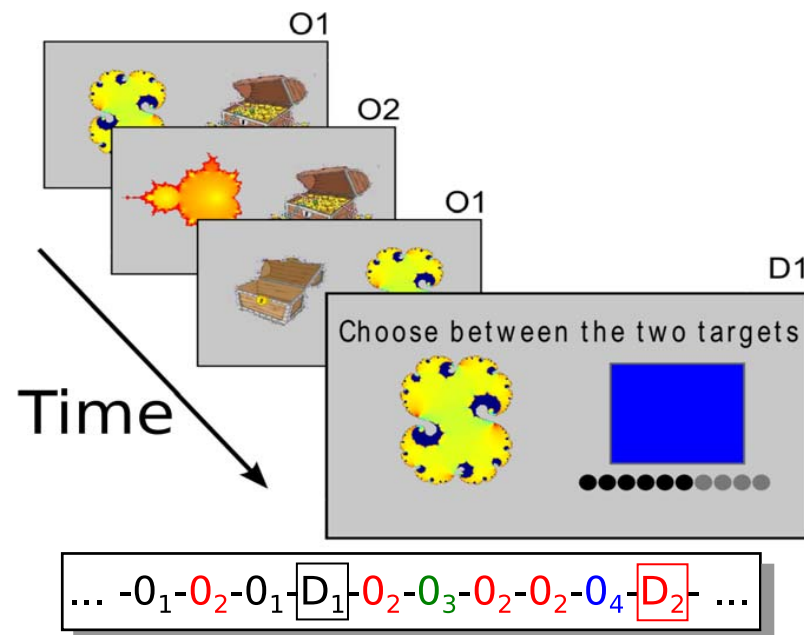
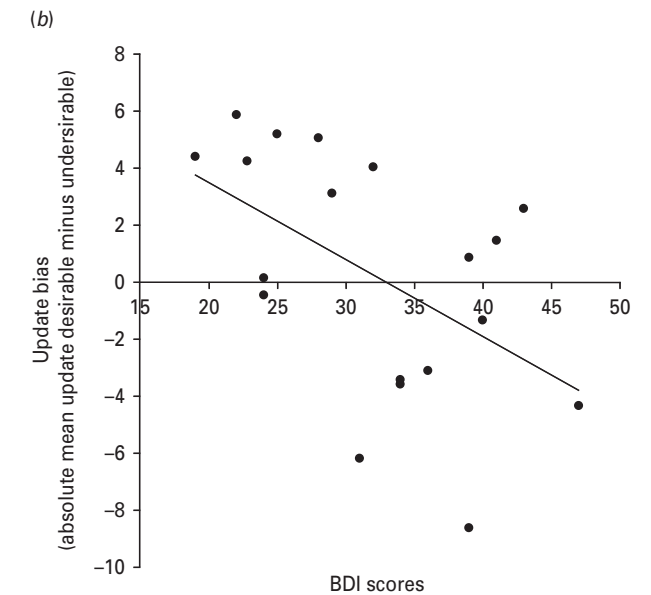
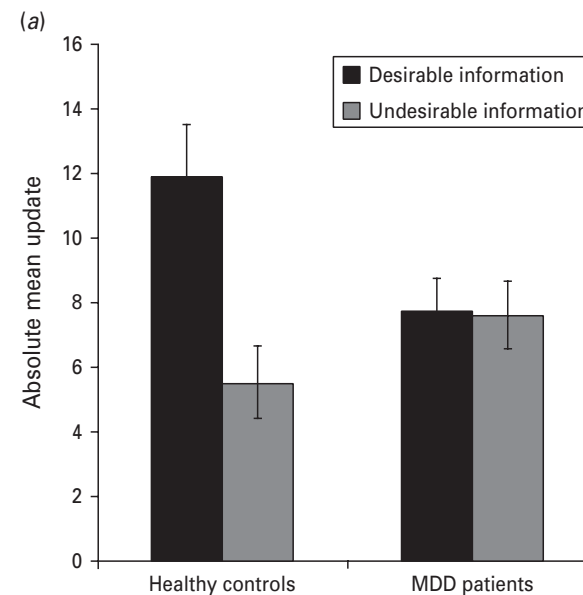
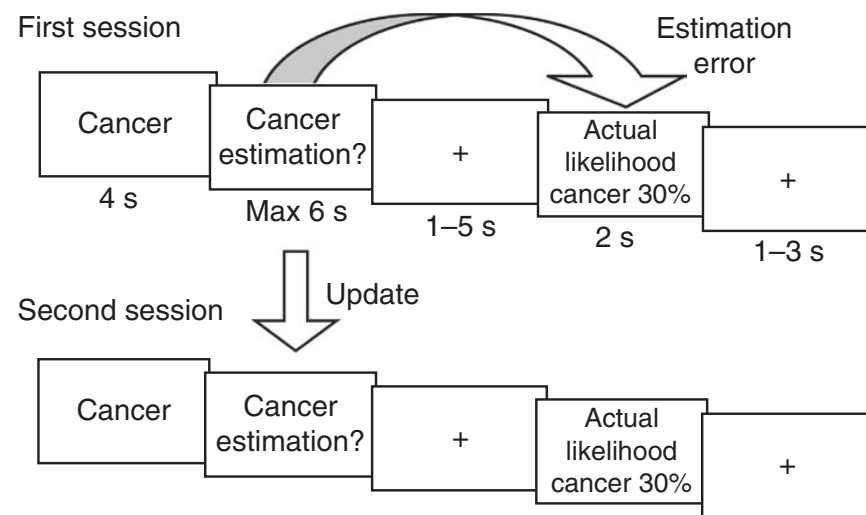
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- partial overlap with PET
 - Thal
 - Caudate
 - pgACC variable - response
 - BA9 vs sgACC inverse corr

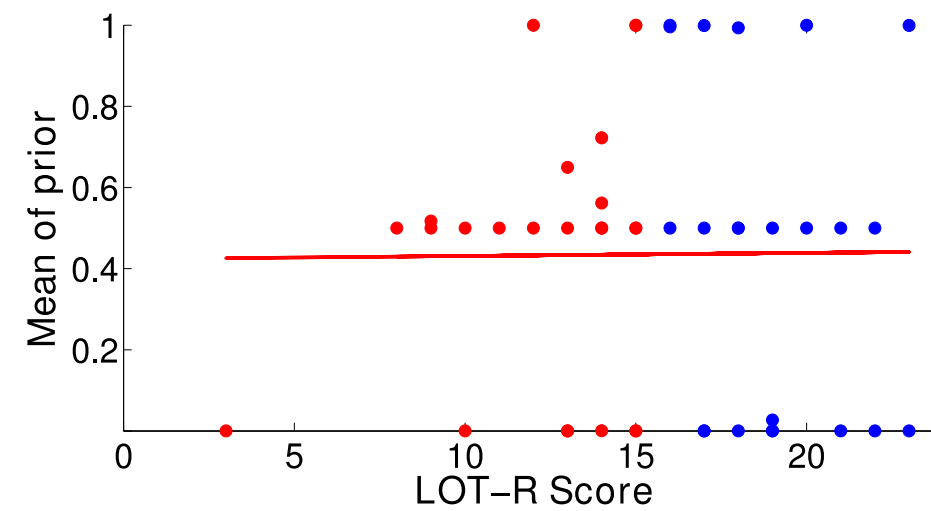
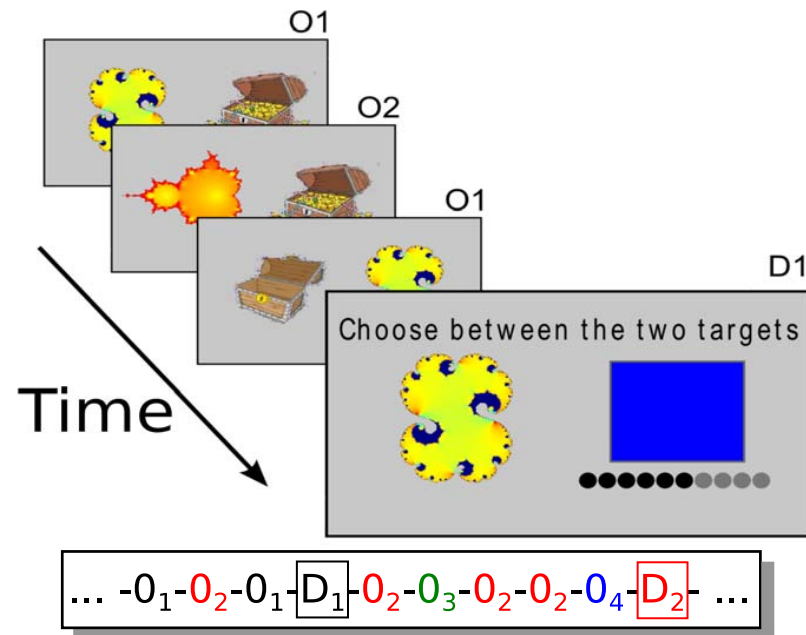
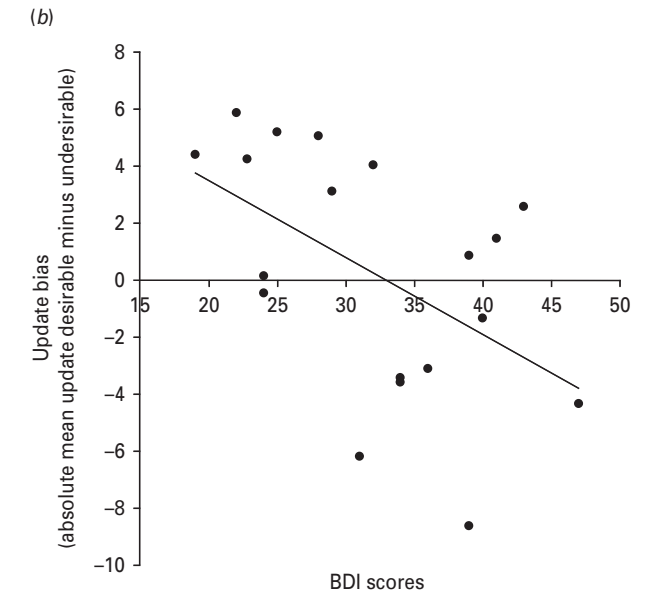
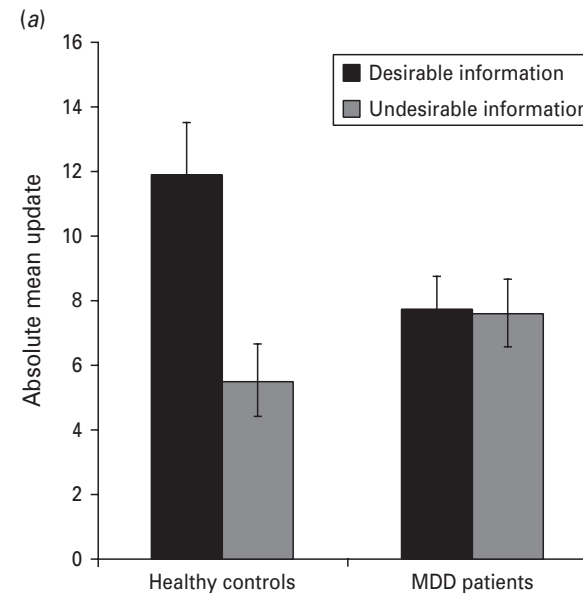
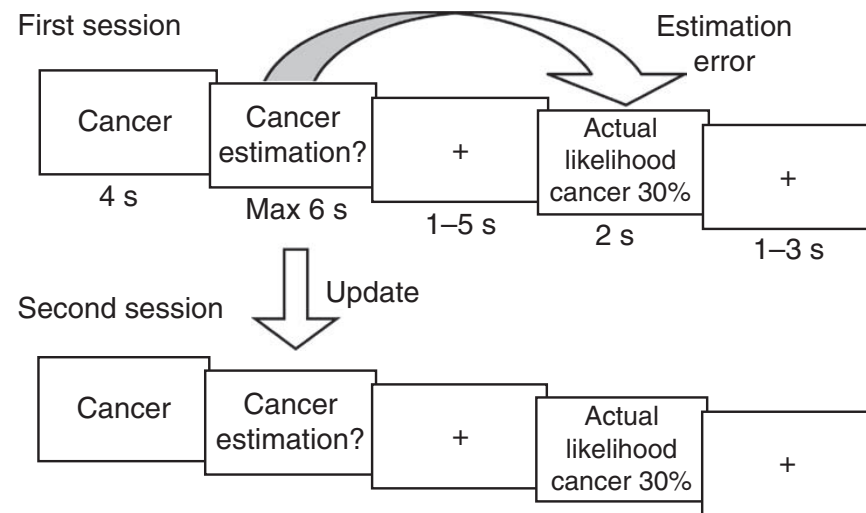


Learning at different conceptual levels



Sharot et al., 2011, Korn et al, 2014, Stankevicius et al., 2014

Learning at different conceptual levels



Sharot et al., 2011, Korn et al, 2014, Stankevicius et al., 2014

- ▶ No primary changes (pain, hedonic taste, sucrose)
- ▶ Reduced emotional responses +<-
- ▶ Attention & memory biased towards negative
 - at conceptual level
 - if allow for elaboration
 - negative conceptual information sticks around longer, positive dissipates away
- ▶ Learning from reinforcement / fMRI reward/loss
 - overall unclear whether learning is impaired or results can be explained by insensitivity to outcomes
 - caudate and ACC appear most robustly involved
- ▶ “Interpretations”

Decision-making in depression

- ▶ Emotional components
- ▶ Cognitive components
- ▶ Neuromodulatory components

Cognitive biases

- ▶ **Extreme thinking**
 - dichotomous - black/white
 - unrealistic expectations - unless perfect it's useless
- ▶ **Selective attention**
 - disqualifying the positive
 - over-generalization
- ▶ **Relying on intuition**
 - jumping to conclusions
 - emotional reasoning
- ▶ **Self-reproach**
 - self-blame, self-criticism
 - taking things personally

Attributional style

► Hopeless attributions are a risk factor for developing depression

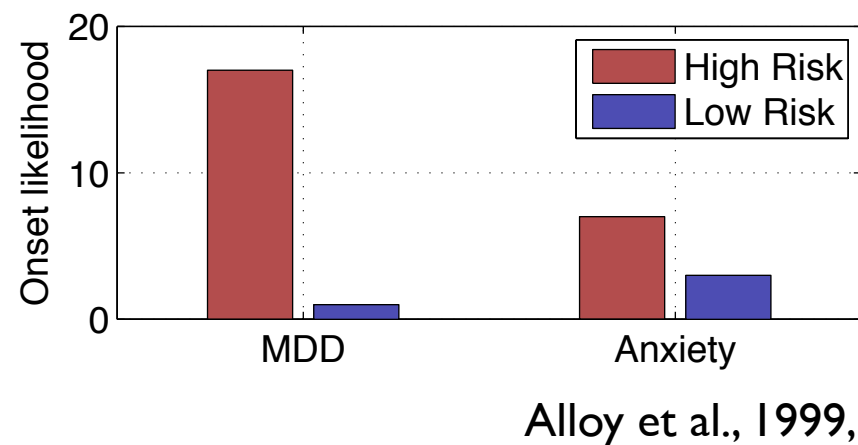


Table 3

Frequency of Symptom Presentation in the Prodromal and Residual Phases (N = 331 Episodes)

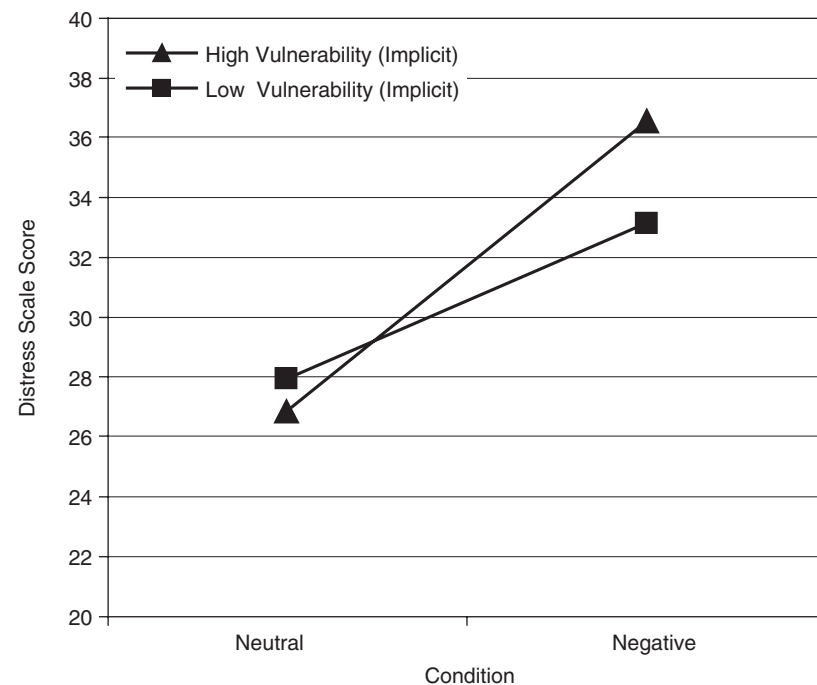
Symptom	Prodromal frequency	Residual frequency
Depressed mood	95	79
Decreased appetite	42	40
Weight loss	13	12
Increased appetite	10	12
Weight gain	20	17
Initial insomnia	29	30
Middle insomnia	13	10
Early waking	11	14
Hypersomnia	23	22
Decreased energy	38	35
Decreased interest or pleasure	82	75
Self-blame	51	55
Decreased concentration	78	75
Indecision	6	8
Suicidality	6	5
Psychomotor agitation	6	5
Psychomotor retardation	10	7
Crying more frequently	34	31
Inability to cry	4	2
Hopelessness	195	201
Worrying/Brooding	104	118
Decreased self-esteem	195	199
Irritability	85	72
Dependency	45	46
Self-pity	24	28
Somatic complaints	5	4
Decreased effectiveness	38	37
Helplessness	35	28
Decreased initiation of voluntary responses	19	23

Iacoviello et al., 2010

Implicit vs explicit attributions

► Acute consequence

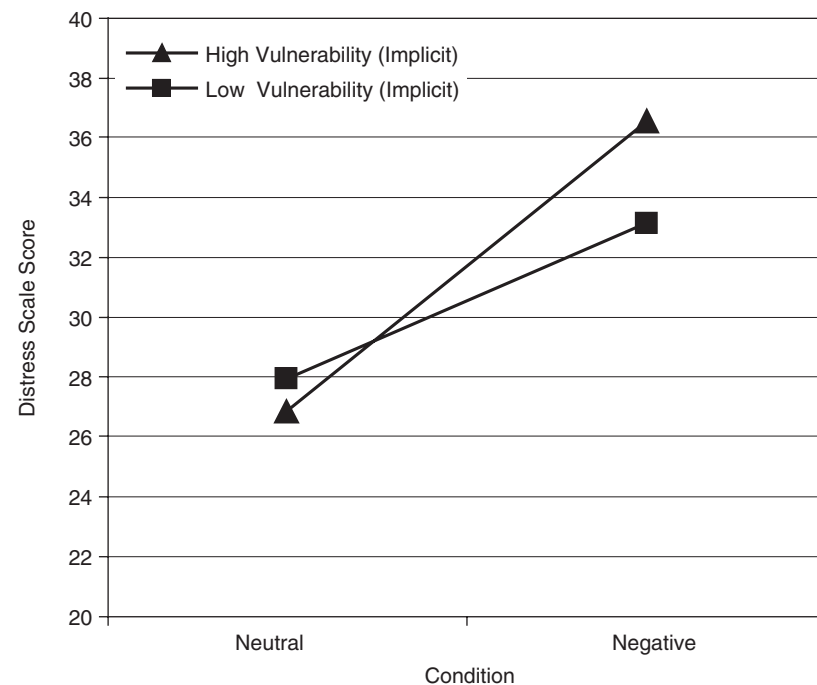
- implicit: IAT self-worth
- explicit: CSQ



Implicit vs explicit attributions

► Acute consequence

- implicit: IAT self-worth
- explicit: CSQ



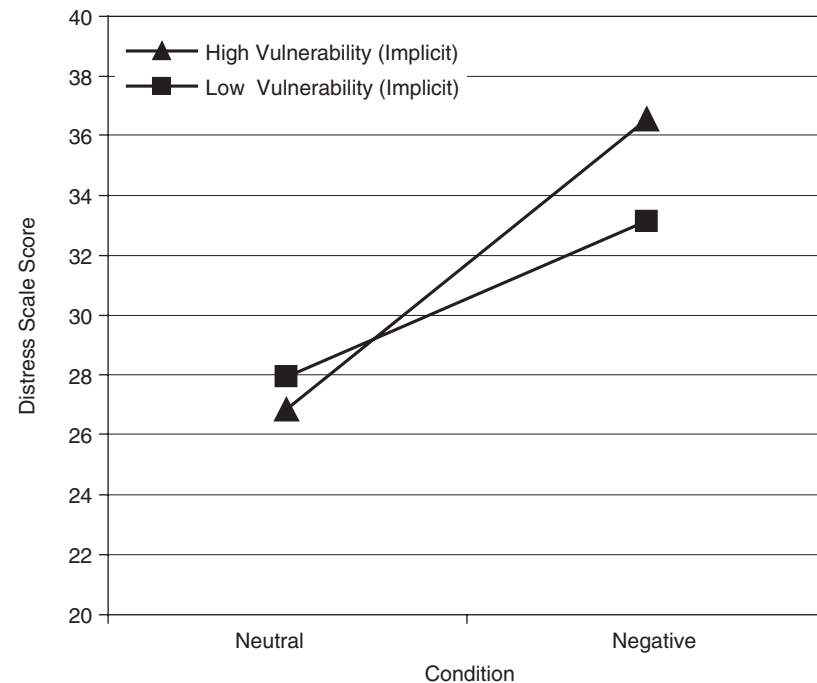
► Chronic consequence

- @ 5 weeks only CSQ survives to predict BDI response to acute life stressor

Implicit vs explicit attributions

► Acute consequence

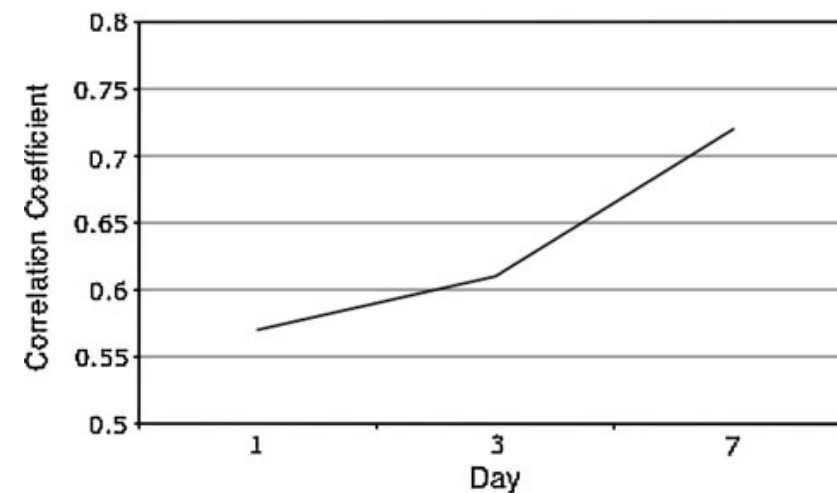
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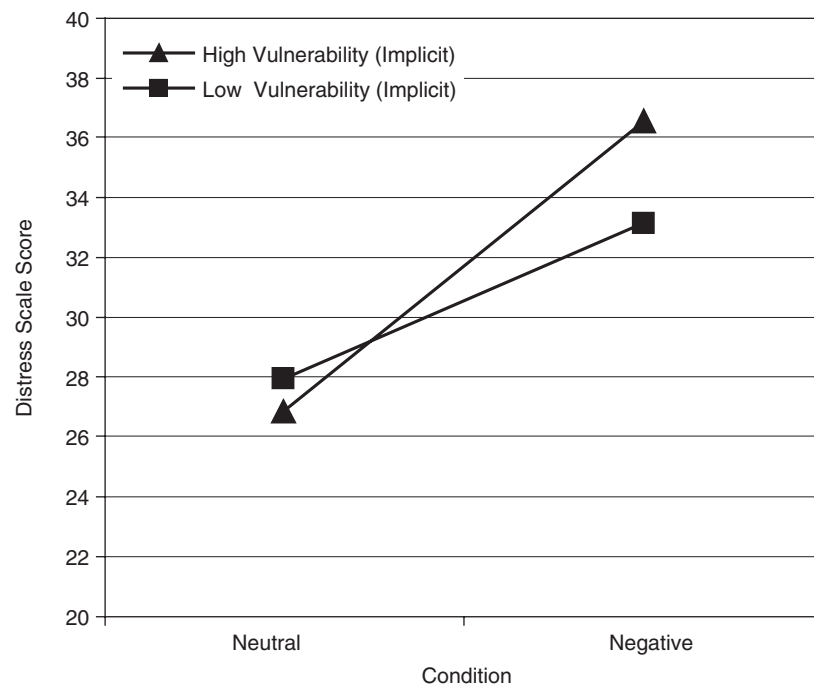
► Evolution over time



Implicit vs explicit attributions

► Acute consequence

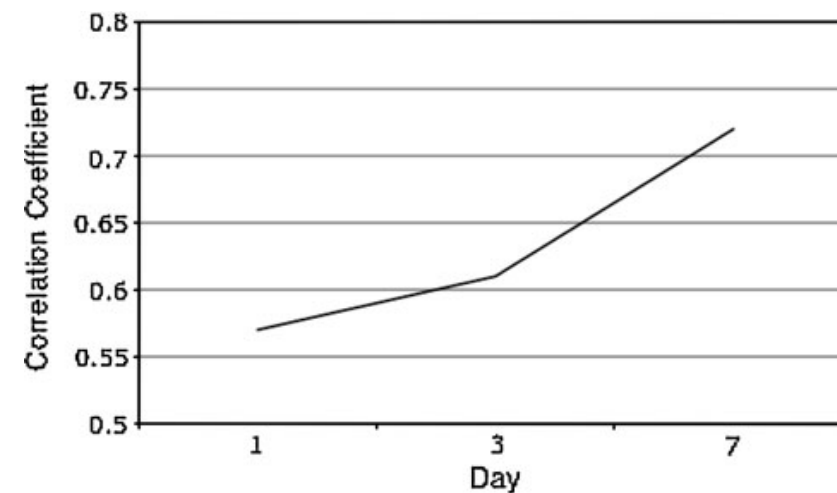
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► Chronic consequence

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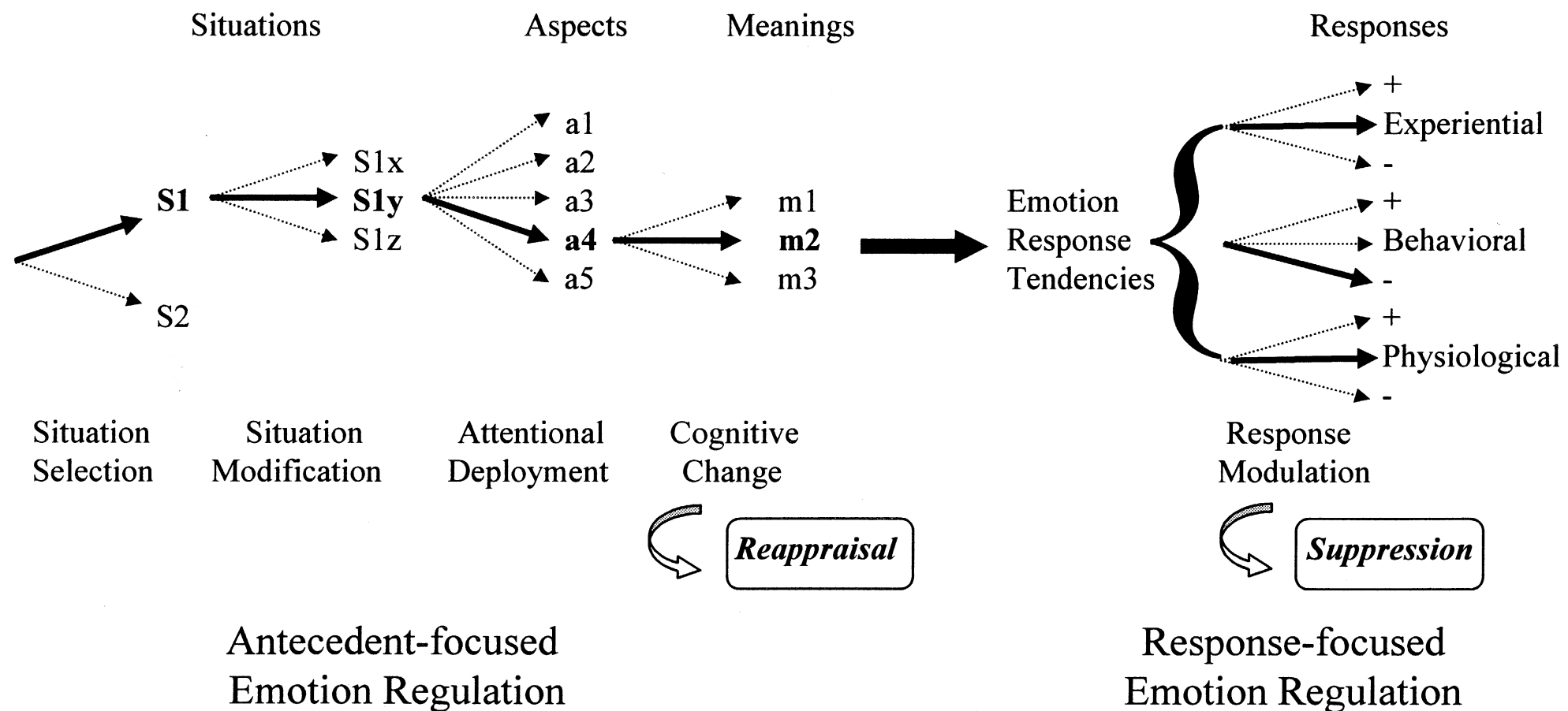
► Evolution over time



- -> explicit interpretations determine long-term outcome
- -> both implicit and explicit determine immediate outcome

Emotion regulation

► Interpretation precedes emotion



Types of emotion regulation

► Habitual emotion regulation strategy

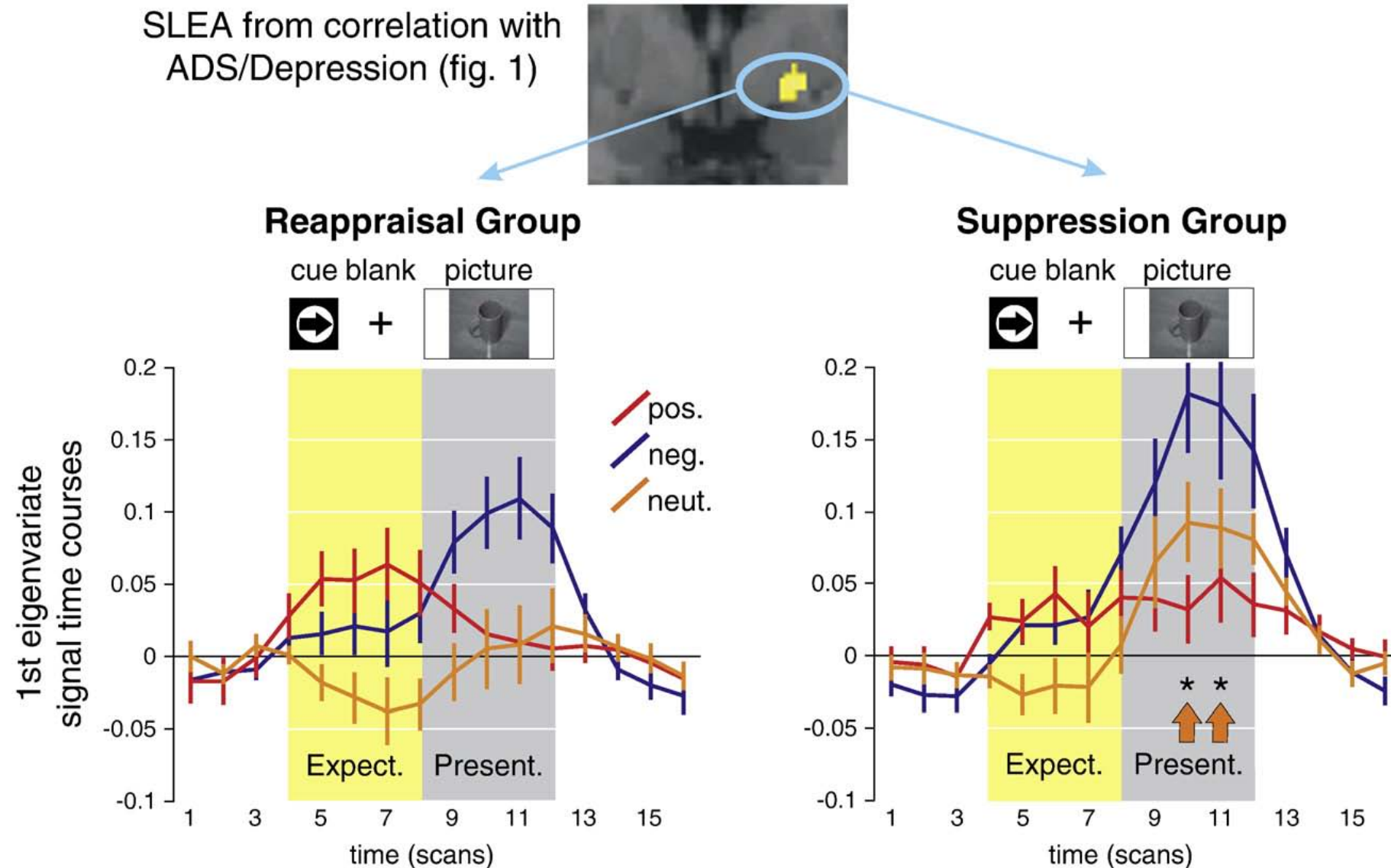
Table 6

Longer Term Implications of Reappraisal and Suppression for Well-Being (Study 5)

	Emotion regulation strategy	
	Reappraisal	Suppression
Depression ^F		
BDI	−.23*	.25*
CES-D	−.25*	.23*
Zung	−.29*	.27*
Life satisfaction ^E	.30*	−.34*
Self-esteem ^E	.30*	−.39*
Optimism ^C	.25*	−.25*
Well-being ^F		
Environmental mastery	.41*	−.23*
Autonomy	.29*	−.22*
Personal growth	.27*	−.28*
Purpose in life	.25*	−.34*
Self-acceptance	.35*	−.38*
Positive relations with others	.23*	−.46*

Habitual ER strategy

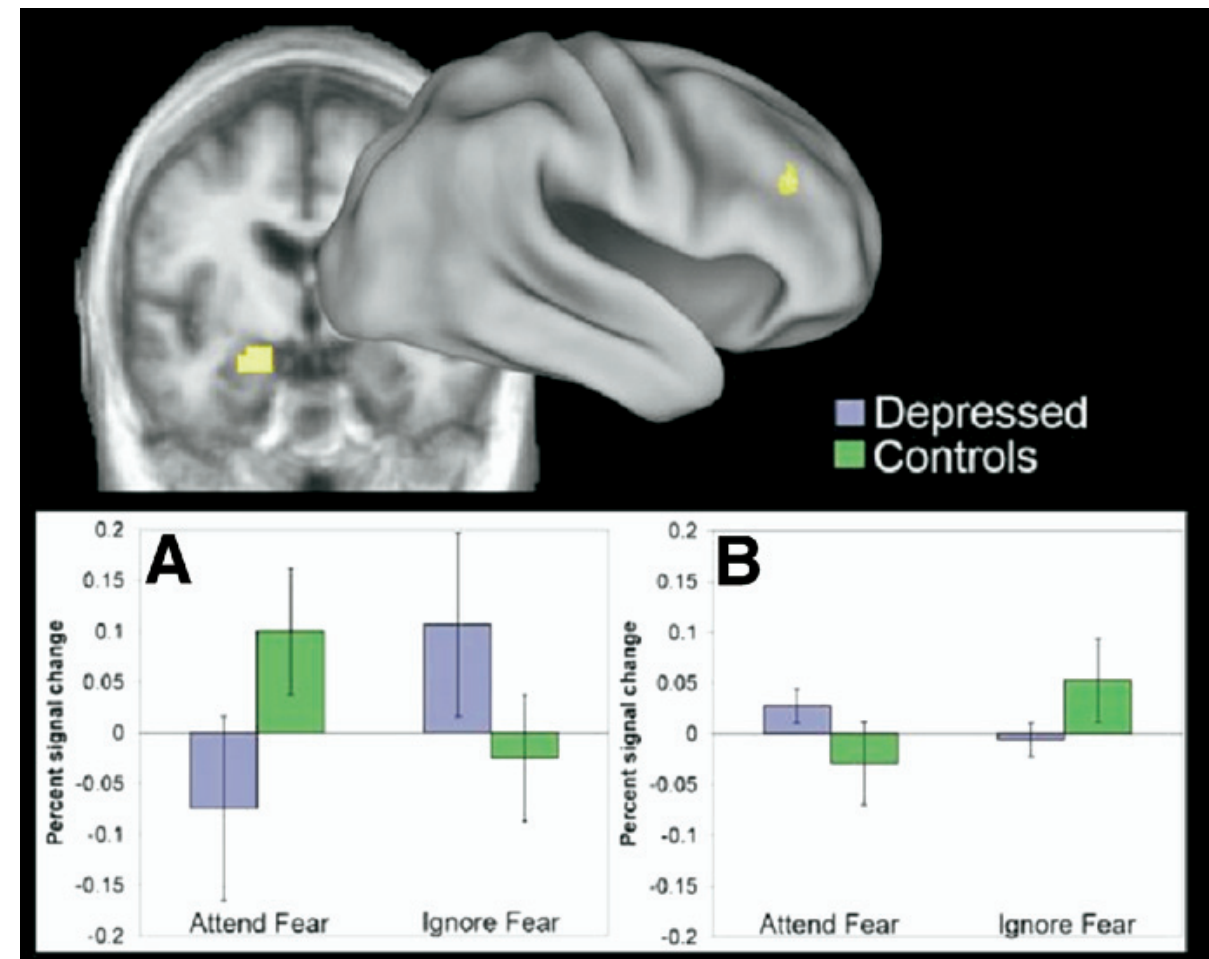
- ▶ Habitual suppression vs reappraisal - alters amygdala reactivity to aversive IAPS images



Depression and emotional control



Depression and emotional control



Cognitive therapy

Mean Pretreatment, Posttreatment, and 6-Month Follow-Up Scores for BDI and HRSD for Four Samples of Participants in Each Treatment Condition

Depression and measure	BA		AT		CT		<i>F(df)</i> and <i>p</i>
	<i>n</i>	<i>M(SD)</i>	<i>n</i>	<i>M(SD)</i>	<i>n</i>	<i>M(SD)</i>	
Total sample (<i>n</i> = 149)							
BDI							
Pre	56	29.3 (6.6)	43	29.1 (6.6)	50	29.8 (6.3)	<i>F</i> (2, 148) < 1, <i>ns</i>
Post	56	9.1 (7.9)	43	10.6 (9.3)	50	10.1 (9.6)	<i>F</i> (2, 145) < 1, <i>ns</i>
6 months	50	8.5 (7.6)	39	9.3 (8.2)	47	10.3 (8.6)	<i>F</i> (2, 132) < 1, <i>ns</i>

Cognitive therapy

- ▶ Identify automatic thoughts
- ▶ Modify them

Mean Pretreatment, Posttreatment, and 6-Month Follow-Up Scores for BDI and HRSD for Four Samples of Participants in Each Treatment Condition

Depression and measure	BA		AT		CT		<i>F(dfs)</i> and <i>p</i>
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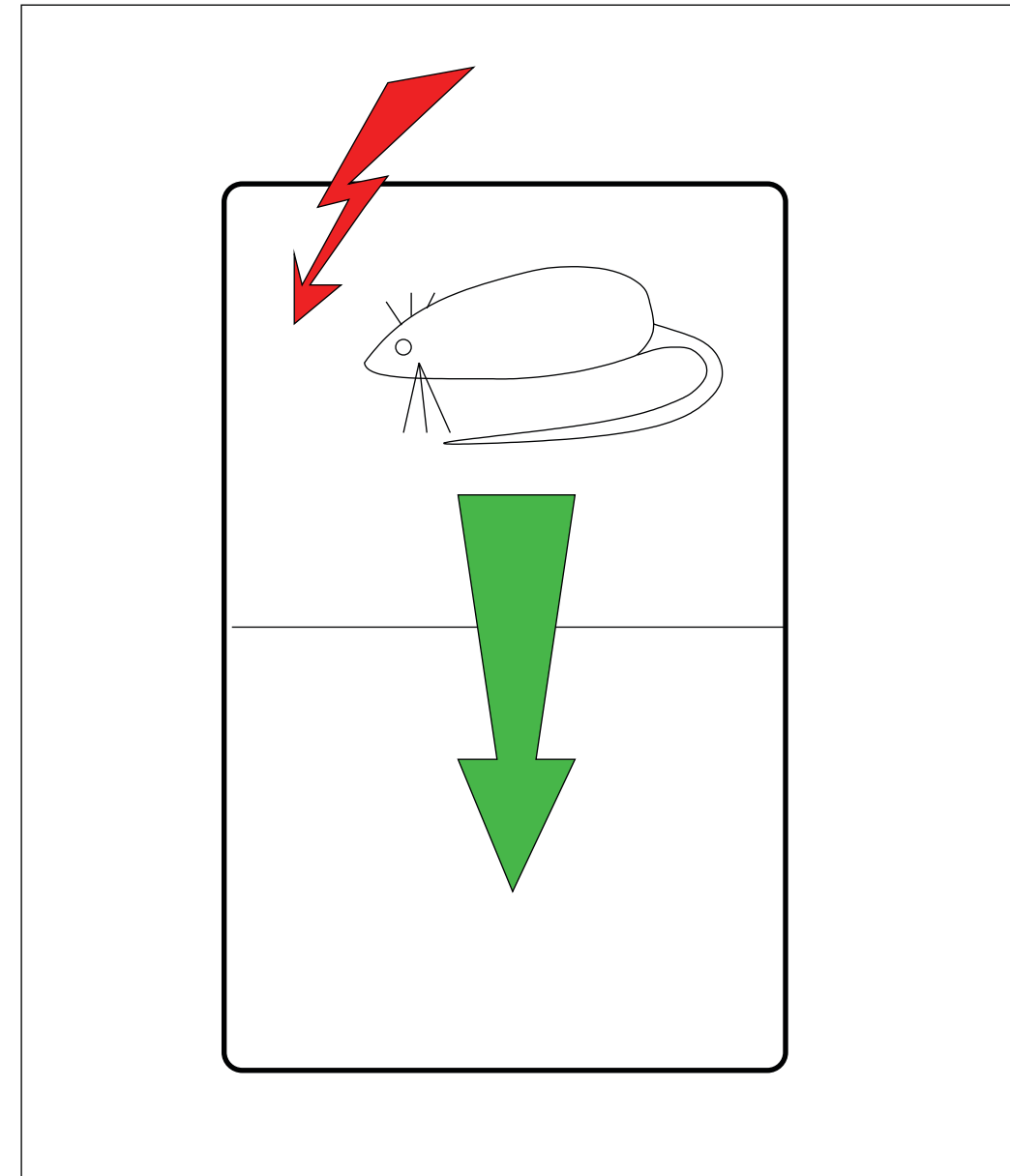
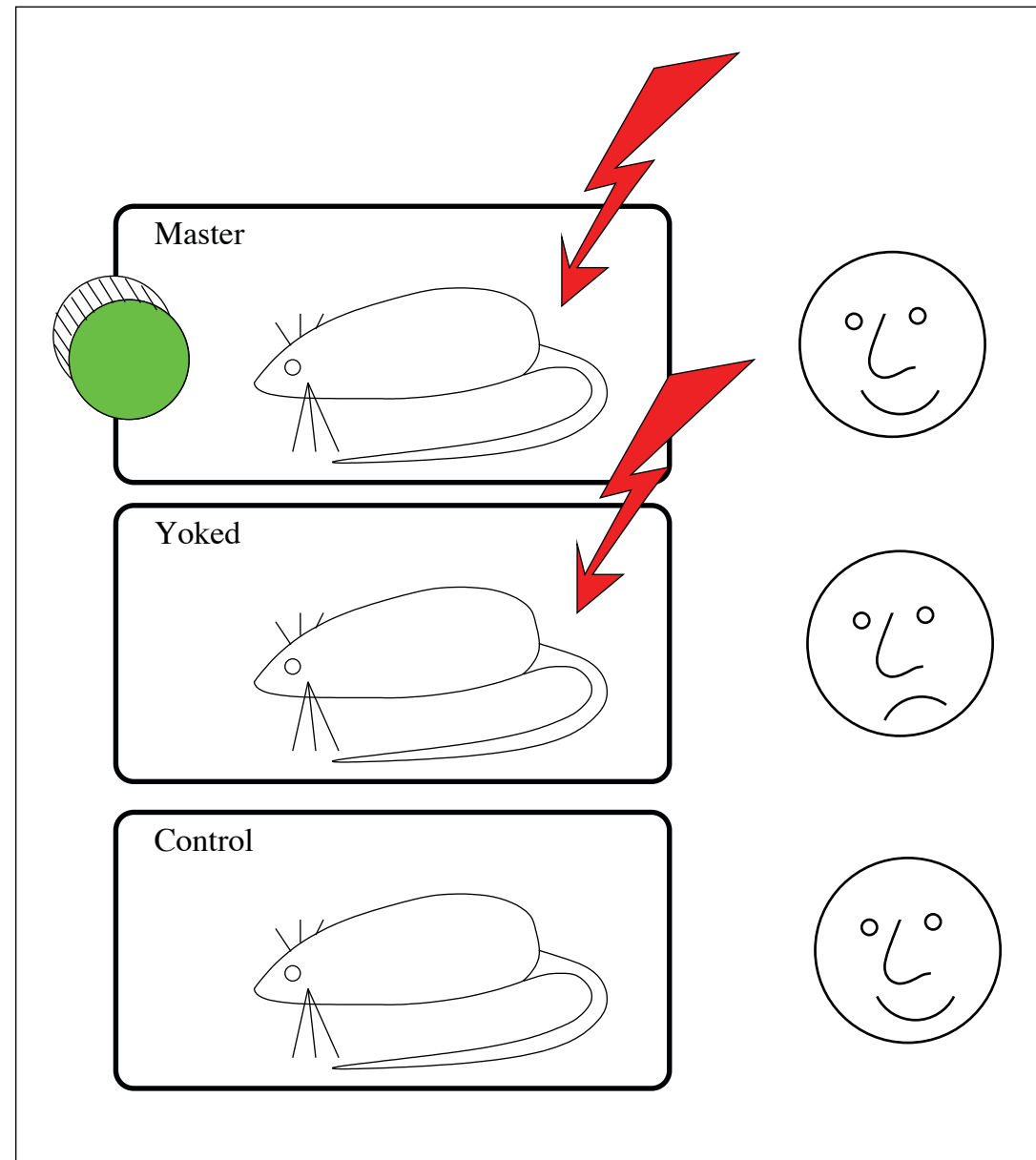
Cognitive therapy

- ▶ Identify automatic thoughts
- ▶ Modify them
- ▶ Is it the active ingredient?

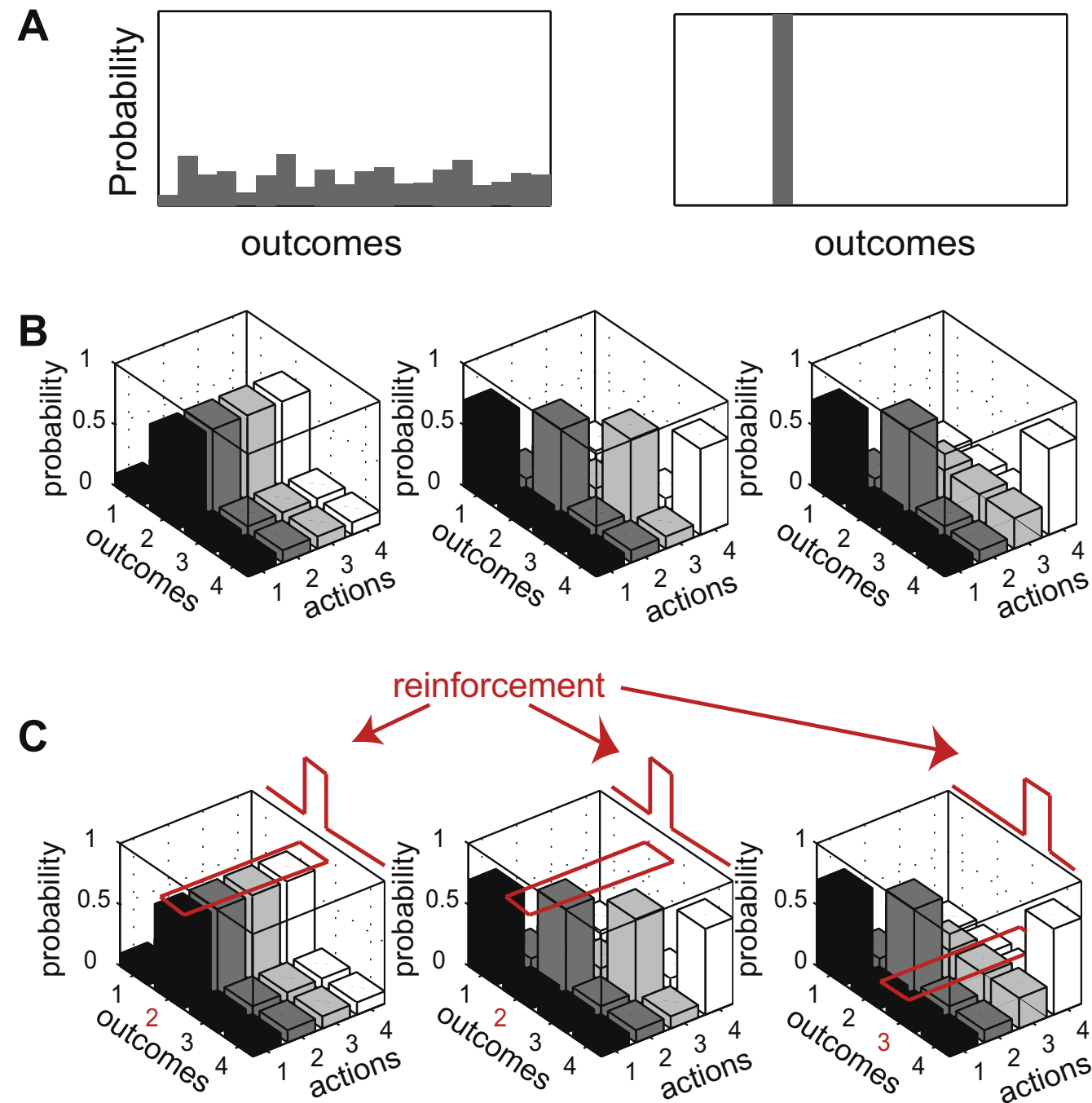
Correlations Between Early Mechanism Change and Late Depression Change in Each Treatment

Mechanism measure	BA	CT
EASQ		
Uncontrollable	-.01	.21
Internal	.27	.14
Stable	.45***	.03
Global	.38*	.22
PES		
Frequency	.17	-.29*
Pleasure	-.26	-.25
DAS	.26	-.02

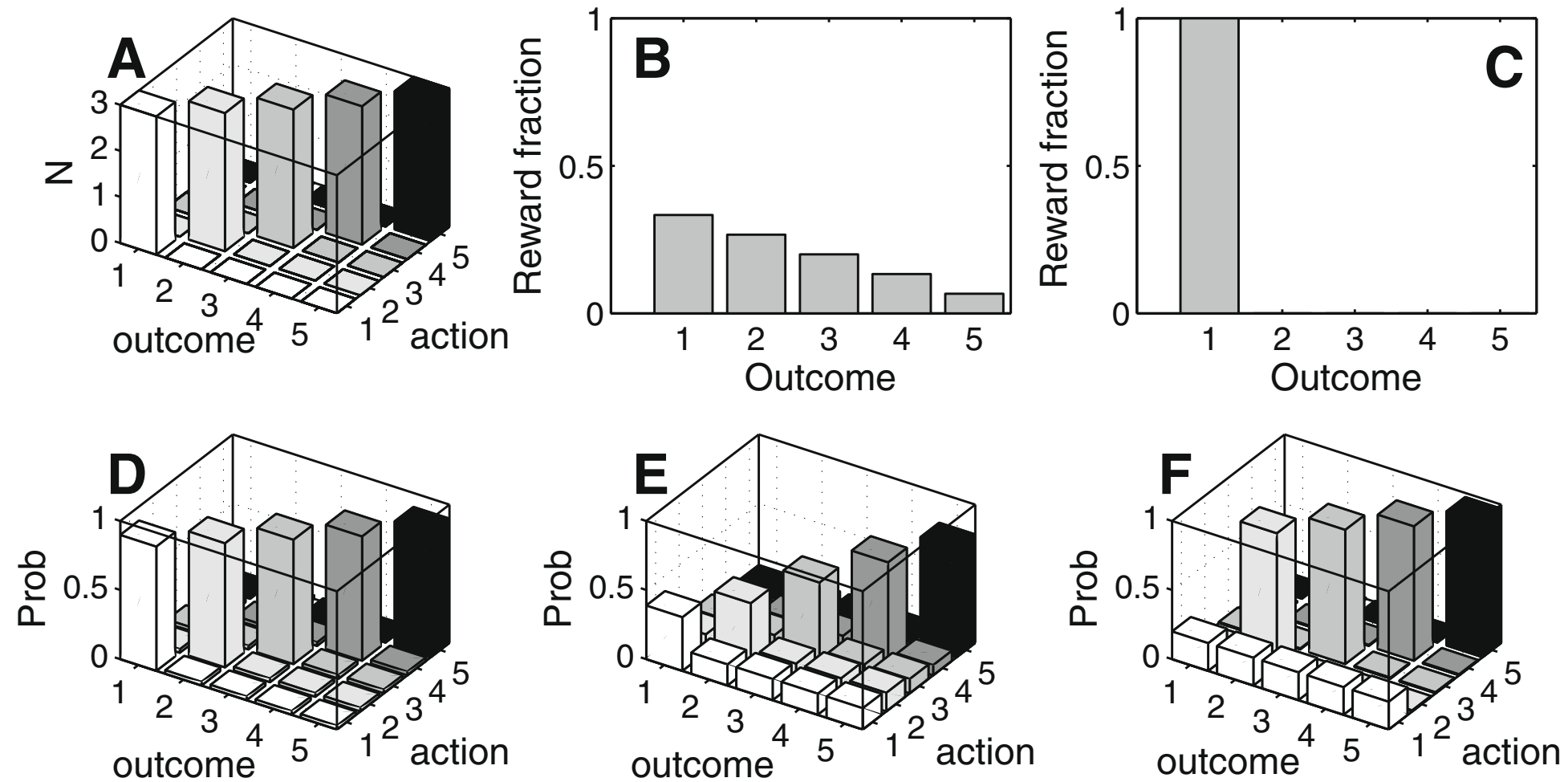
Bad data: helplessness



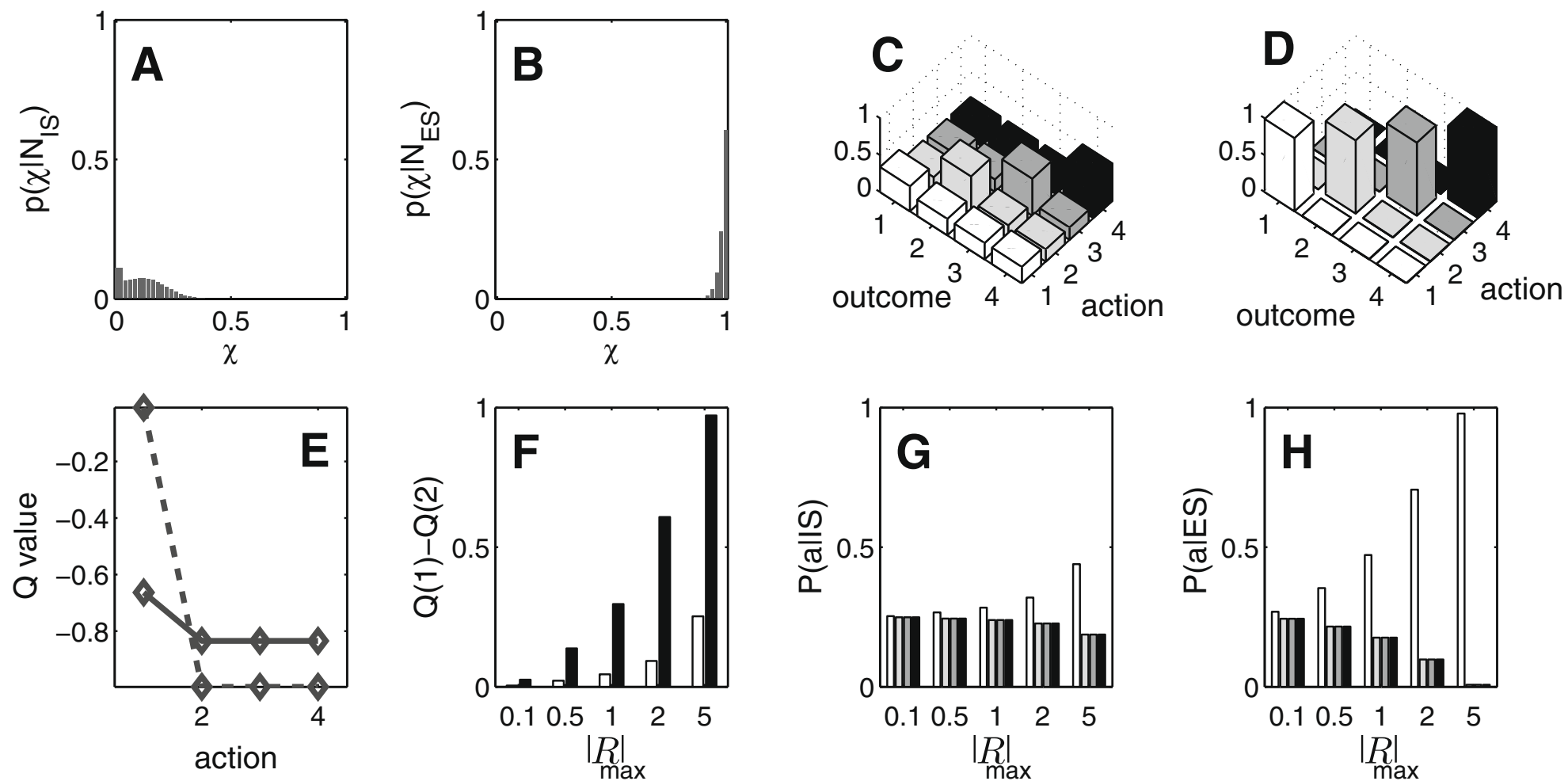
Notions of control



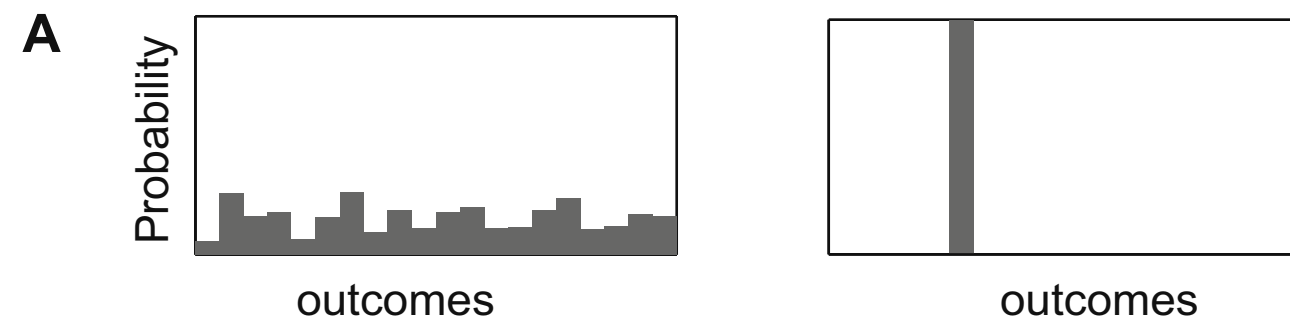
Reward-sensitive control predictions



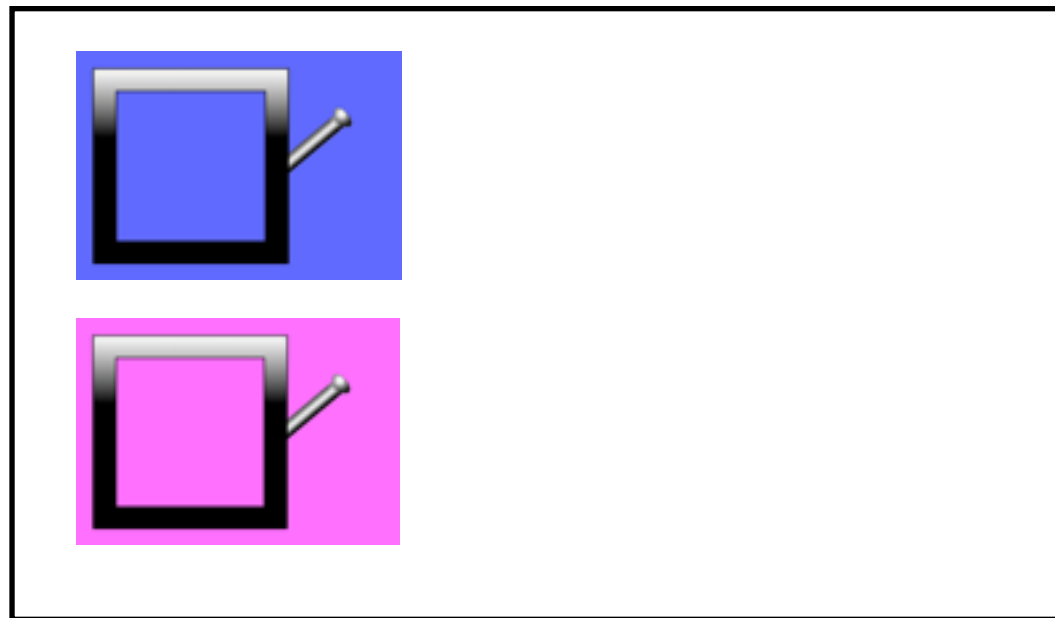
Modelling learned helplessness



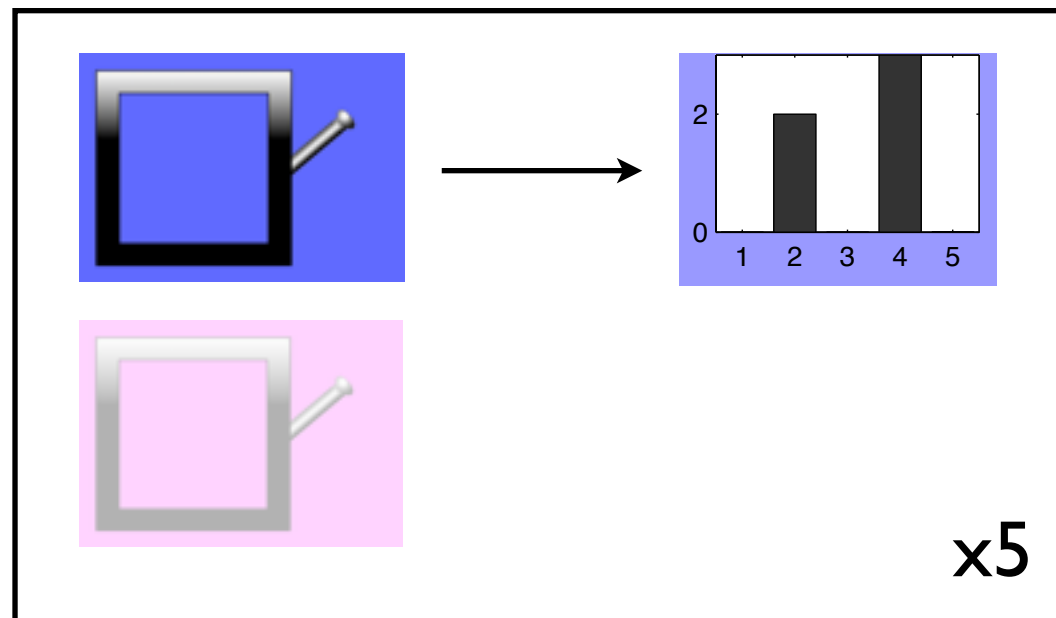
Hopelessness and uncontrollability?



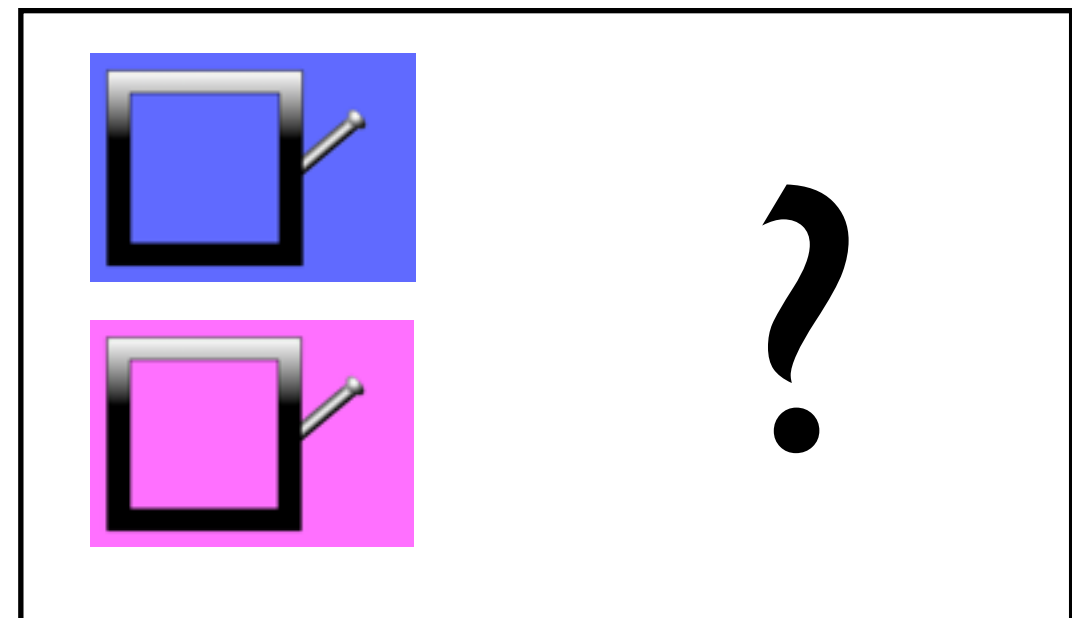
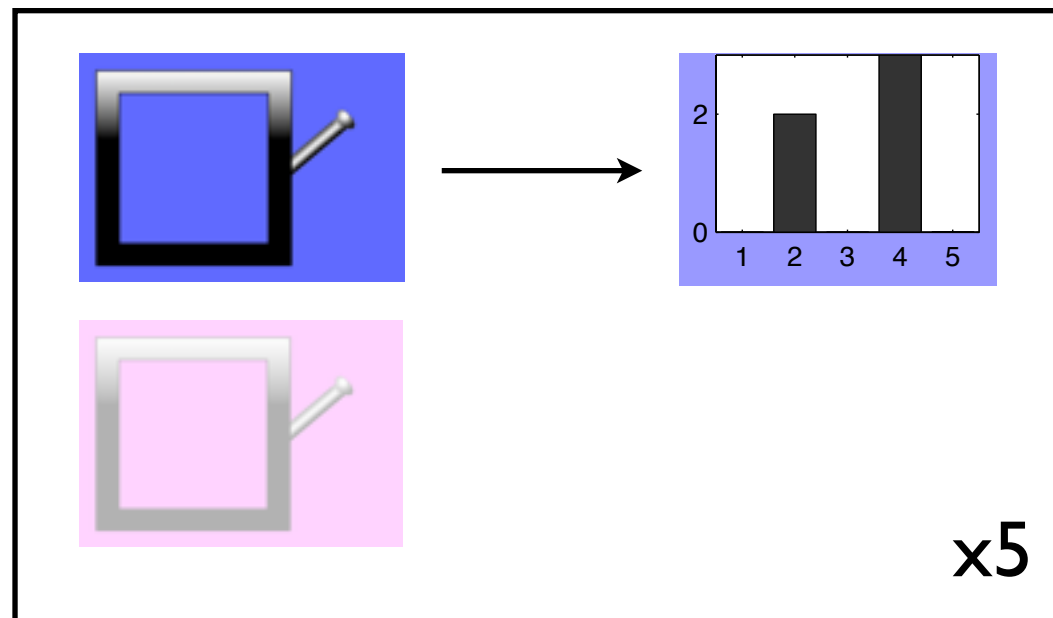
Consequences of beliefs about control



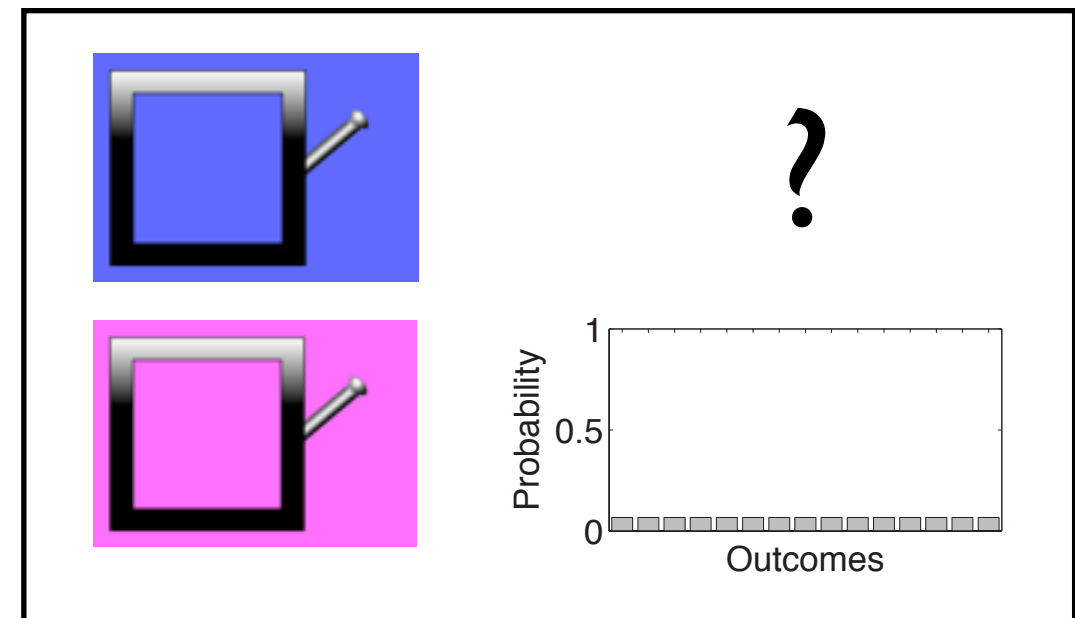
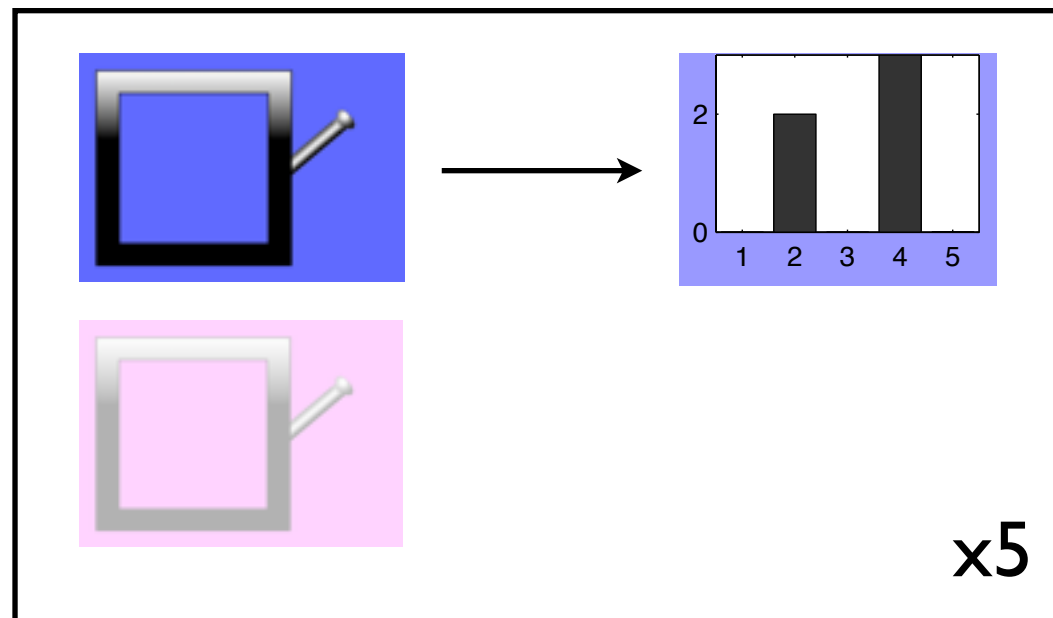
Consequences of beliefs about control



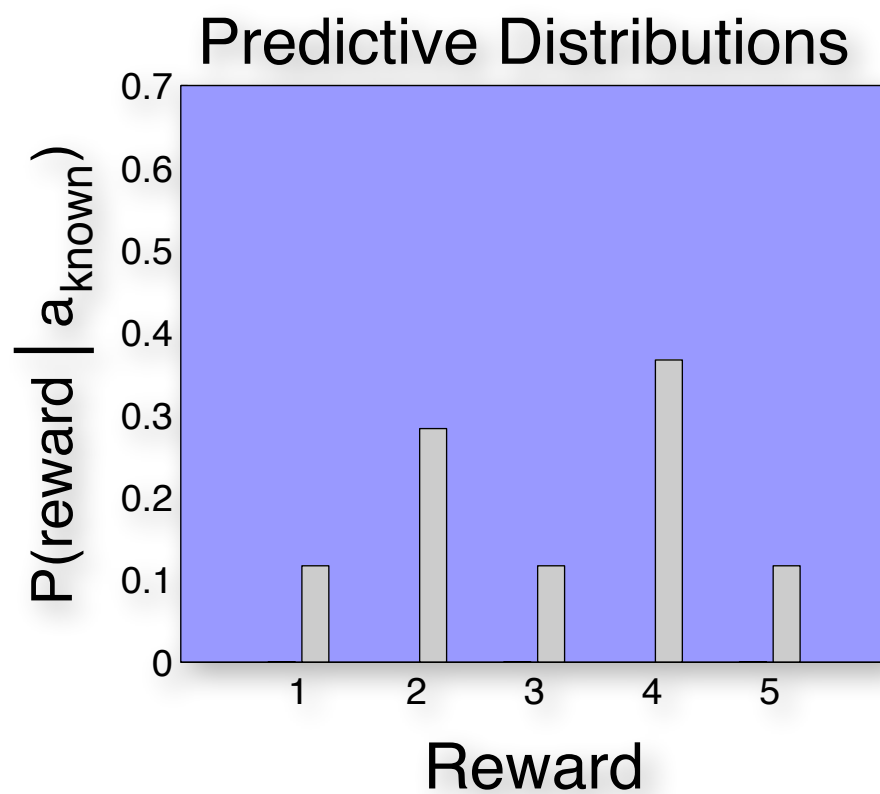
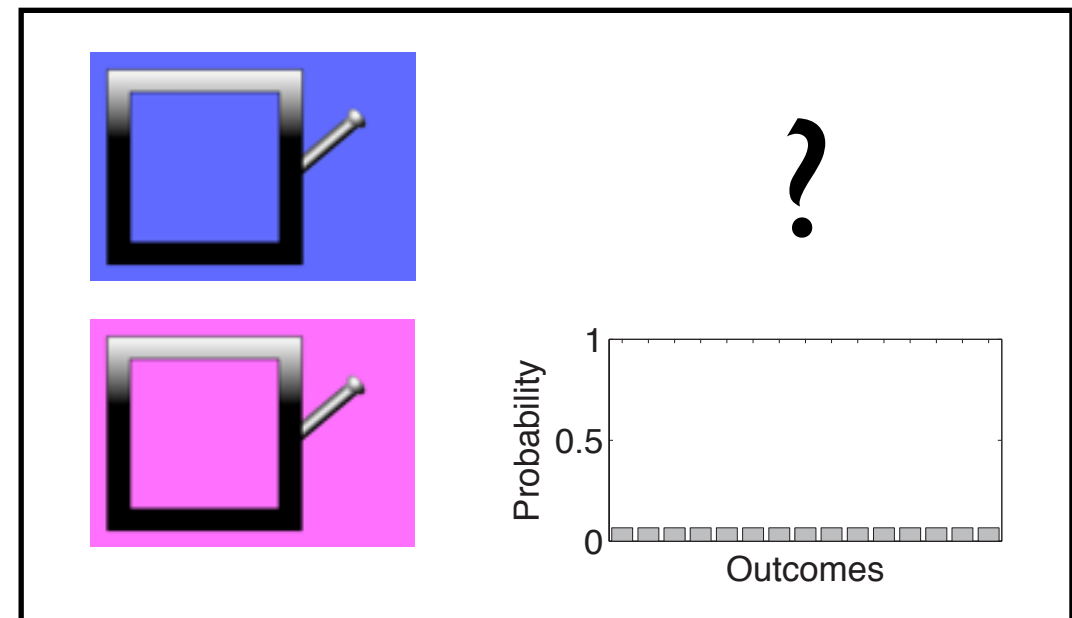
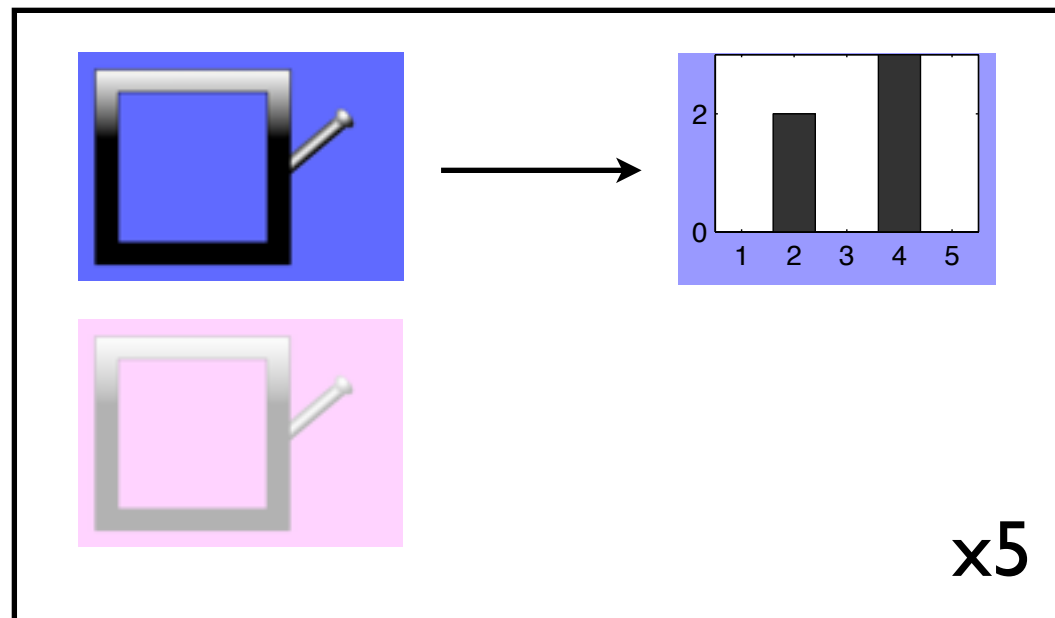
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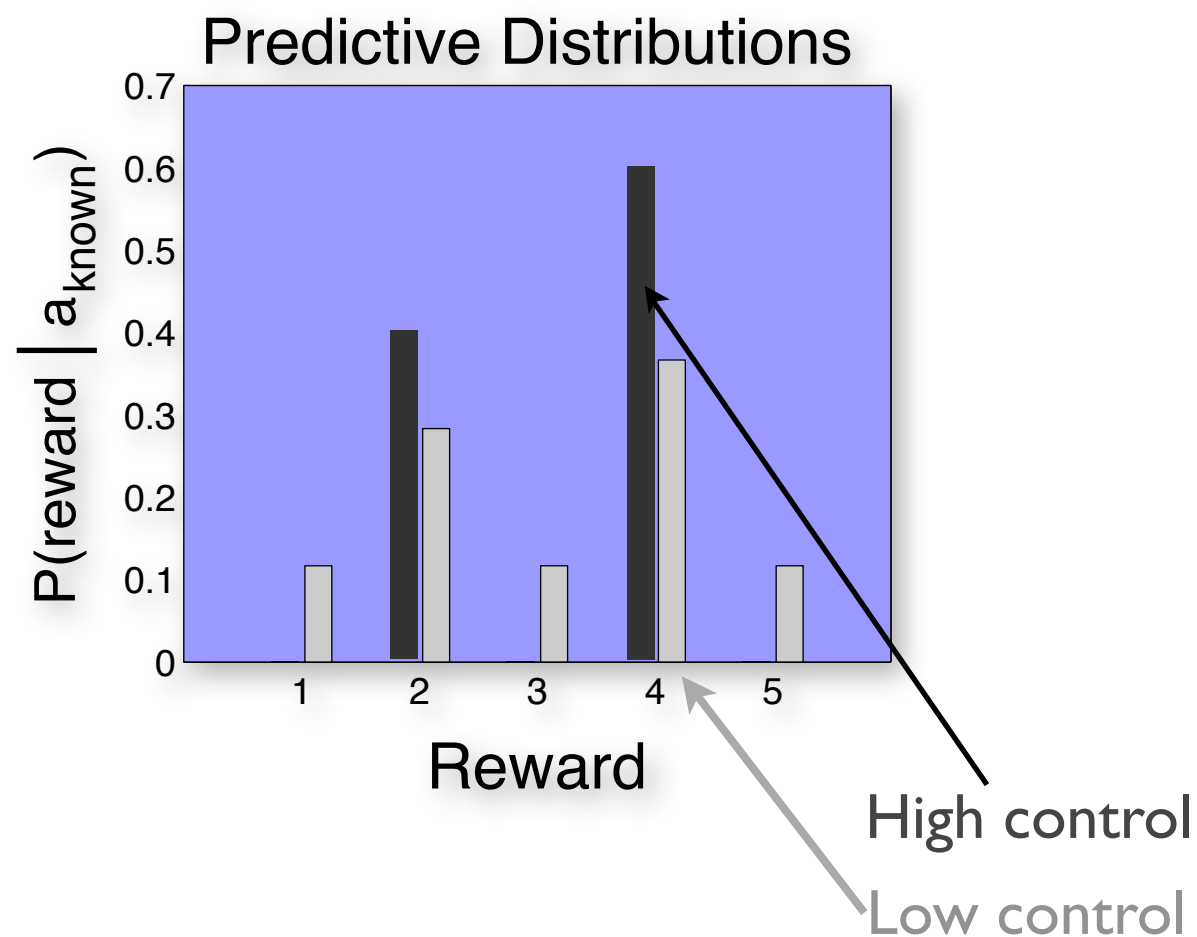
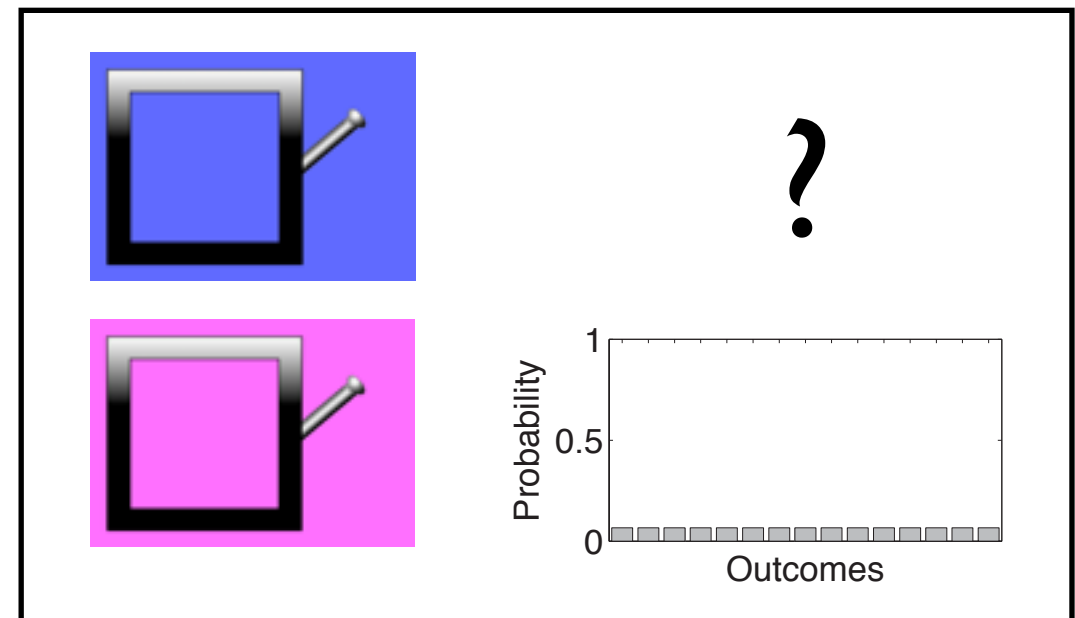
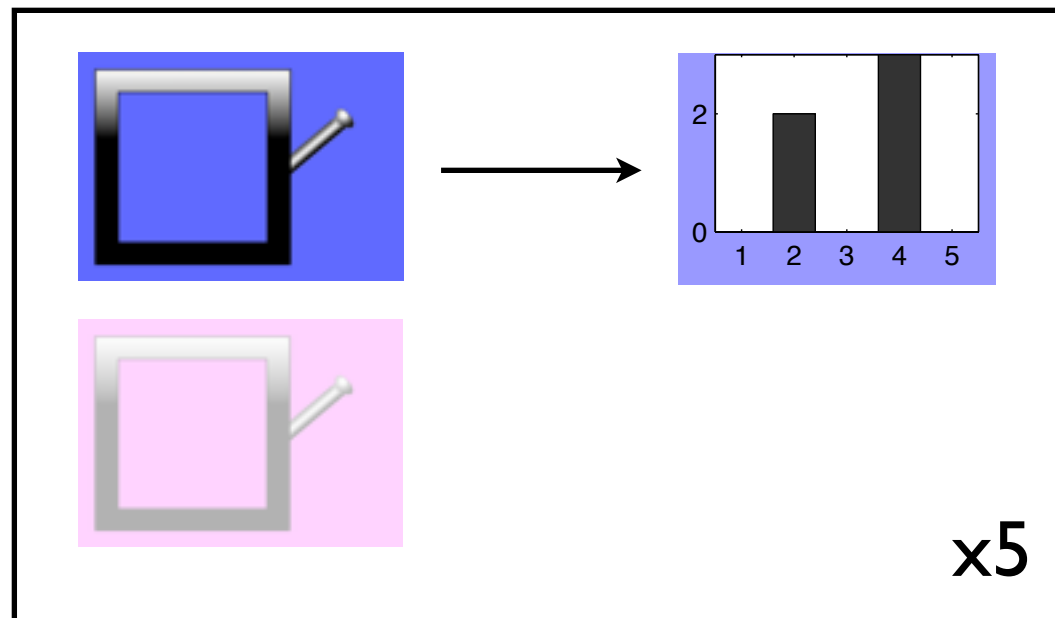
Consequences of beliefs about control



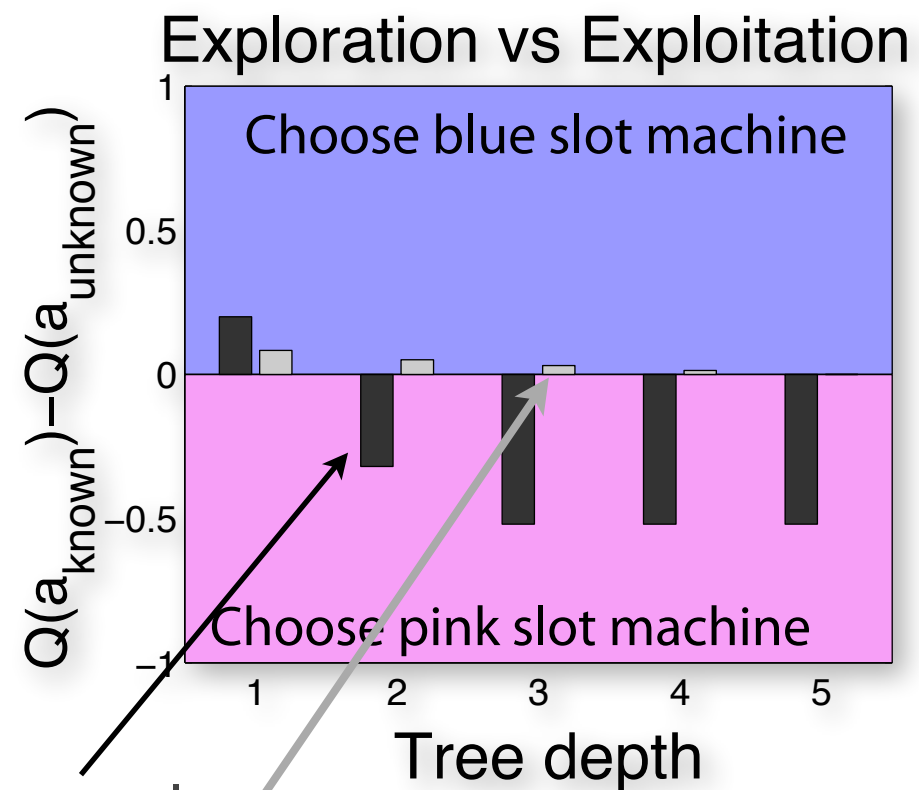
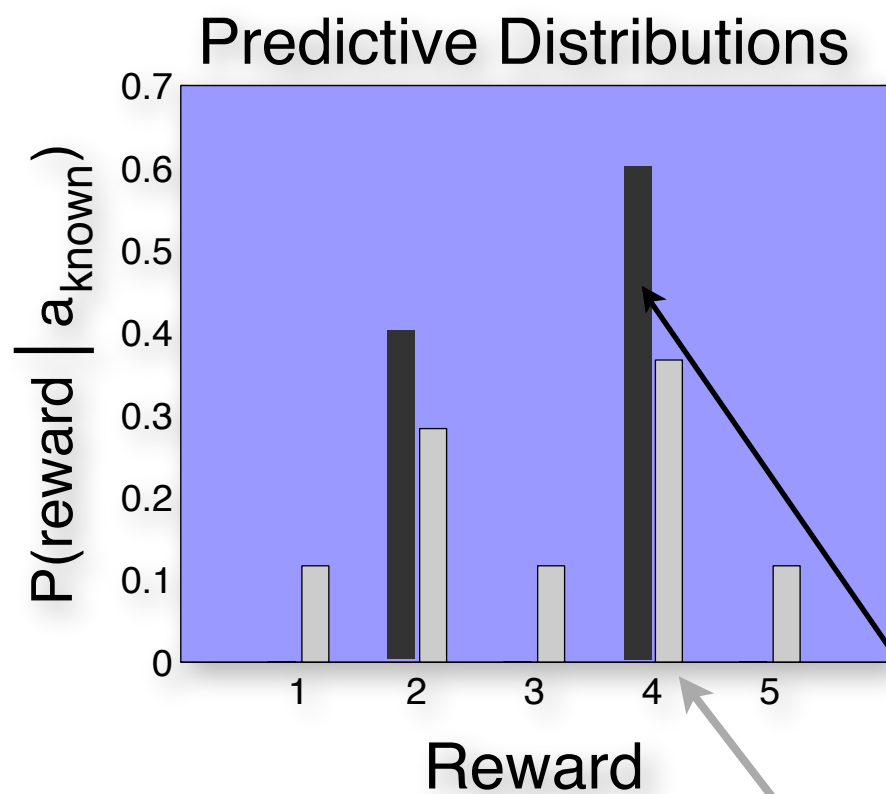
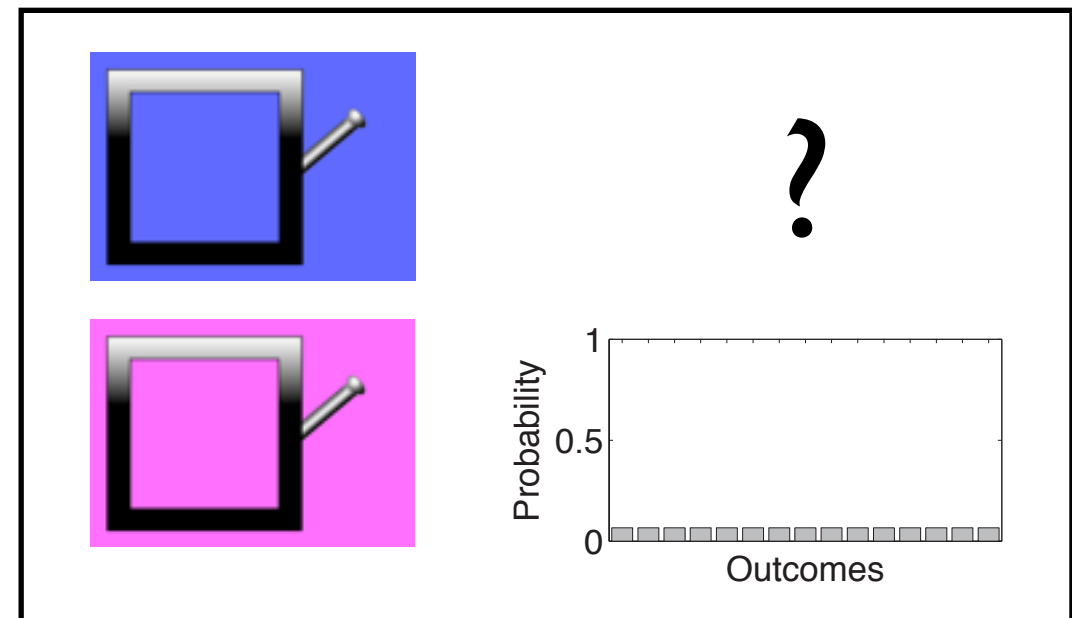
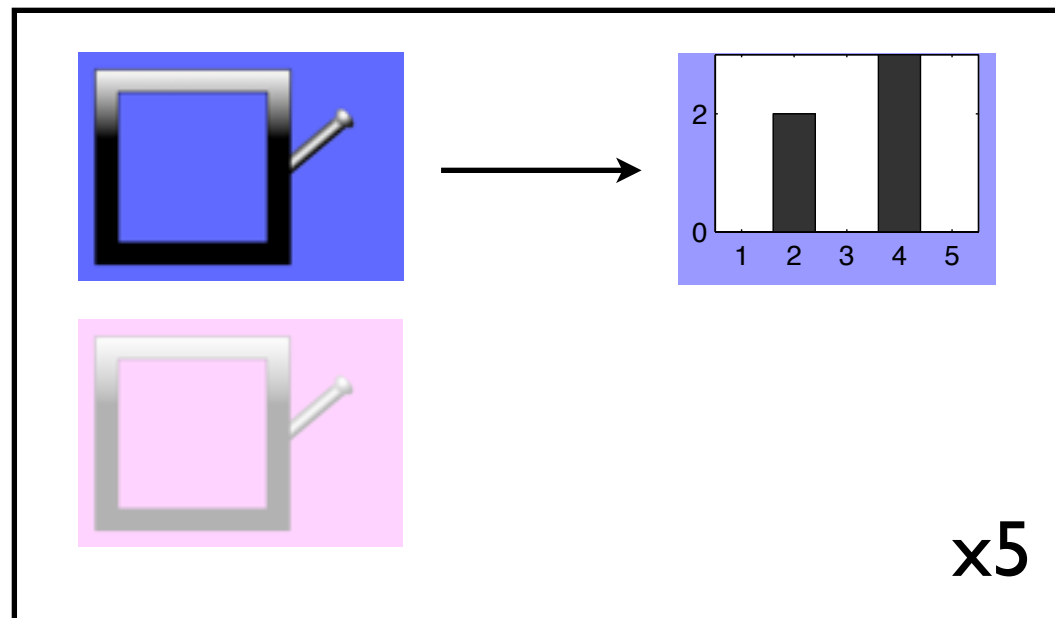
Consequences of beliefs about control



Consequences of beliefs about control



Consequences of beliefs about control



High control
Low control

Choice probability as function of prior belief

► Bellman equation

$$Q(a, s) = \sum_{s'} \mathcal{T}_{s,s'}^a [\mathcal{R}_{s,s'}^a + \operatorname{argmax}_{a'} Q(a', s')]$$

► Dirichlet prior

- on entropy of each machine a

$$\mathcal{T}_{s,s'}^a = P(r|N_t, a, \alpha)$$

Choice probability as function of prior belief

► Bellman equation

$$Q(a, s) = \sum_{s'} \mathcal{T}_{s,s'}^a [\mathcal{R}_{s,s'}^a + \operatorname{argmax}_{a'} Q(a, s')]$$

► Dirichlet prior

- on entropy of each machine a

$$\mathcal{T}_{s,s'}^a = P(r|N_t, a, \alpha)$$

► Value of each machine by evaluating tree weighted by belief-dependent outcome probabilities

$$Q_t(a|N_t, \alpha) = \sum_r p(r|N_t, a, \alpha) [r + \operatorname{argmax}_{a'} Q_t(a'|N_{t+1}(r), \alpha)]$$

Casino Task

Imagine you are in a Casino.
With lots and lots of rooms.

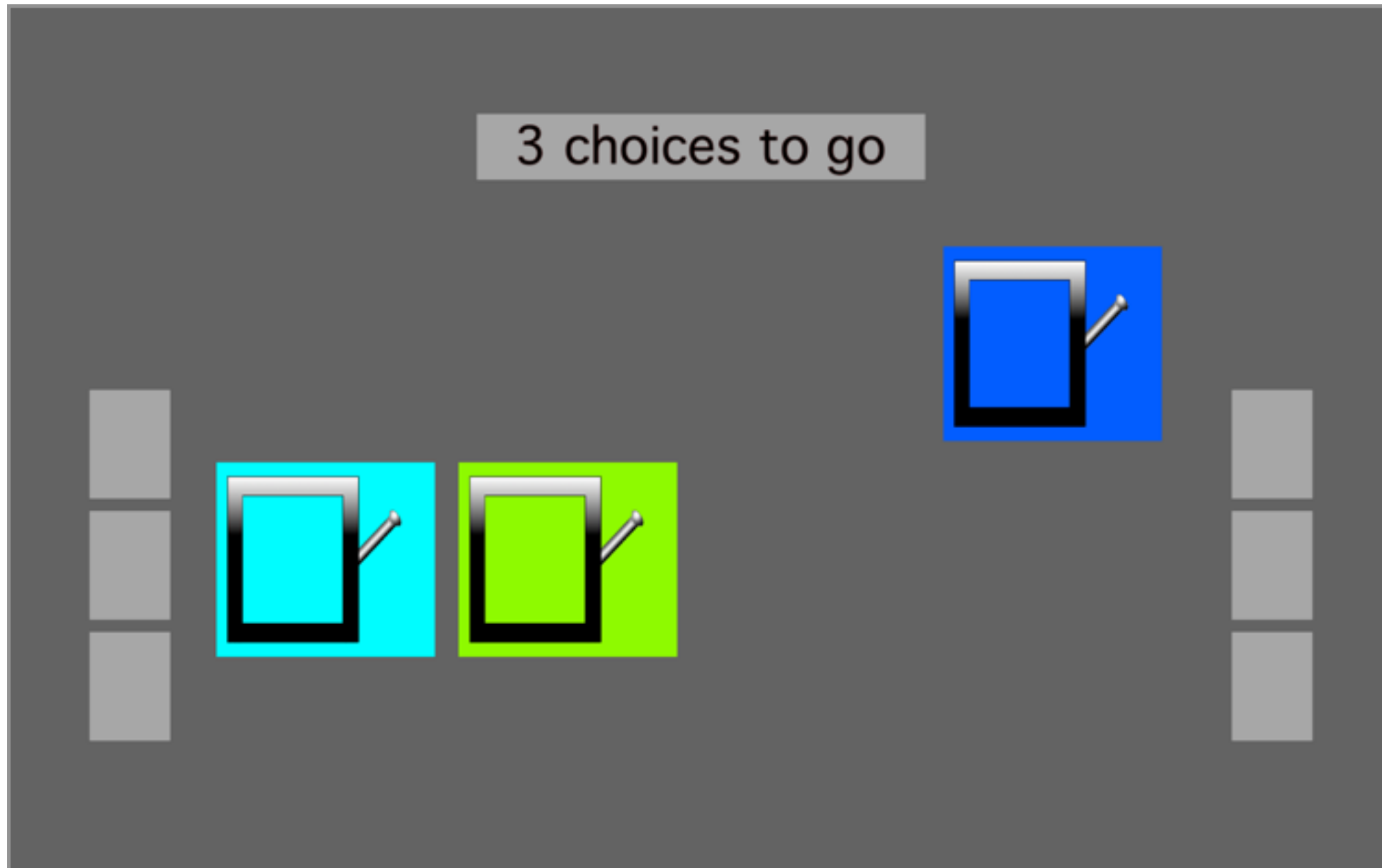
Casino Task

In each room, you can choose between
slot machines.

You will go through 100 different rooms.

In each room, you get to choose
8 times.

Casino Task



Anhedonia or helplessness?

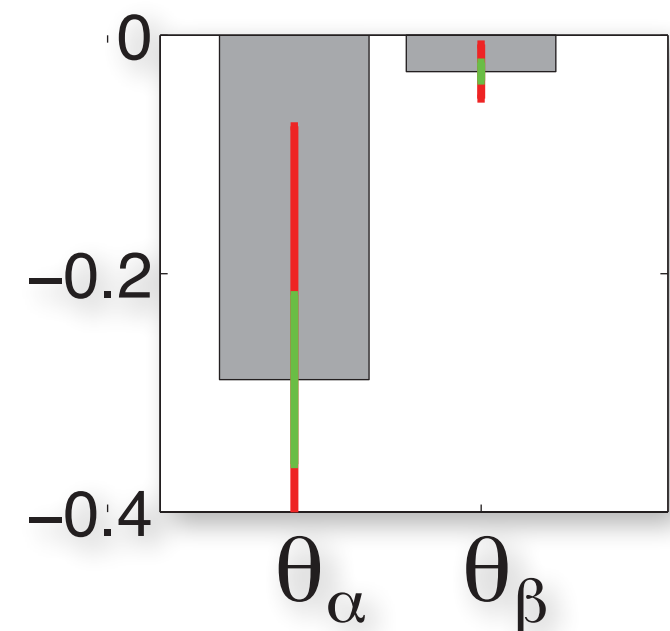
$$p(a|N_t, \alpha, \beta) = \frac{e^{\beta Q(a; N_t, \alpha)}}{\sum_{a'} e^{\beta Q(a'; N_t, \alpha)}}$$

Anhedonia?

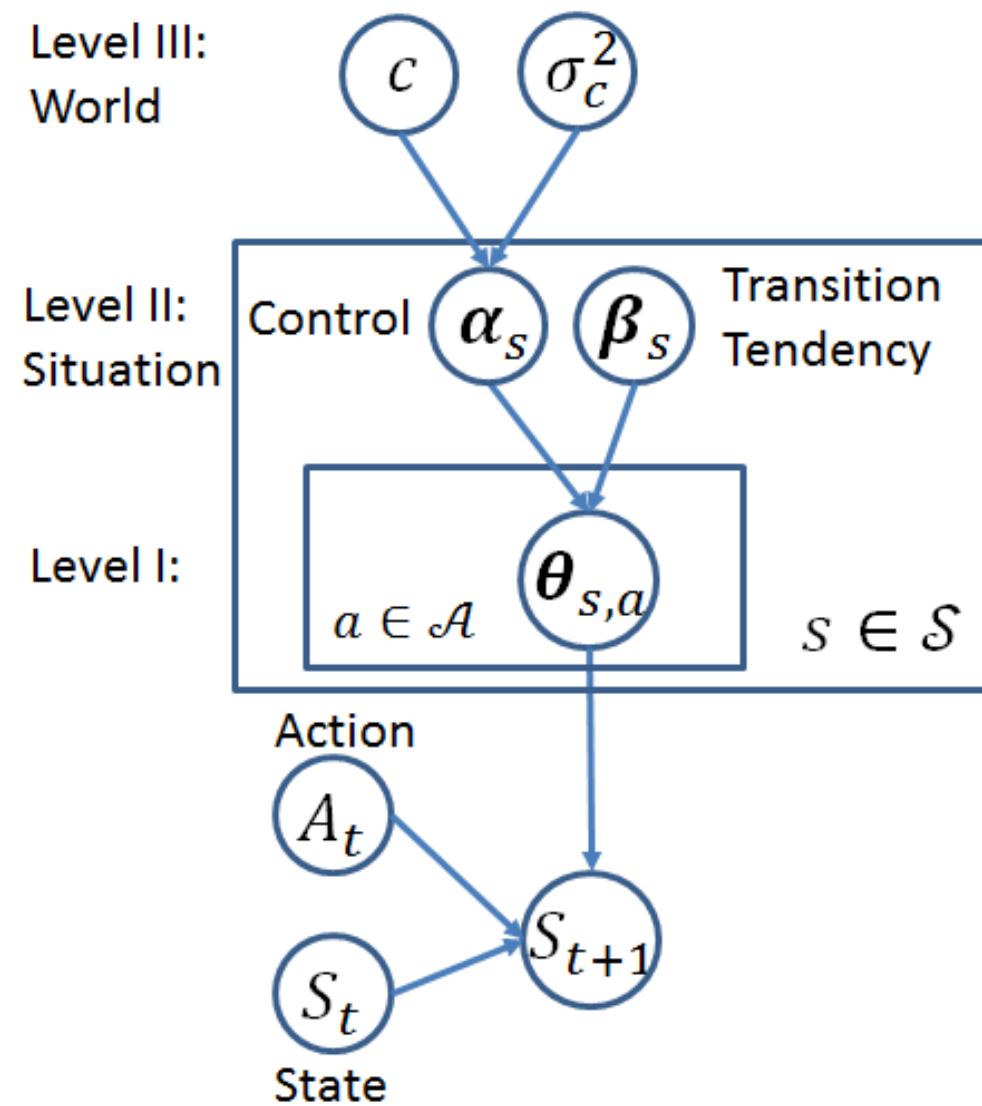
Helplessness?

$$\alpha = \theta_\beta BDA + \theta'_\alpha BHS + \dots$$

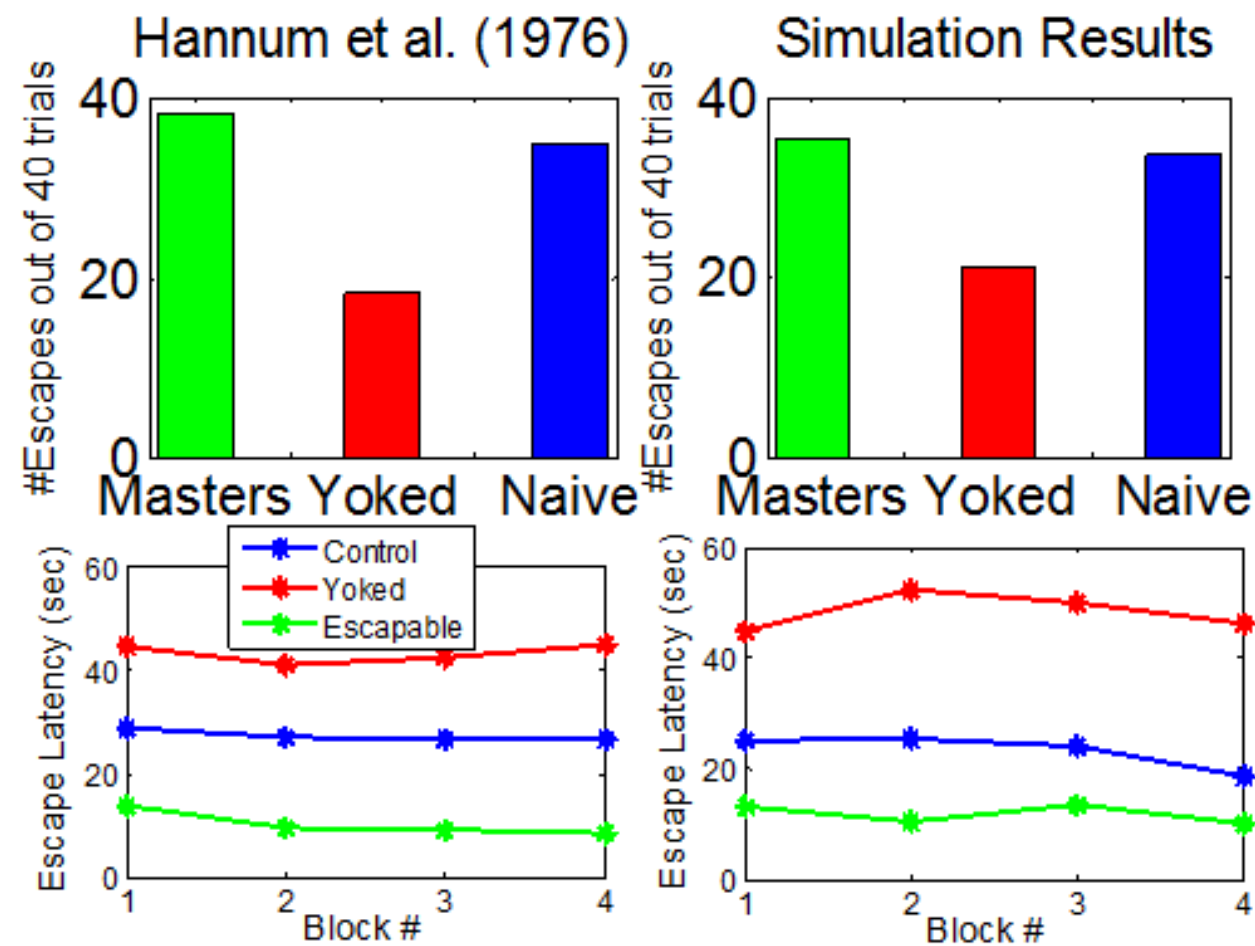
$$\beta = \theta'_\beta BDA + \theta_\alpha BHS + \dots$$



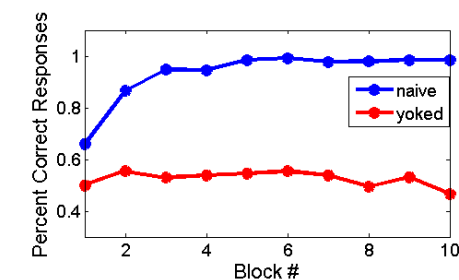
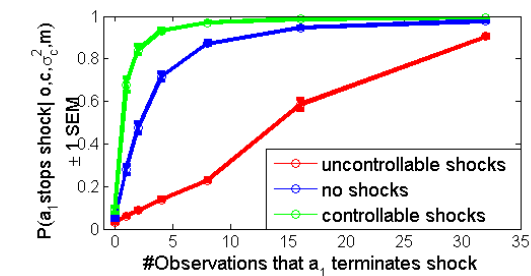
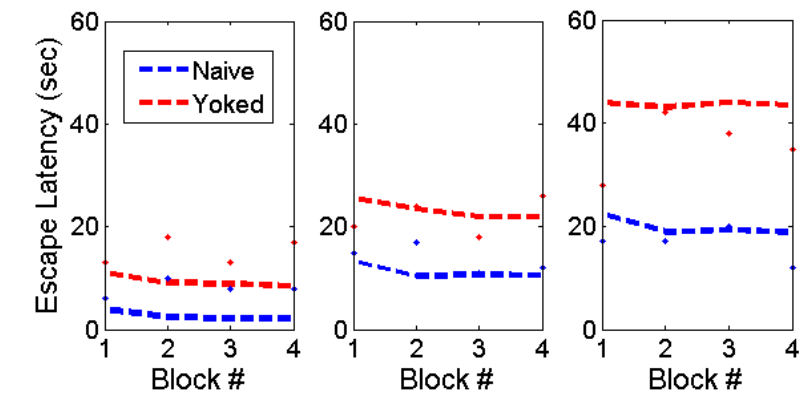
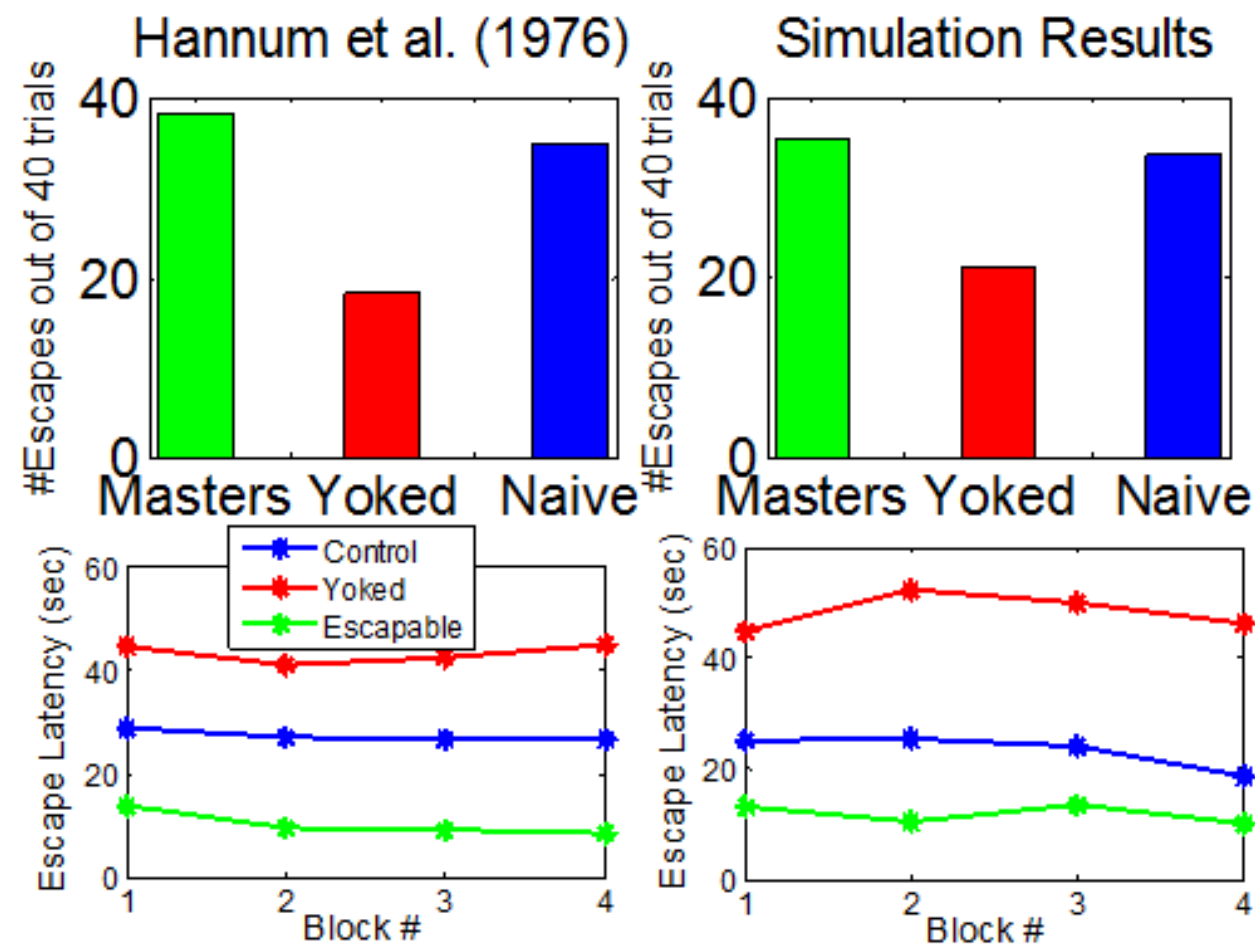
Helplessness as normative generalisation



Helplessness as optimal inference



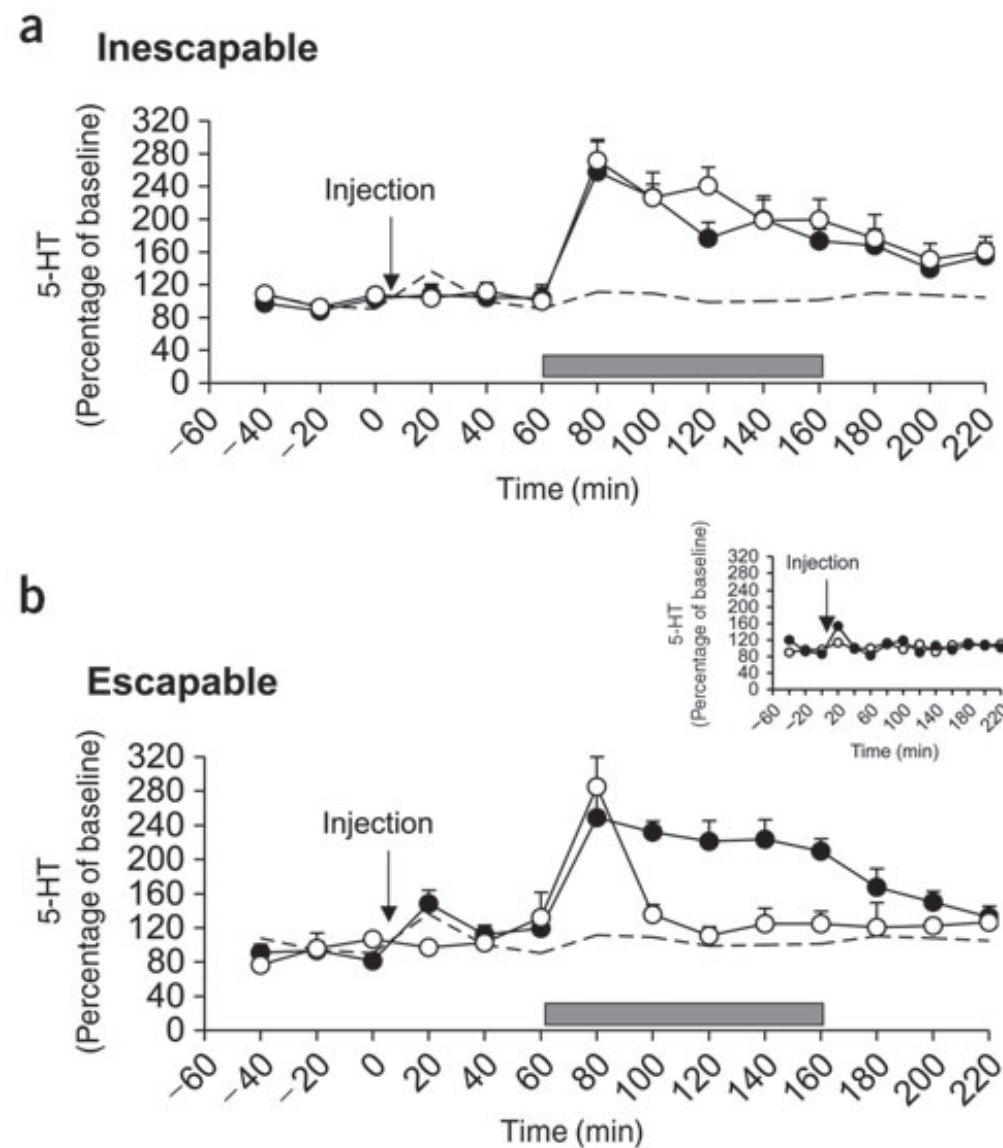
Helplessness as optimal inference



Lieder, Goodman and Huys, 2013

Helplessness - goal-directed decisions

► Matches the neurobiology



So...

▶ Emotional component

- No primary changes (pain, hedonic taste, sucrose)
- Negative “emotional” biases & decision-making
 - conceptual -> interpretation?

▶ Cognitive component

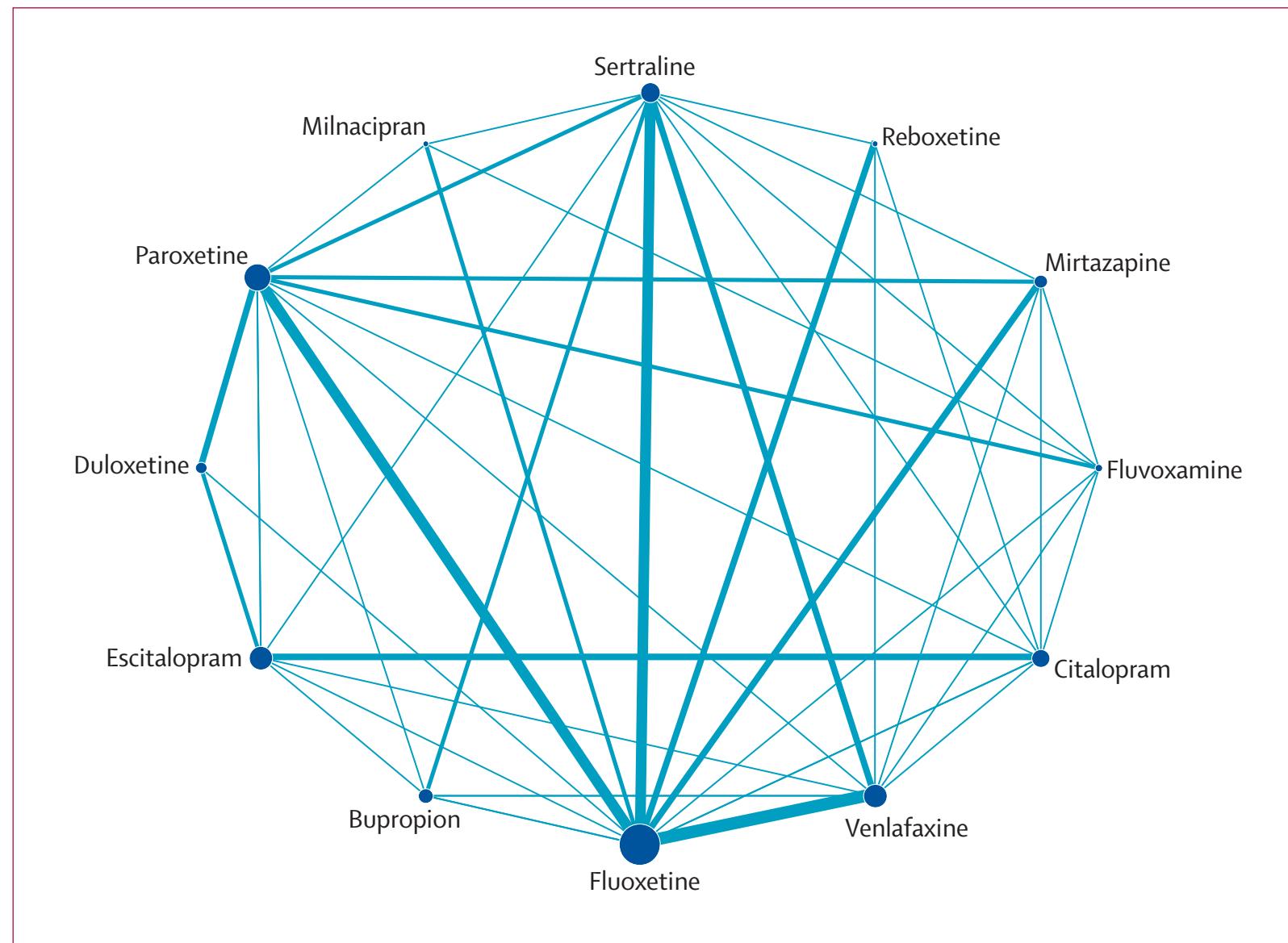
- Helplessness
- Goal-directed “interpretations”

▶ Neuromodulators: 5HT

▶ Cognitive Neuropsychological model: emotional biases lead to cognitive biases

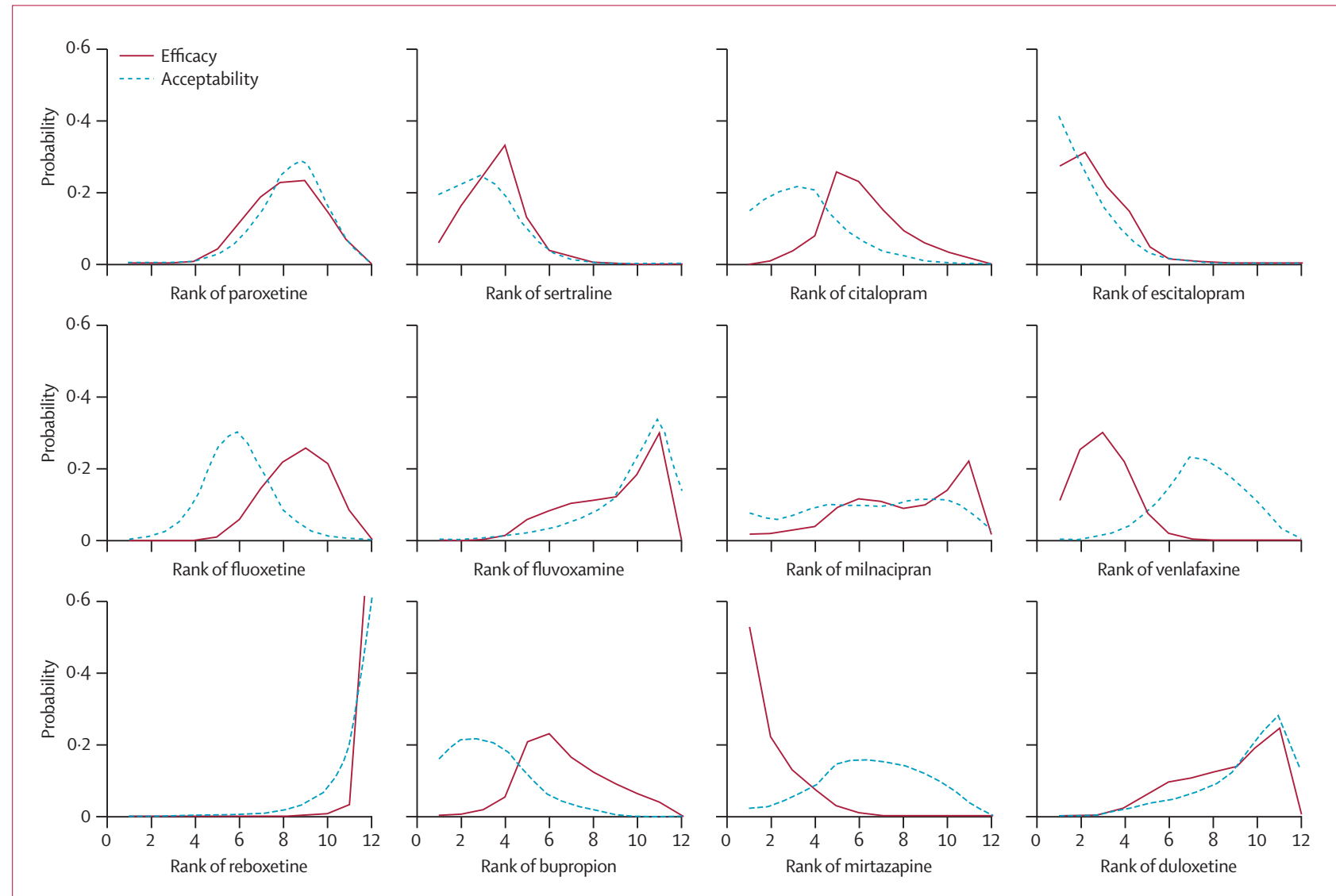
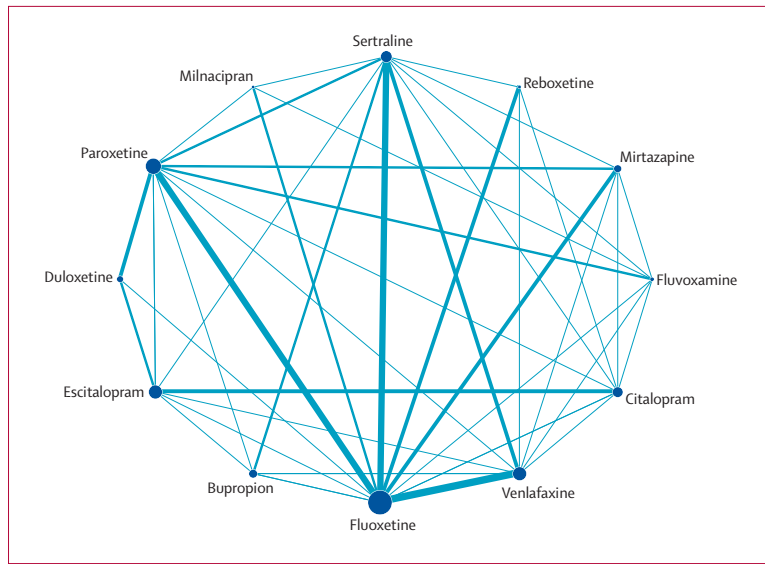
- How?

► Main treatment modality



► the more specific the better?

► Main treatment modality

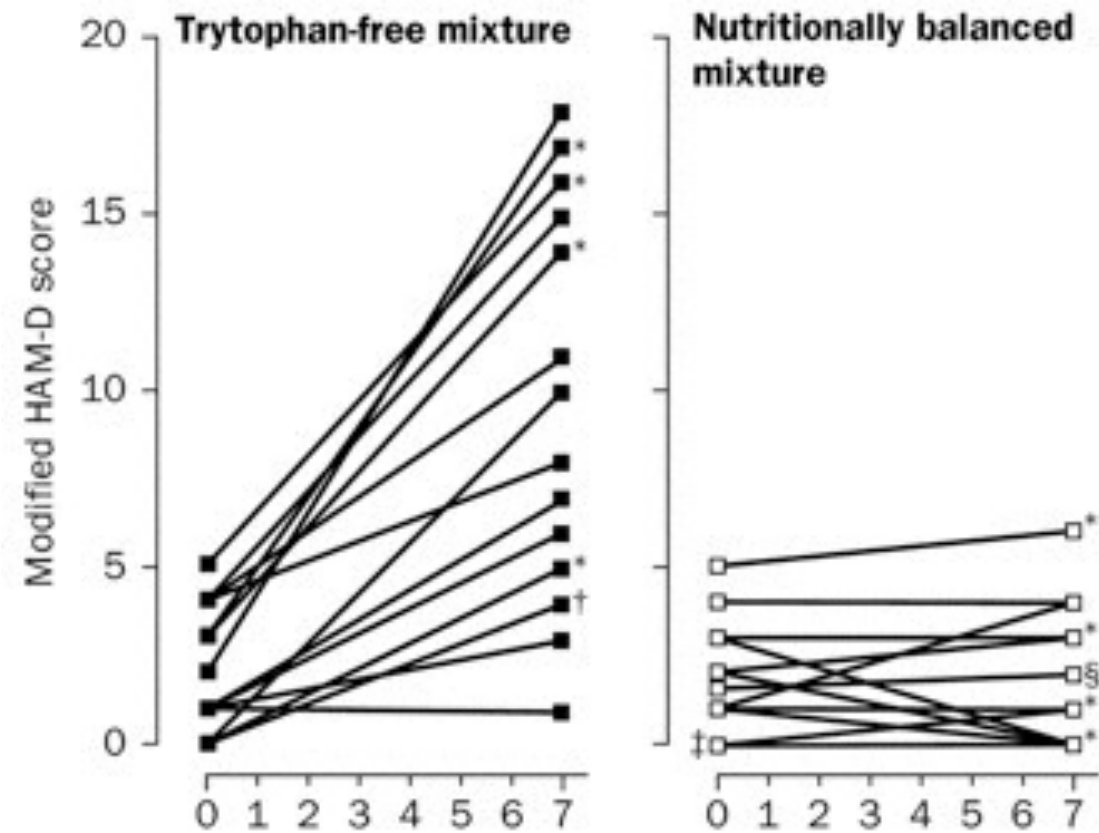


► the more specific the better?

Acute tryptophan depletion

- ▶ 80% in patients who have responded to SSRIs. 16% in those who have not.
- ▶ AMT: similar for NA -> converse picture

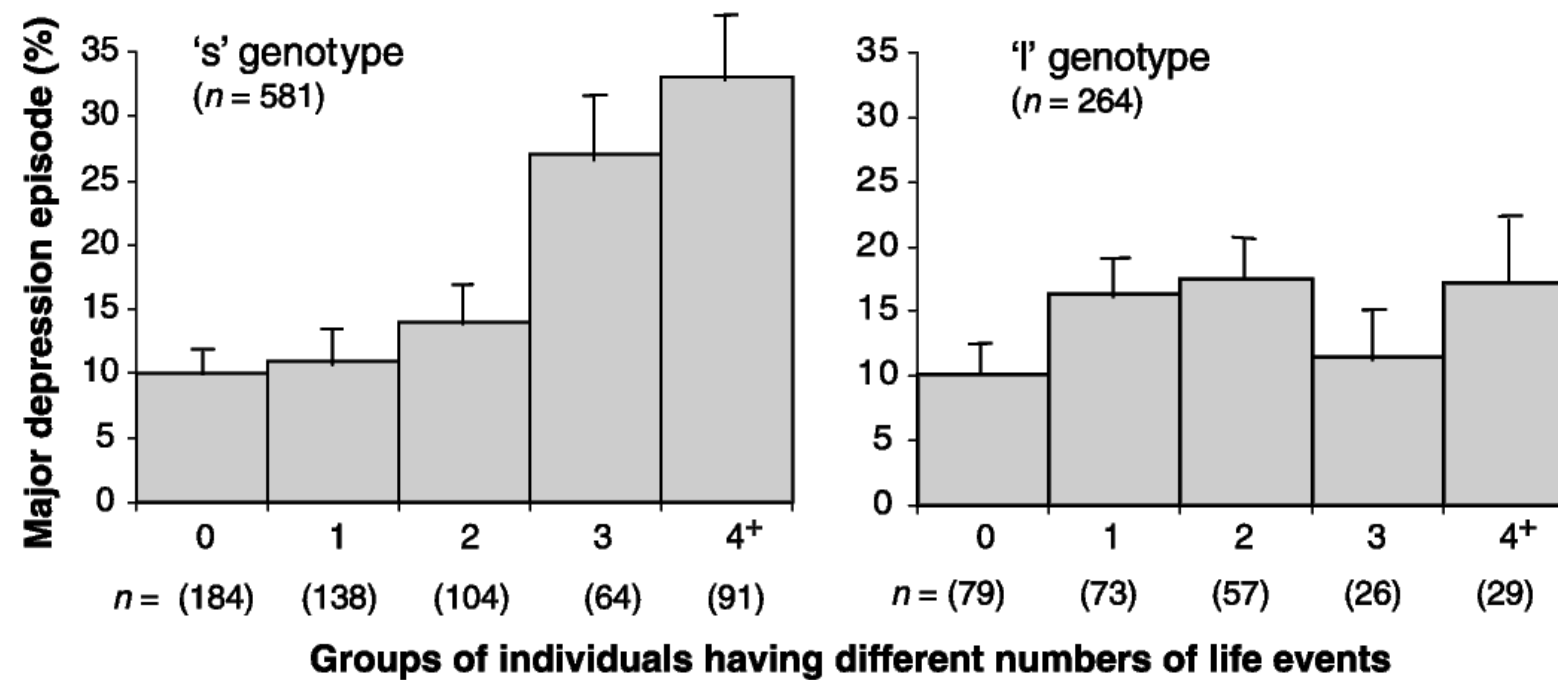
Acute tryptophan depletion



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Serotonin in MDD: 5HTT

Serotonin in MDD: 5HTT



Caspi et al. 2003

Caspi et al., 2003

Serotonin and depression

SSRI

Effect

inhibit reuptake

increase 5HT??

Depression

treats

Serotonin and depression

SSRI

Effect

inhibit reuptake

increase 5HT??

Depression

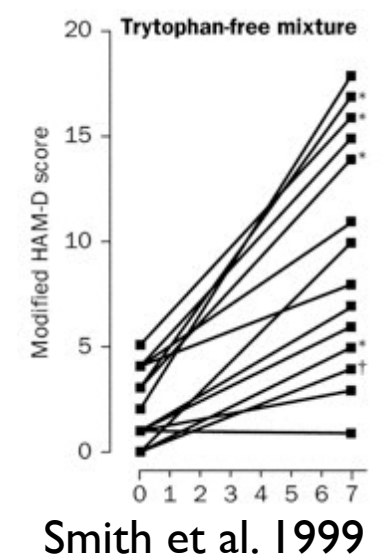
treats

Serotonin and depression

	SSRI	5HTTLPR
Effect	inhibit reuptake increase 5HT??	inefficient reuptake increase 5HT??
Depression	treats	causes

Serotonin and depression

	SSRI	5HTTLPR	Tryptophan depletion
Effect	inhibit reuptake increase 5HT??	inefficient reuptake increase 5HT??	reduce 5HT
Depression	treats	causes	acute relapse



Serotonin in helplessness

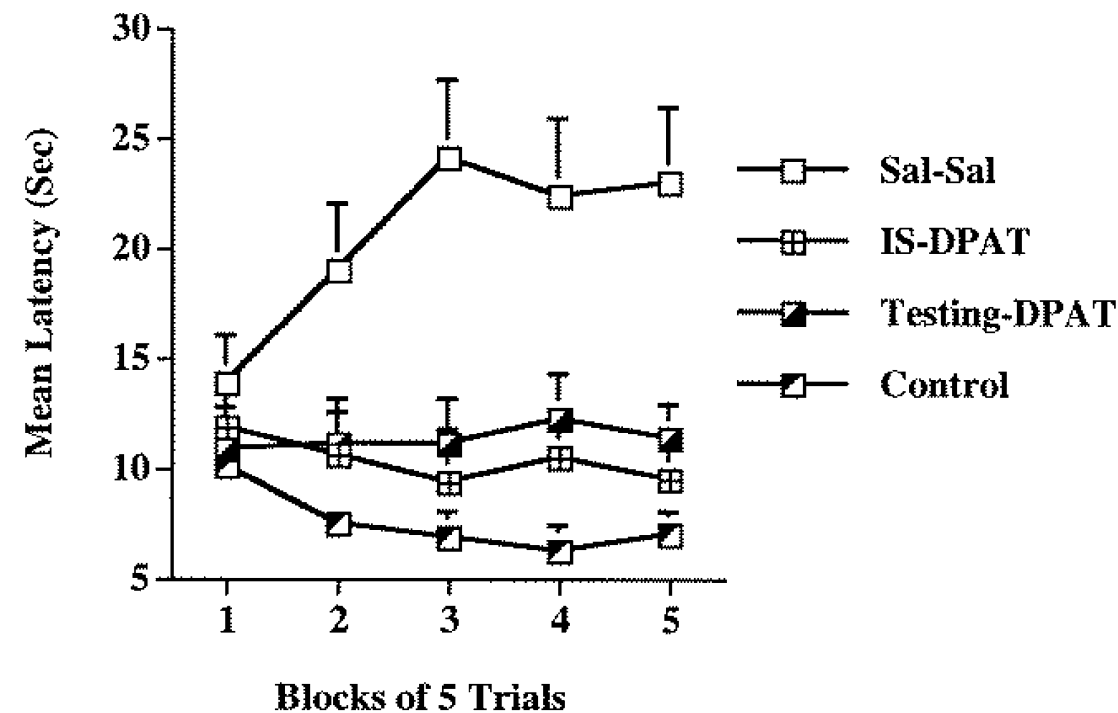
Table 2

Effects of inescapable shock on the number of Fos+ 5-HT cells and Fos+ TH cells.

Nuclei	Cage control	Shocks			
		0	10	50	100
DRN	7.8 ± 1.7	76.8 ± 12.6**	98.7 ± 14.0**	155.0 ± 16.6***,††,§	162.3 ± 17.8***,††,§
MRN	1.8 ± 1.2	7.8 ± 1.8	9.0 ± 1.9	18.7 ± 3.4***,††,§§	24.0 ± 2.0***,†††,§§§
NRM	1.8 ± 0.5	31.3 ± 2.1**	33.3 ± 4.8*	40.2 ± 4.0***	45.0 ± 11.9**
NRO	0.5 ± 0.3	9.7 ± 1.8*	10.5 ± 0.8*	9.5 ± 3.0*	11.3 ± 2.5*
NRP	2.3 ± 0.5	9.3 ± 2.5	6.3 ± 2.2	7.2 ± 2.1	8.5 ± 2.2
LC	49.0 ± 15.2	332.3 ± 31.2***	390.3 ± 32.5***	506.5 ± 47.9***,††,§	531.2 ± 41.6***,††,§

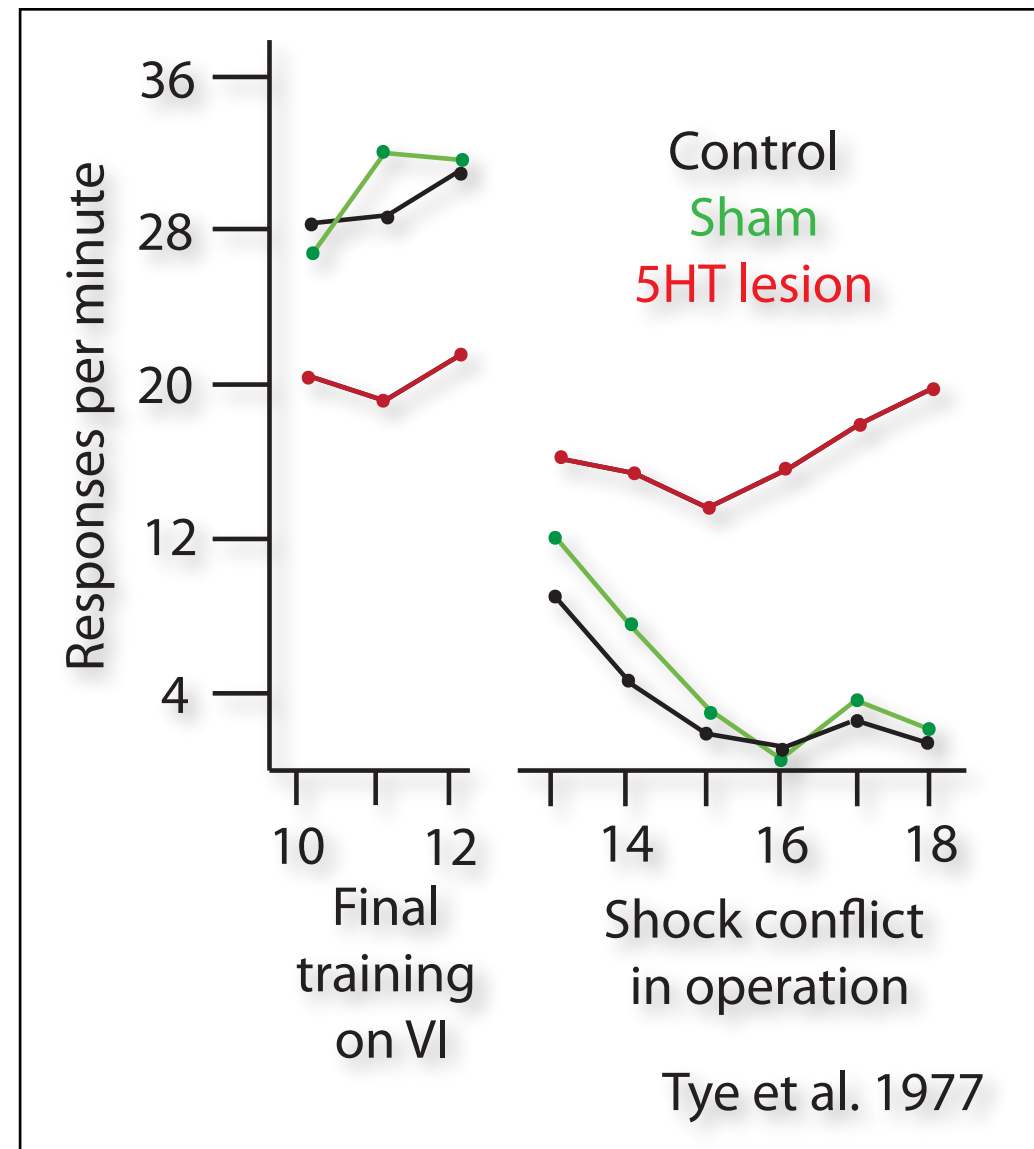
Values are means ± S.E.M.; $n = 4$ for cage control; $n = 6$ for 0, 10, 50 and 100 shocks. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$ vs. cage control; †† $p < 0.01$; ††† $p < 0.001$ vs. 0 shocks; § $p < 0.05$; §§ $p < 0.01$; §§§ $p < 0.001$ vs. 10 shocks; by one-way ANOVA and Newman–Keuls multiple comparison test.

Takase et al., 2005



Maier and Watkins, 2005

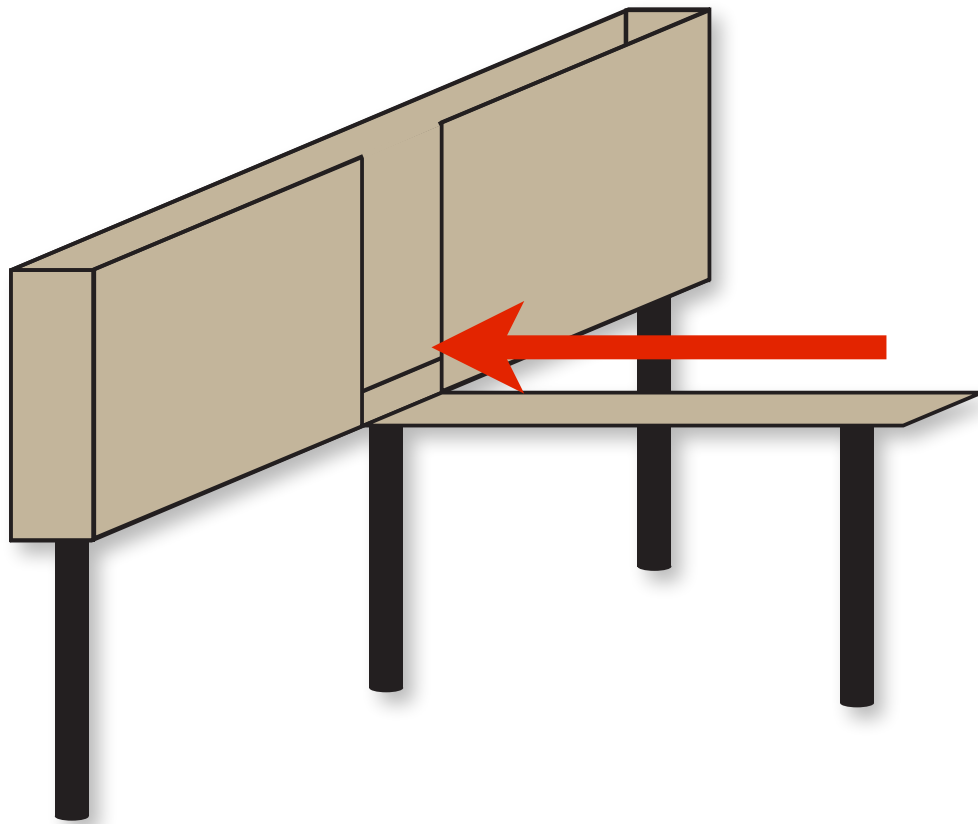
Behavioural inhibition and 5HT



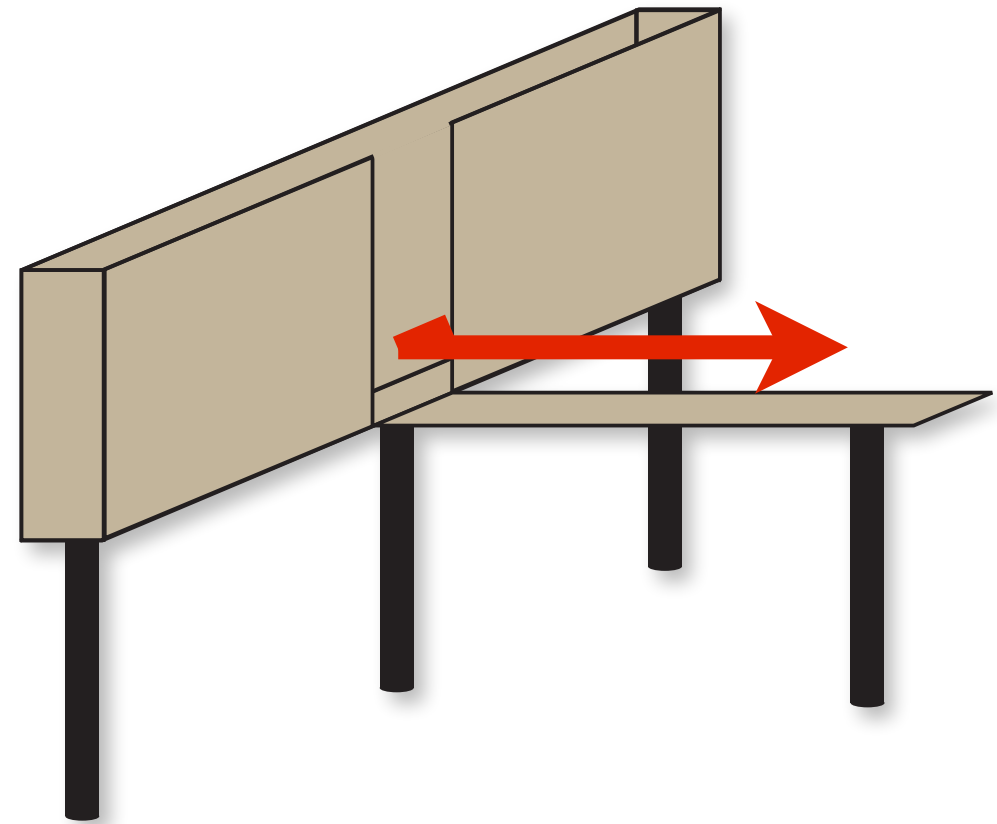
Release of punishment-suppressed responding
= anxiolysis

5HT: Panic and anxiety

Deakin, Graeff, Gray et al.



Panic

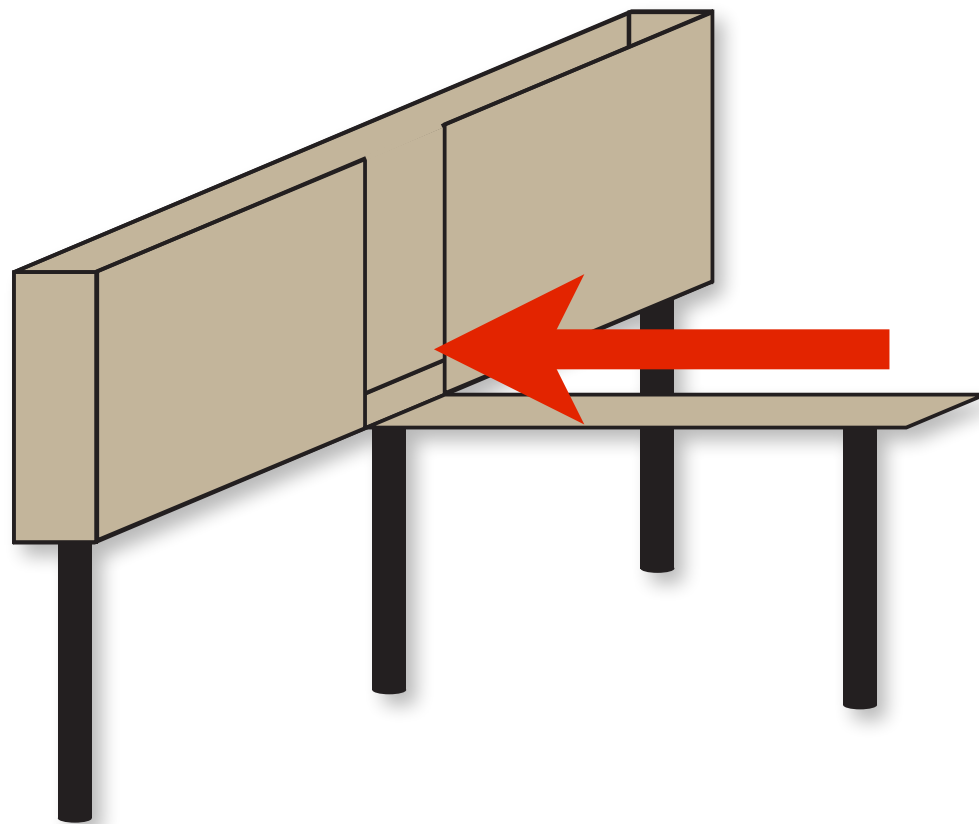


Anxiety

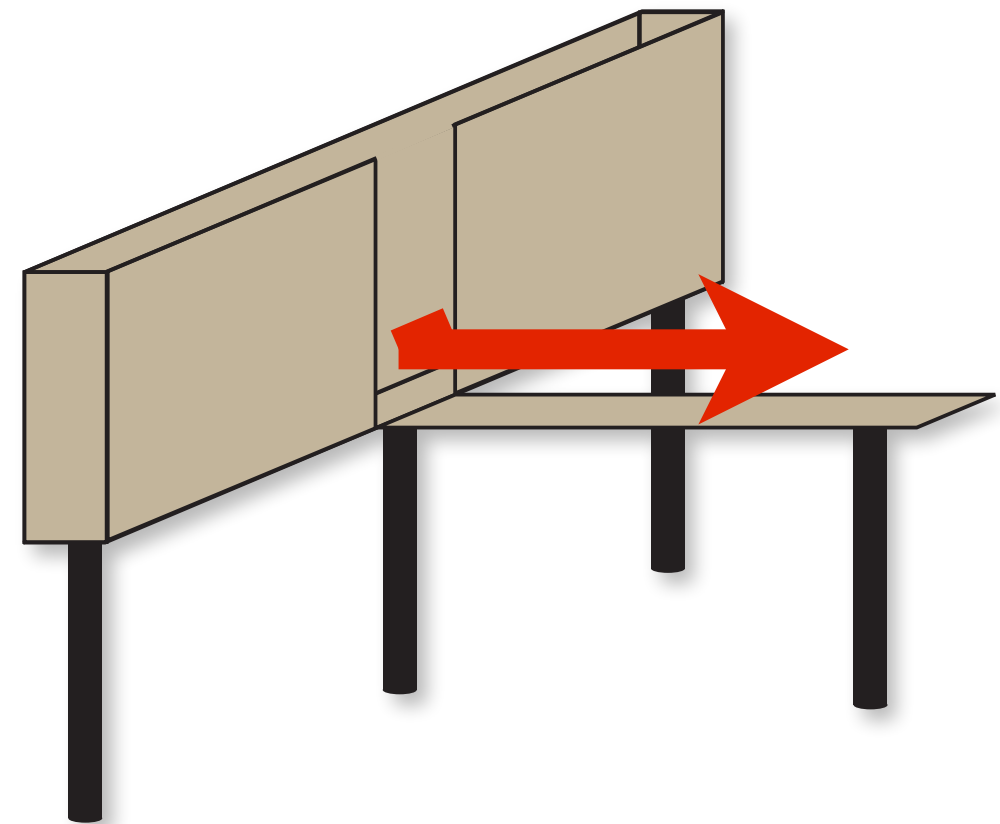
Soubrie 1986, Deakin & Graeff 1996, Dayan & Huys 2009

5HT: Panic and anxiety

Deakin, Graeff, Gray et al.



↑ Panic



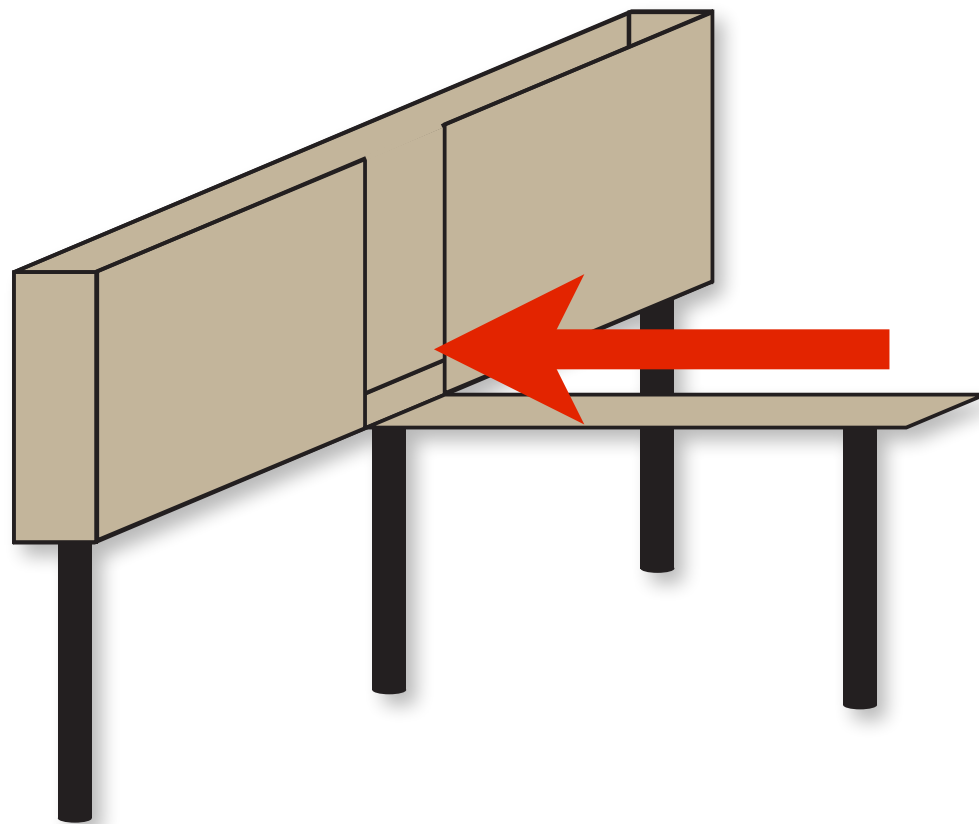
↓ Anxiety

↓ 5HT

Soubrie 1986, Deakin & Graeff 1996, Dayan & Huys 2009

5HT: Panic and anxiety

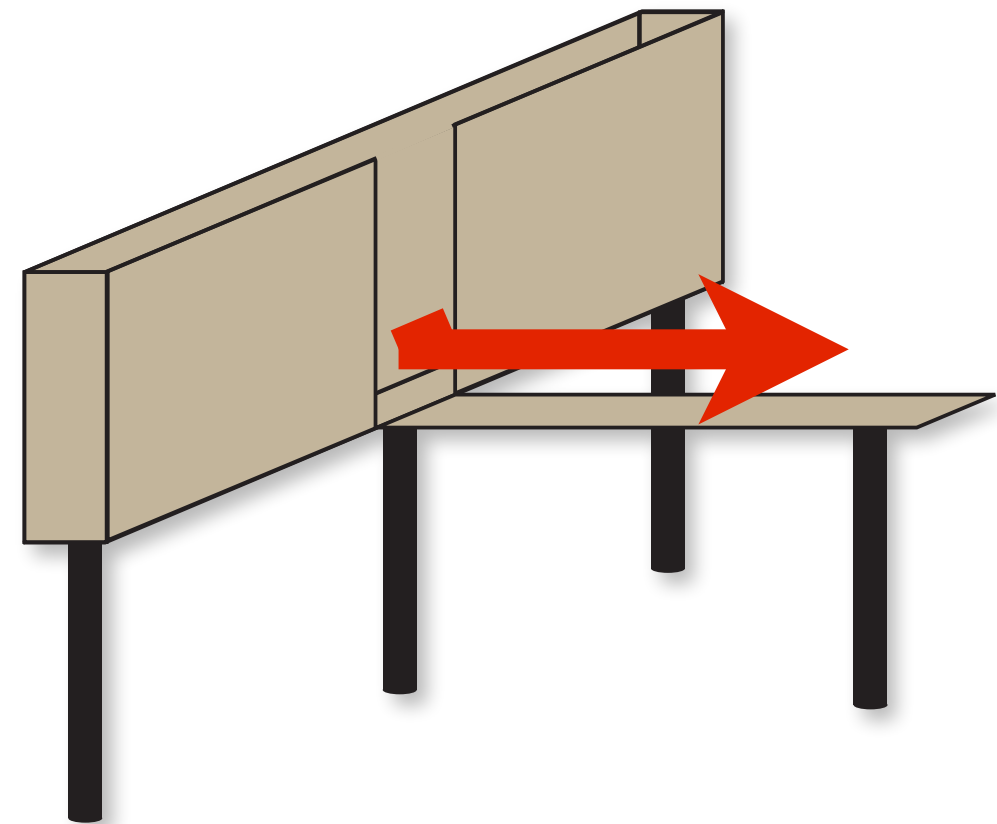
Deakin, Graeff, Gray et al.



↑
Panic

↑
Behaviour

↓
5HT



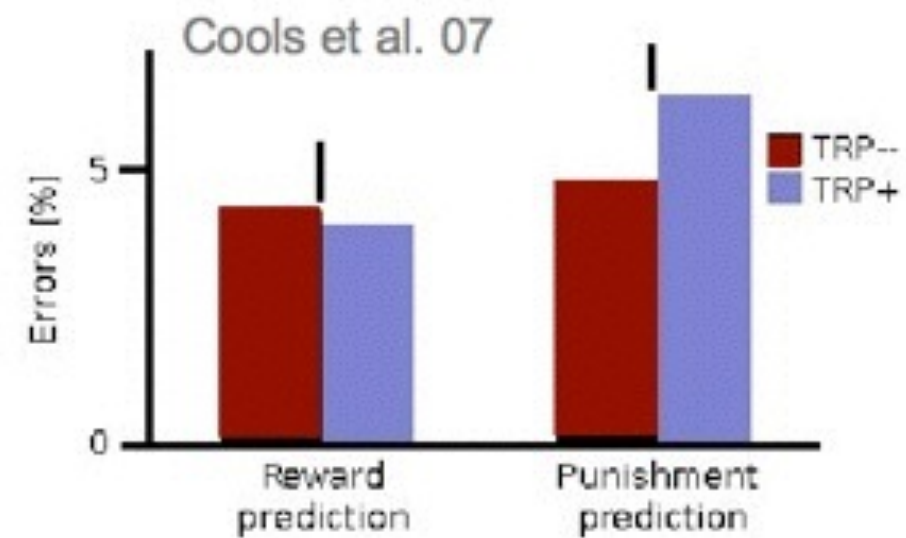
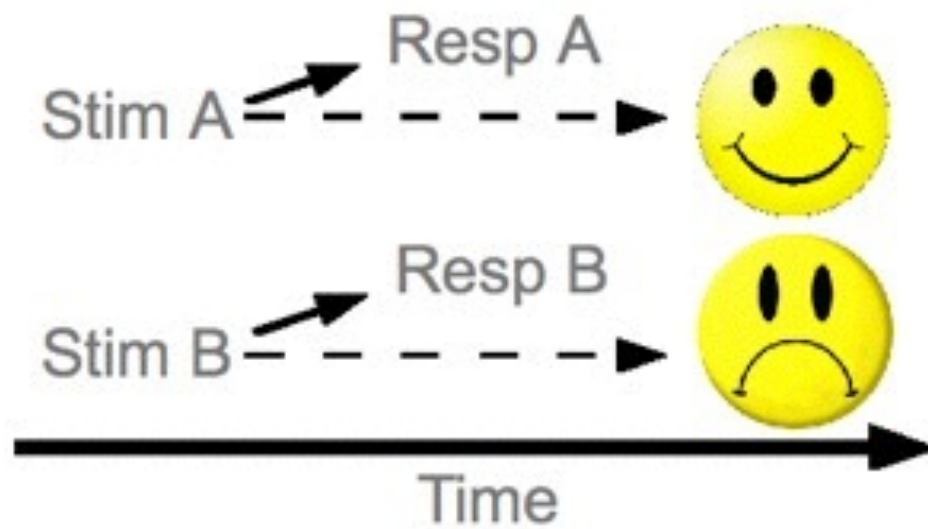
↓
Anxiety

↑
Behaviour

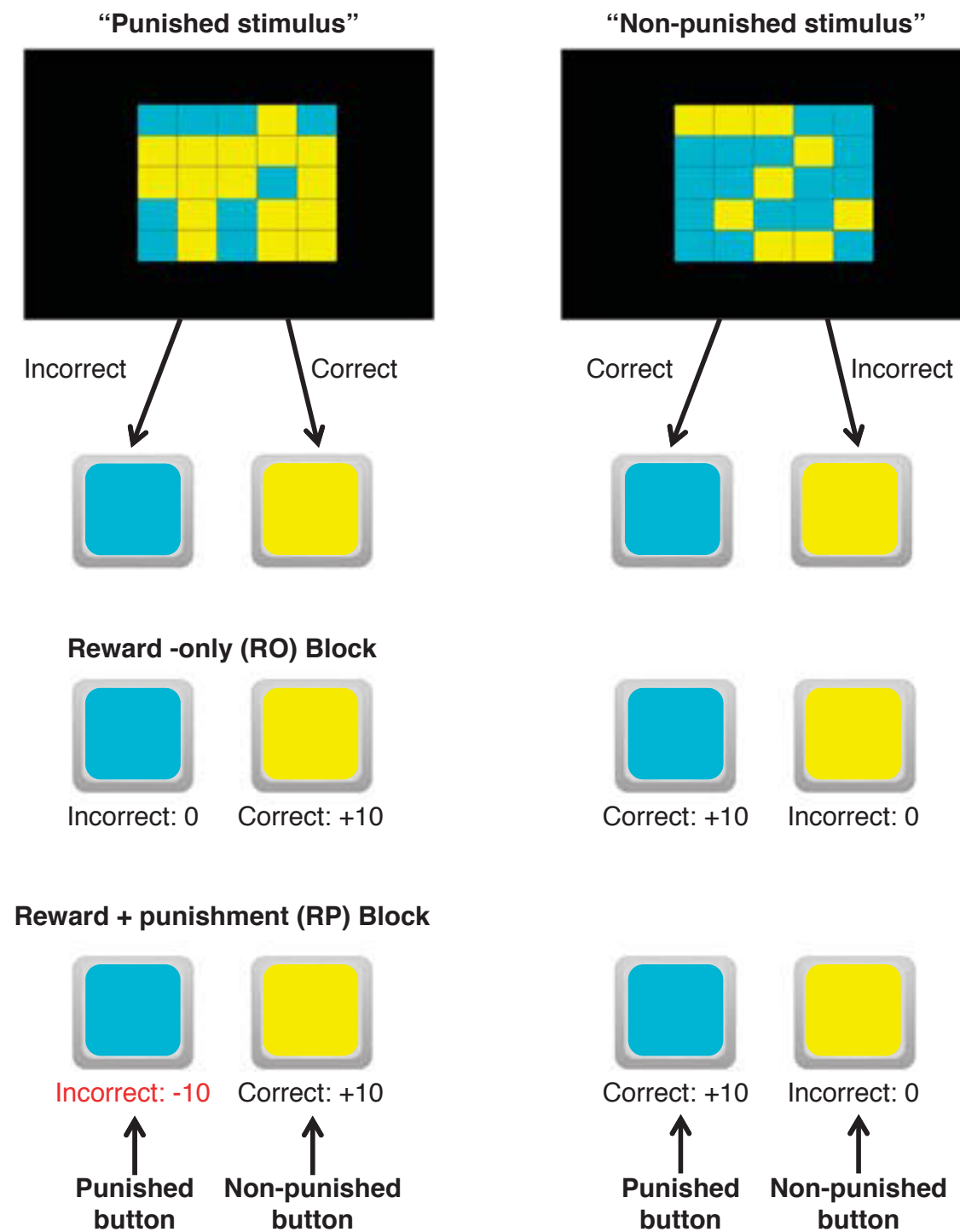
Soubrié (1986) - not anxiety, but behavioural suppression

Soubrie 1986, Deakin & Graeff 1996, Dayan & Huys 2009

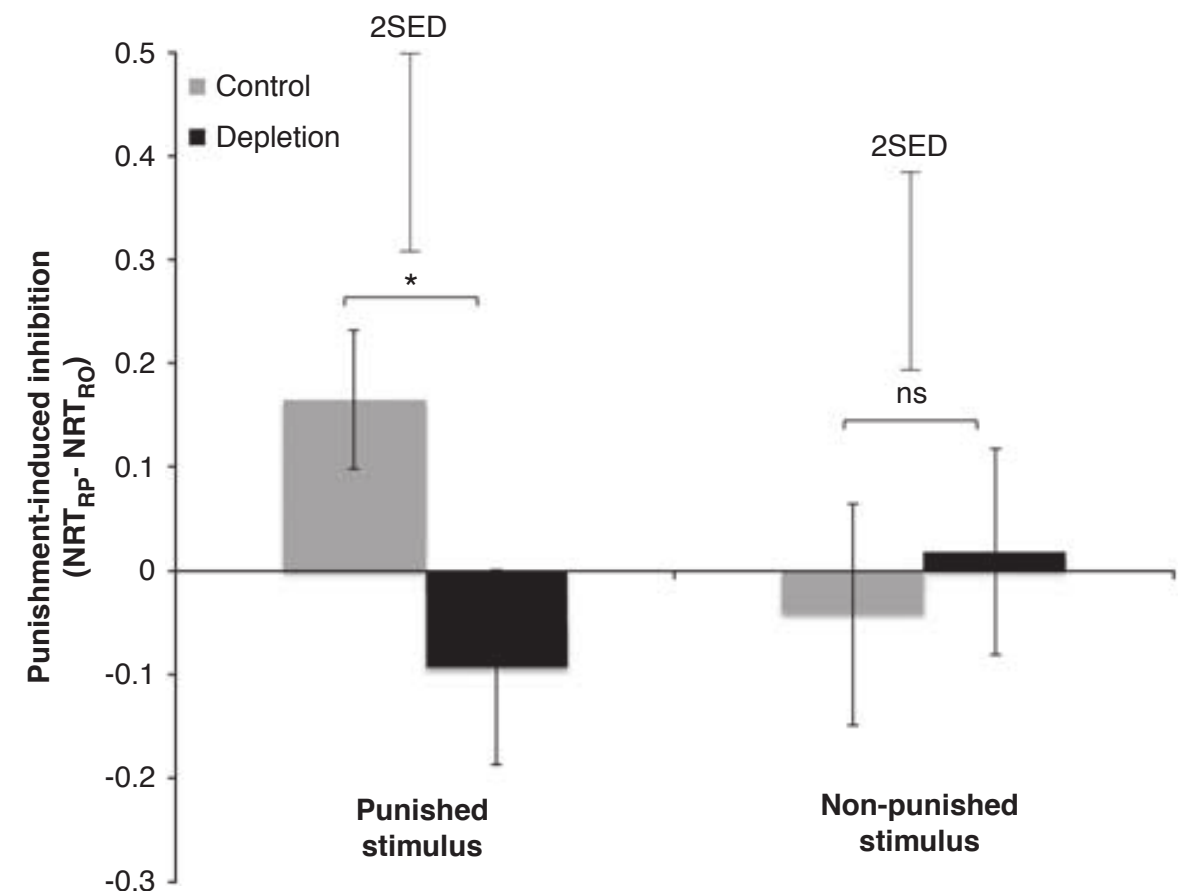
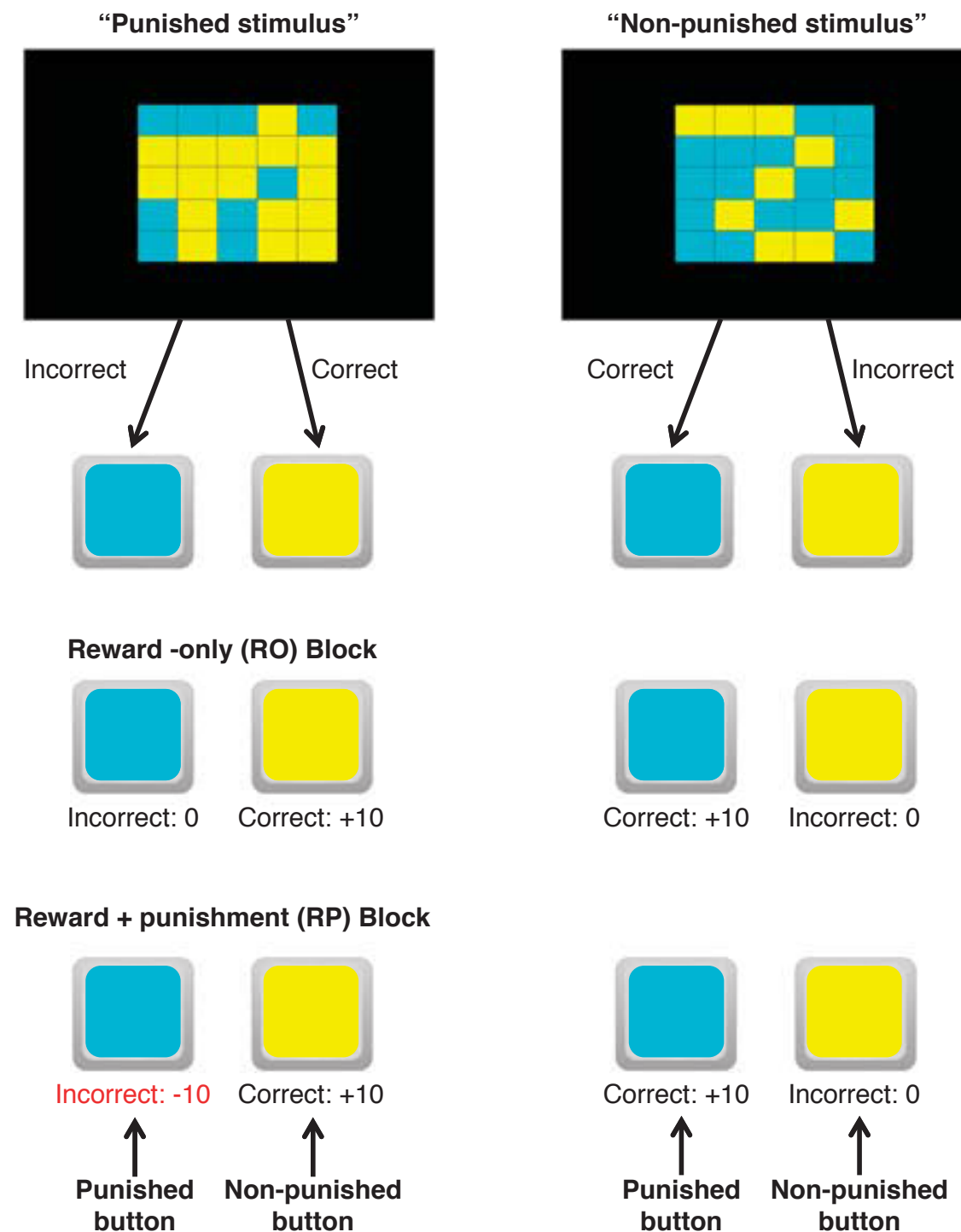
Inhibition with aversive expectations?



ATD abolishes Pavlovian inhibition in humans

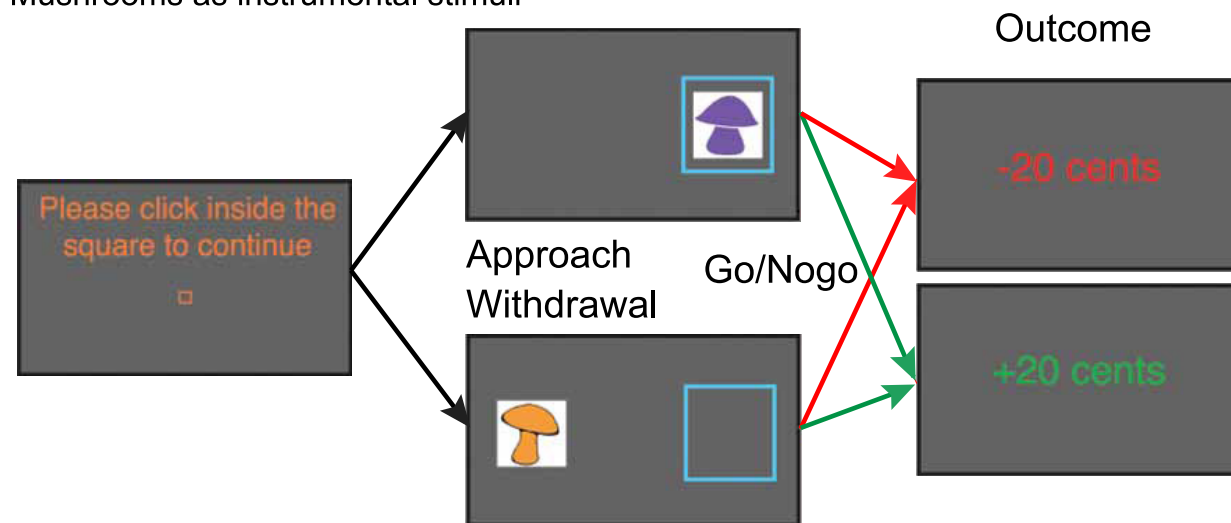


ATD abolishes Pavlovian inhibition in humans



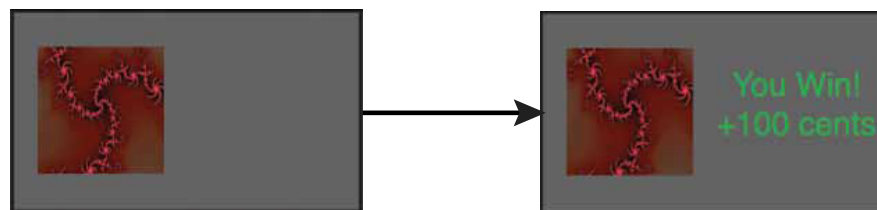
A Instrumental training

Mushrooms as instrumental stimuli



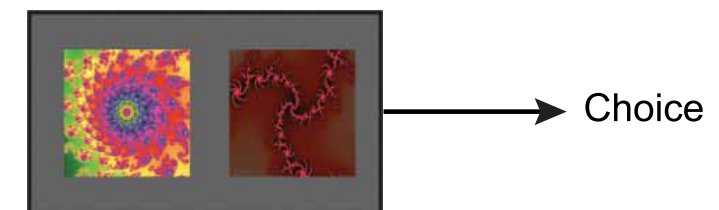
B Pavlovian training

Fractals and tones as Pavlovian stimuli



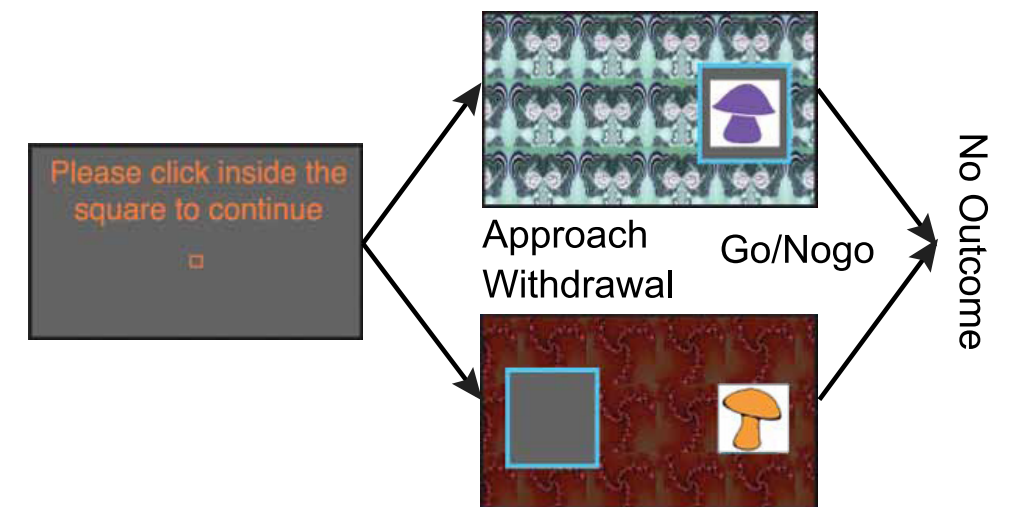
C Pavlovian query trials

Fractals and tones as Pavlovian stimuli

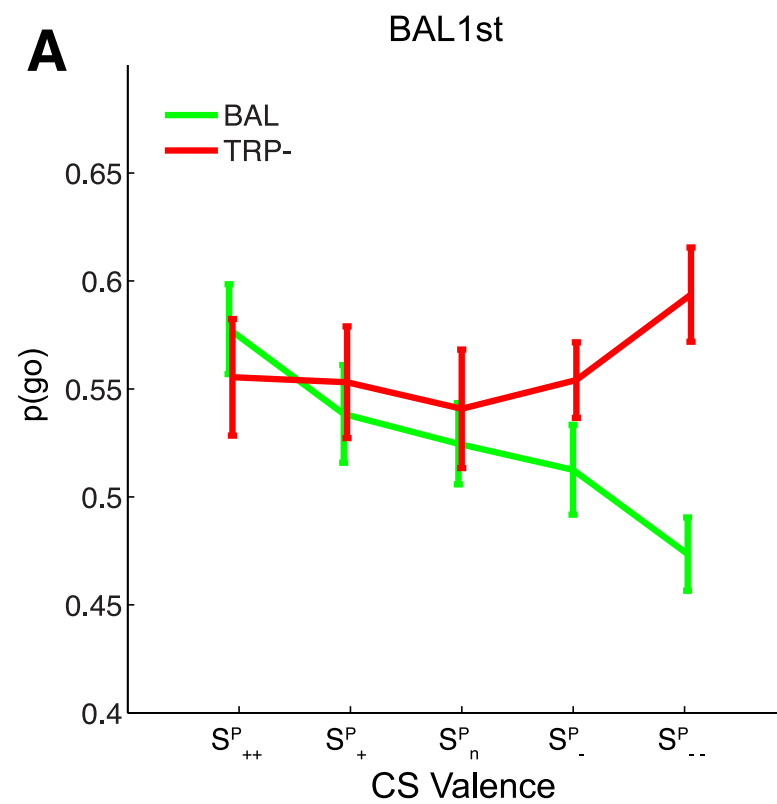


D Pavlovian-instrumental transfer

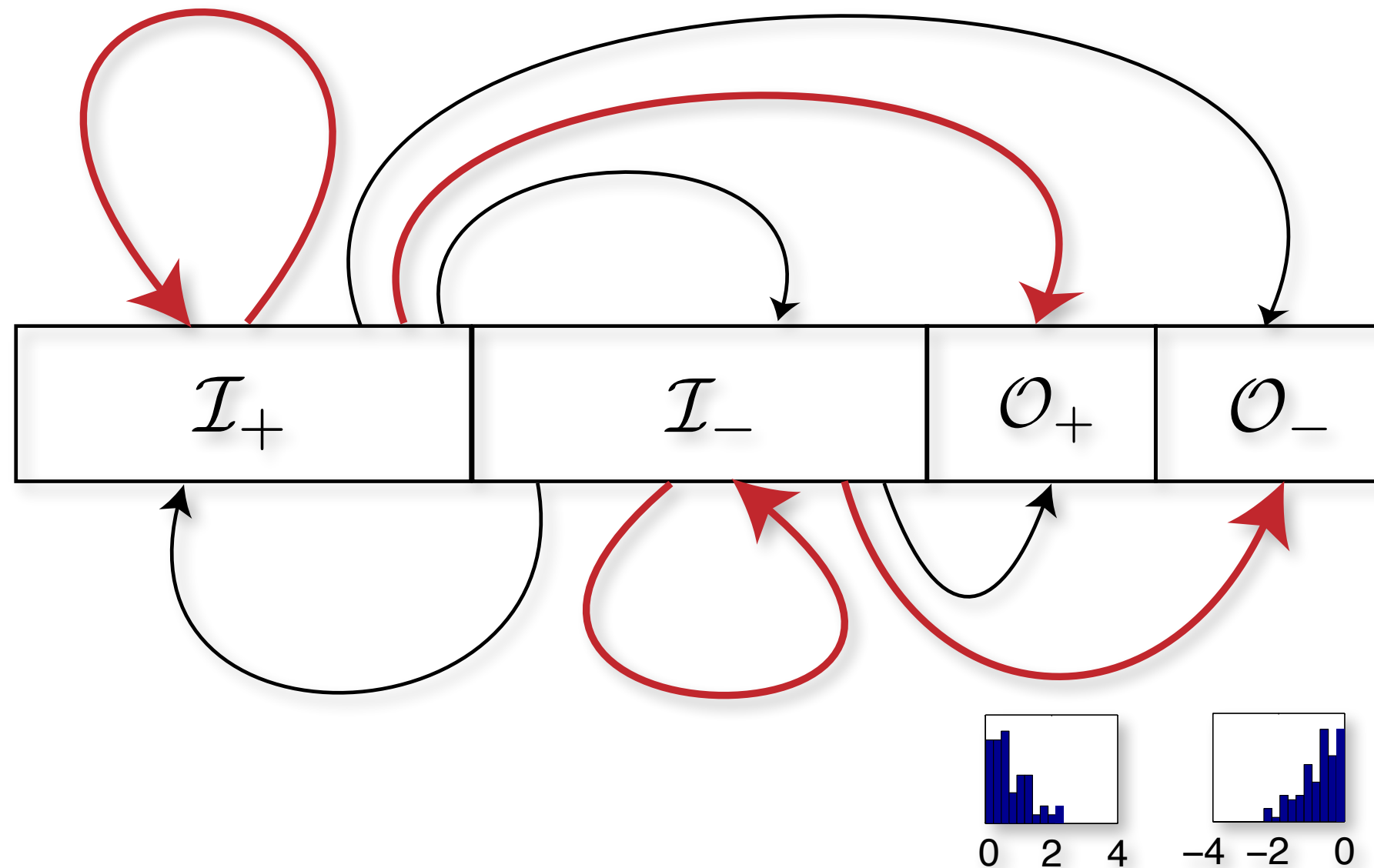
Instrumental stimuli on background of Pavlovian stimuli



Conditioned suppression, ATD

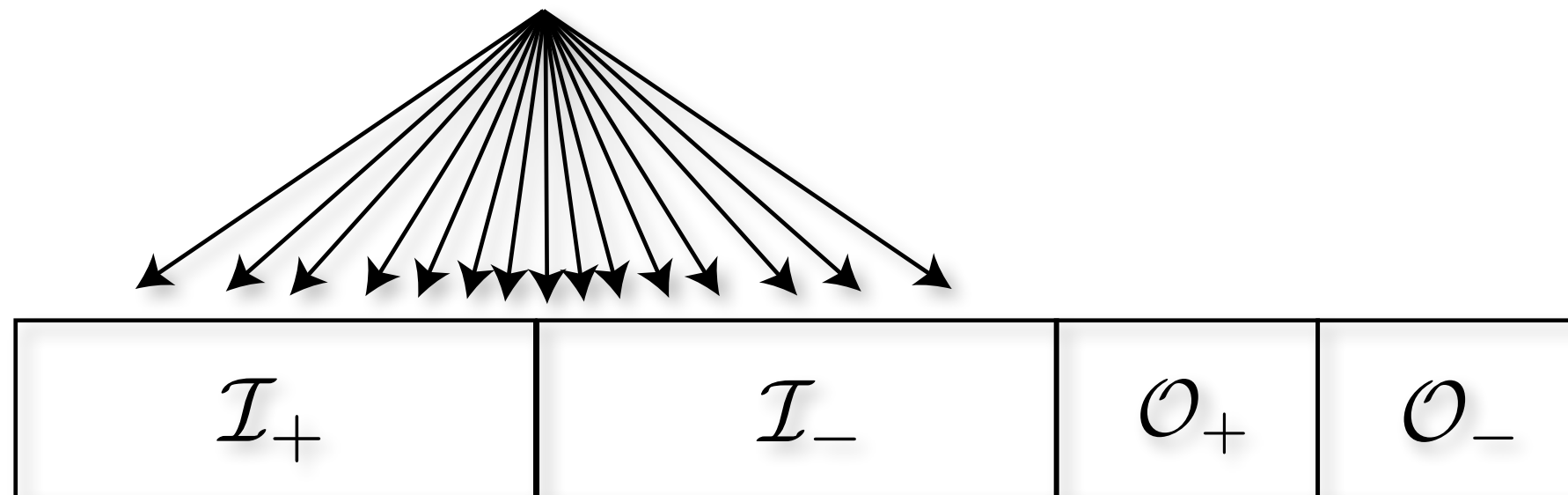


Modelling Pavlovian inhibition



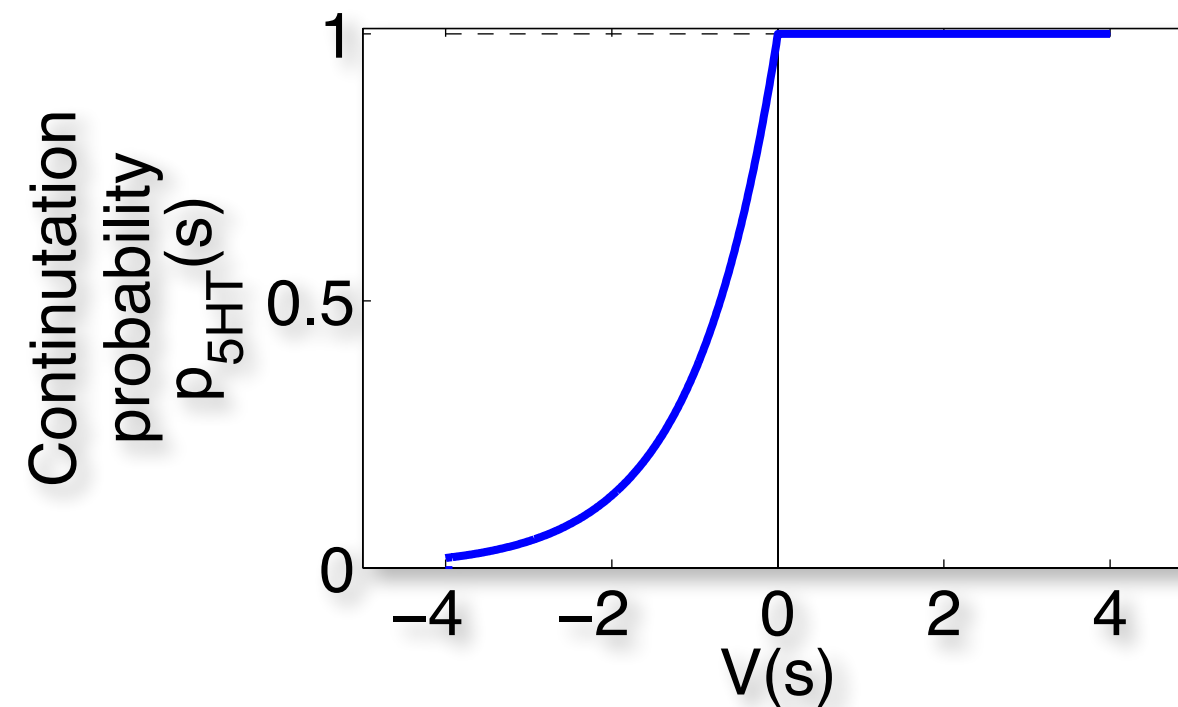
Either proceed according to the fixed arrows
OR
inhibit and restart randomly in \mathcal{I}

Inhibit and restart

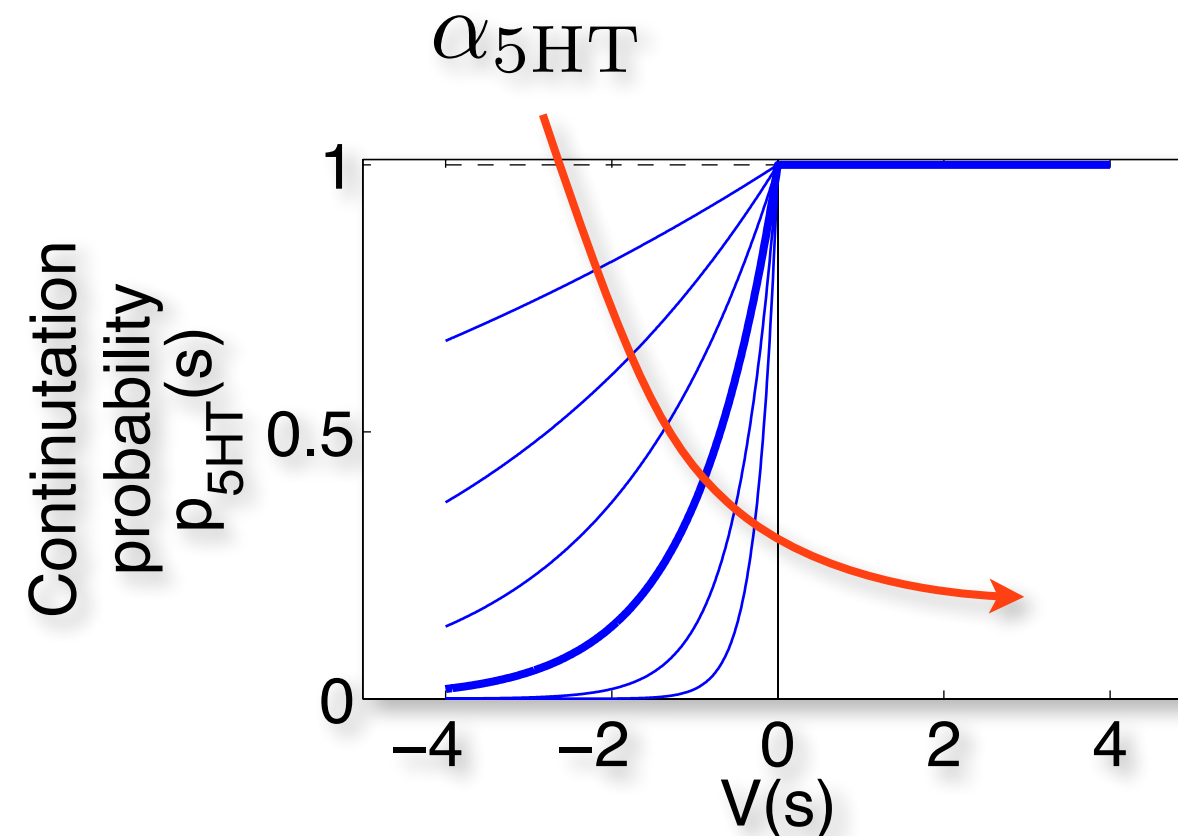


Either proceed according to the fixed arrows
OR
inhibit and restart randomly in \mathcal{I}

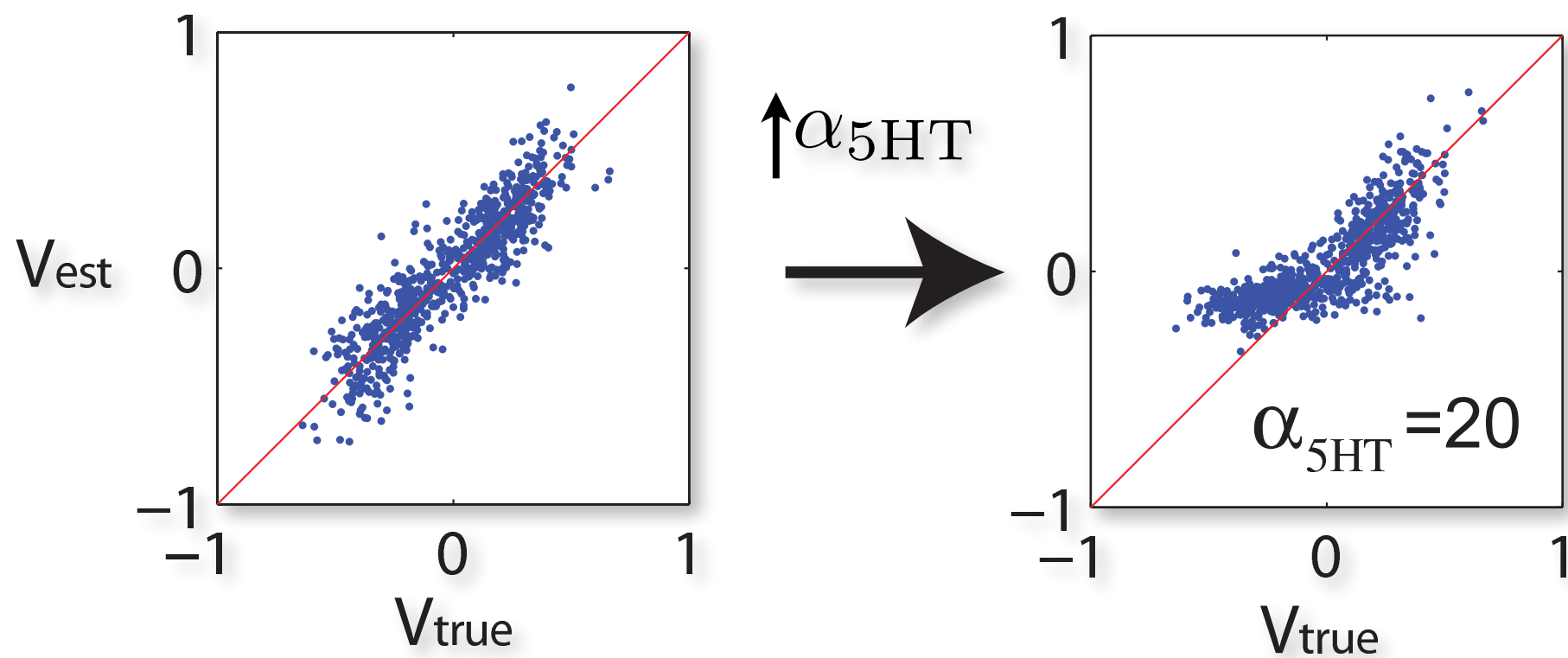
Inhibit if faced with aversive prediction V



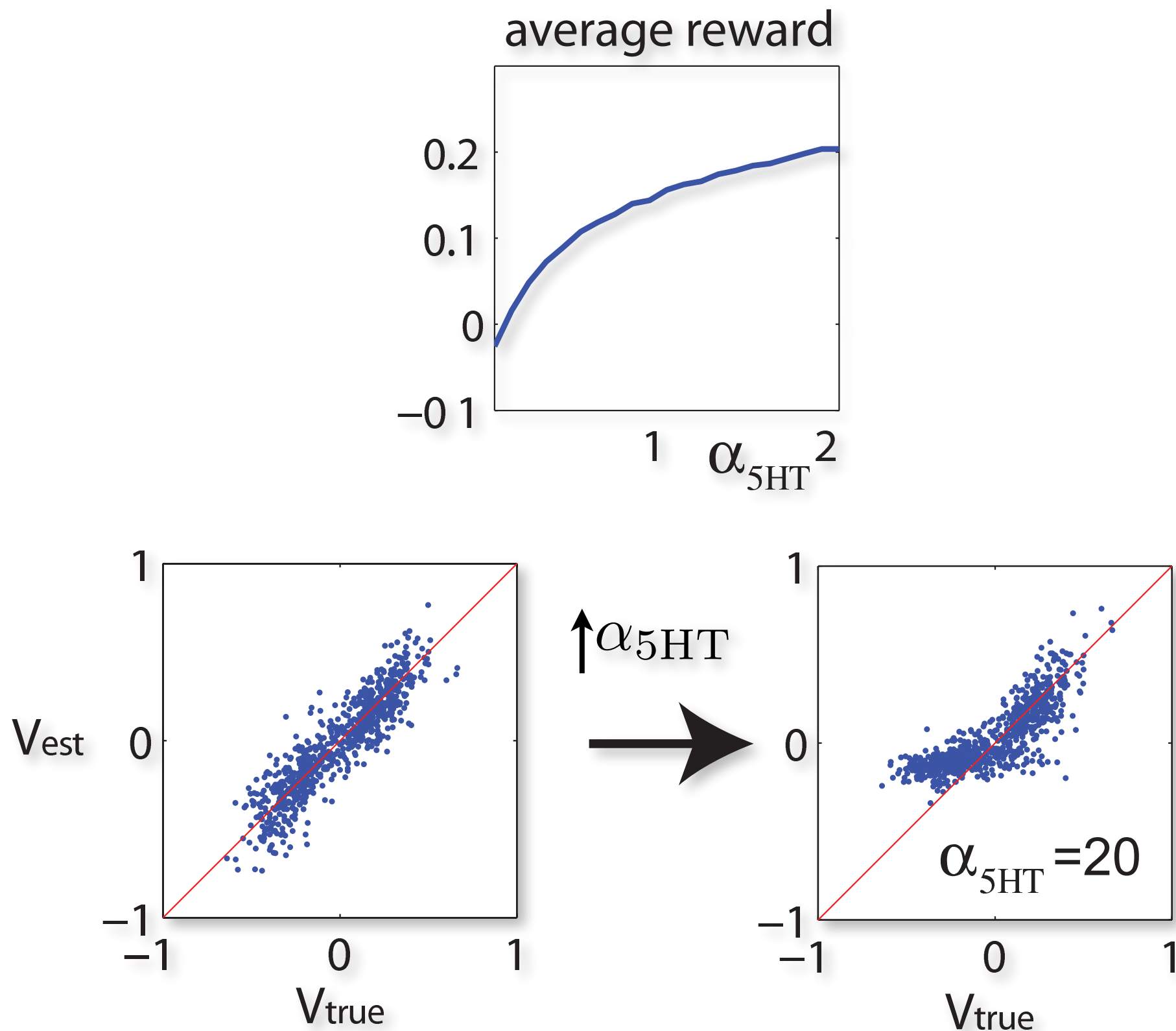
Inhibit if faced with aversive prediction V



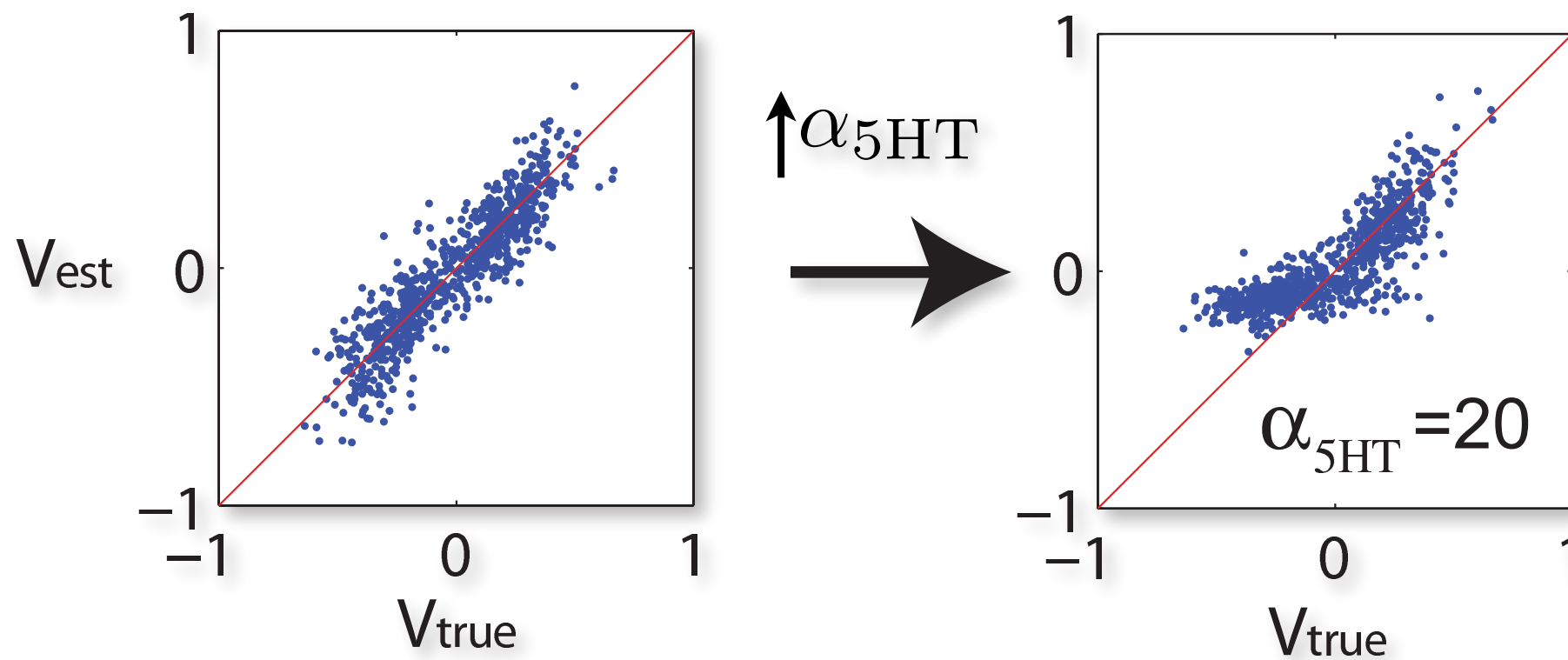
Punishment sensitivity supports optimism



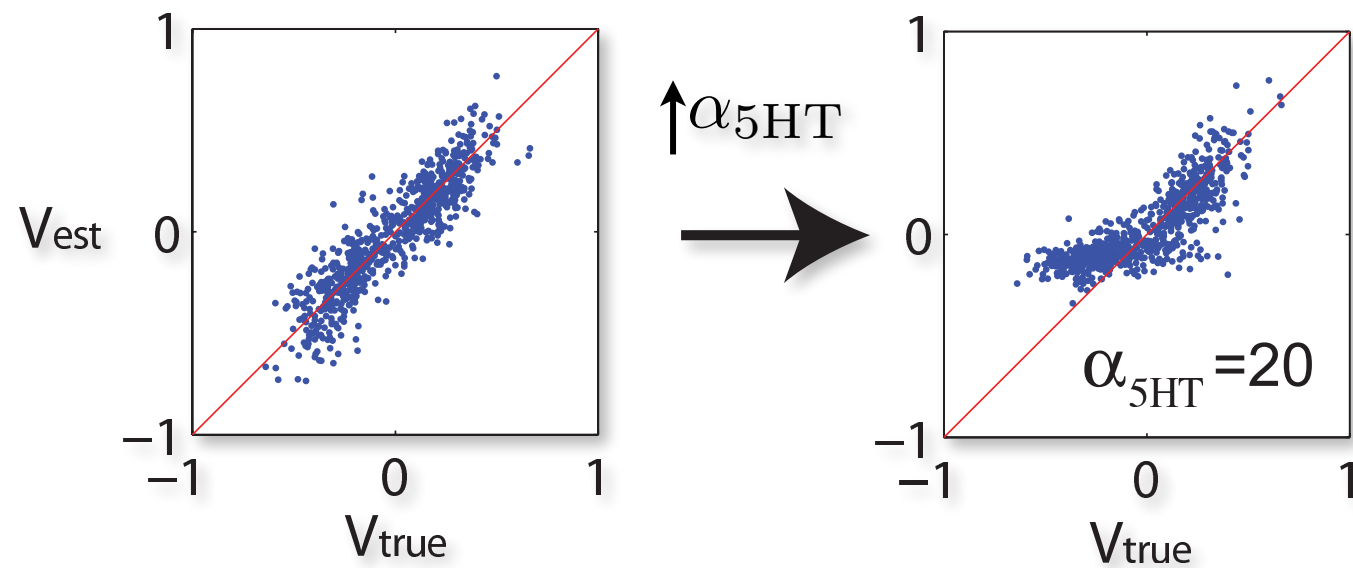
Punishment sensitivity supports optimism



Serotonin and depression

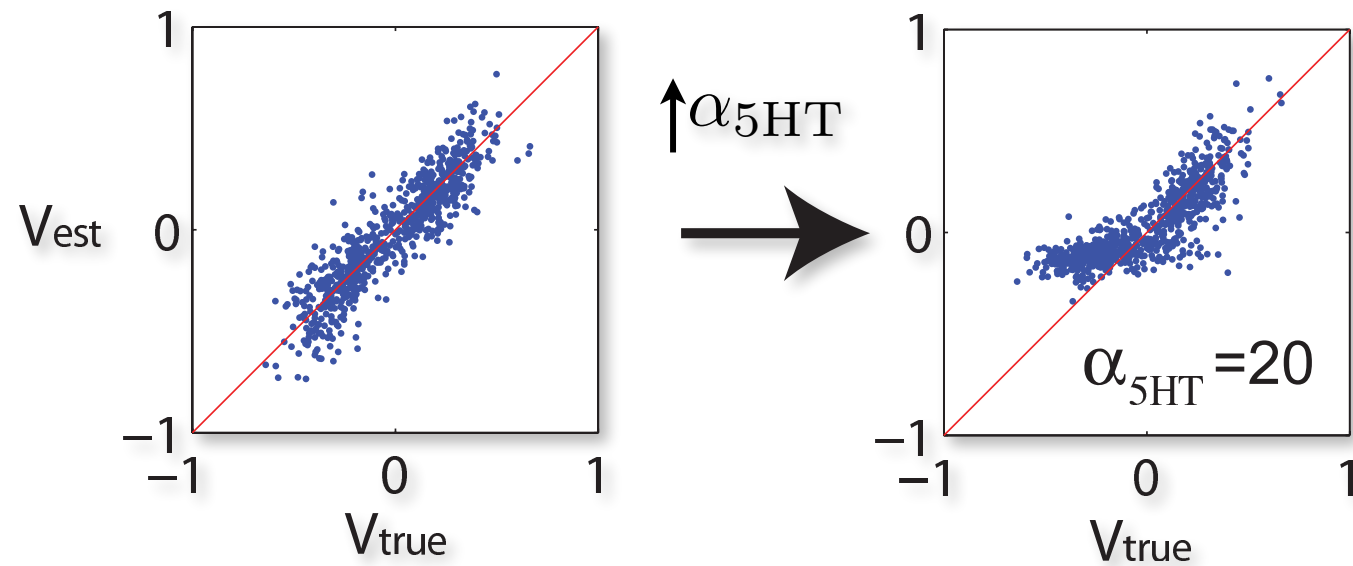


Serotonin and depression



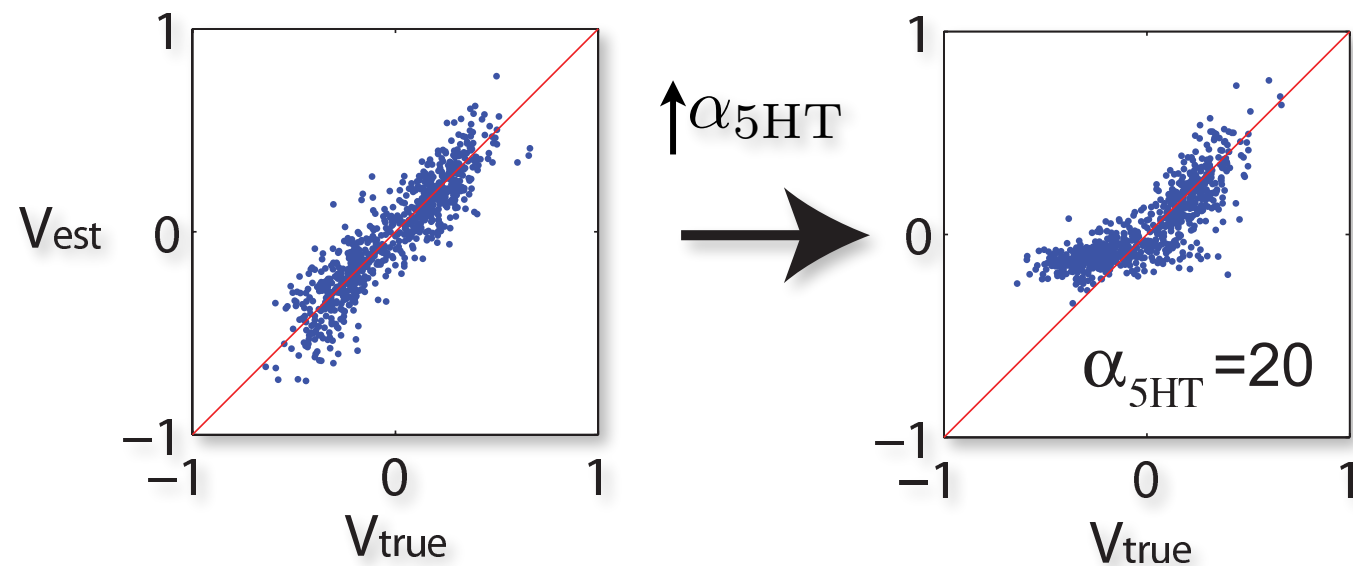
Serotonin and depression

5HTTLPR → increased 5HT tone



Serotonin and depression

5HTTLPR → increased 5HT tone

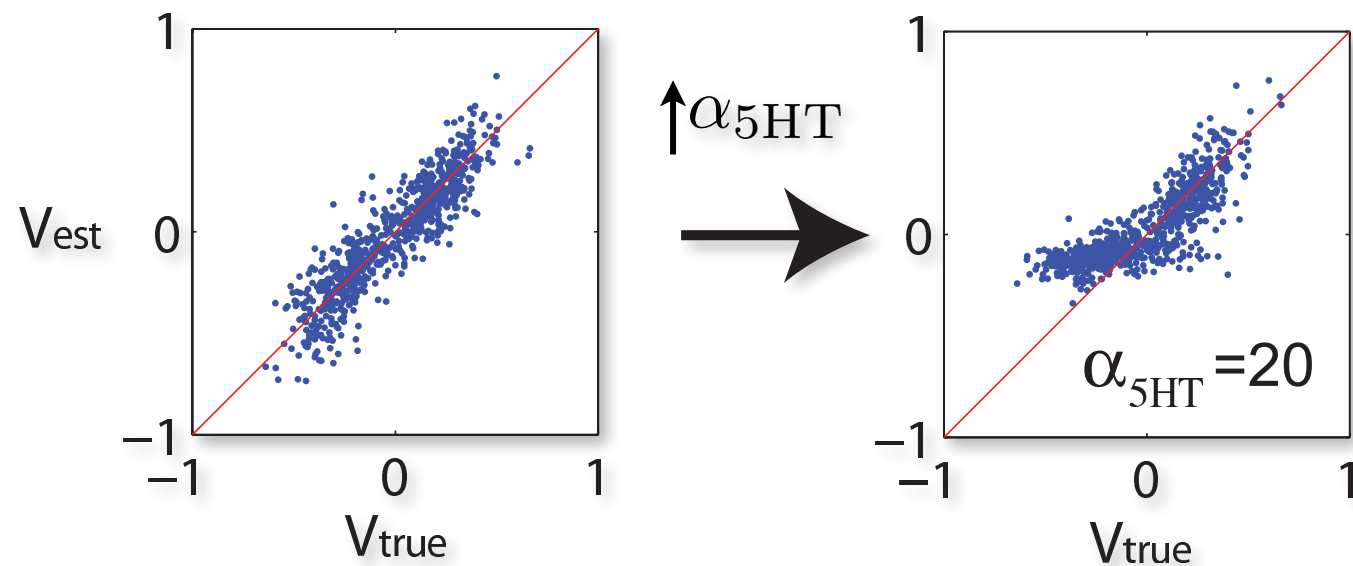


acute reduction

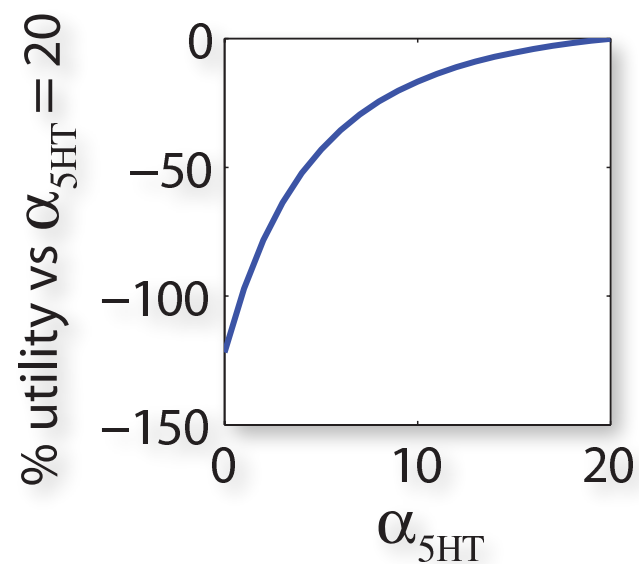


Serotonin and depression

5HTTLPR → increased 5HT tone

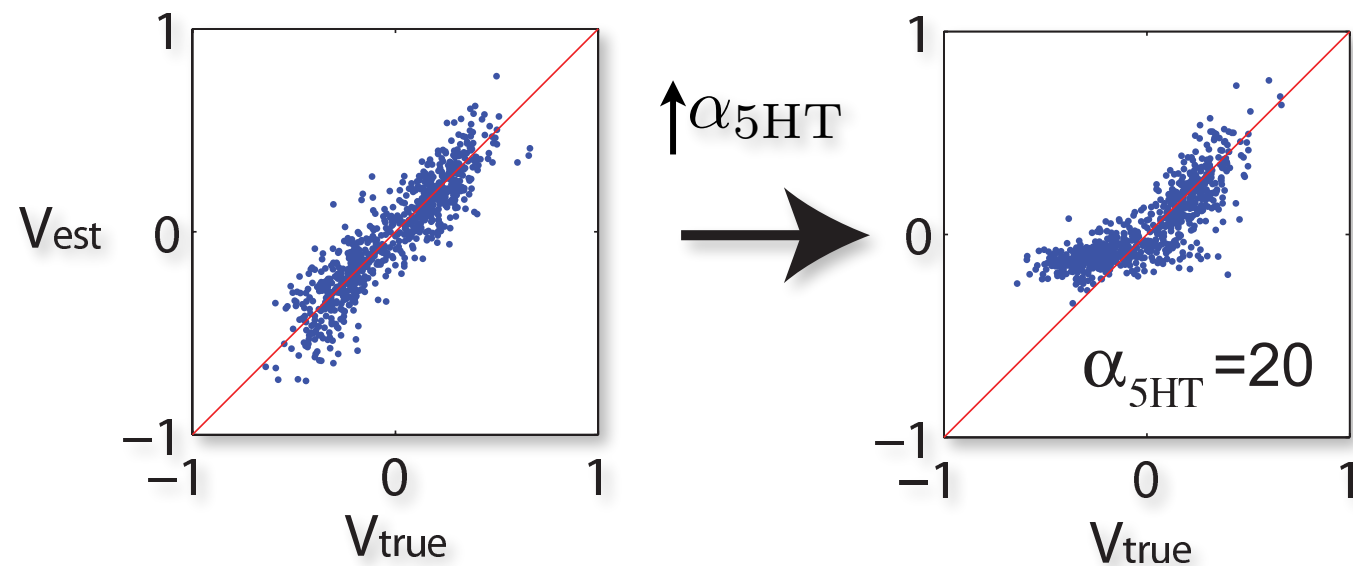


acute reduction

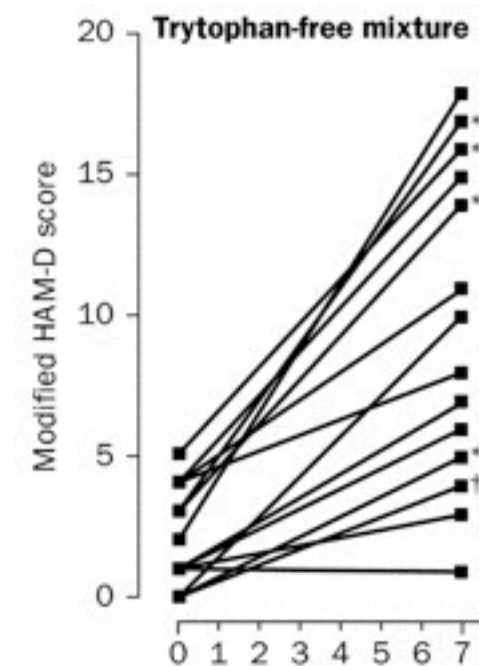
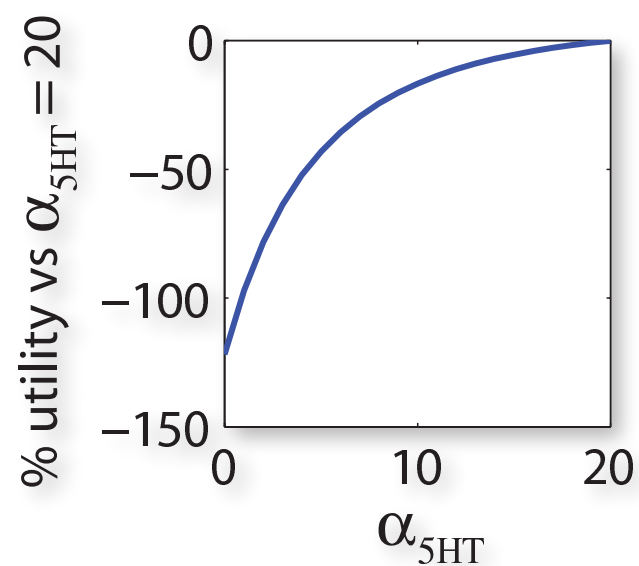


Serotonin and depression

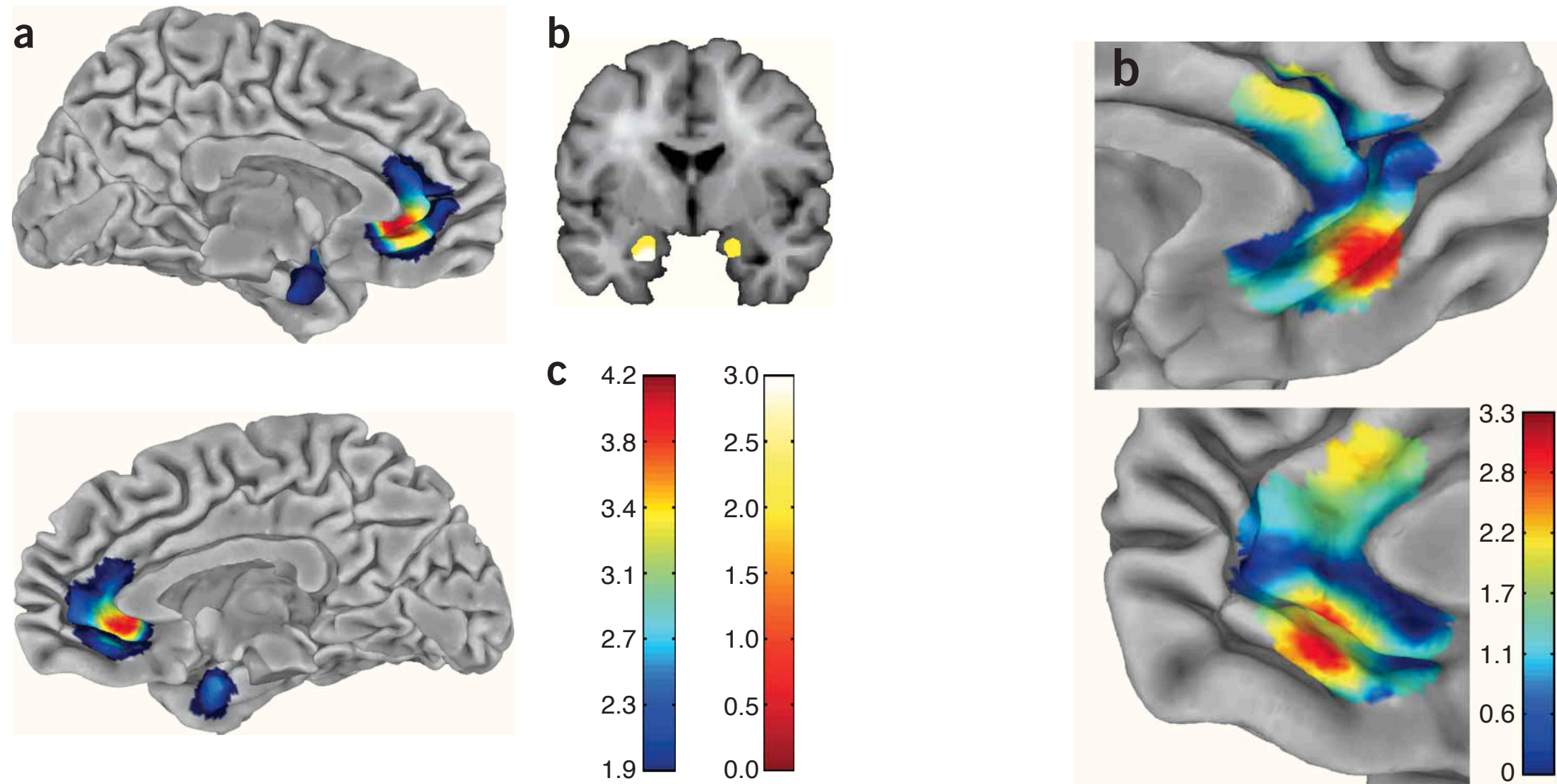
5HTTLPR → increased 5HT tone



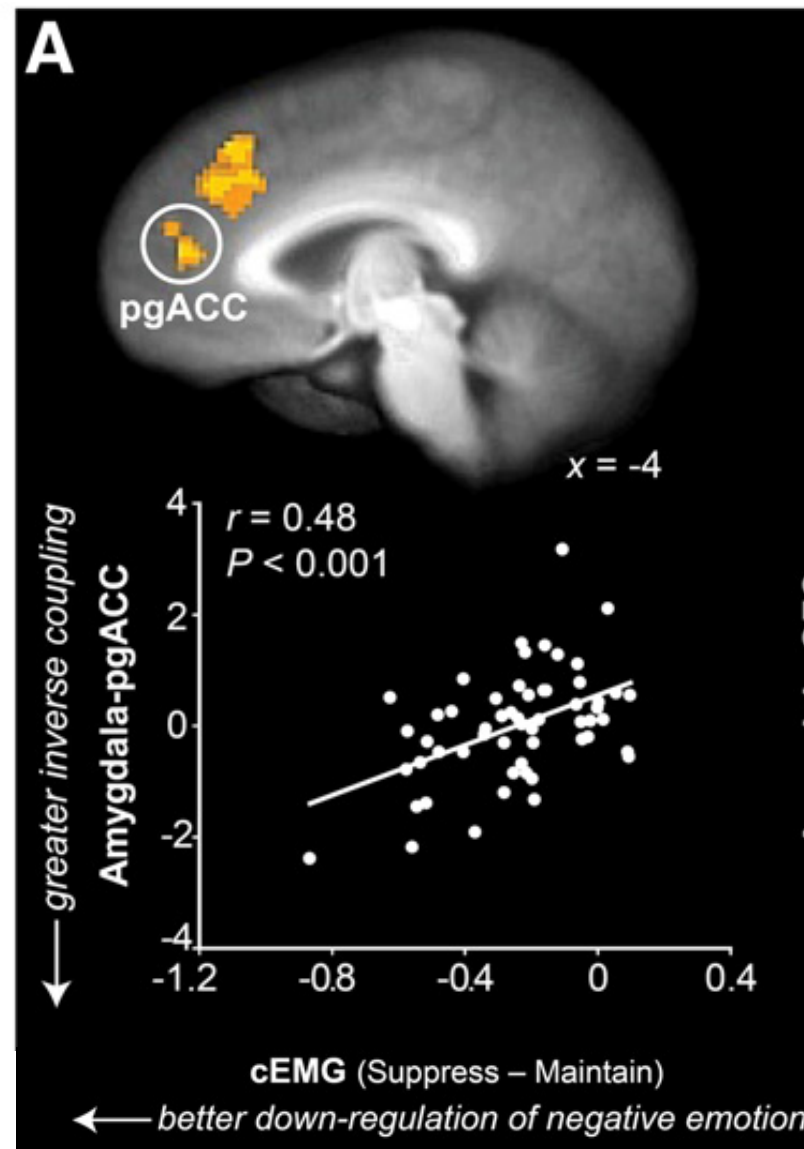
acute reduction



5HTTLPR affects Amg-PFC connectivity

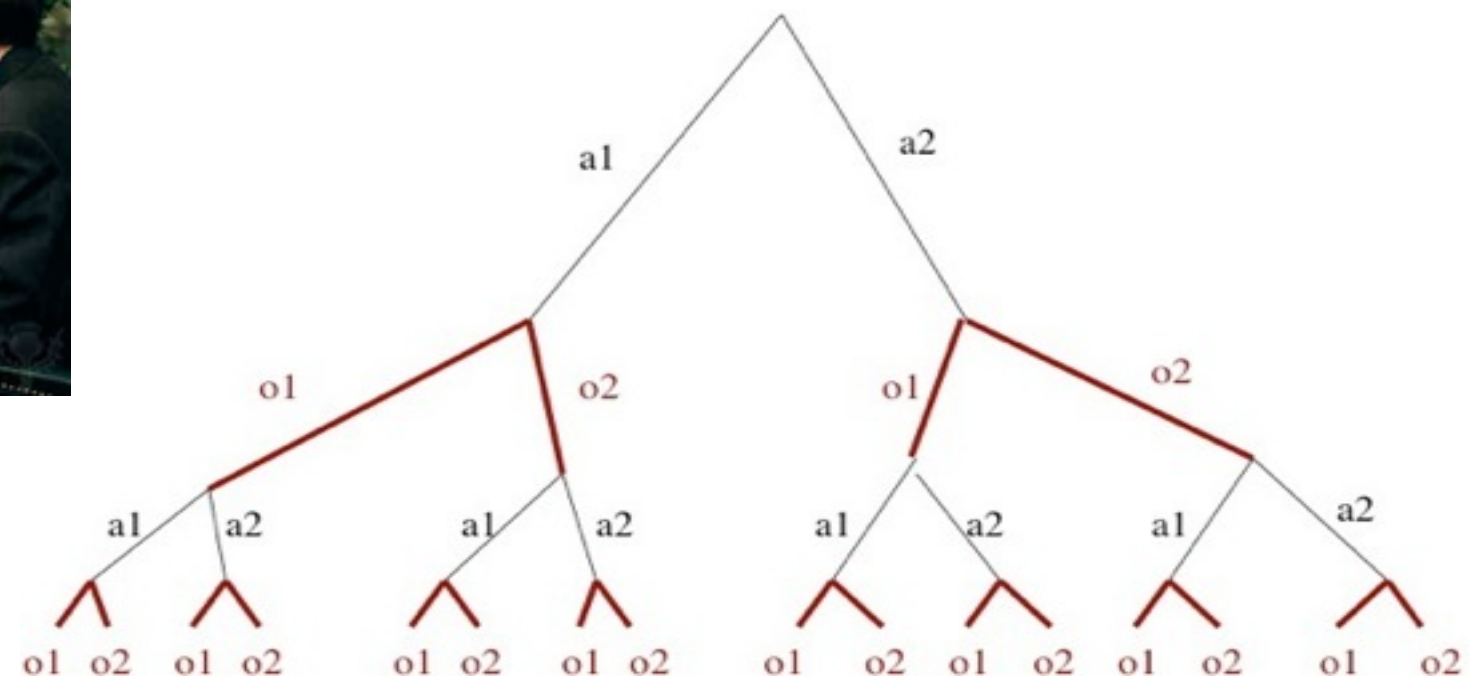


pgACC - amygdala connectivity & ER

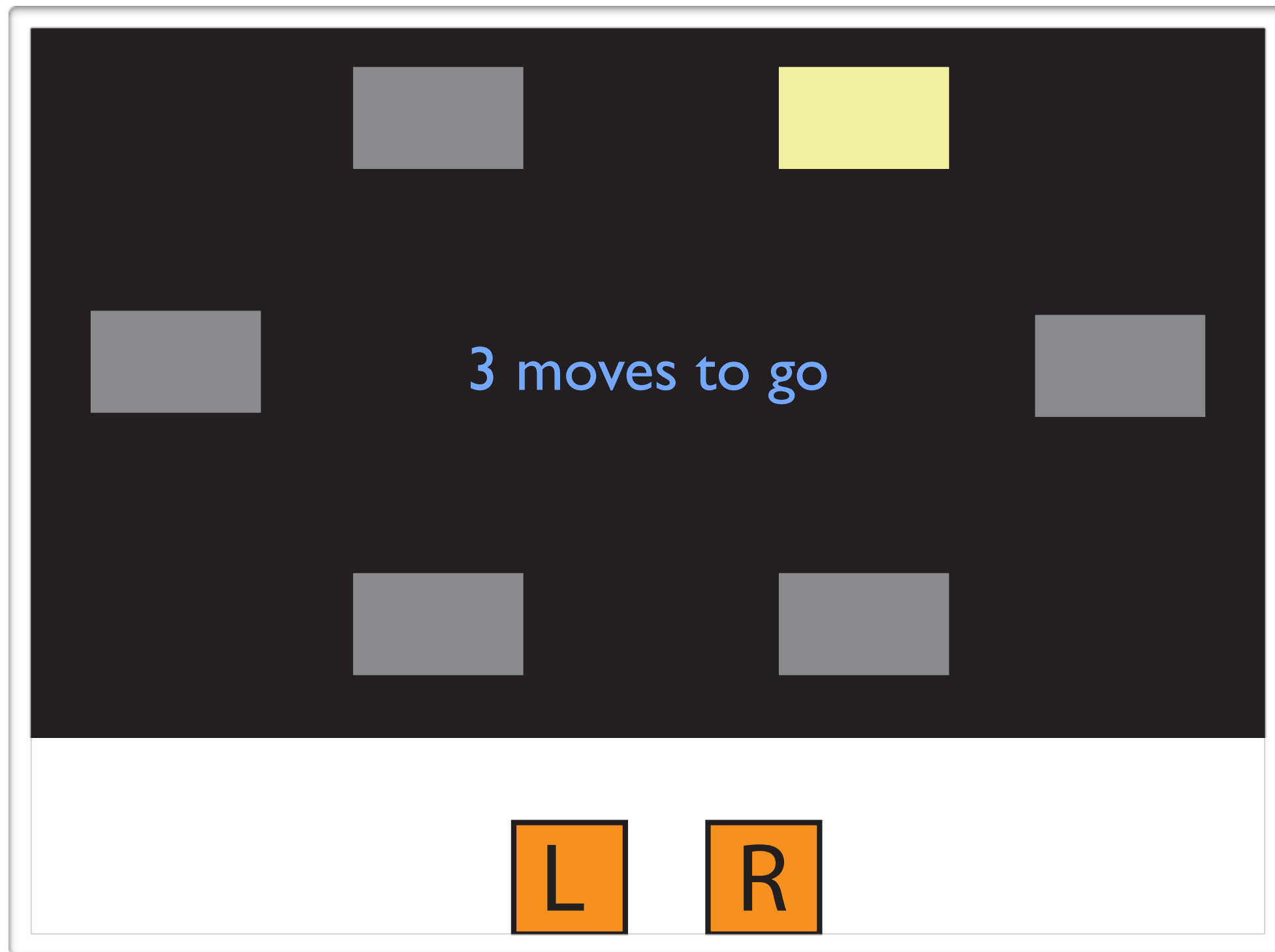


Pruning one's thoughts

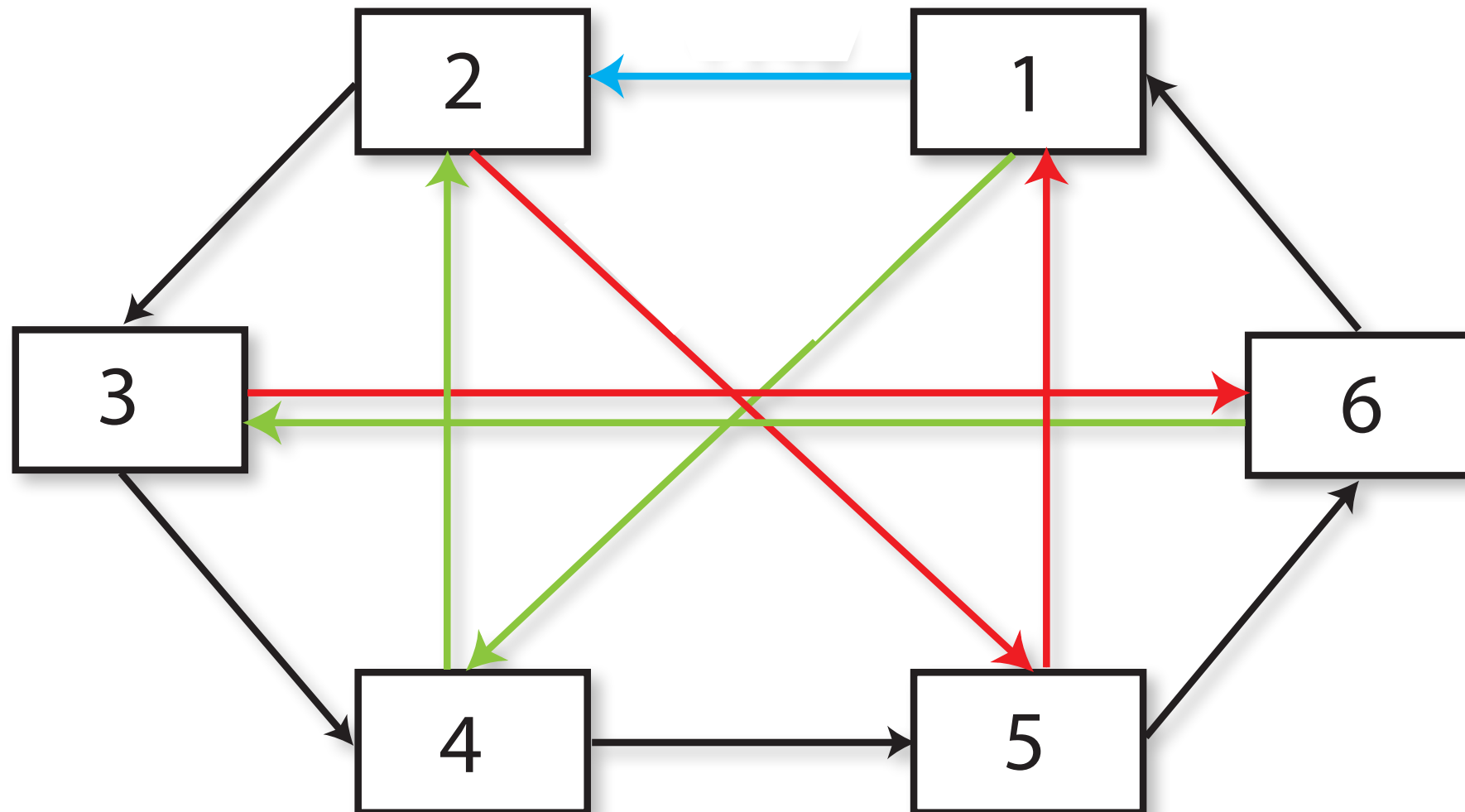
- ▶ Could reflexive (serotonergic) inhibition also apply to internal thought processes?
- ▶ Pruning to approximate goal-directed problems we can't solve



Psychochess

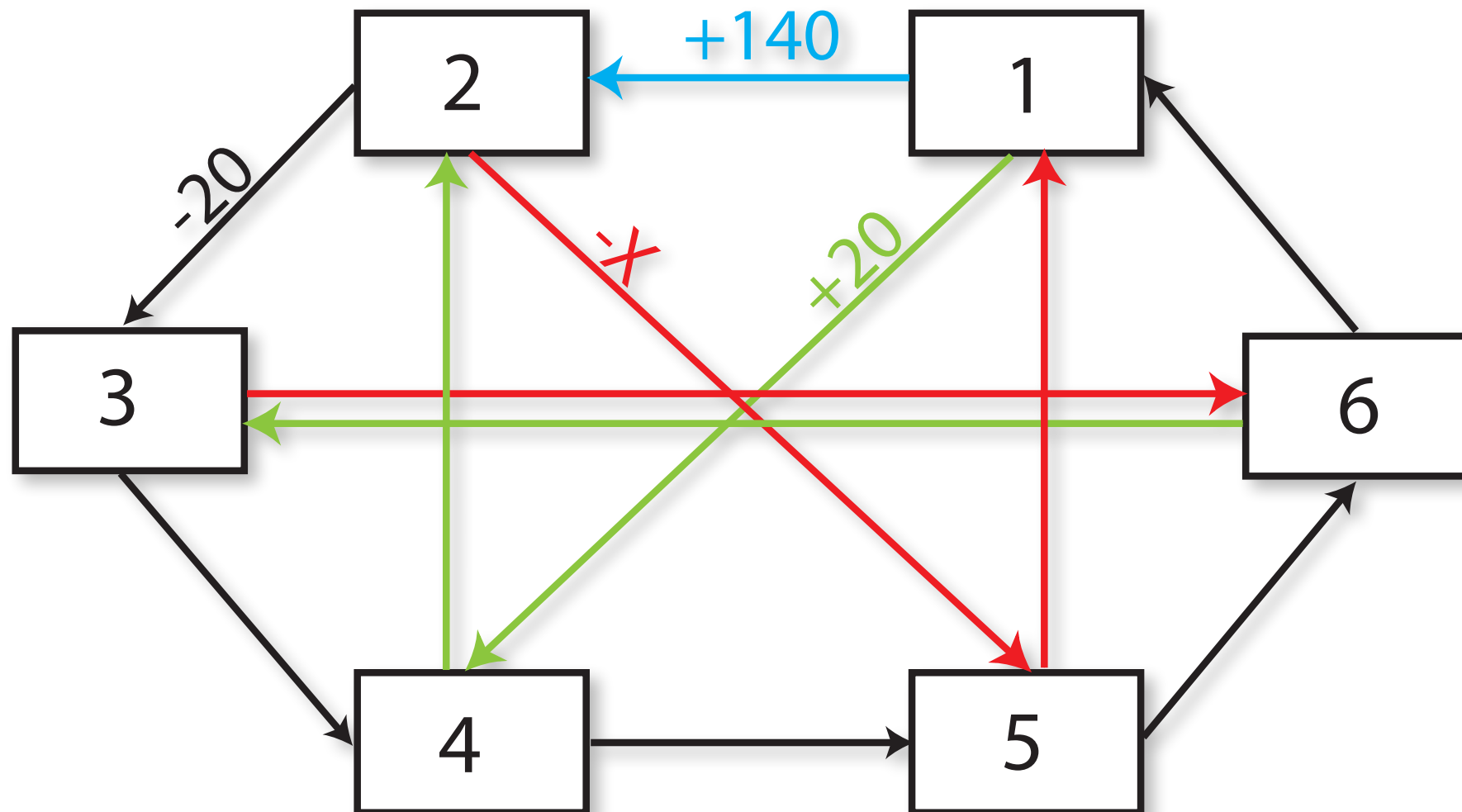


A poor experimental psychologist's version of chess



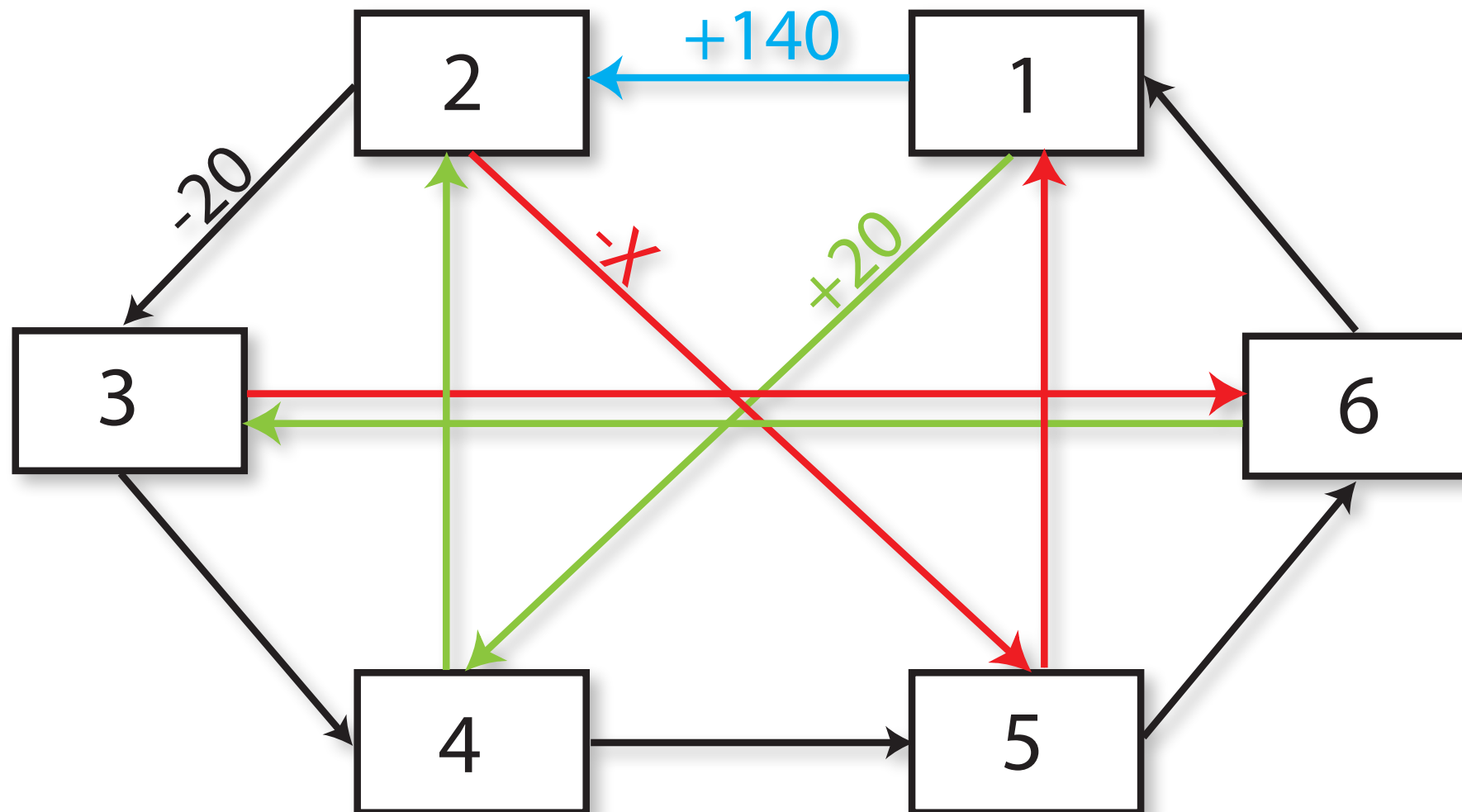
A tree search task

A poor experimental psychologist's version of chess



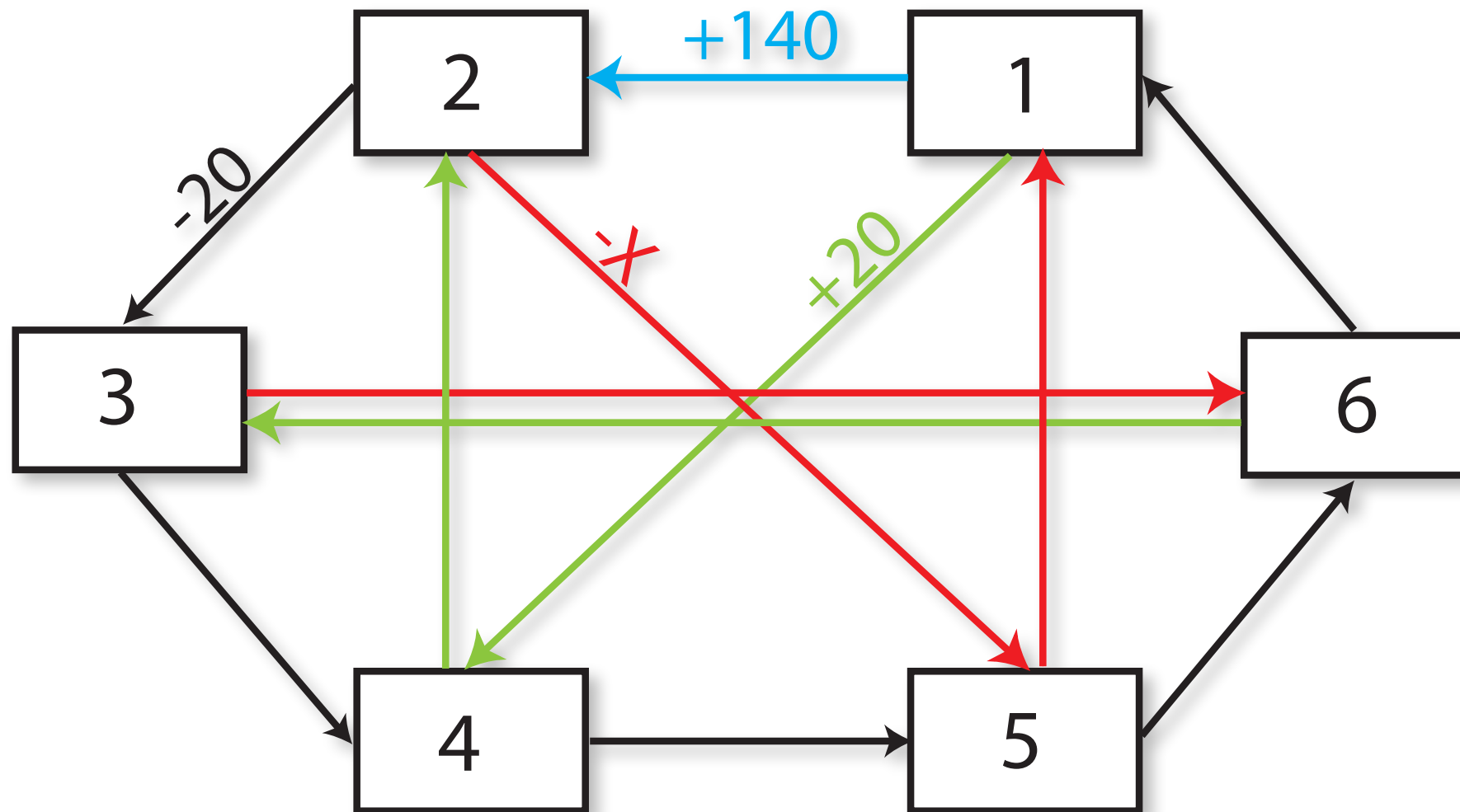
A tree search task

Make a choice...



$$X = 70$$

Make a choice...



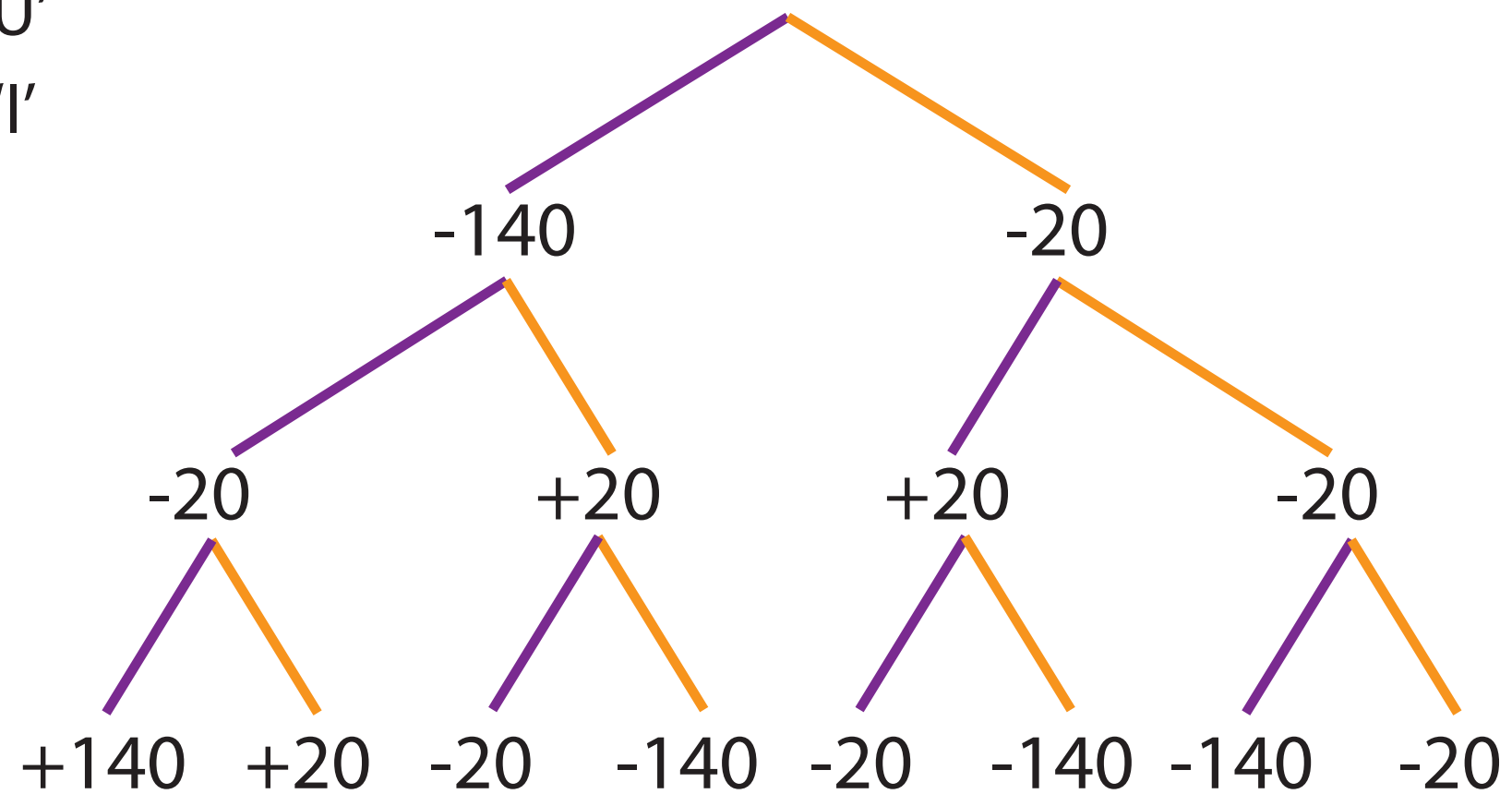
Optimal choices depend on the depth
There are $S \times D$ optimal paths.

~~X~~ = 70

Text

Approximate planning

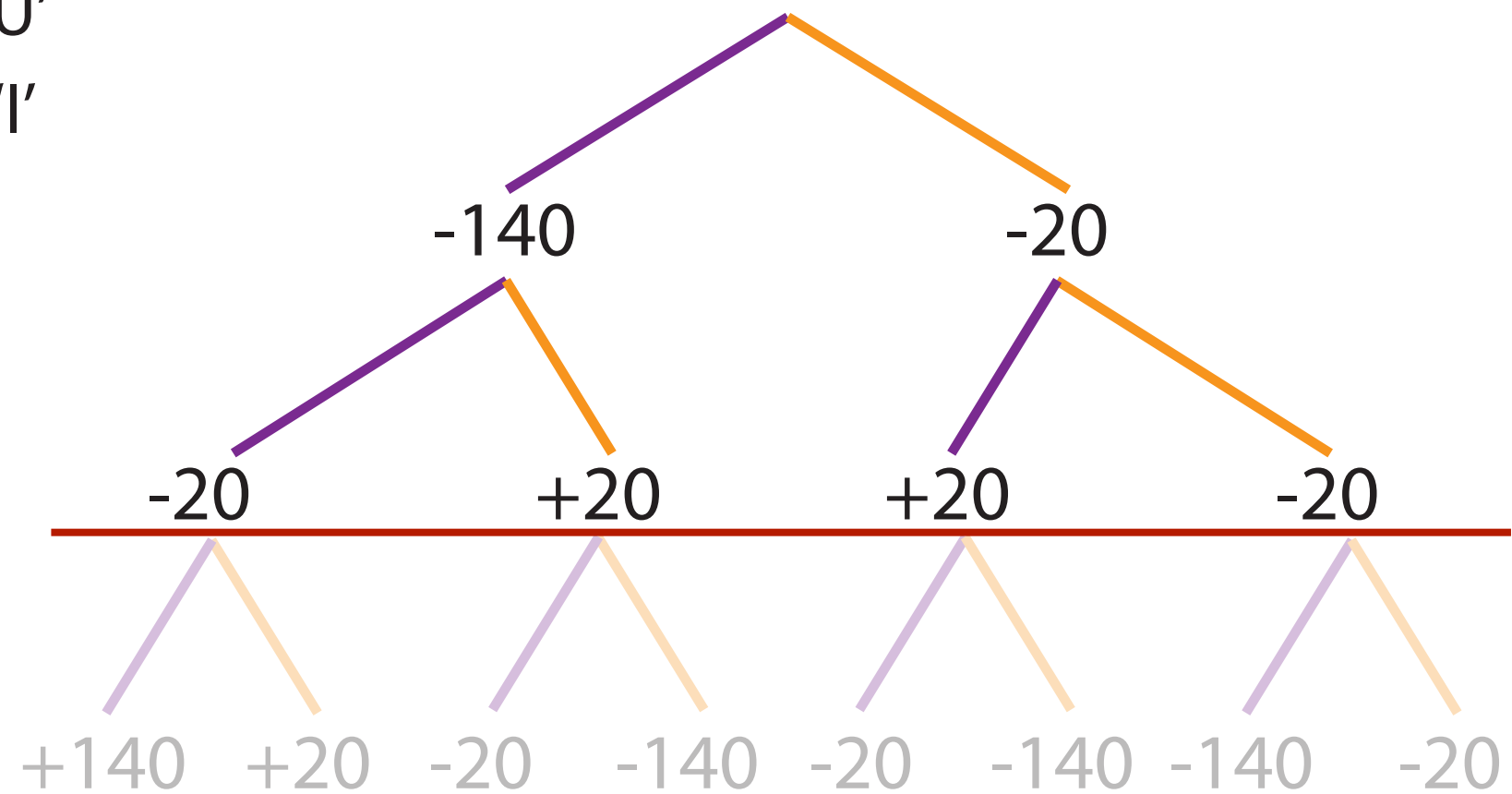
■ key 'U'
■ key 'I'



Text

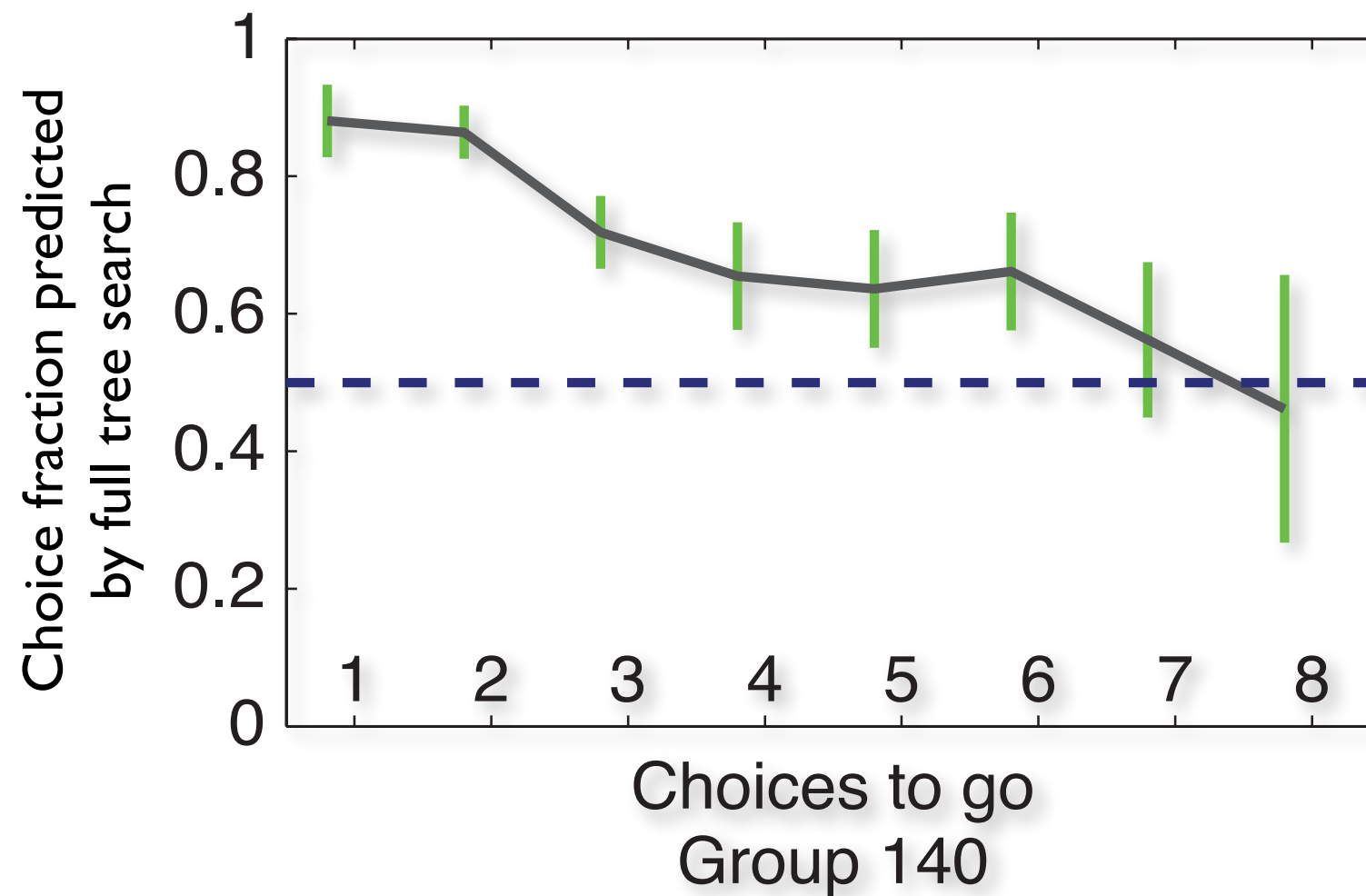
Approximate planning

■ key 'U'
■ key 'I'

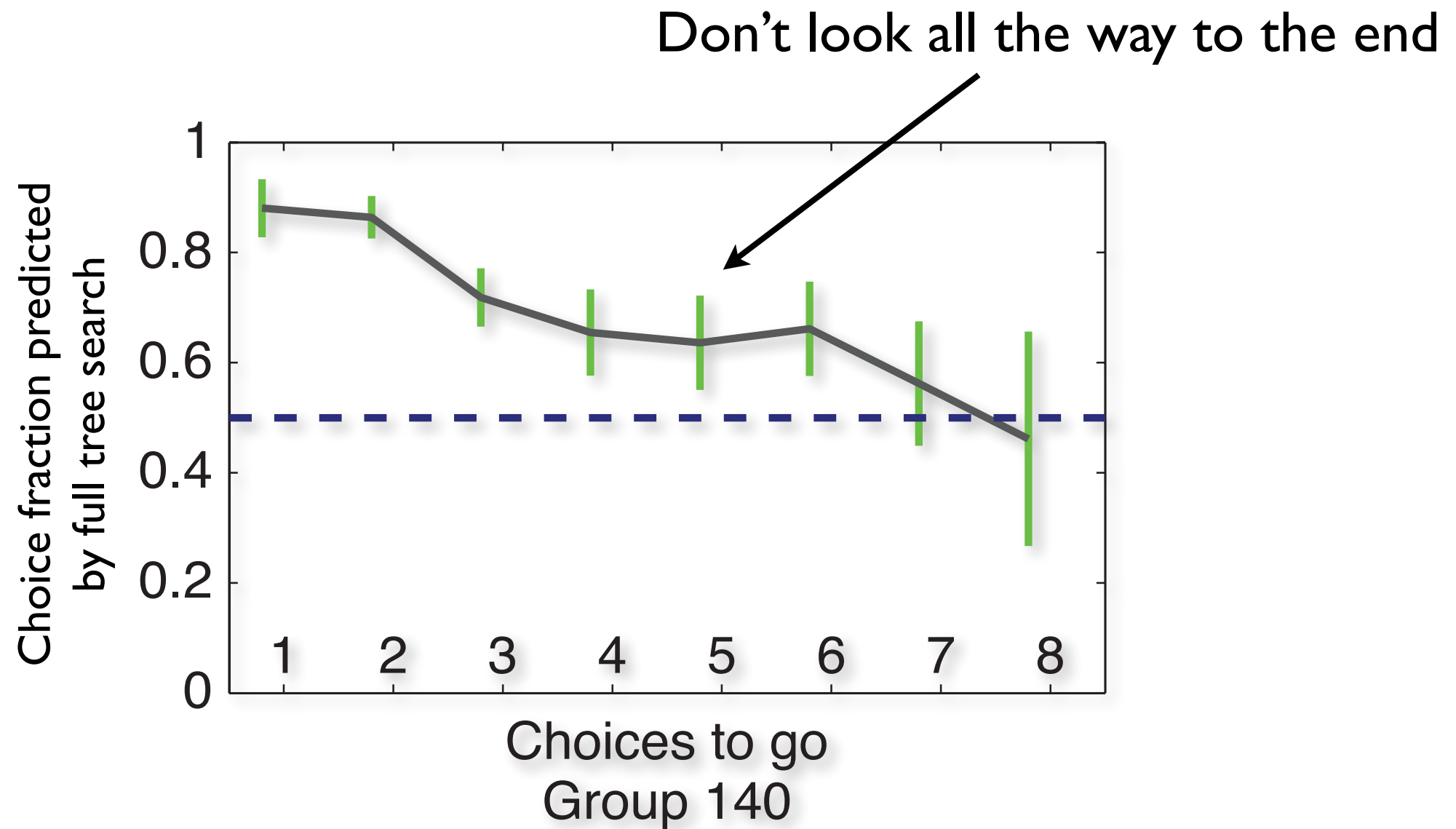


Text

Approximate planning

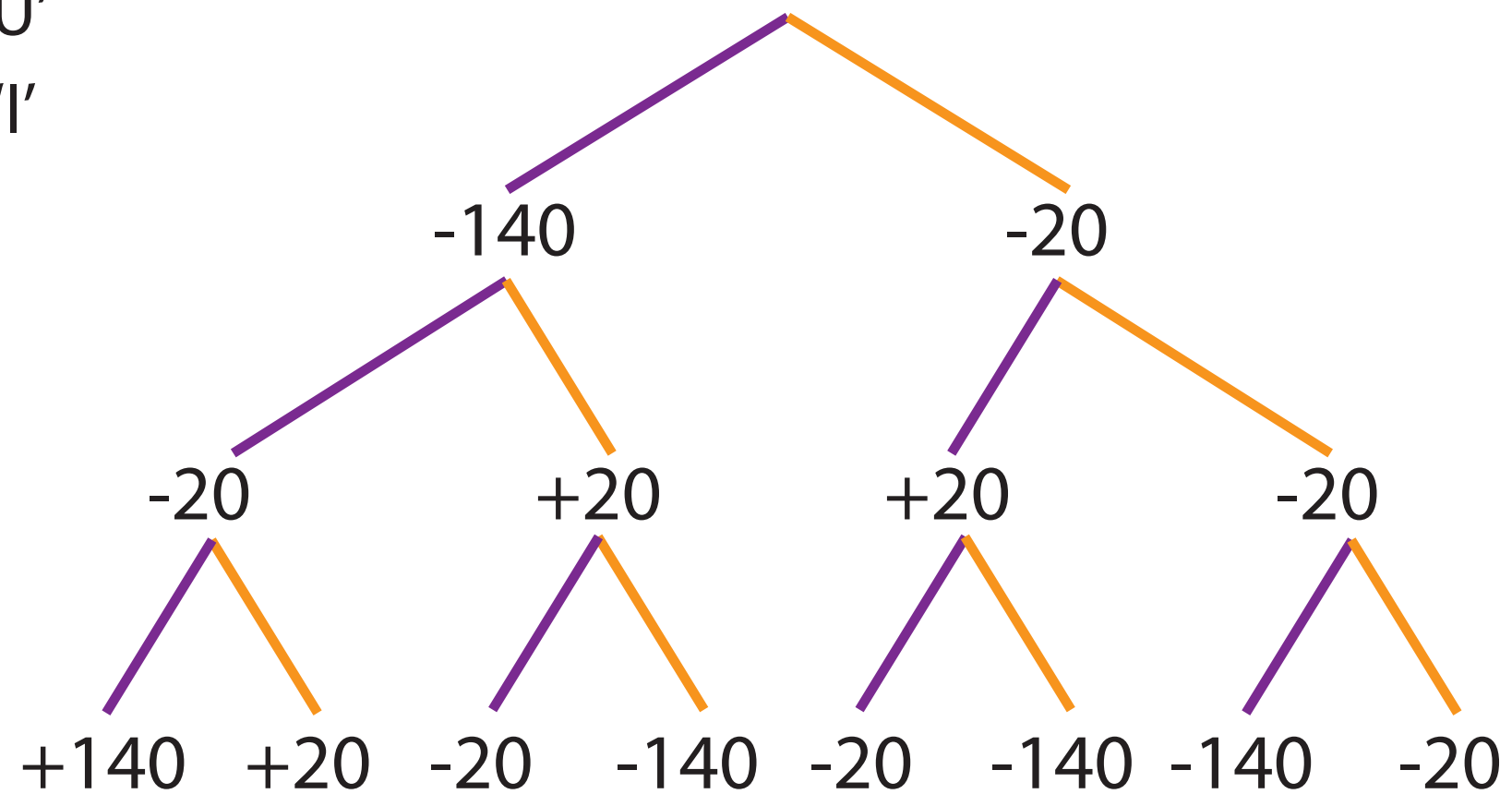


Approximate planning



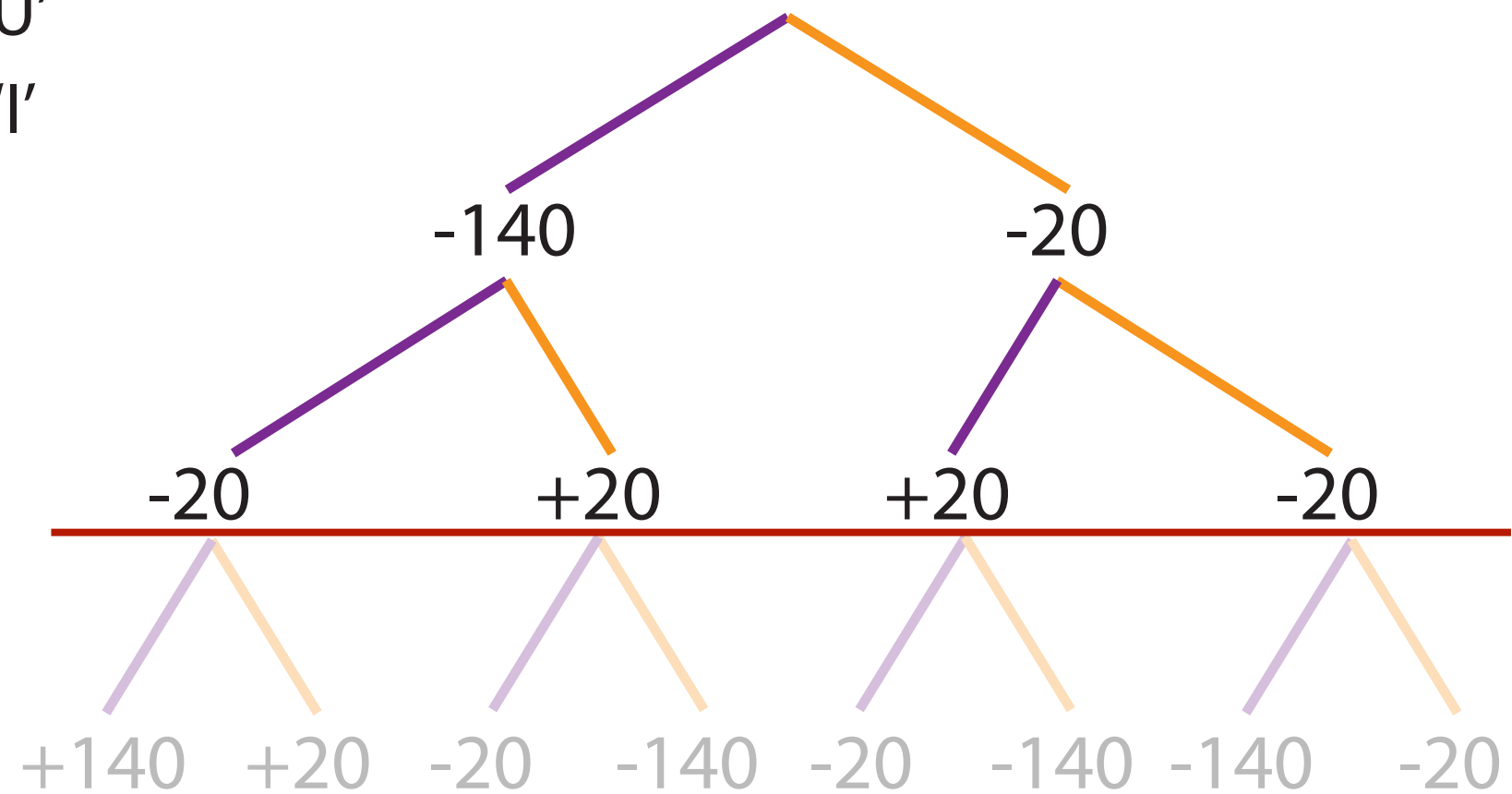
Pruning

■ key 'U'
■ key 'I'



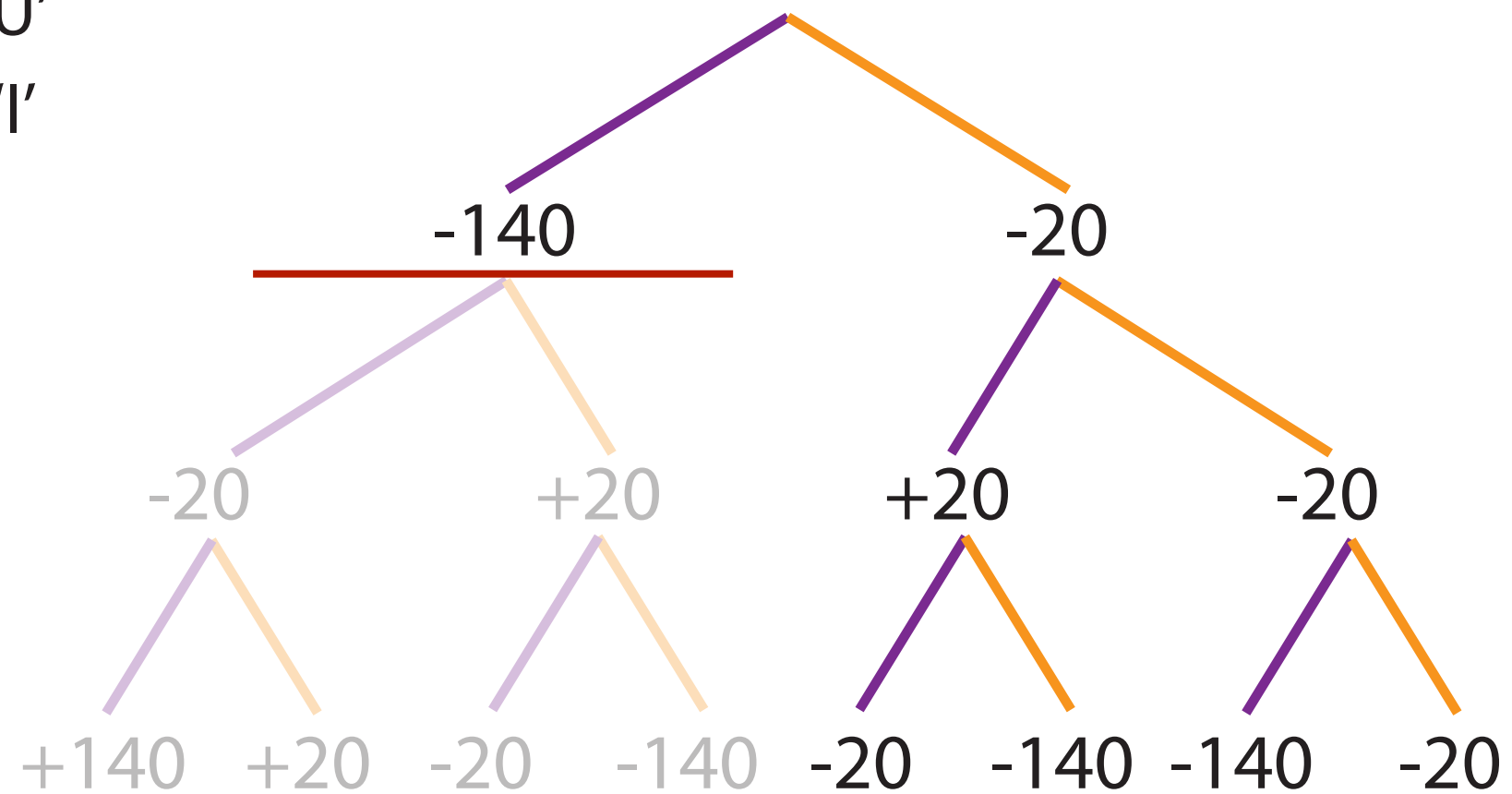
Pruning

■ key 'U'
■ key 'I'



Pruning

■ key 'U'
■ key 'I'



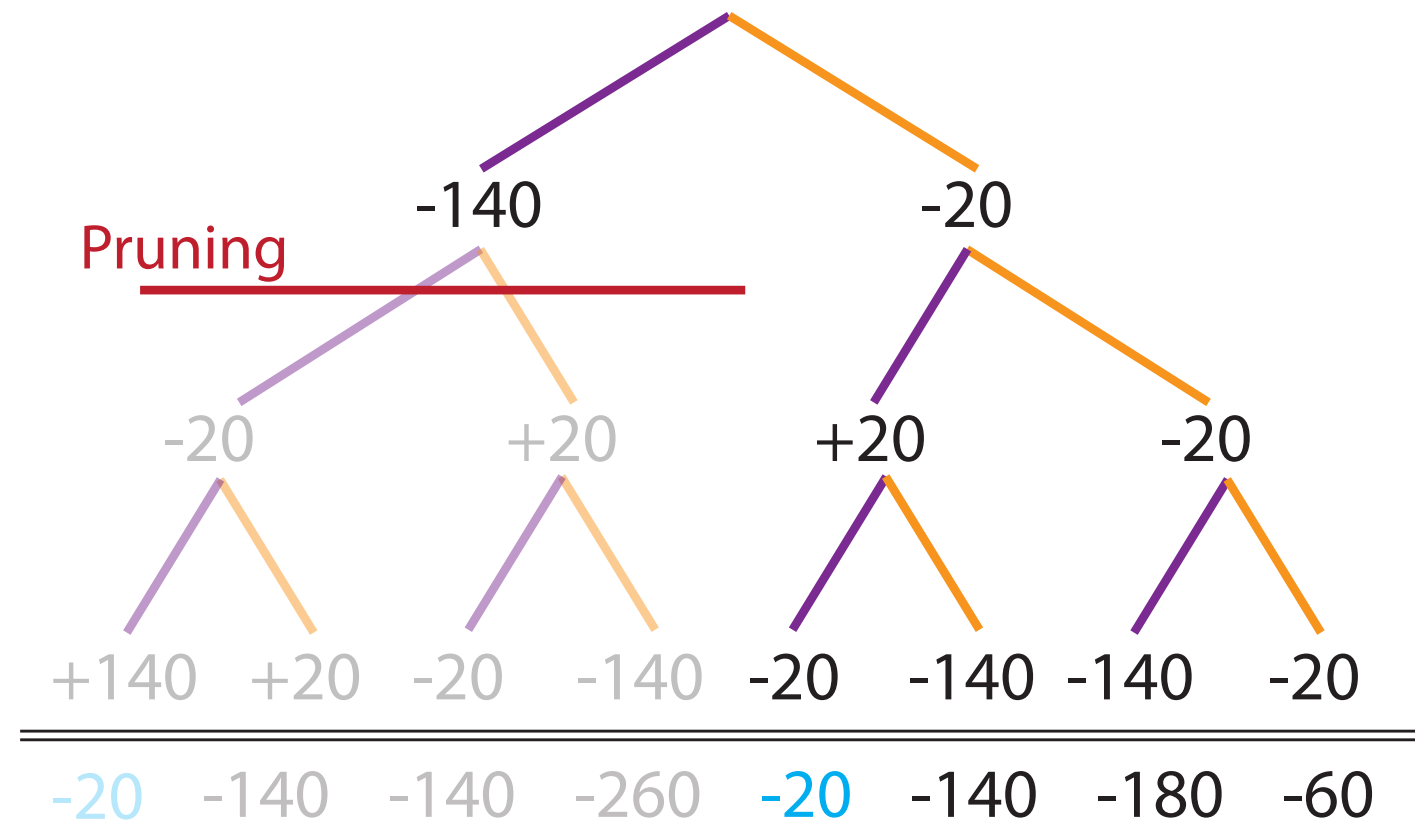
Pavlovian pruning

► Optimality

- conserve guarantees
- difficult & computationally expensive

► Approximate

- trade optimality for speed



Pavlovian pruning

► Optimality

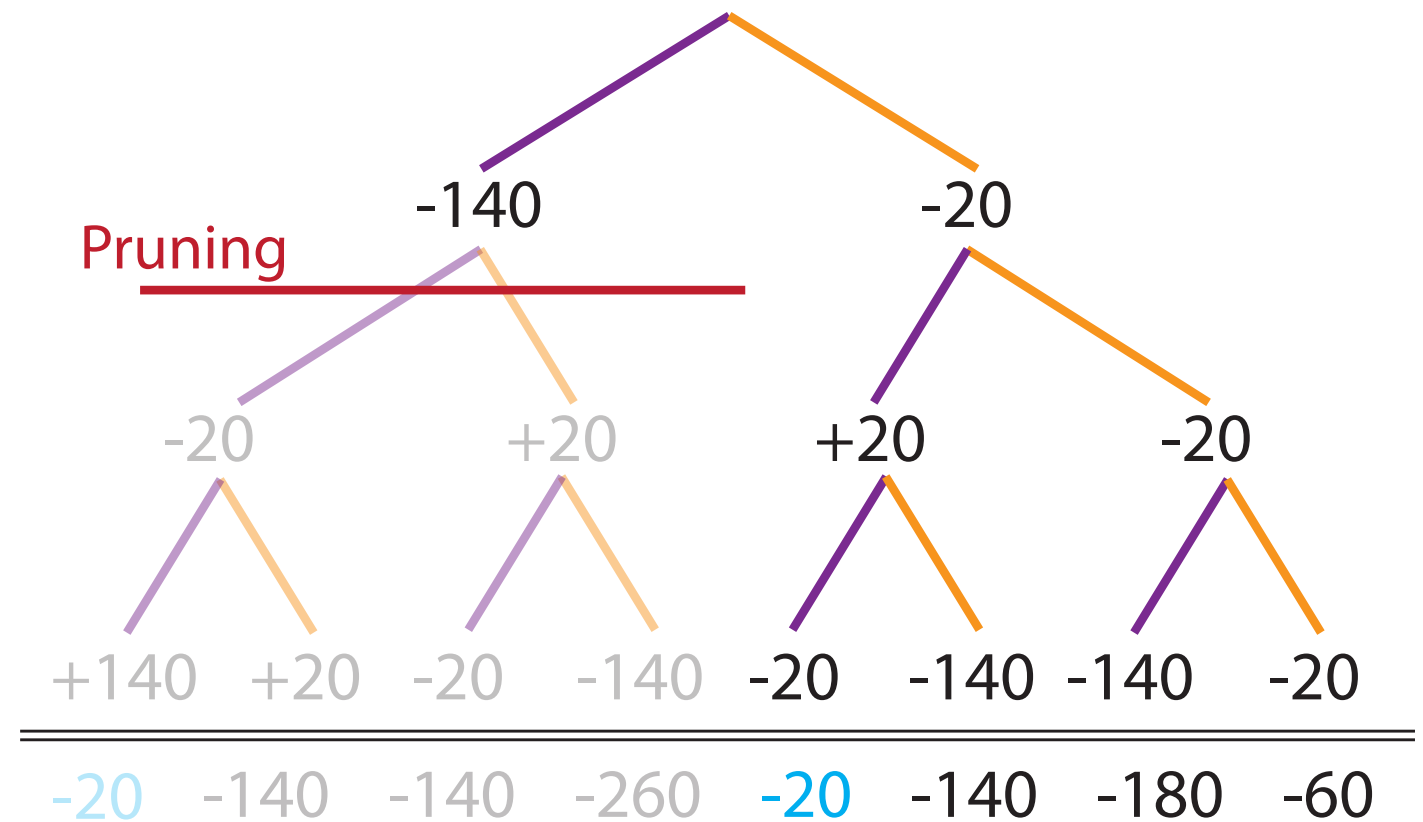
- conserve guarantees
- difficult & computationally expensive

► Approximate

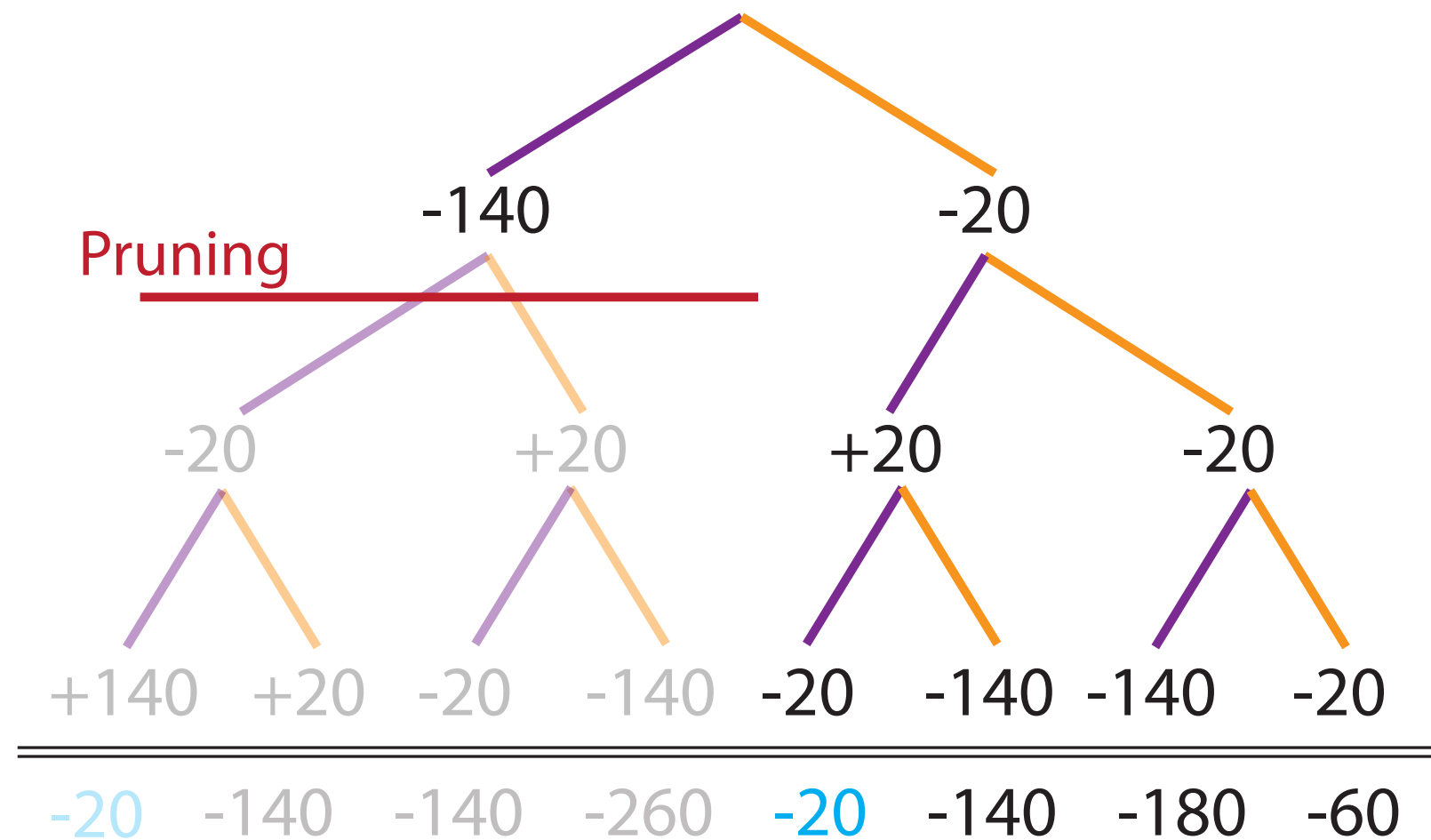
- trade optimality for speed

► Pavlovian

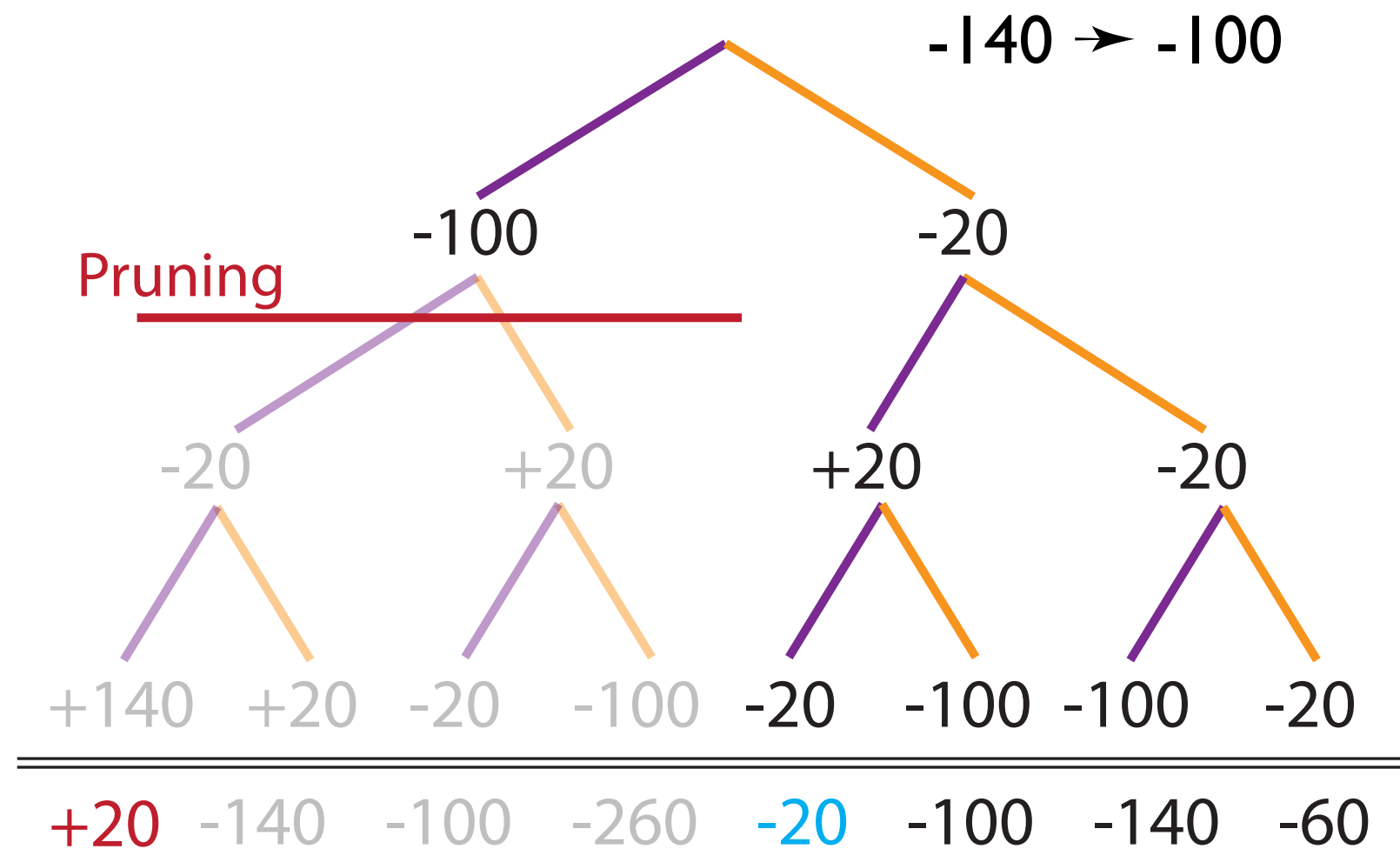
- reflexively prune on encountering a punishment



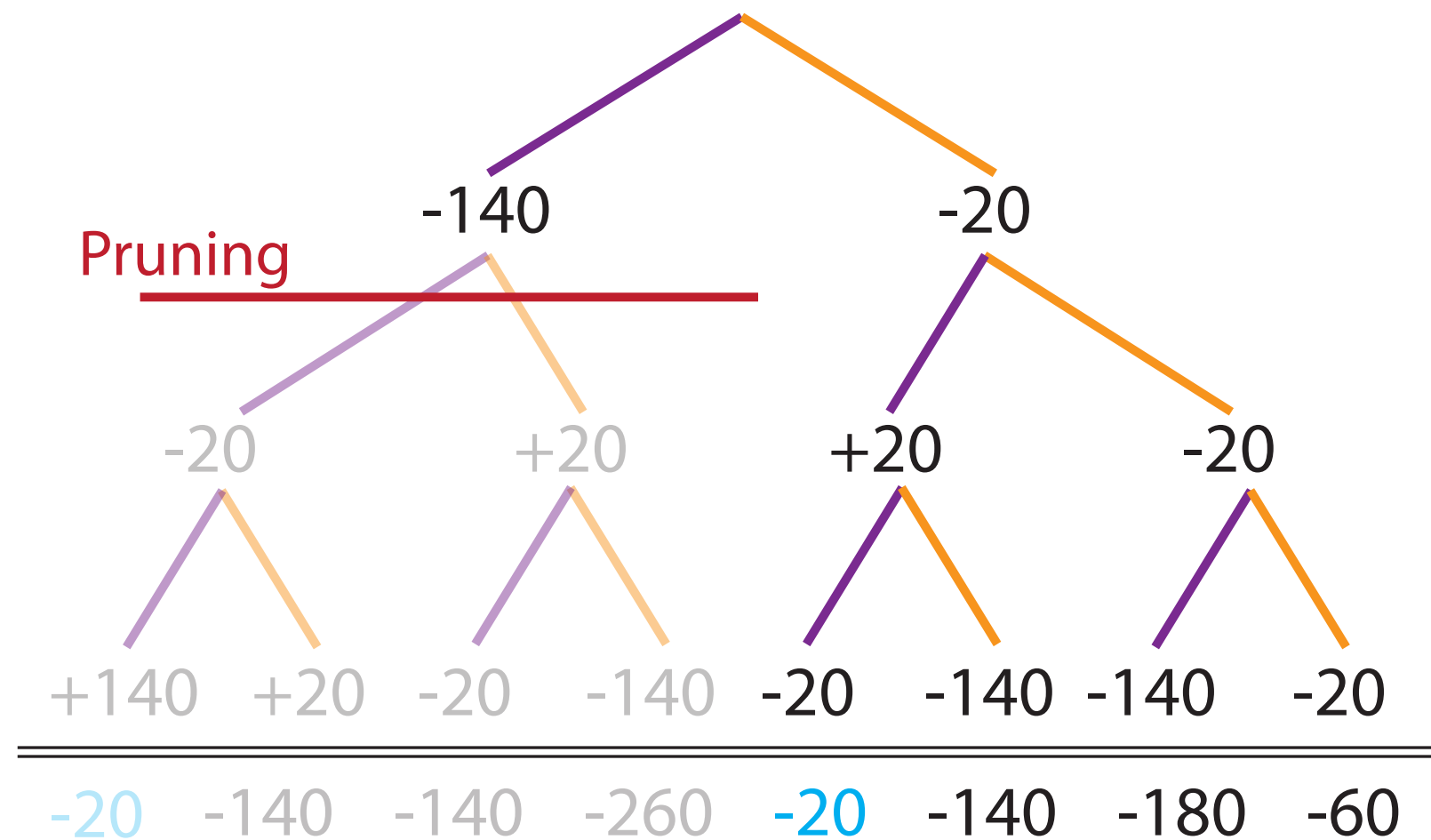
Pavlovian?



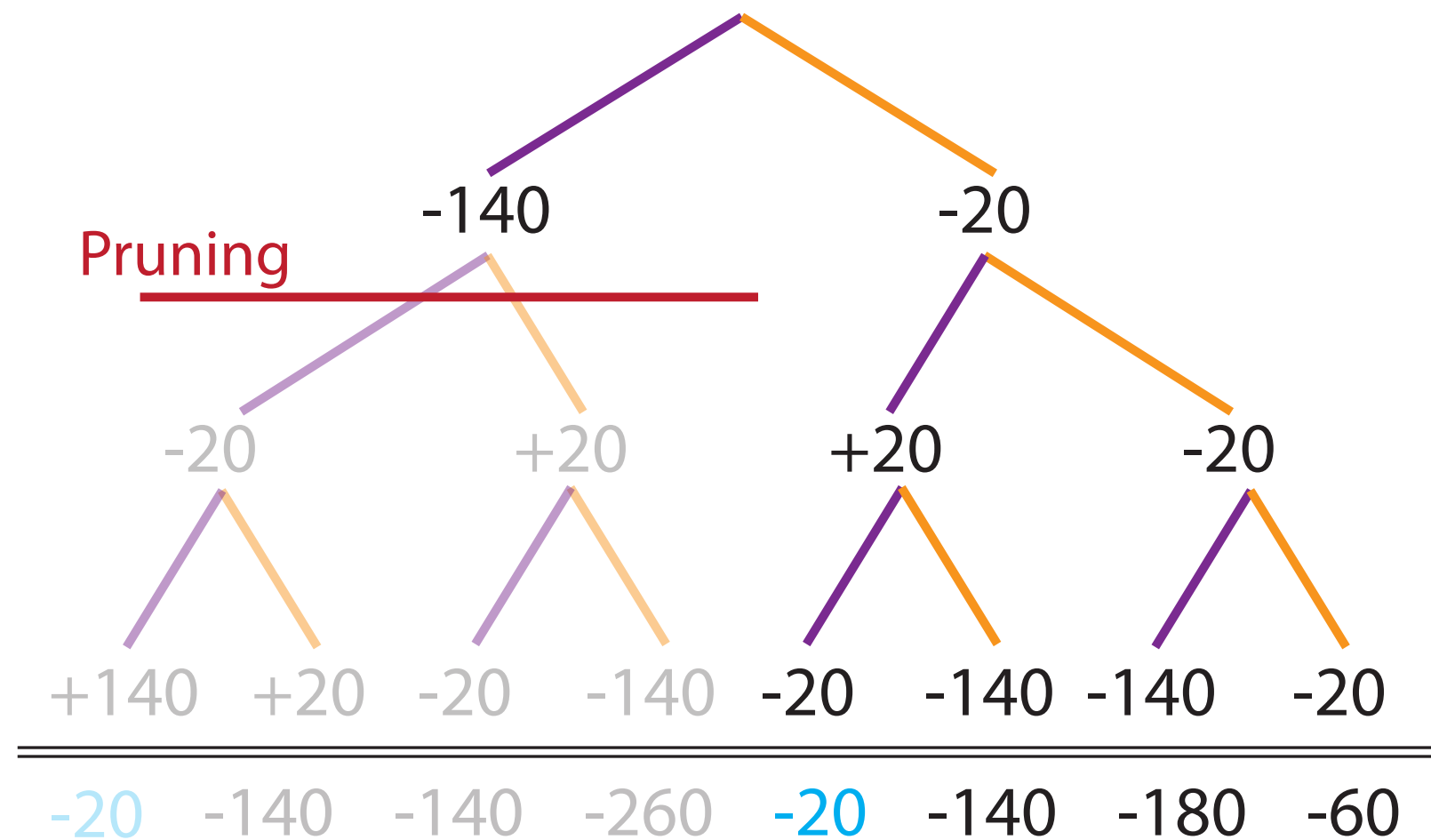
Pavlovian?



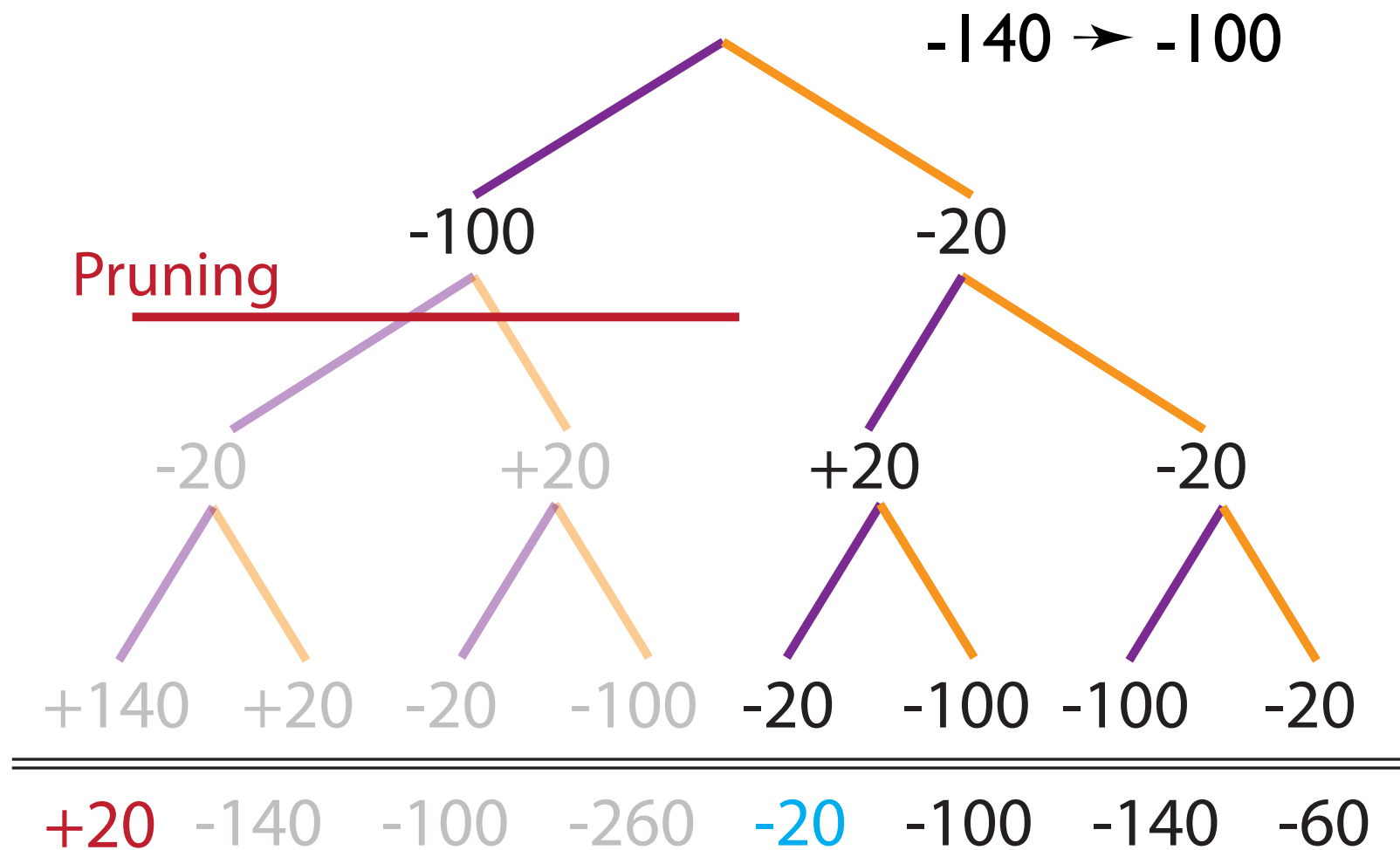
Pavlovian?



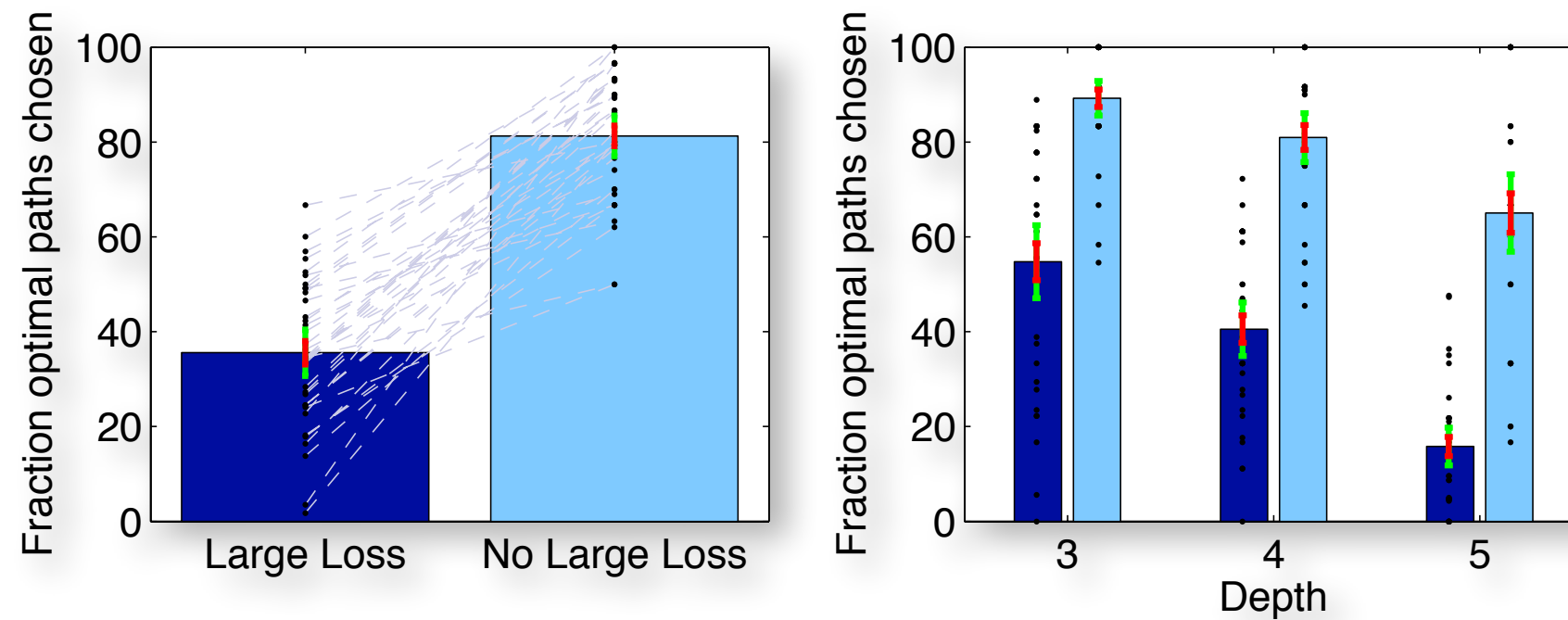
Pavlovian?



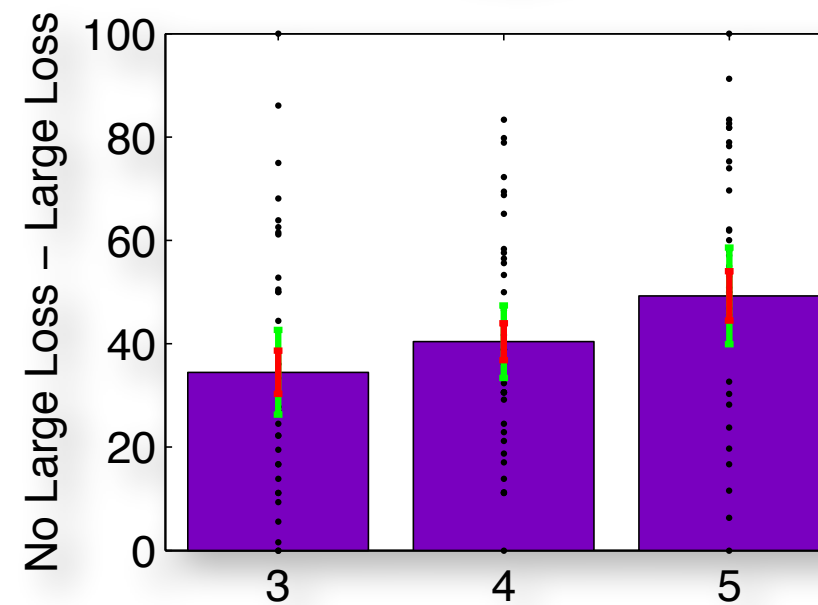
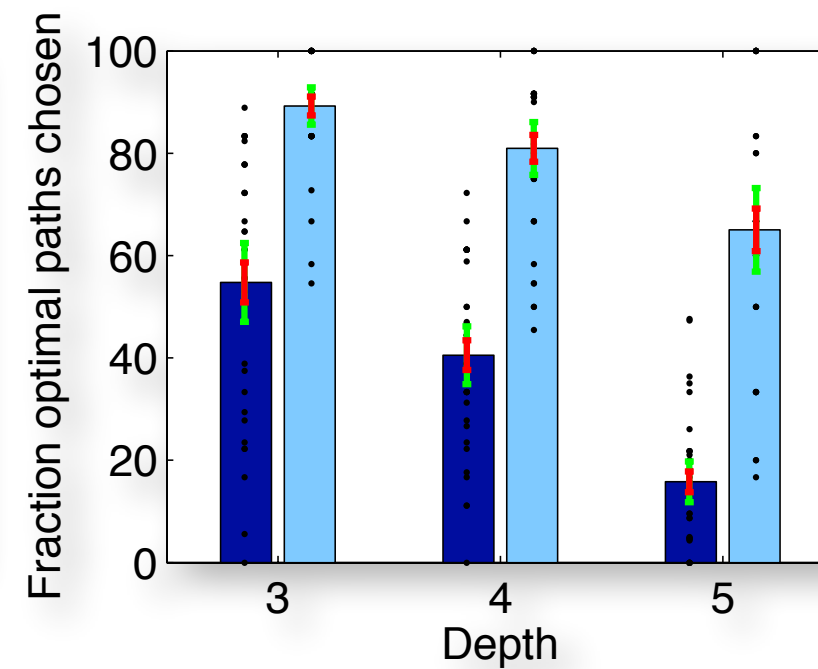
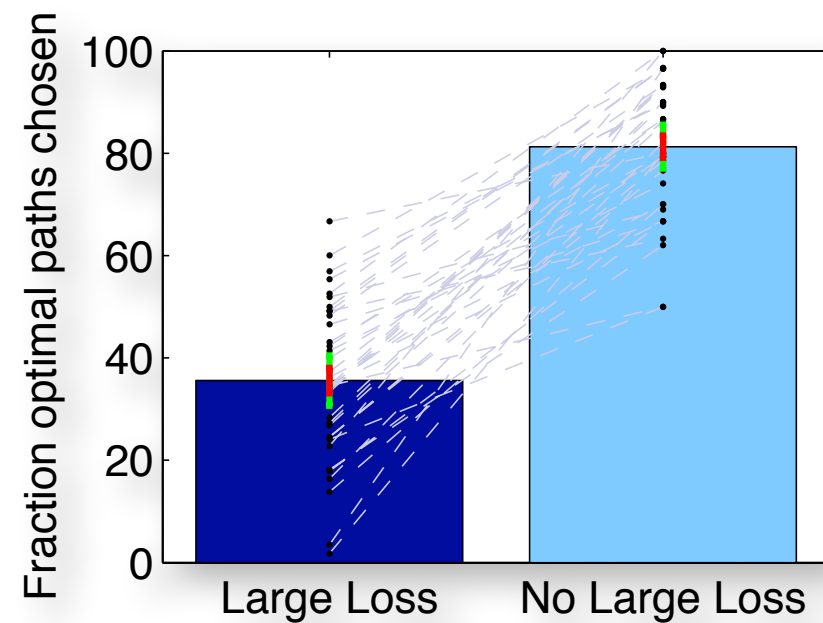
Pavlovian?



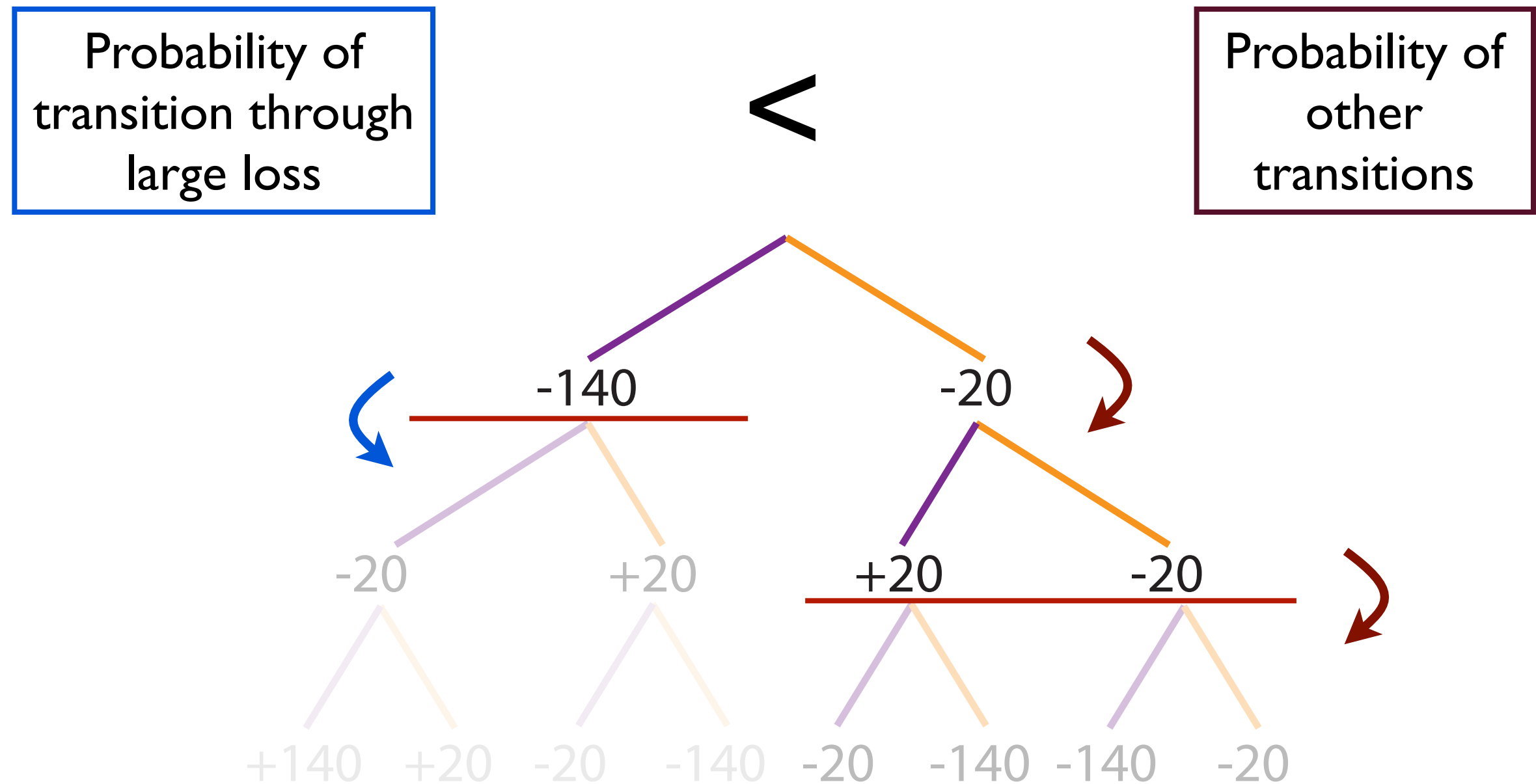
Optimal sequences containing losses



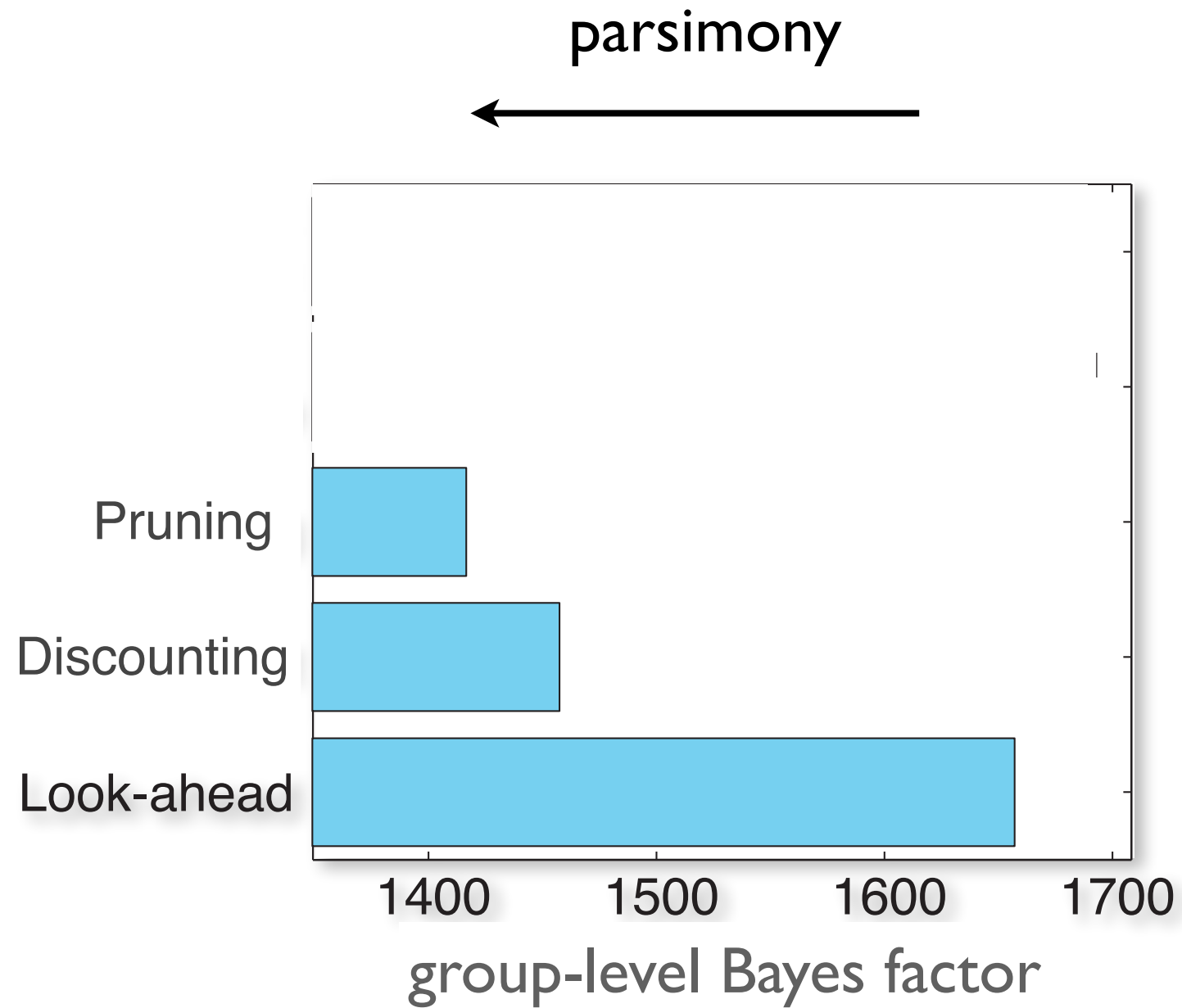
Optimal sequences containing losses



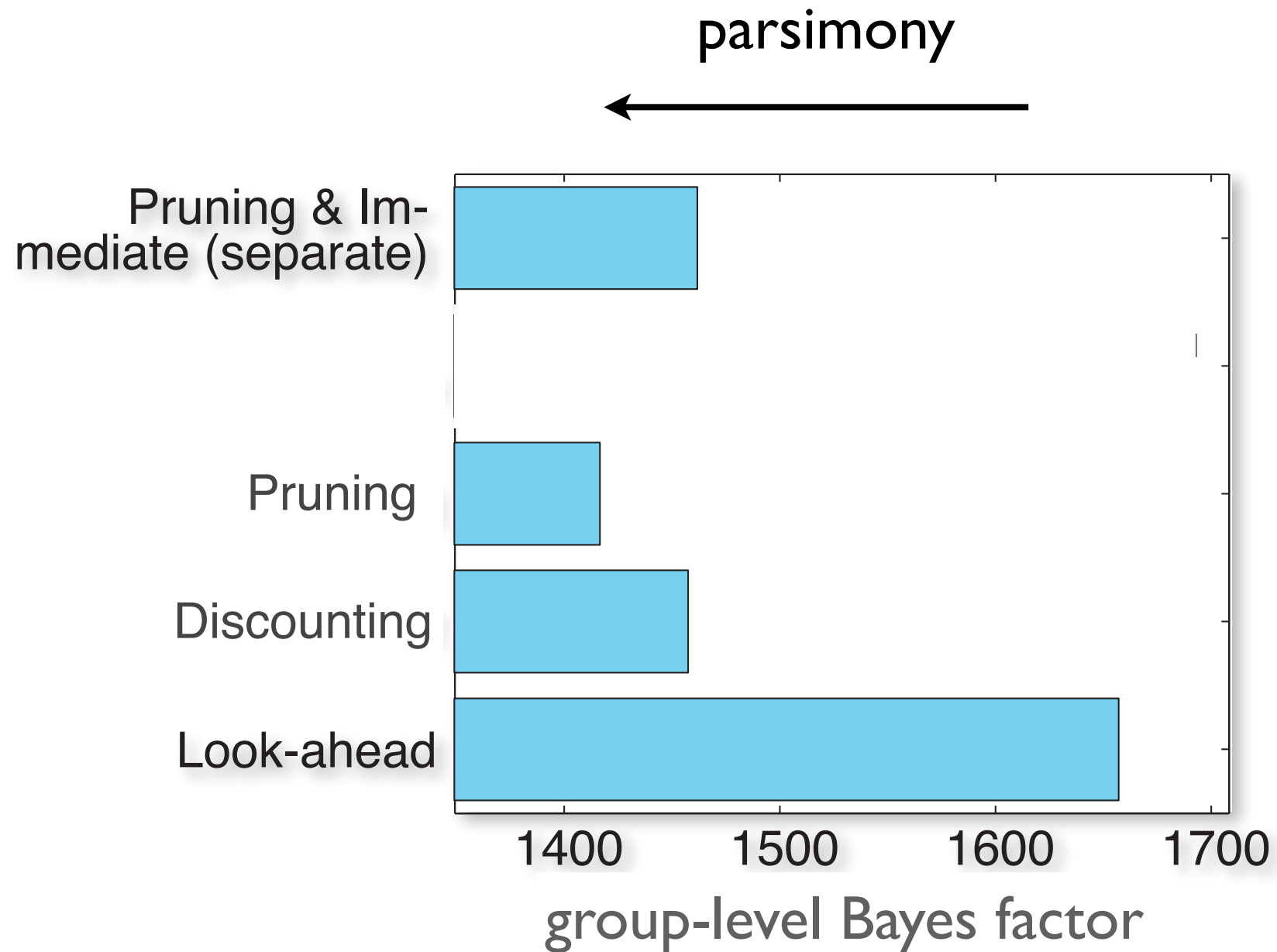
Adaptive pruning model



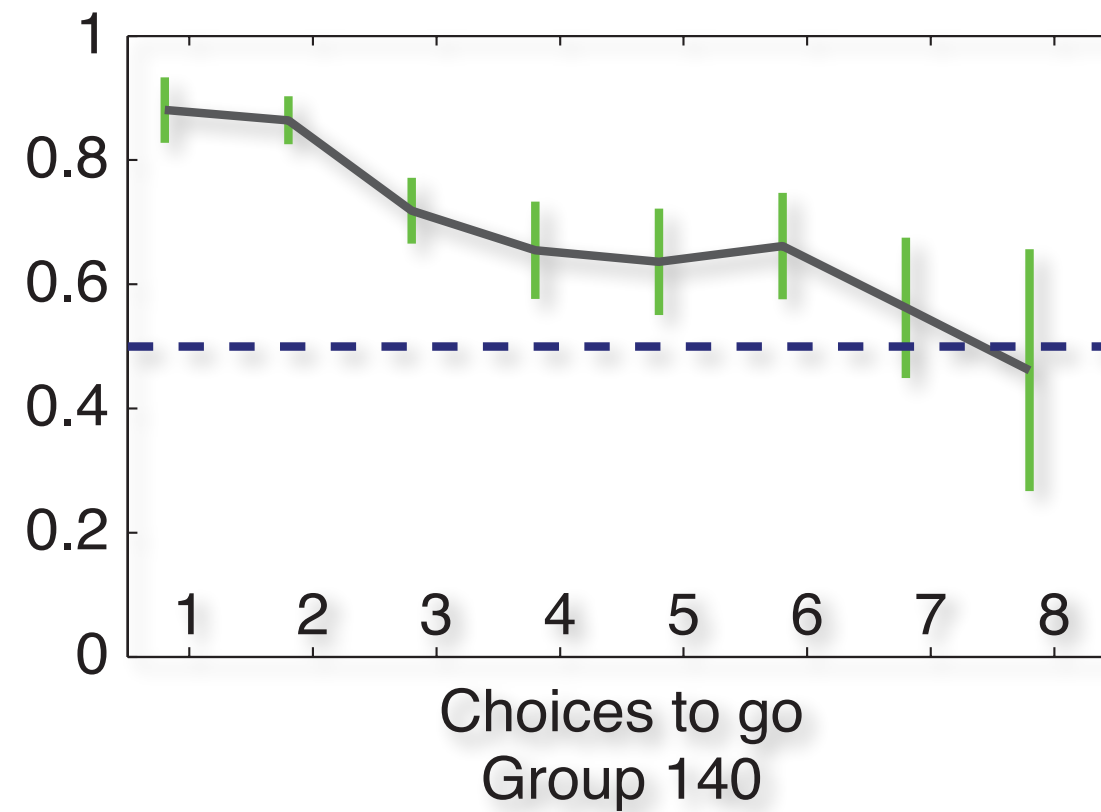
Adaptive pruning wins



Adaptive pruning wins



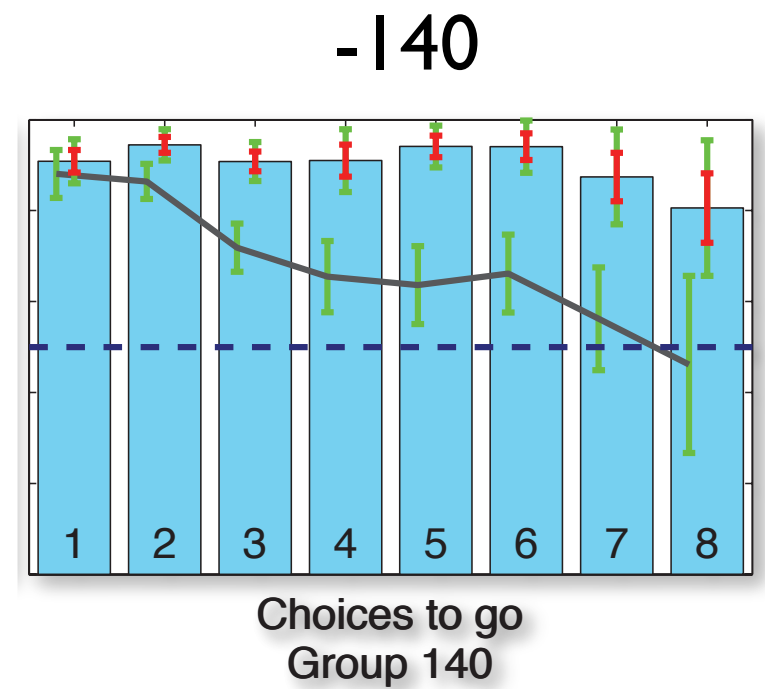
Pruning is Pavlovian



Pruning is Pavlovian

Maximal loss

% choices pre-
dicted by model



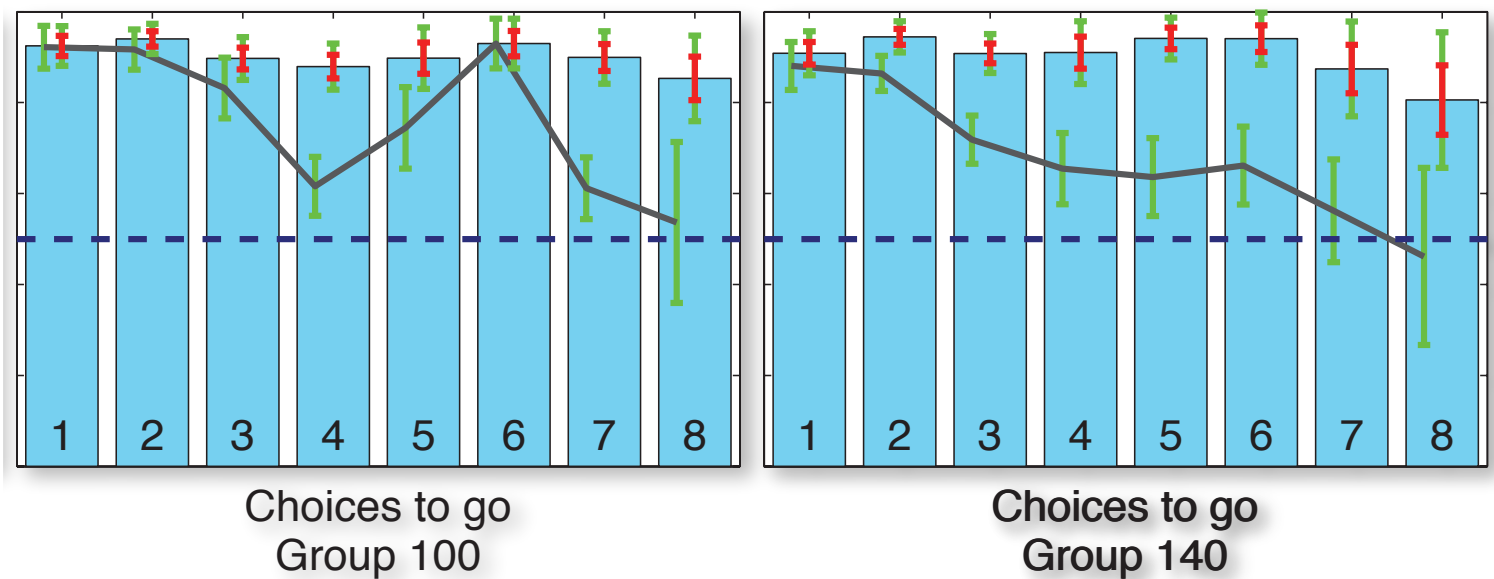
Pruning is Pavlovian

Maximal loss

-100

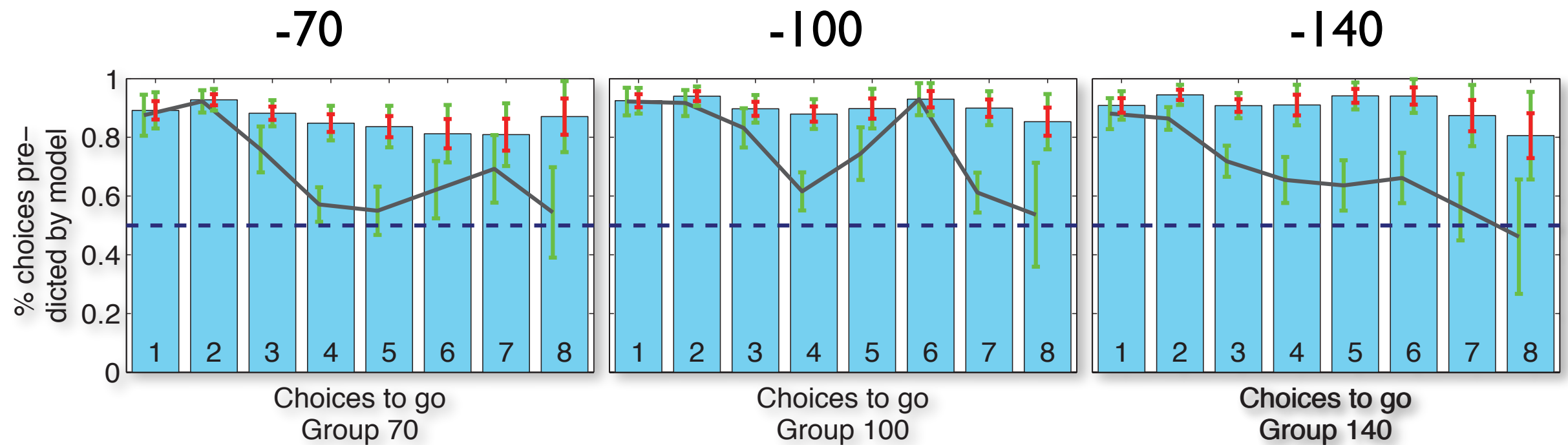
-140

% choices pre-
dicted by model



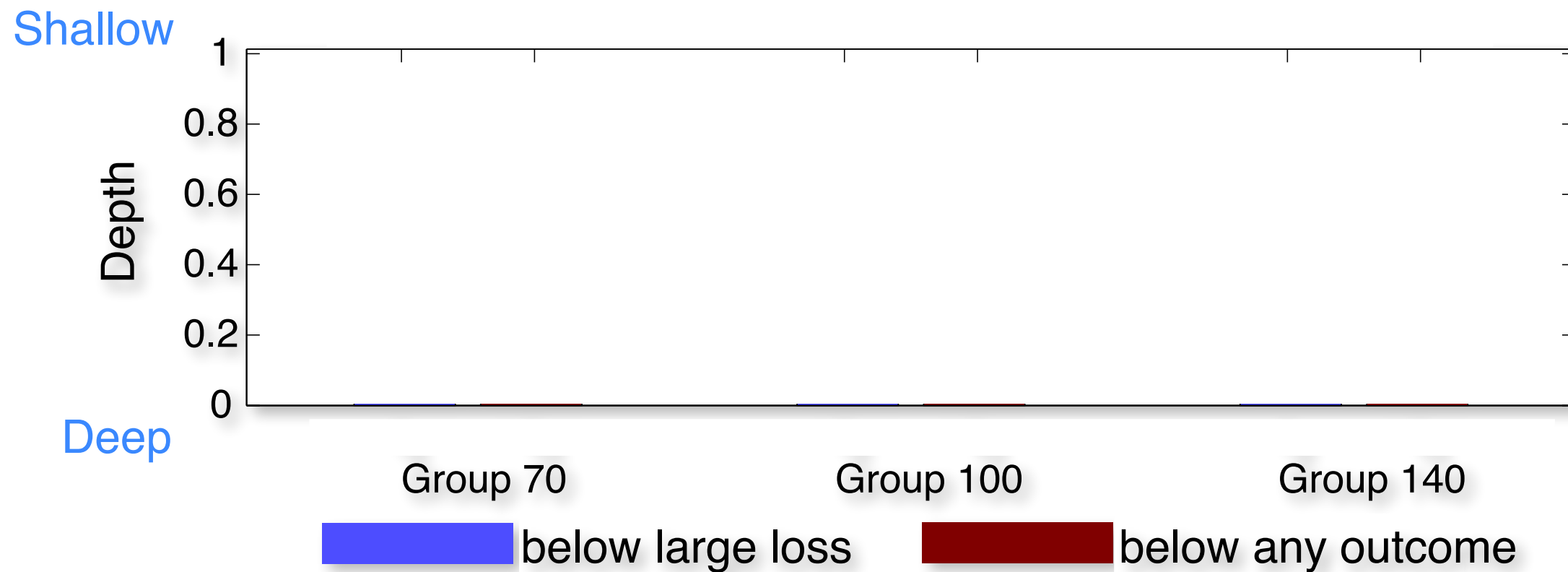
Pruning is Pavlovian

Maximal loss



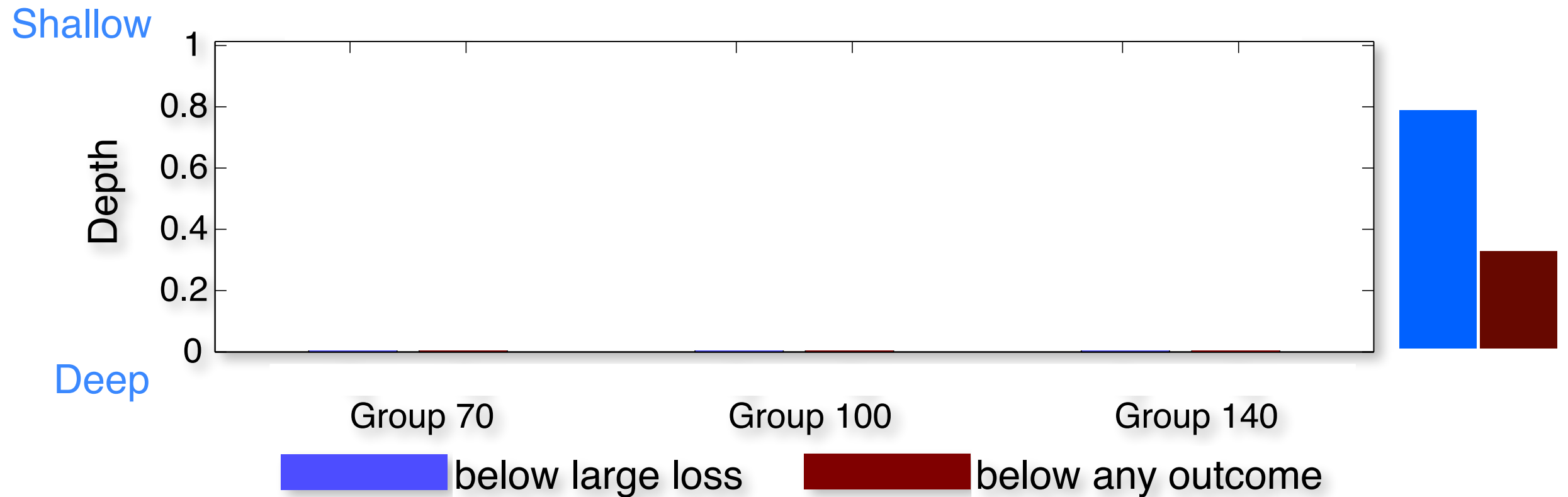
Pruning parameters

- ▶ Given the model, can now look at parameters



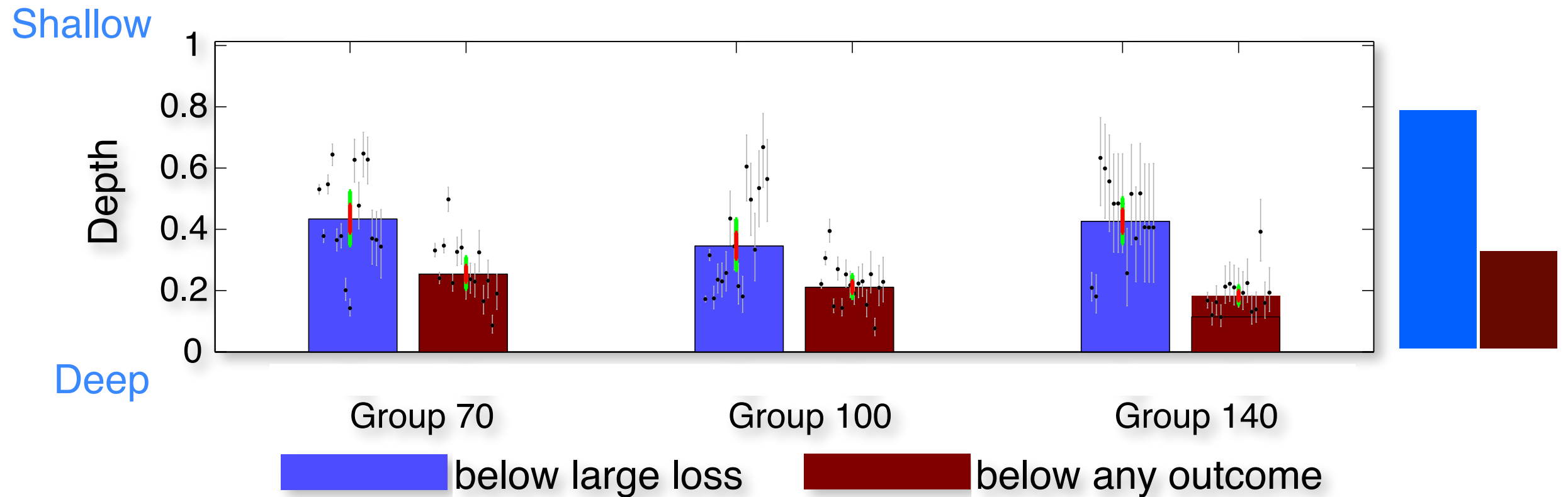
Pruning parameters

- ▶ Given the model, can now look at parameters



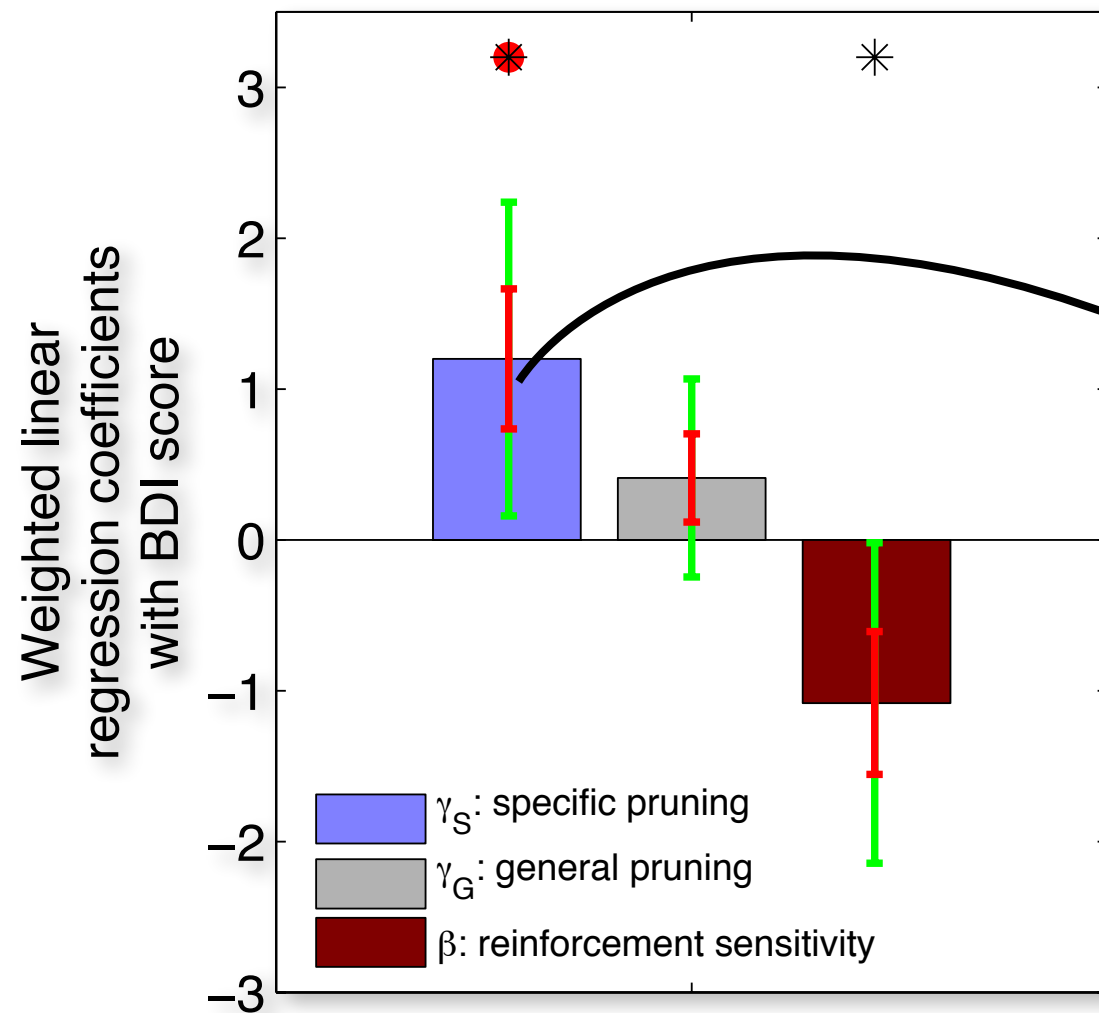
Pruning parameters

- ▶ Given the model, can now look at parameters



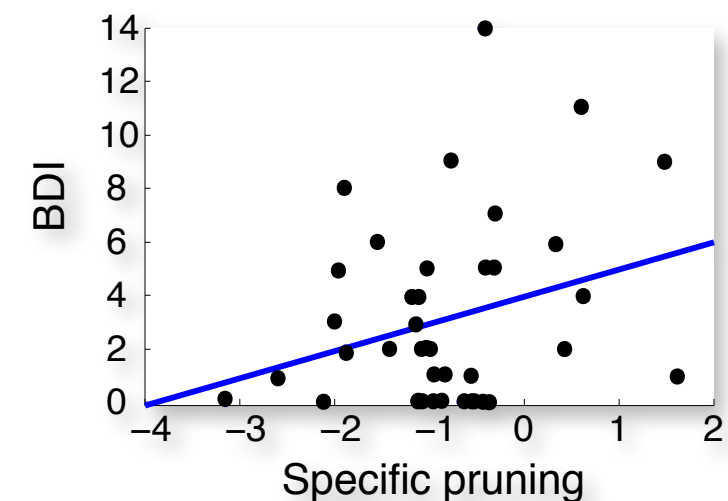
Minor symptoms of depression increase pruning

- ▶ leads to increased pruning



More pruning

- more dependence on pruning
- more sensitivity to drops in 5HT?



- ▶ prediction: in MDD less pruning

Discussion I

▶ Emotional component

- No primary changes (pain, hedonic taste, sucrose)
- Negative “emotional” biases & decision-making
 - conceptual -> interpretation?

▶ Cognitive component

- Helplessness
- Goal-directed “interpretations”

▶ Serotonin

▶ Pavlovian influence on goal-directed thought processes as one influence of emotion on cognition.