

A computational approach to understanding motivational dysfunction in depression

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Computational Psychiatry Course Zurich 2021



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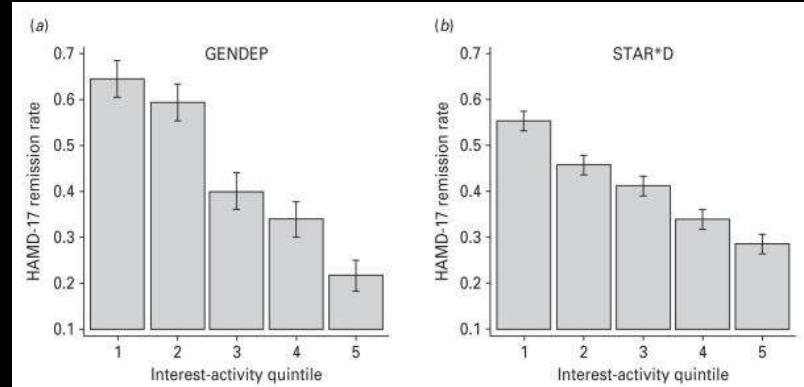
Yumeya Yamamori

Depression is a devastating condition

- The impact of depression:
 - High lifetime incidence (10-20%)
 - Life-threatening - more UK deaths due to suicide in depression than due to road accidents
 - In 2011, estimated cost to the UK economy:
~£20b per year (cf £7.9b current UKRI budget)
 - Has a larger impact on real-world function and wellbeing than angina, arthritis and diabetes
 - Effective treatment takes months; <50% respond to the first treatment they try

Motivation is central to depression

- Anhedonia
 - Loss of interest or pleasure
 - Cardinal symptom of depression
- Fatigue
- Difficulty in decision-making
- “Interest-activity” cluster of symptoms predicts poor response to treatment
- Subjective effort discounting in depression

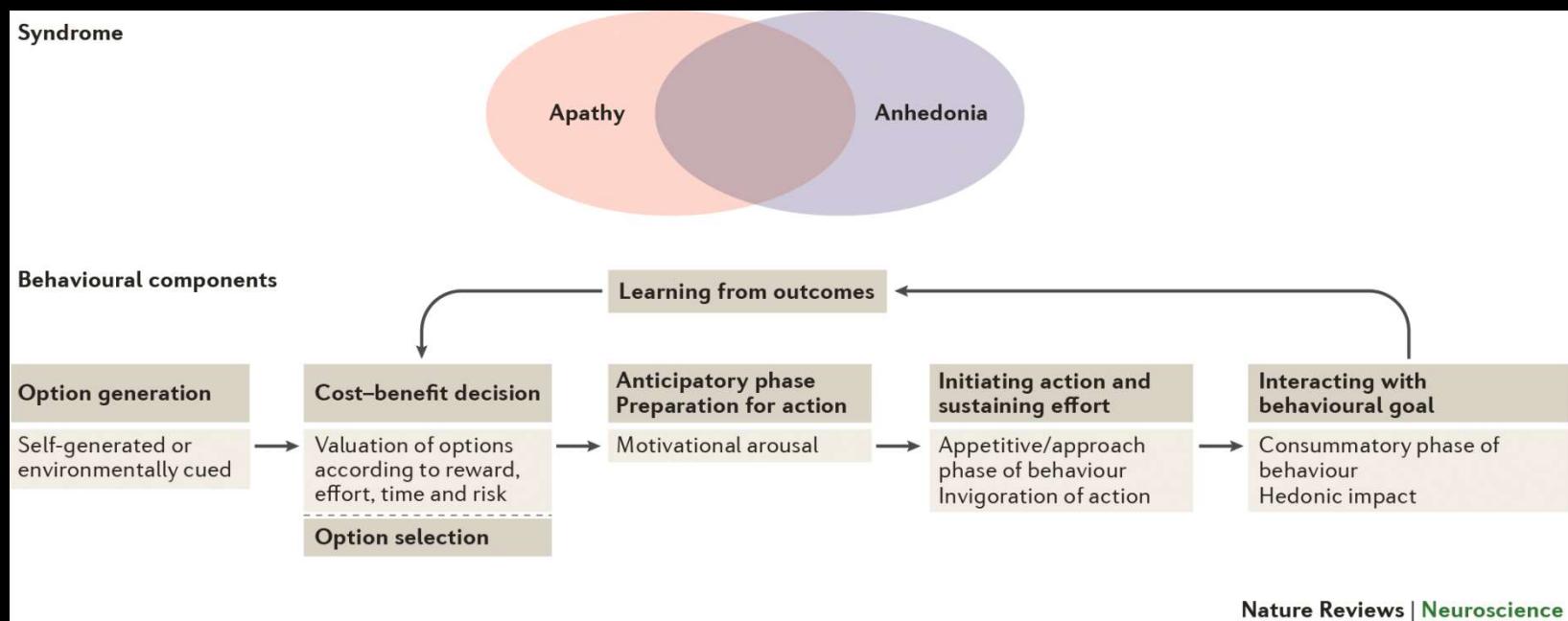


REVIEW

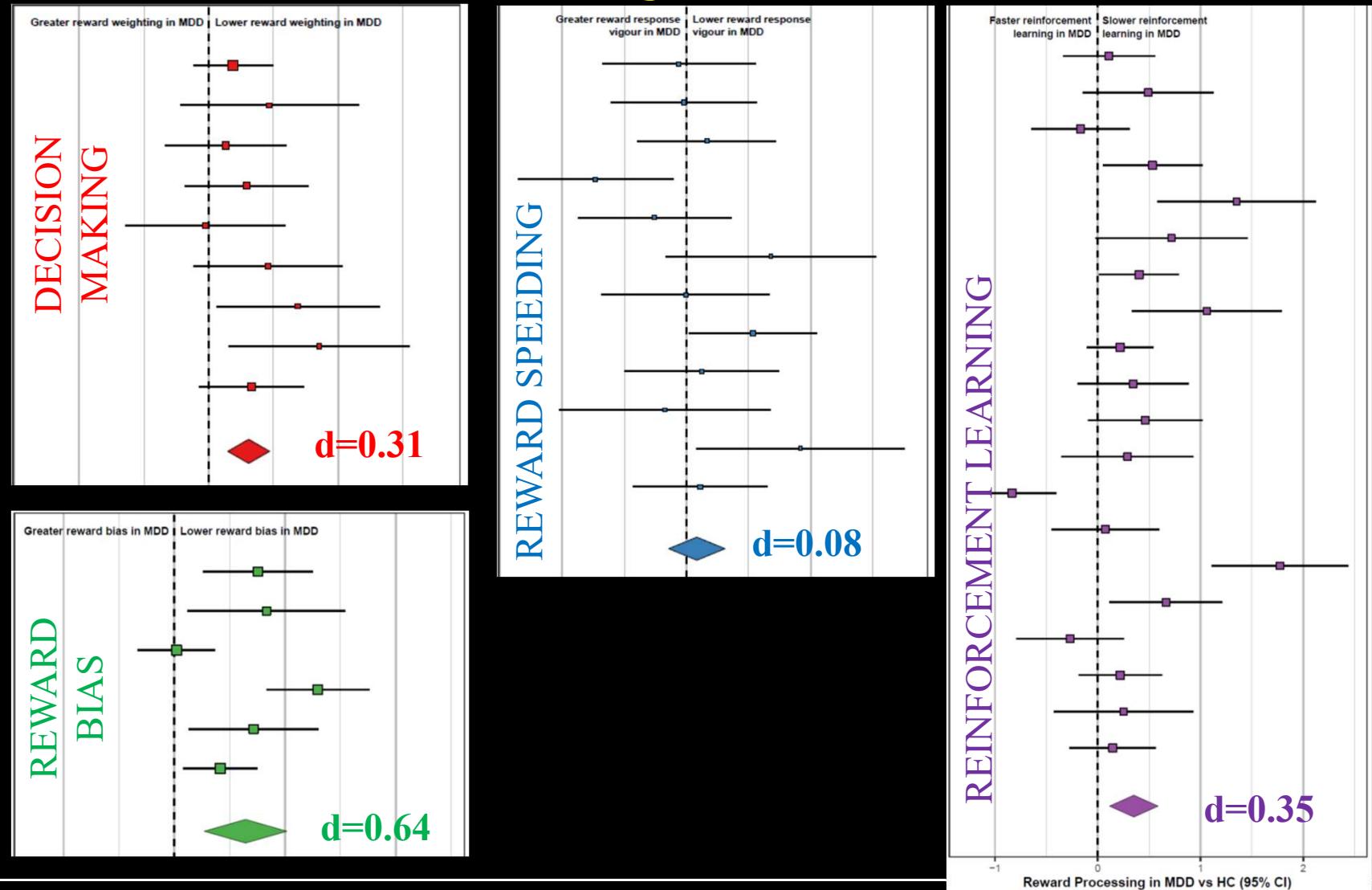
Reward and Punishment Processing in Depression

Neir Eshel and Jonathan P. Roiser

Cognitive processes and amotivation



Reward processing in depression



Motivation in the lab

The willingness to engage in an effortful activity (cost) in order to attain an outcome (reward)

Depends on:

- Magnitude of the anticipated rewards
- Effort required (cost)



Motivation in the lab

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Motivation in the lab

The willingness to engage in an effortful activity (cost) in order to attain an outcome (reward)

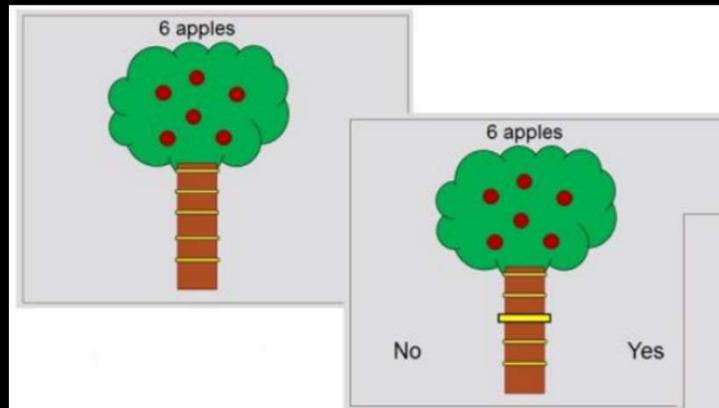
Depends on:

- Magnitude of the anticipated rewards
- Effort required (cost)



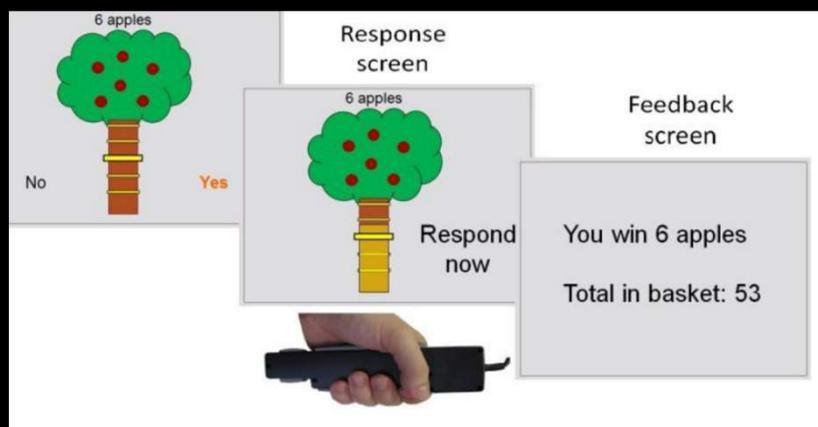
The Apple Gathering Task

- Effort-based decision-making task



- 5 blocks, 16 trials (80 total)

- 4 reward levels
 - 3, 6, 9, 12 points



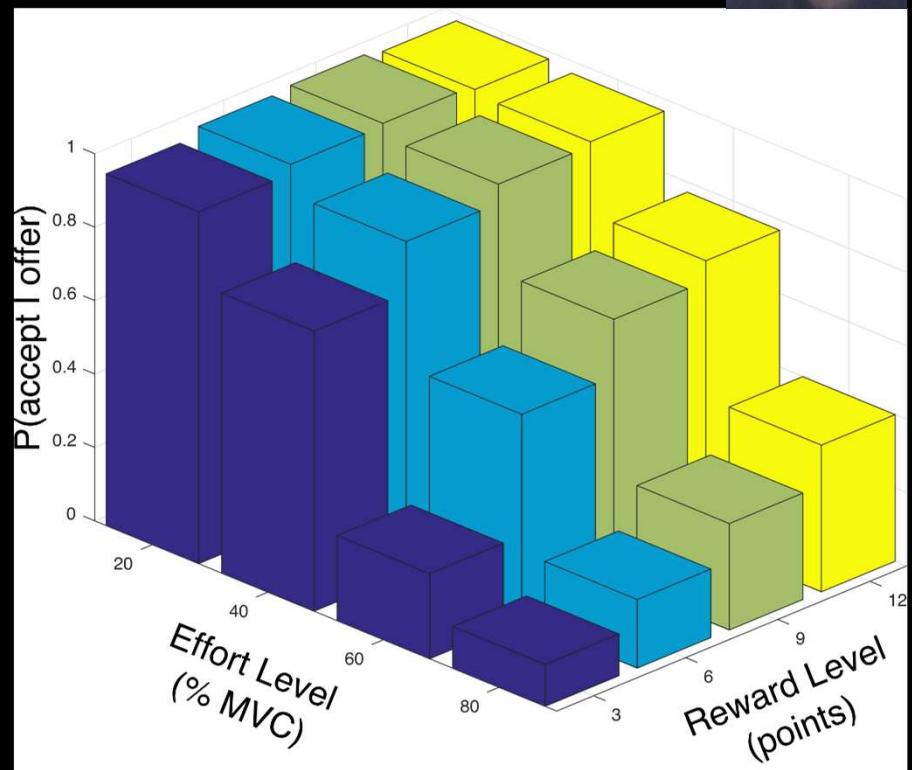
- 4 effort levels
 - 20%, 40%, 60%, 80% of maximum strength (calibrated individually)

Decisions affected by reward and effort



Alan Gray

- 102 healthy controls (12 excluded), N=90 analyzed
- Probability of accepting an offer
 - Significant effect of effort $F(1.813, 161.34)=185.22, p<0.001$
 - Significant effect of reward $F(1.812, 161.23)=107.73, p<0.001$
 - Significant effort x reward interaction $F(5.14, 458.24)=20.08, p<0.001$



Theory-driven Computational Psychiatry

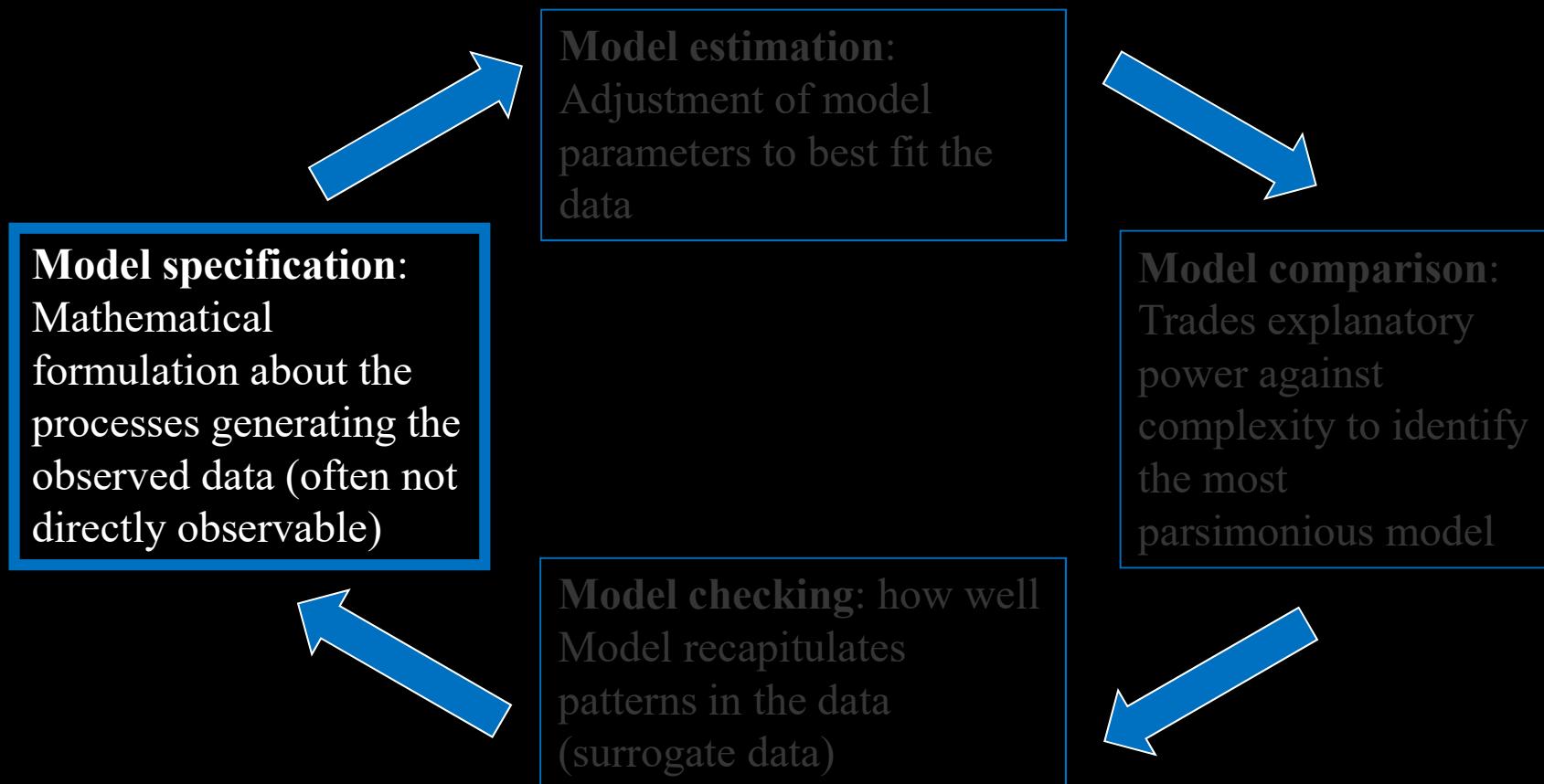
Model specification:
Mathematical formulation about the processes generating the observed data (often not directly observable)

Model estimation:
Adjustment of model parameters to best fit the data

Model comparison:
Trades explanatory power against complexity to identify the most parsimonious model

Model checking: how well model recapitulates patterns in the data (surrogate data)

Theory-driven Computational Psychiatry





Model specification

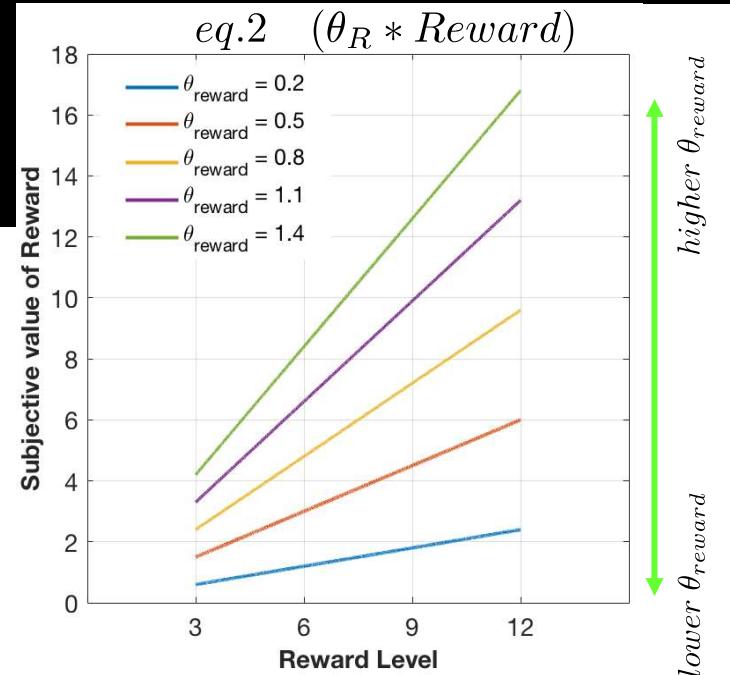
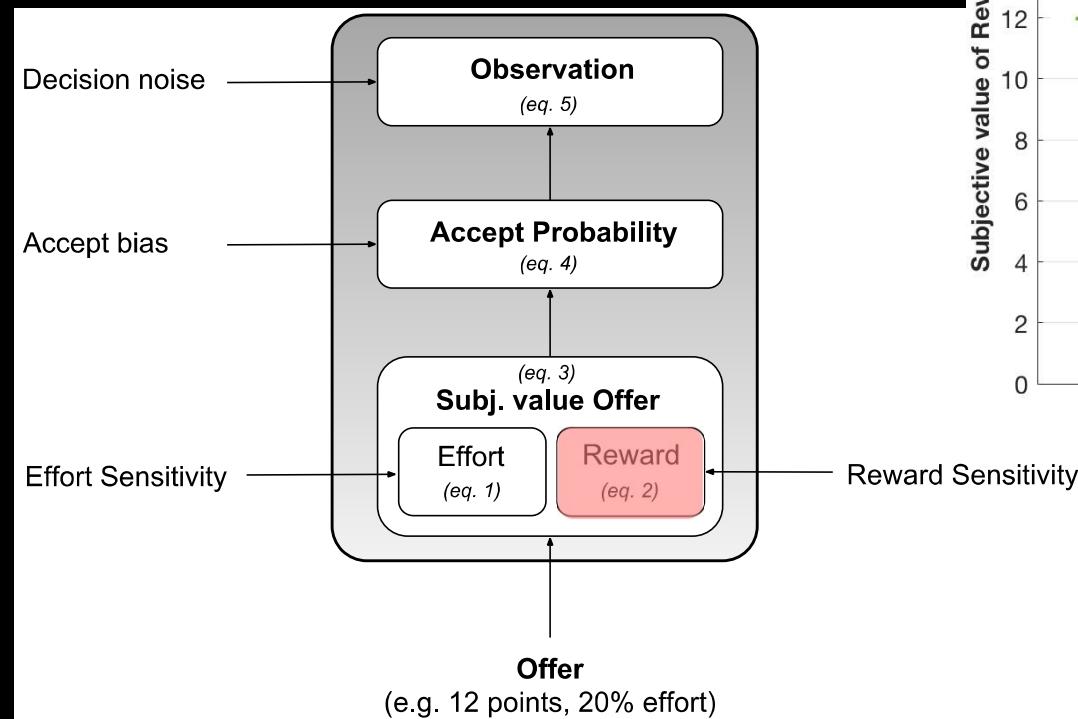
$$eq.5 \quad (\theta_{noise} * \frac{1}{2}) + ((1 - \theta_{noise}) * Bernoulli(eq.4))$$

$$eq.4 \quad inv_logit(\theta_{bias} + eq.3)$$

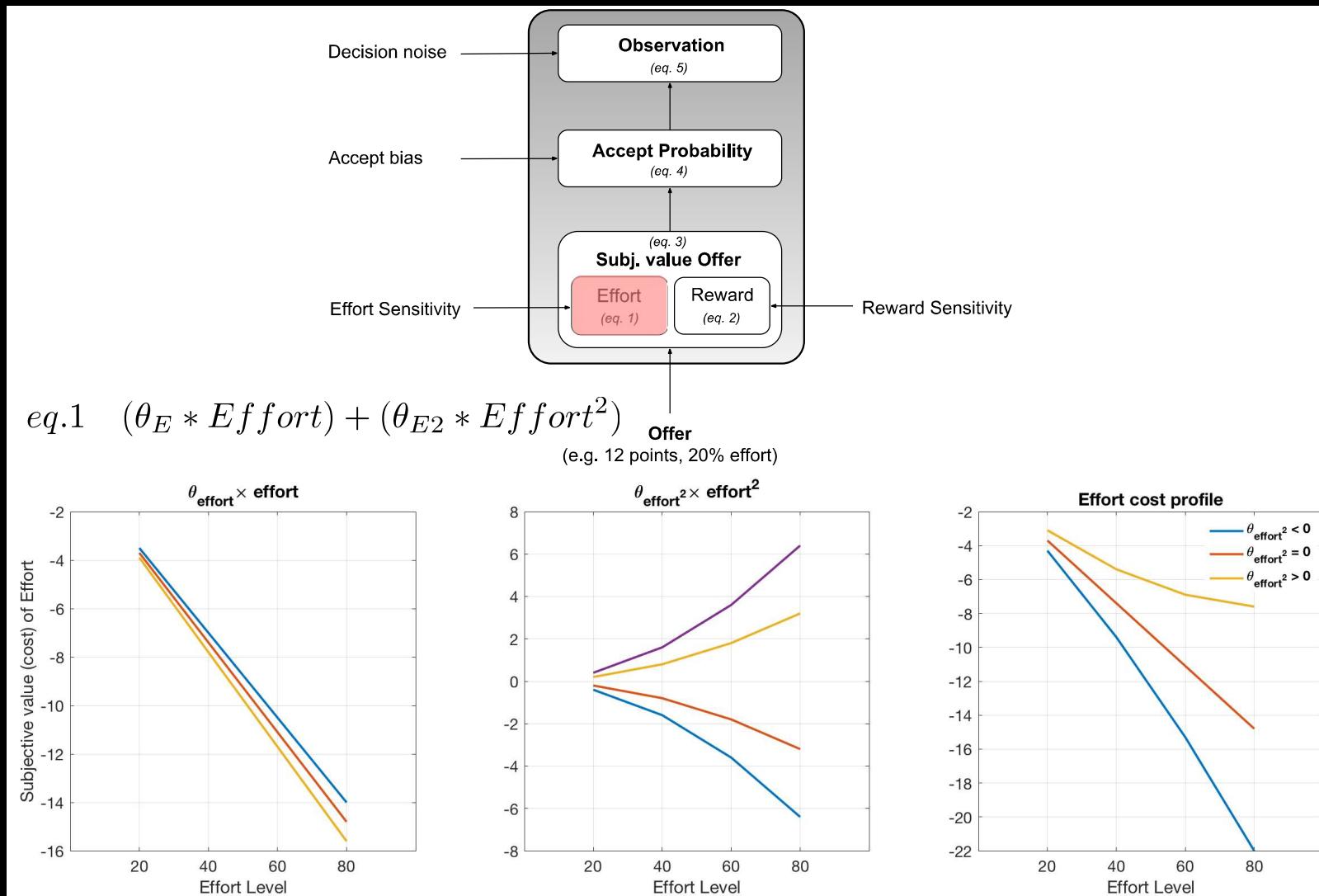
$$eq.3 \quad (eq.1) + (eq.2)$$

$$eq.2 \quad (\theta_R * Reward)$$

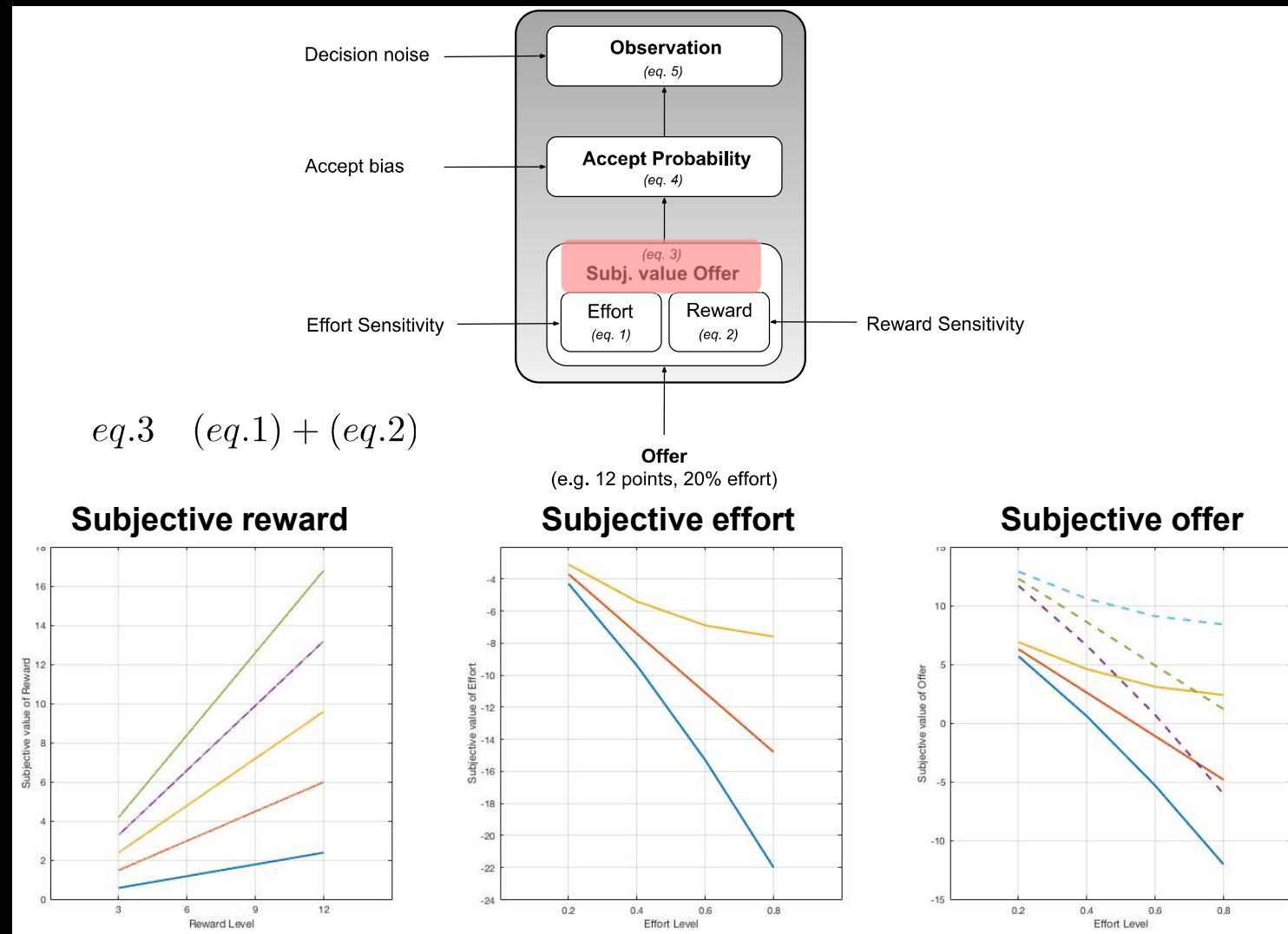
$$eq.1 \quad (\theta_E * Effort) + (\theta_{E2} * Effort^2)$$



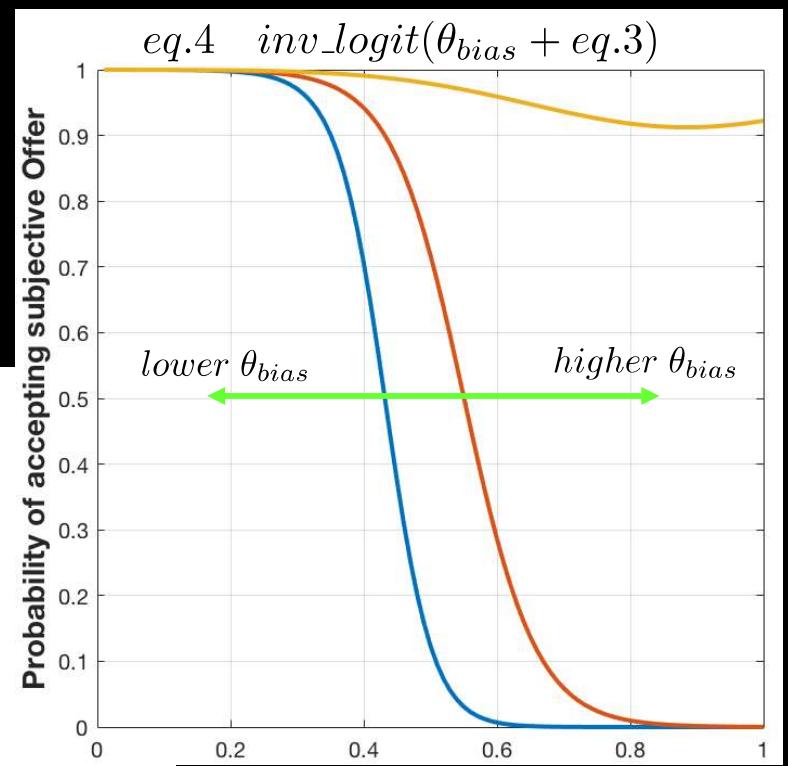
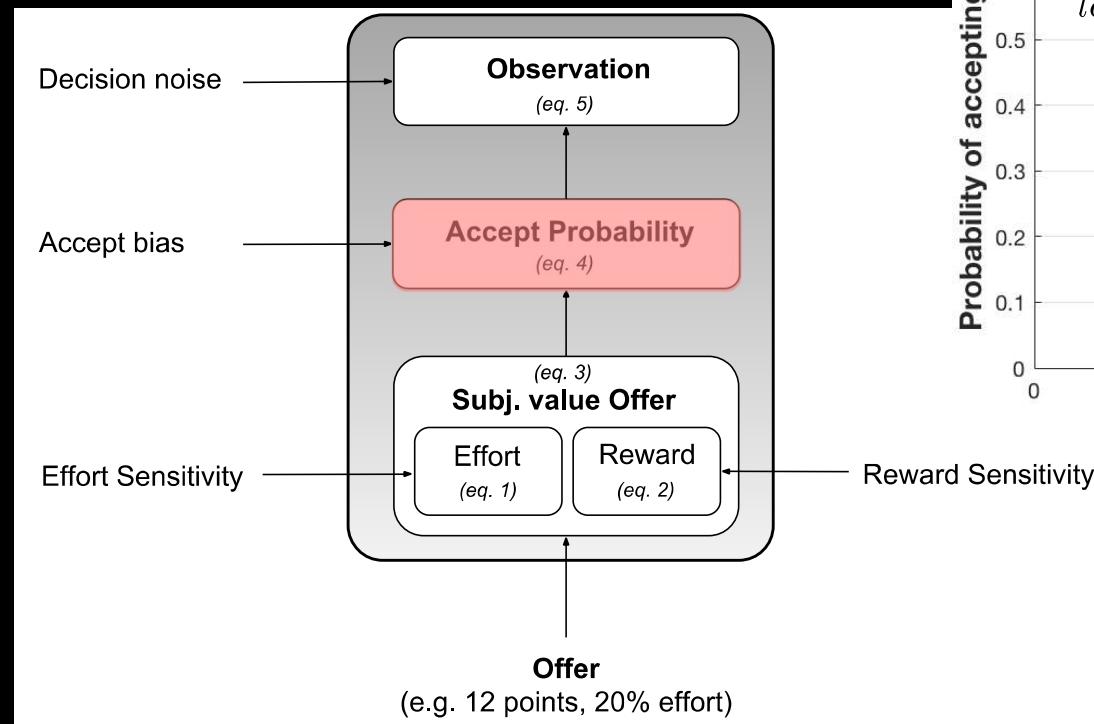
Model specification



Model specification



Model specification



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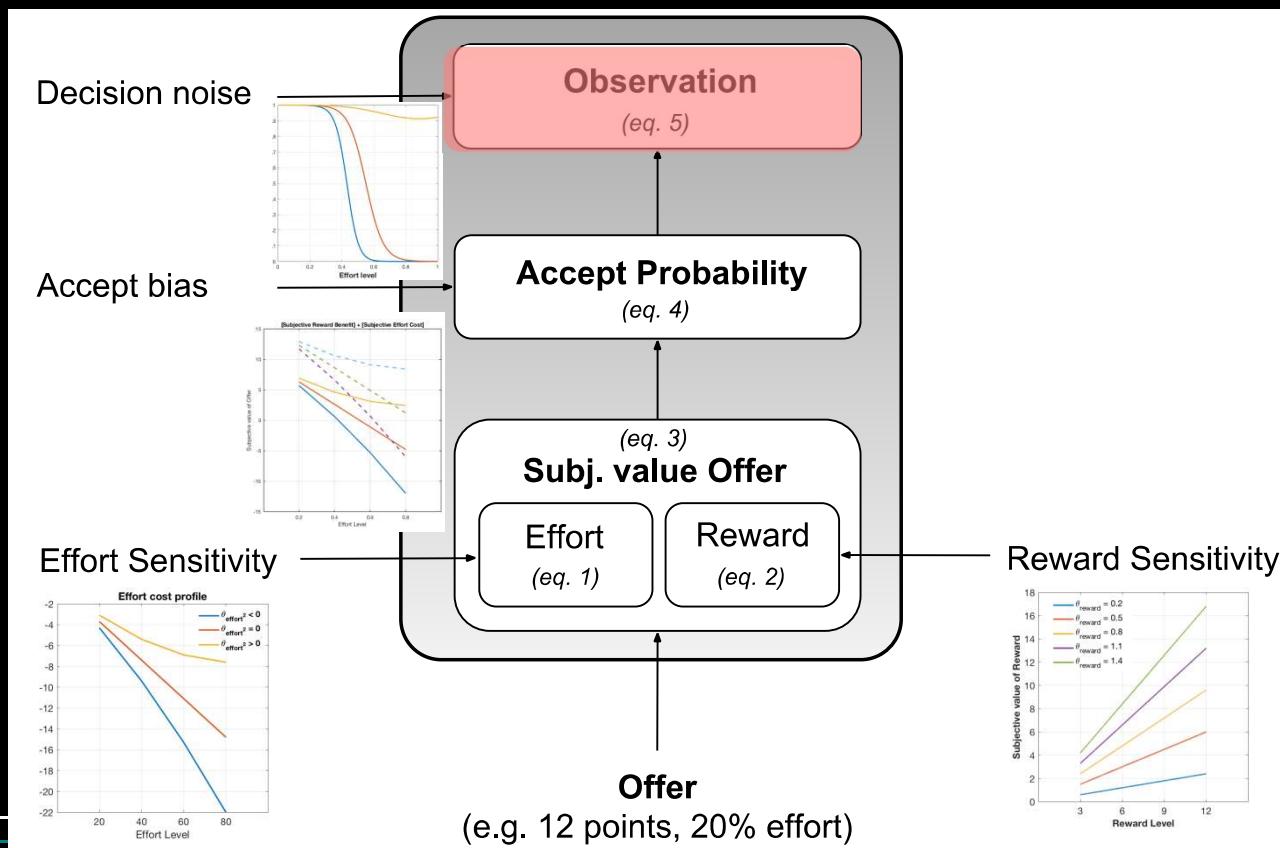
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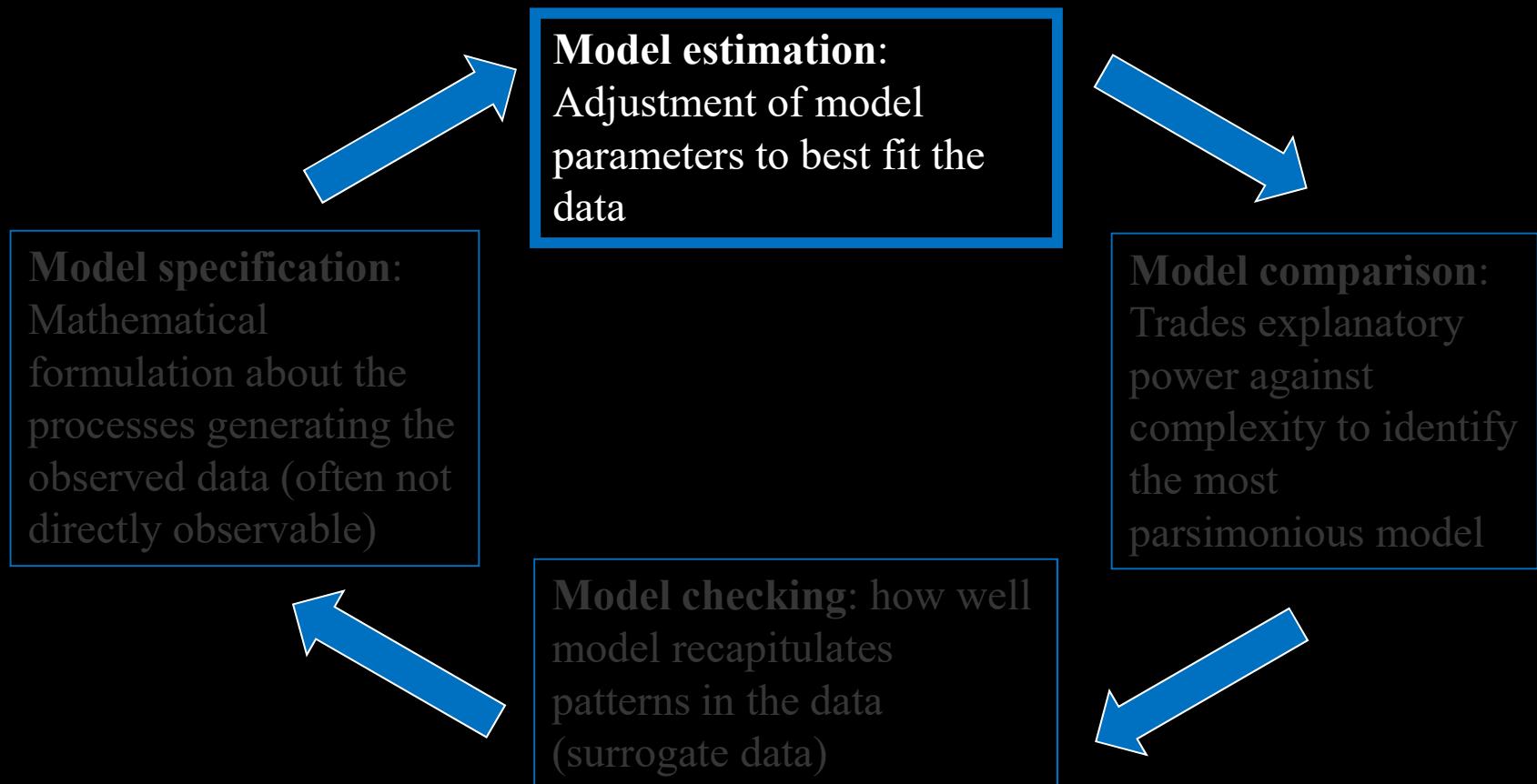
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$$eq.5 \quad (\theta_{noise} * \frac{1}{2}) + ((1 - \theta_{noise}) * Bernoulli(eq.4))$$

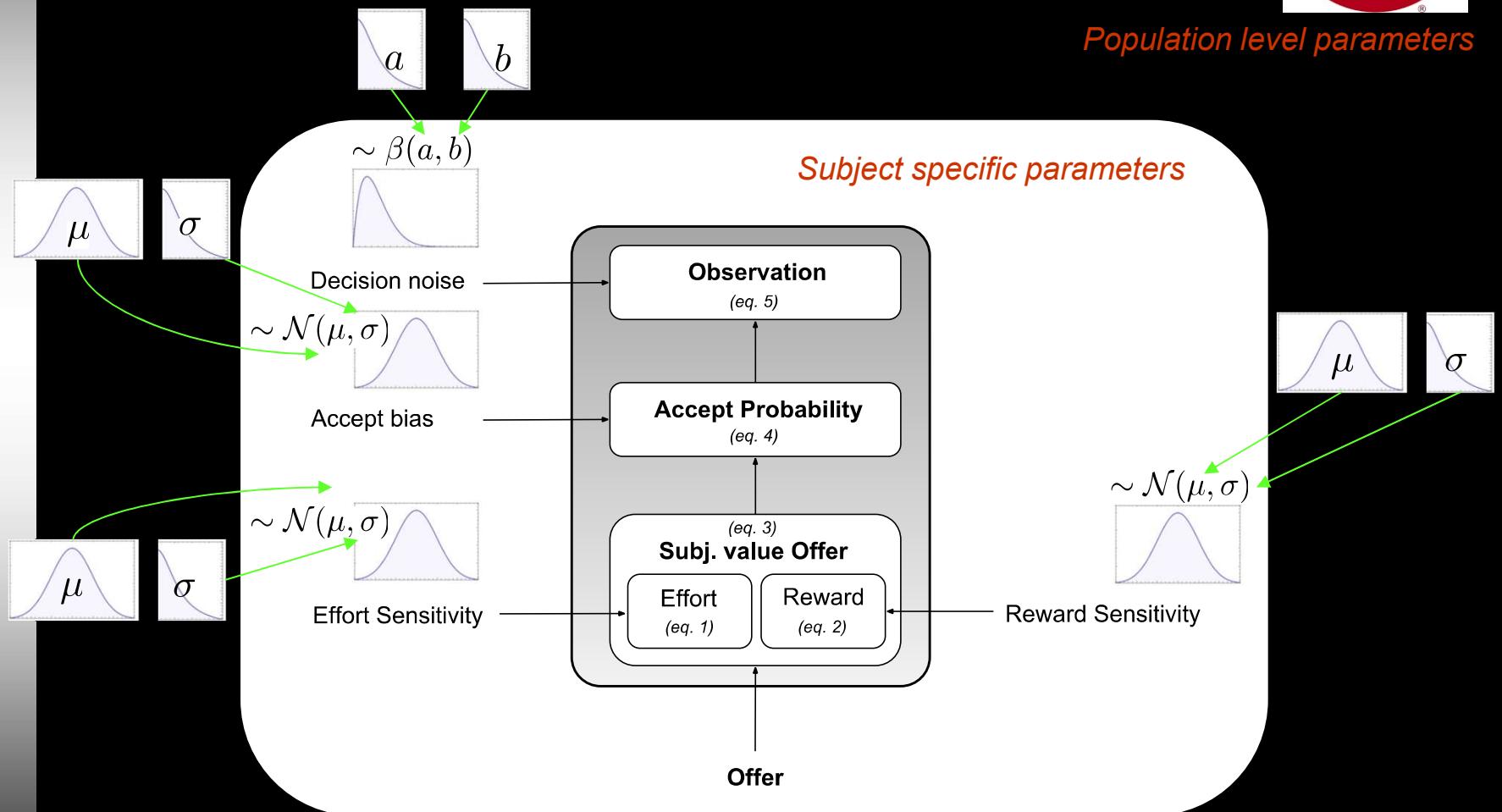


Theory-driven Computational Psychiatry

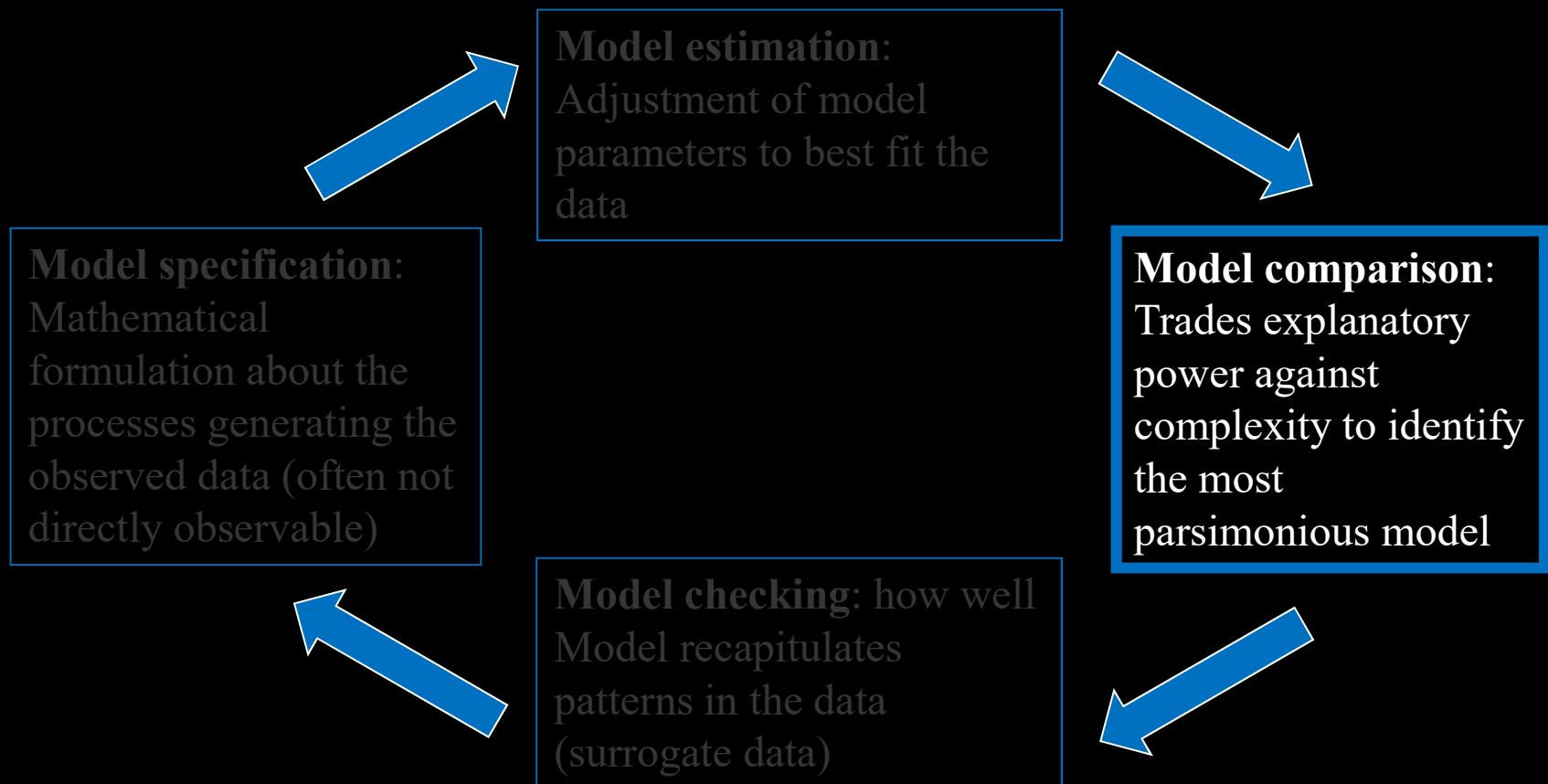


Model estimation

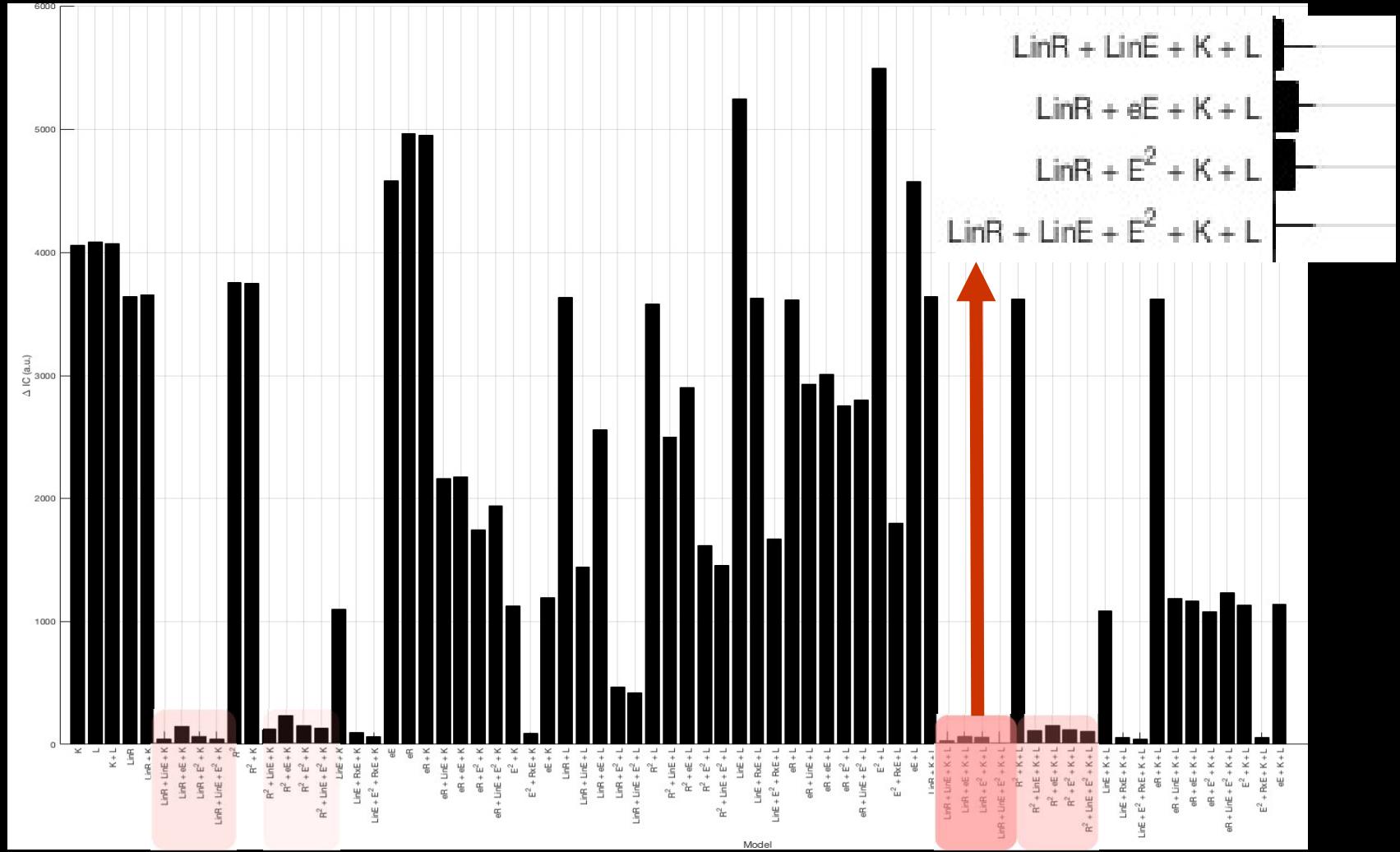
Hierarchical parameter estimation using Stan (MCMC)



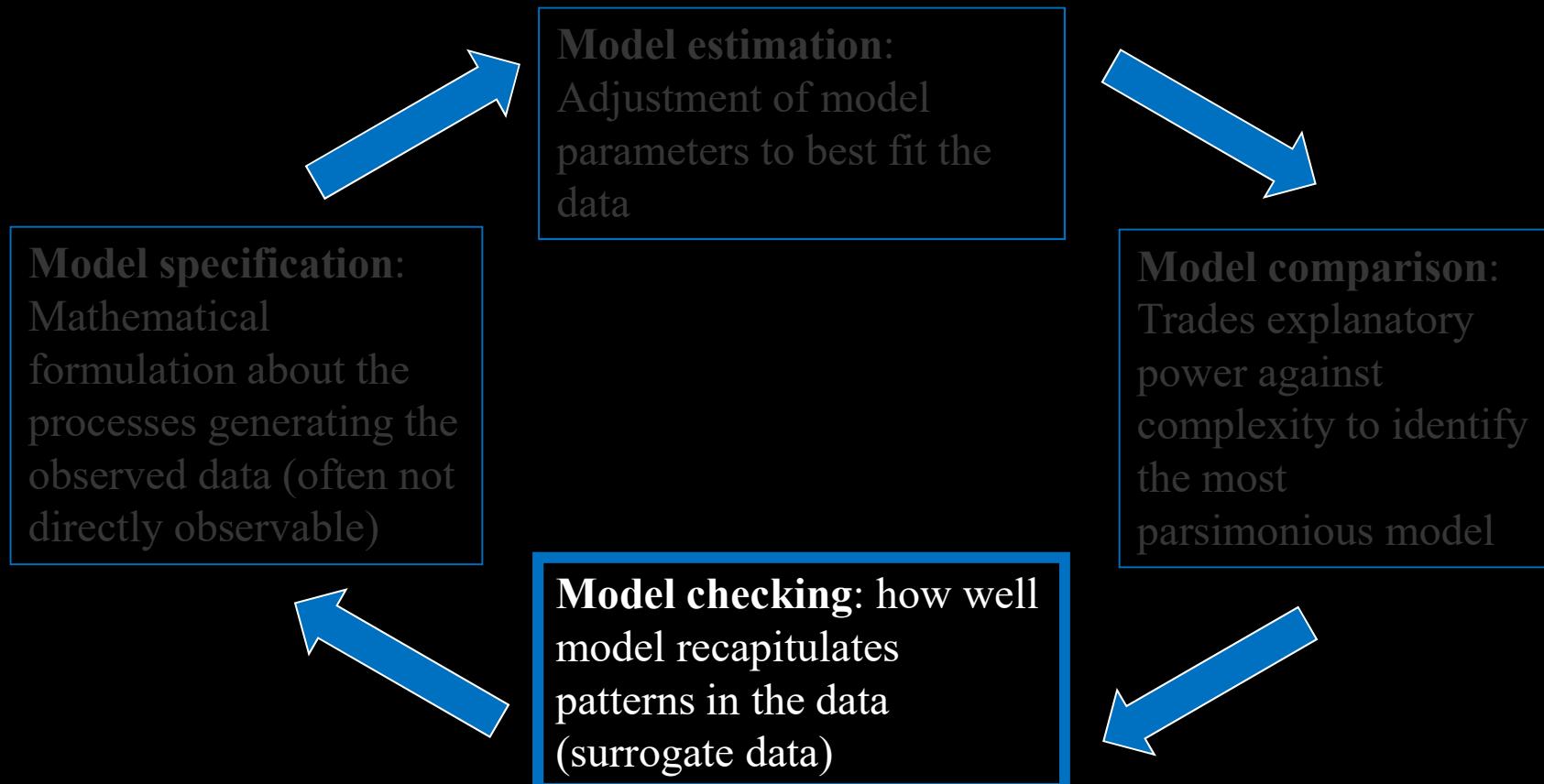
Theory-driven Computational Psychiatry



Model comparison

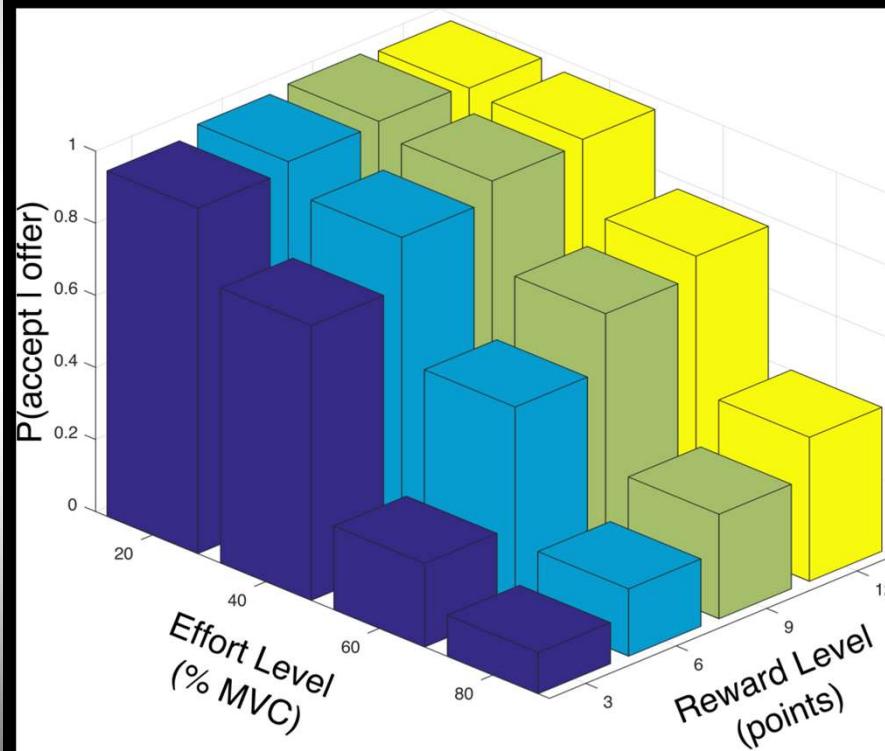


Theory-driven Computational Psychiatry

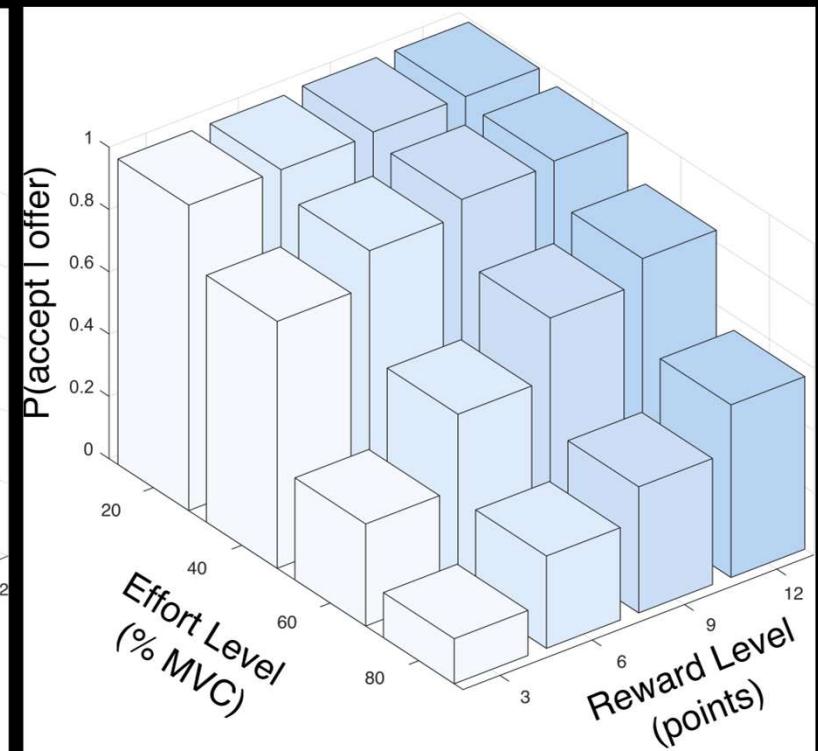


Model checking

Simulated behaviour from estimated parameters over all participants



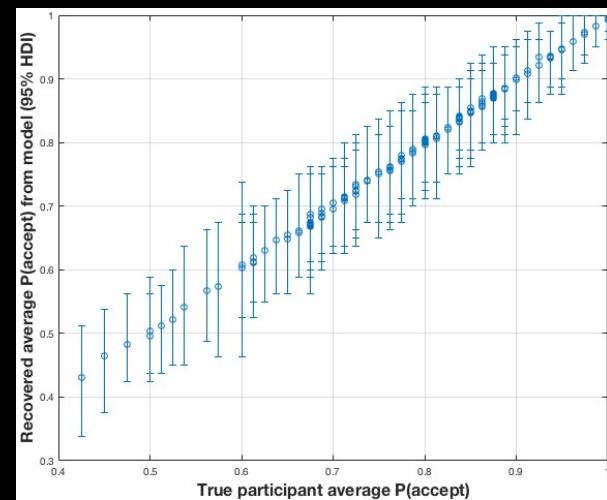
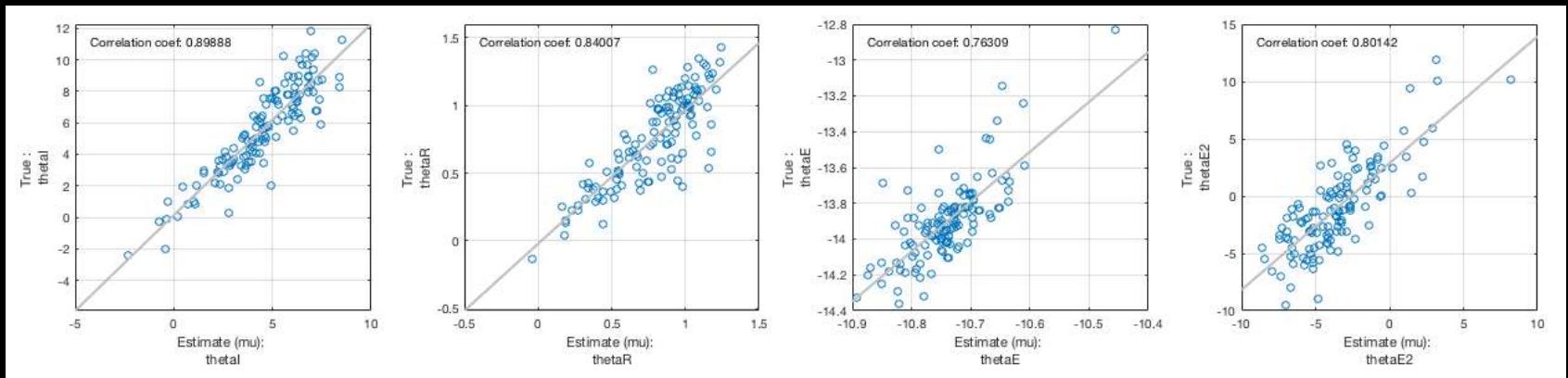
Data



Model

Model checking

Parameter recovery (parameter/model identifiability) and recovery of model-agnostic measures



Symptoms

Latent variables from symptom scales

		Factor 1	Factor 2	Factor 3	Factor 4
AES	BDI	0.5967			
	Cog. Apathy		0.6590		
	Beh. Apathy		0.5356		
	Emo. Apathy		0.3457		
	Other Apathy		0.7928		
LOTR	CPAS			-0.8955	
	DAS Scale 1				0.8234
	DAS Scale 2				0.8391
	Optimism	-0.4747			
STAI	SHAPS			0.3660	
	STAI state	0.7296			
	STAI trait	0.8503			
TEPS	TEPS anticip.			0.3312	
	TEPS consum.			0.8345	
	Neg. Urg.	0.6673			
UPPS	Lack Premedit.		0.5067		
	Sens. seeking			0.3926	
	Pos. Urgency	0.6423			
	Lack of Persev.		0.6240		

- (F1) Low Mood / Anxiety
- (F2) Apathy
- (F3) Anhedonia
- (F4) Dysfunctional attitudes

BDI = Beck depression inventory

AES = Apathy evaluation scale

CPAS = Chapman physical
Anhedonia Scale

DAS = Dysfunctional attitudes scale

LOTR = Life orientation test

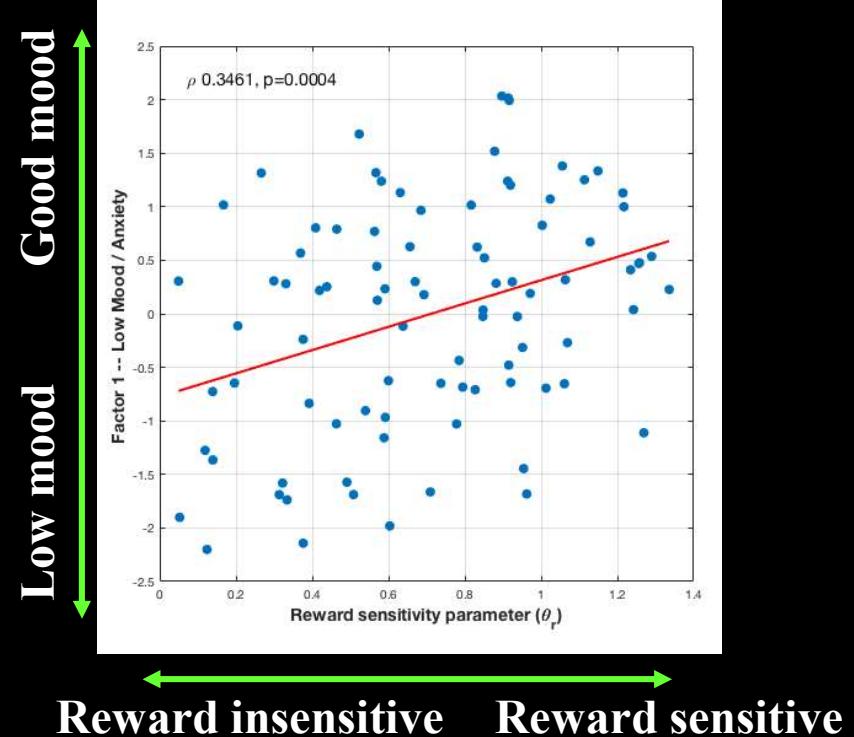
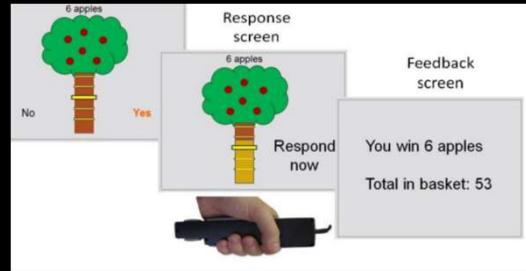
SHAPS = Snaith-Hamilton pleasure
scale

STAI = State/trait anxiety inventory

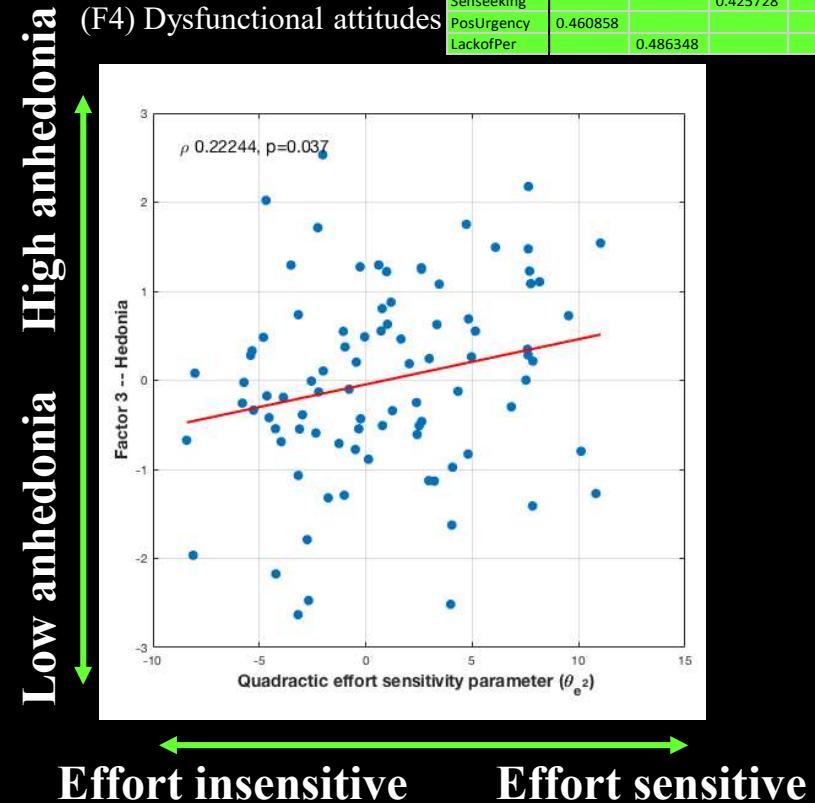
TEPS = Temporal experience of
pleasure scale

UPPS = Urgency, premeditation,
perseverance, sensation seeking, and
positive urgency

Symptom correlations

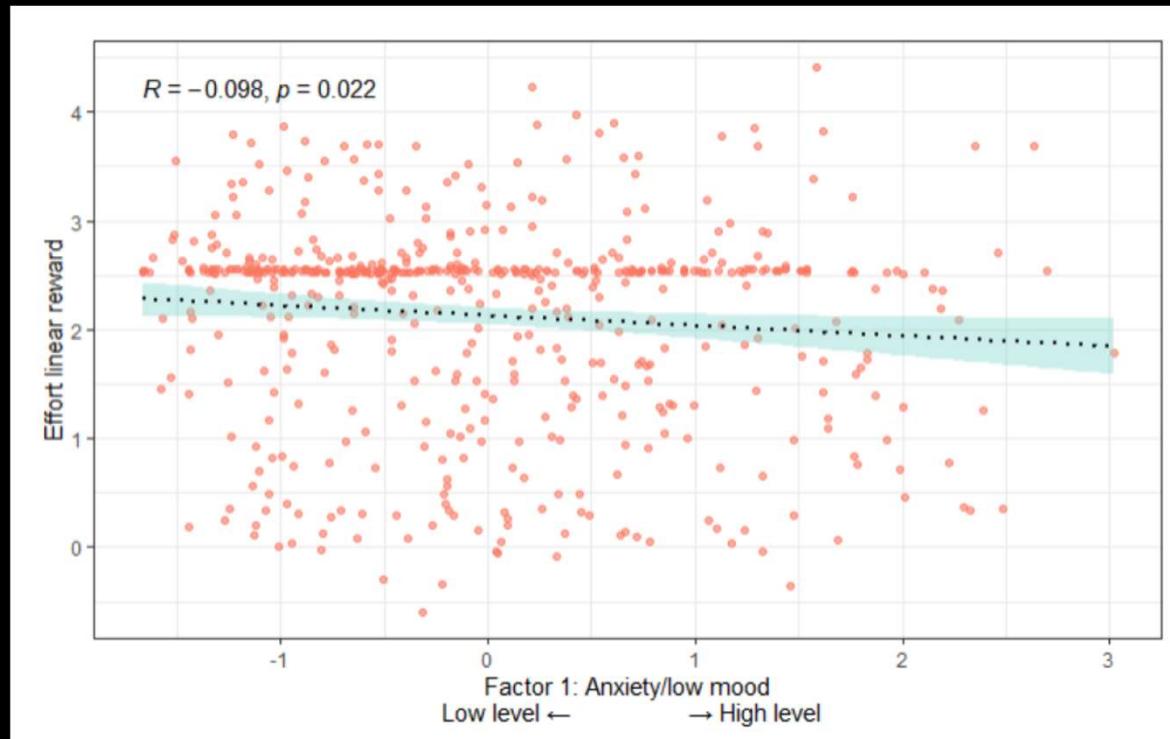


- (F1) Low mood / anxiety
- (F2) Apathy
- (F3) Anhedonia
- (F4) Dysfunctional attitudes



	F1	f2	f3	f4
BDI	0.55379			
CogApathy		0.903325		
BehApathy	0.357154	0.506497		
EmoApathy		0.486473	-0.32731	
OthApathy		0.631454		
PAS		0.429155	-0.46439	
DAS1				0.965774
DAS2				0.714758
Optimism	-0.55013			
SHAPS	0.923372			
STAIs				
STAlt	0.950164			
TEPa			0.837838	
TEPc			0.96338	
NegUrg	0.559472			
LackofPre				
Senseeking			0.425728	
PosUrgency	0.460858			
LackofPer		0.486348		

Symptom correlations – replication in online sample (cognitive effort)



Switching task in N~500; 2 week test-retest reliability in N~100 ranged from fair (reward sensitivity: ICC~0.5) to good (effort sensitivity & bias: ICC~0.7)

Case-control study



Anahit Mkrtchian

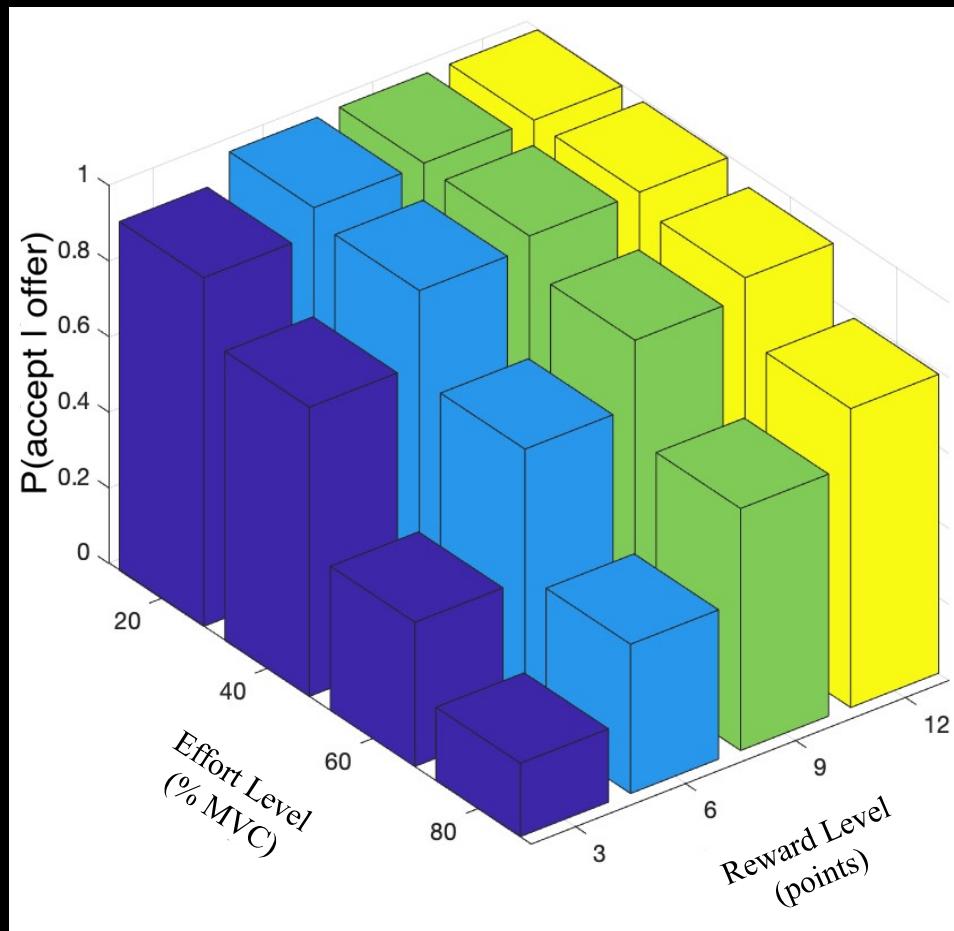


Madeleine Payne

	CTR (n=59)	REL (n=37)	REM (n=50)	MDD (n=48)	Statistics
Age	26.46 (8.10)	25.91 (8.12)	27.52 (8.00)	29.71 (11.0)	$F(3,190)=1.64$, $p>.05$
Gender	18 M / 41 F	13 M / 24 F	18 M / 32 F	14 M / 34 F	$X^2(1)=0.74$, $p>.05$
WTAR IQ	111.5 (7.62)	113.2 (7.47)	116.3 (7.82)	114.9 (9.51)	$F(3,188)=3.37$, $p<.05$
Years education	16.46 (2.81)	17.03 (3.10)	17.16 (2.74)	15.96 (2.53)	$F(3,190)=1.85$, $p>.05$
Ham-D	0.62 (1.06)	1.02 (1.34)	1.28 (1.91)	16.92 (5.27)	--
BDI	2.06 (2.67)	2.81 (4.02)	4.76 (5.09)	28.60 (7.89)	--
STAI trait	33.05 (7.56)	35.03 (11.5)	38.66 (9.30)	62.77 (8.04)	--
SHAPS	22.08 (5.36)	21.76 (4.68)	23.08 (5.44)	36.79 (5.44)	--
TEPS ant.	44.75 (7.00)	46.30 (7.91)	43.86 (6.50)	30.63 (8.41)	--
TEPS con.	35.85 (5.94)	37.59 (6.17)	36.92 (6.79)	26.23 (7.47)	--

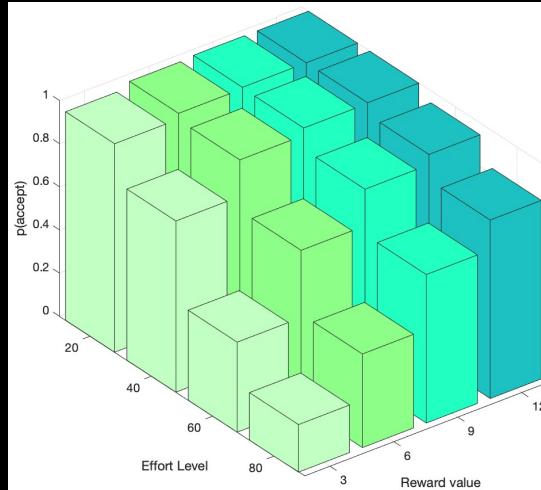
Behavioural results (all groups)

- N=194 (out of 202) analysed
- Excluded 8
 - N=2 calibration
 - N=5 clinical
 - N=1 outlier on several tests
- Significant effect of effort
 $F(1.735,329.722)=391.041, p<0.001$
- Significant effect of reward
 $F(1.614,306.680)=326.428, p<0.001$
- Significant effort x reward interaction
 $F(5.098,968.691)=90.547, p<0.001$
- Significant effect of group
 $F(3,190)=3.345, p<0.02$

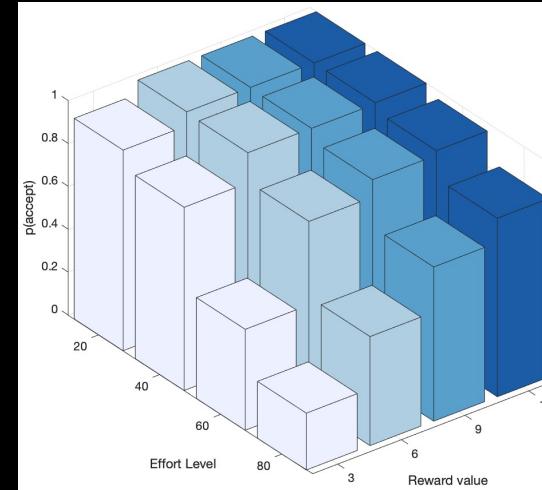


Behavioural results (by group)

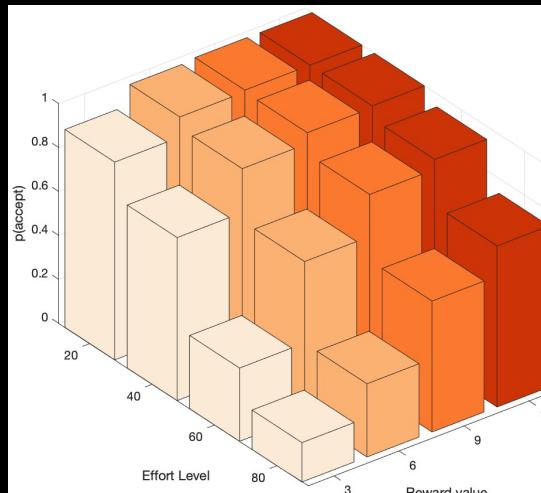
CTR



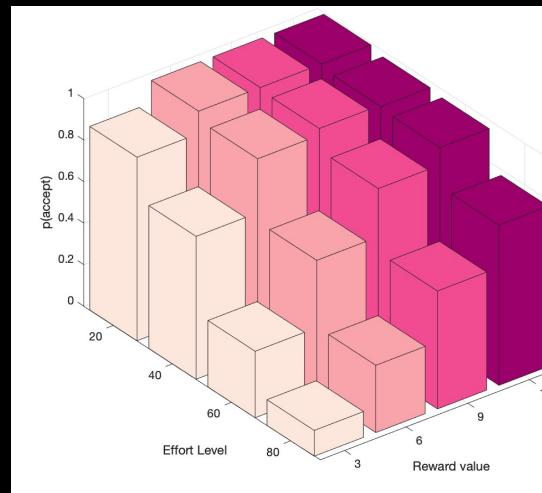
REL



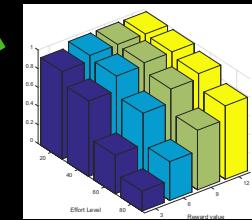
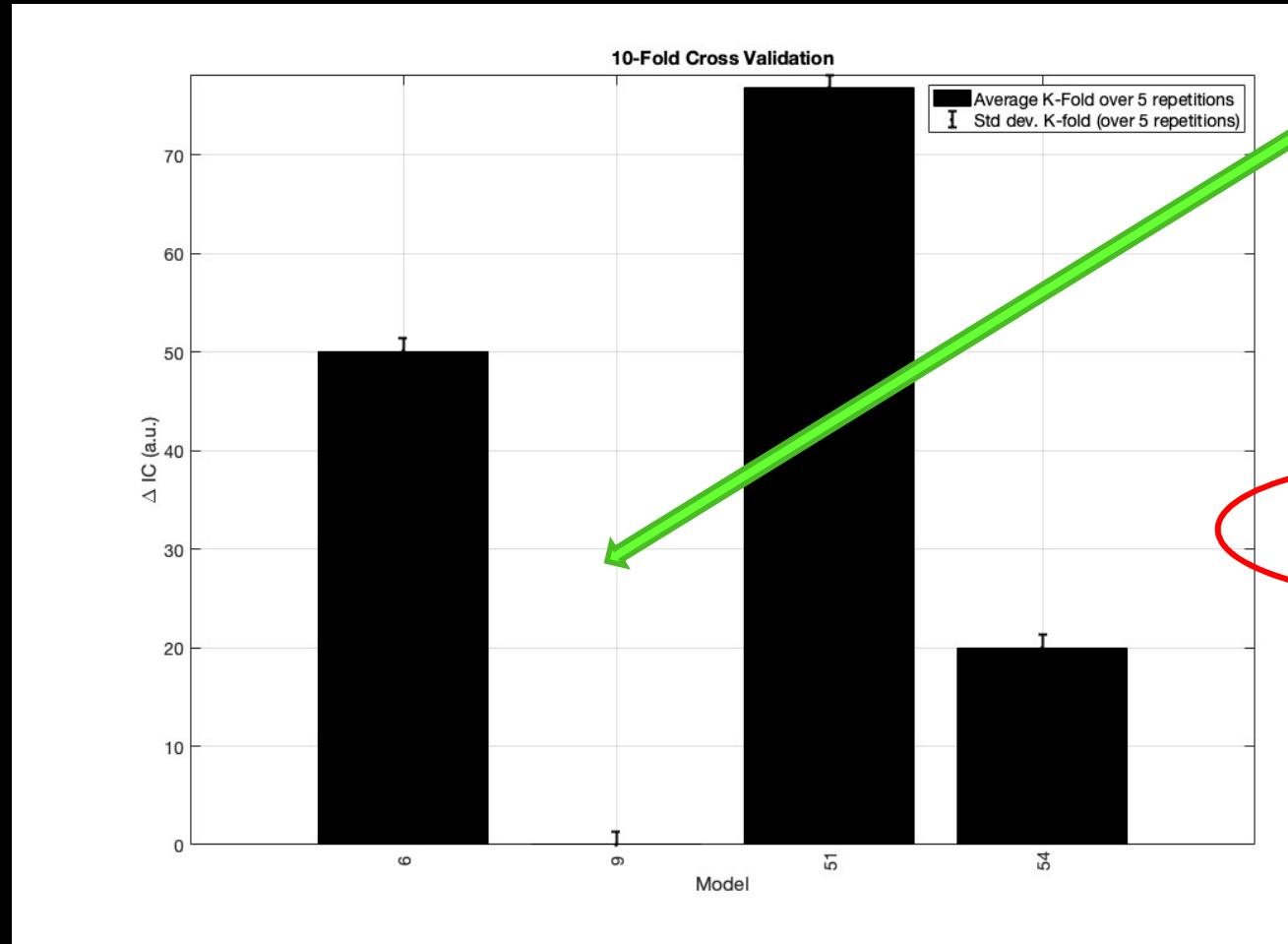
MDD



REM



Model comparison



Model 6 : Bias +
LinR + LinE

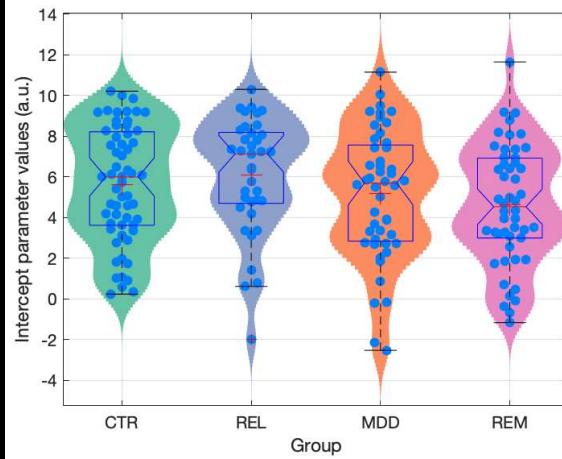
Model 9 : Bias +
LinR + LinE + E²

Model 51 : Bias +
LinR + LinE + Guess

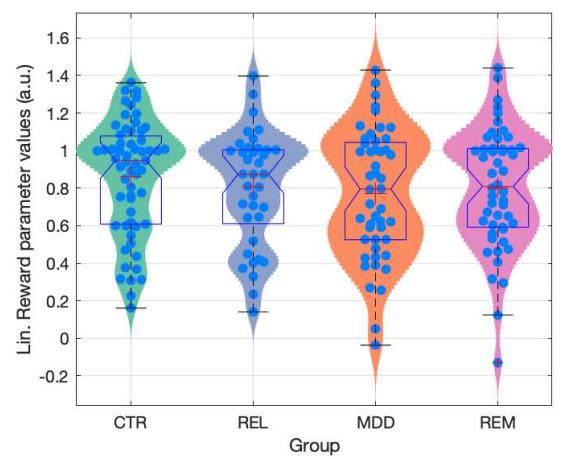
Model 54 : Bias +
LinR + LinE + E² +
Guess

Parameter estimates

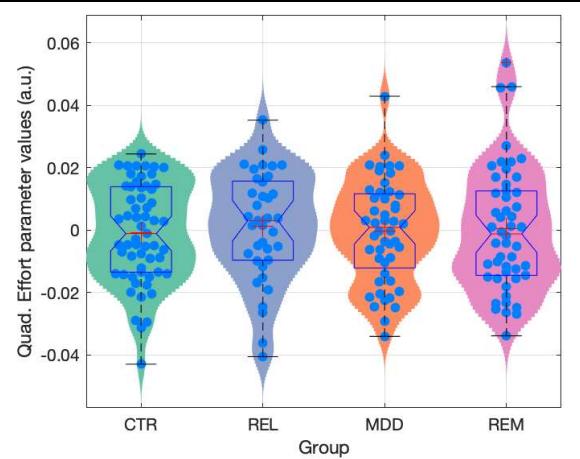
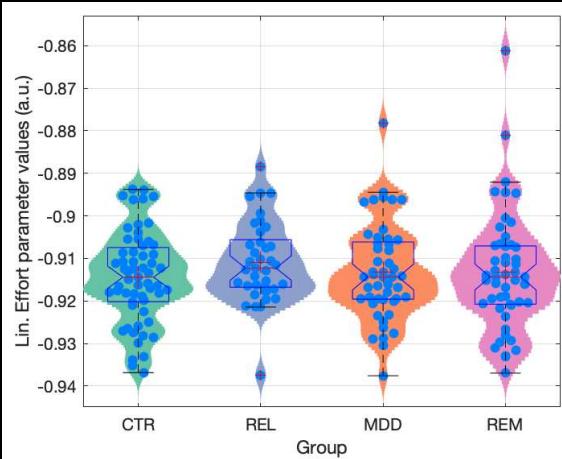
Bias



Reward



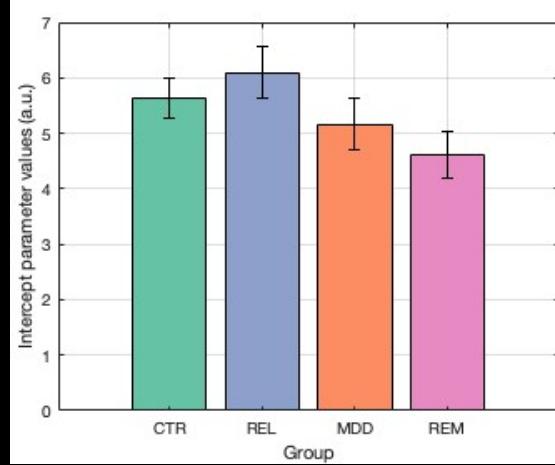
Effort



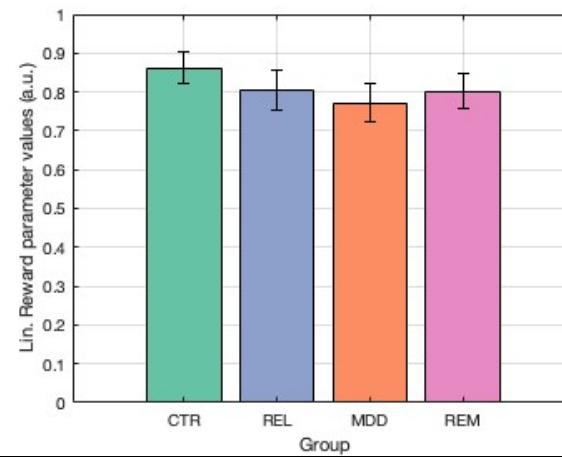
Parameter estimates

Bias*

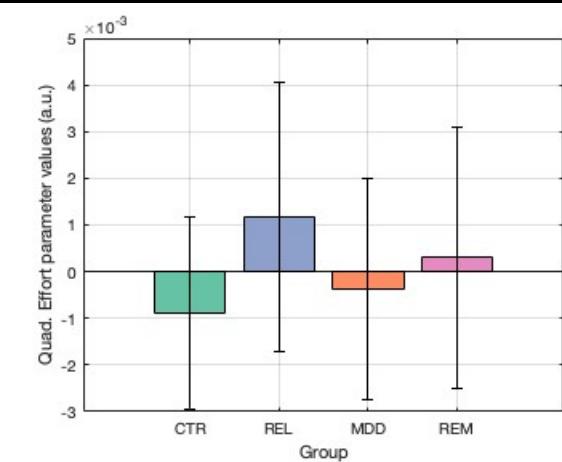
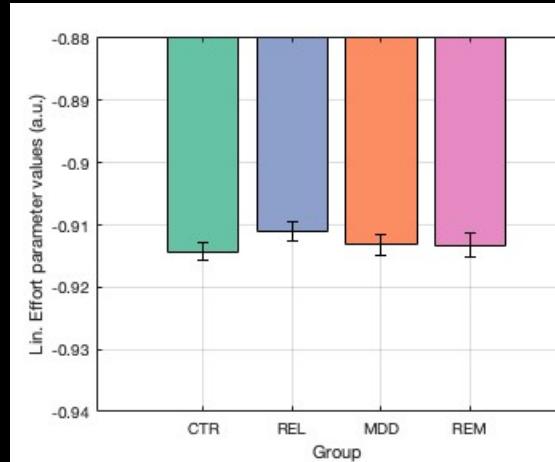
CTR+REL>
DEP+REM



Reward



Effort



L-Dopa study



Karel Kieslich

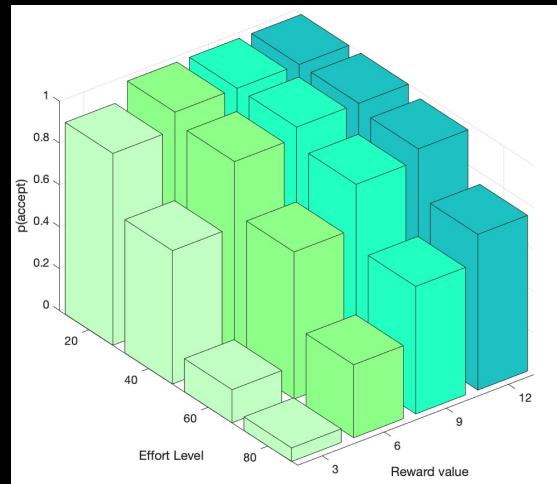


Chamith Halahakoon

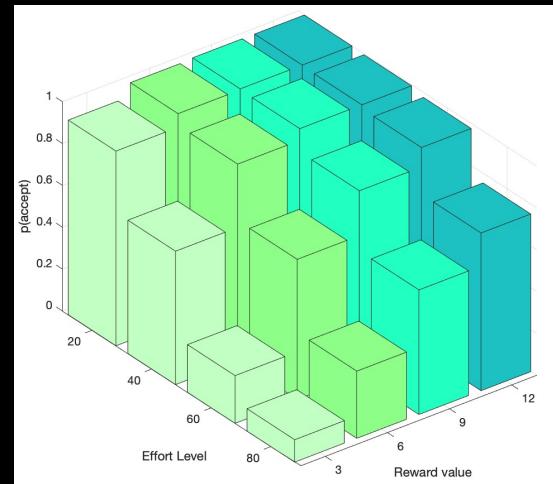
	CTR (n=43)	MDD (n=43)	Stats
Age	24.79 (6.25)	24.91 (4.85)	$F(1,84)=0.009, p>.05$
Gender (m/f)	25/18	27/16	$X^2(1)=0.194, p>.05$
Weight	65.35 (12.09)	70.74 (21.05)	$F(1,84)=2.121, p>.05$
IQ (Ravens)	8.97 (2.31)	8.37 (2.34)	$F(1,83)=1.433, p>.05$
Digit Span (Fwd.)	9.14 (1.99)	9.19 (1.79)	$F(1,83)=0.015, p>.05$
Digit Span (Bkwd.)	7.51 (1.76)	6.71 (2.09)	$F(1,83)=3.601, p>.05$
Ham-D	0.41 (0.76)	20.86 (6.22)	--
BDI	1.44 (2.63)	29.45 (8.19)	--
STAI trait	30.71 (7.15)	60.30 (11.55)	--
SHAPS	24.47 (9.77)	36.28 (6.63)	--
TEPS ant.	46.23 (5.72)	30.16 (7.82)	--
TEPS con.	38.56 (6.59)	26.35 (8.71)	--

L-Dopa: Behavioural results

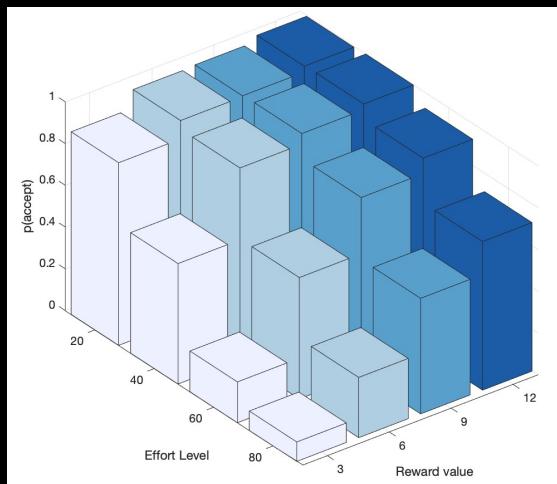
PLA



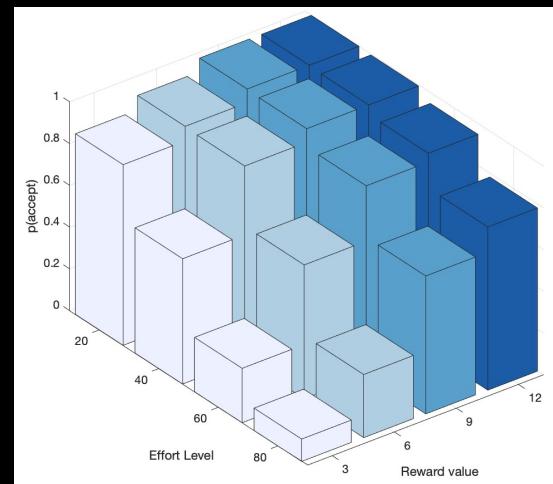
DOPA



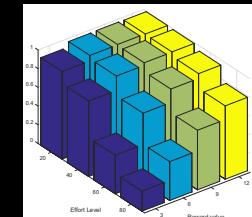
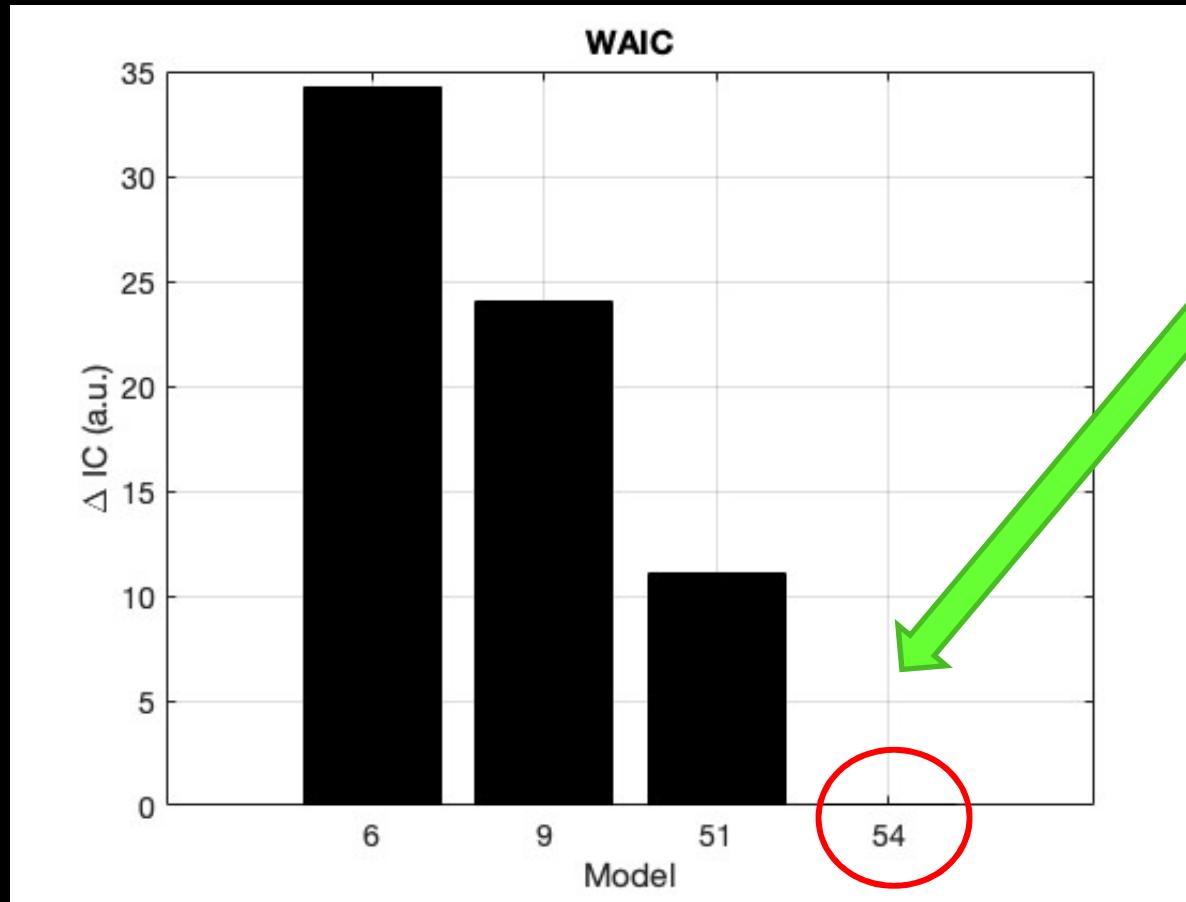
CTR



MDD



L-Dopa: Model comparison



Model 6 : Bias + LinR
+ LinE

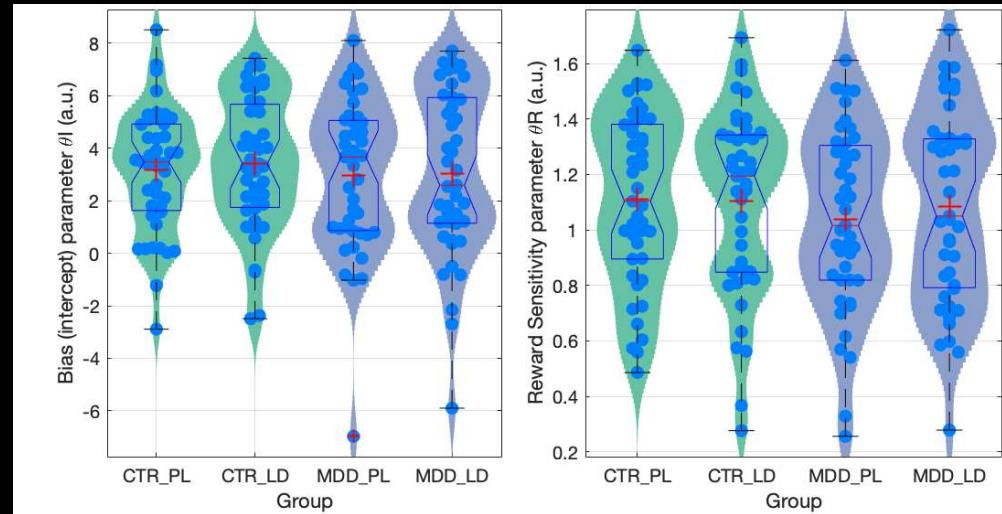
Model 9 : Bias + LinR
+ LinE + E²

Model 51 : Bias + LinR
+ LinE + Guess

Model 54 : Bias + LinR
+ LinE + E² + Guess

L-Dopa: Parameter estimates

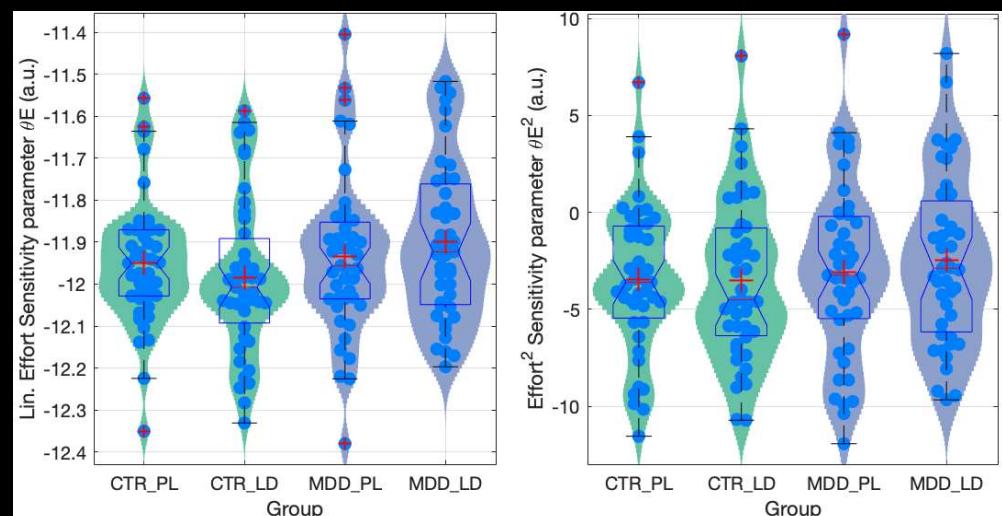
Bias



PL = Placebo
LD = L-Dopa

Reward

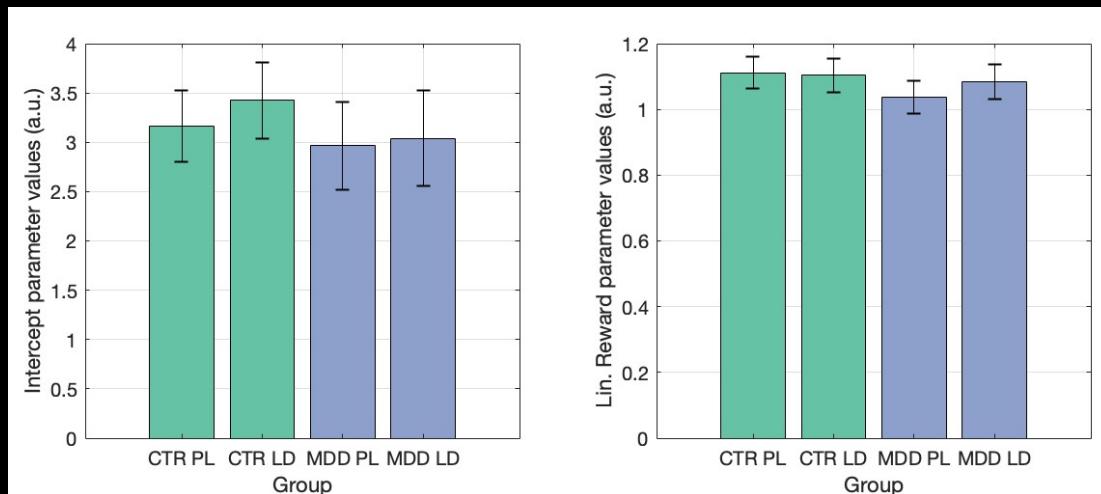
Effort



Effort²

L-Dopa: Parameter estimates

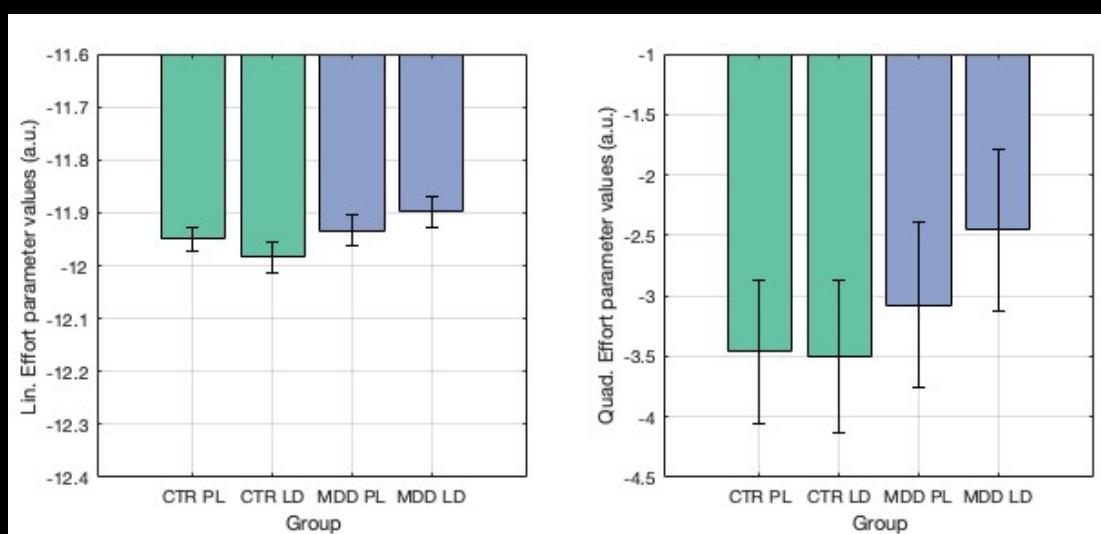
Bias



PL = Placebo
LD = L-Dopa

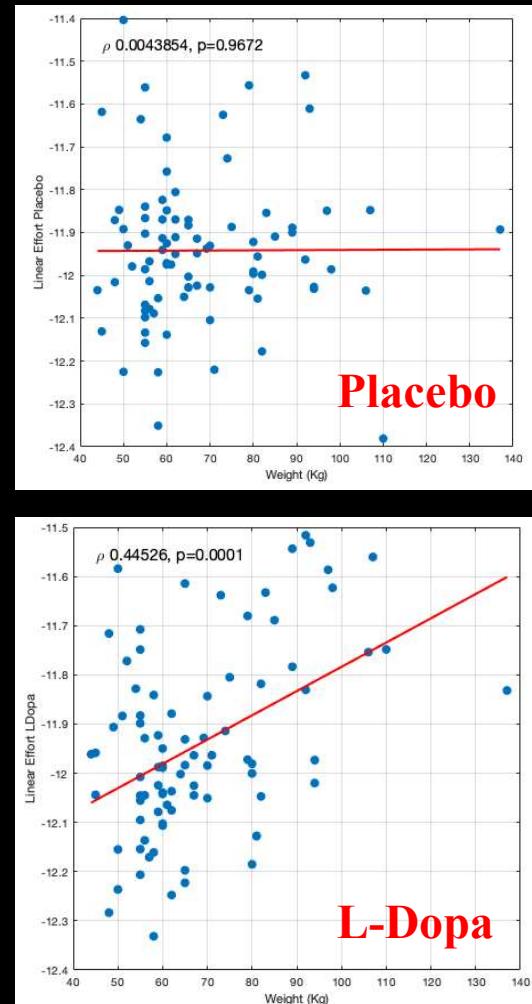
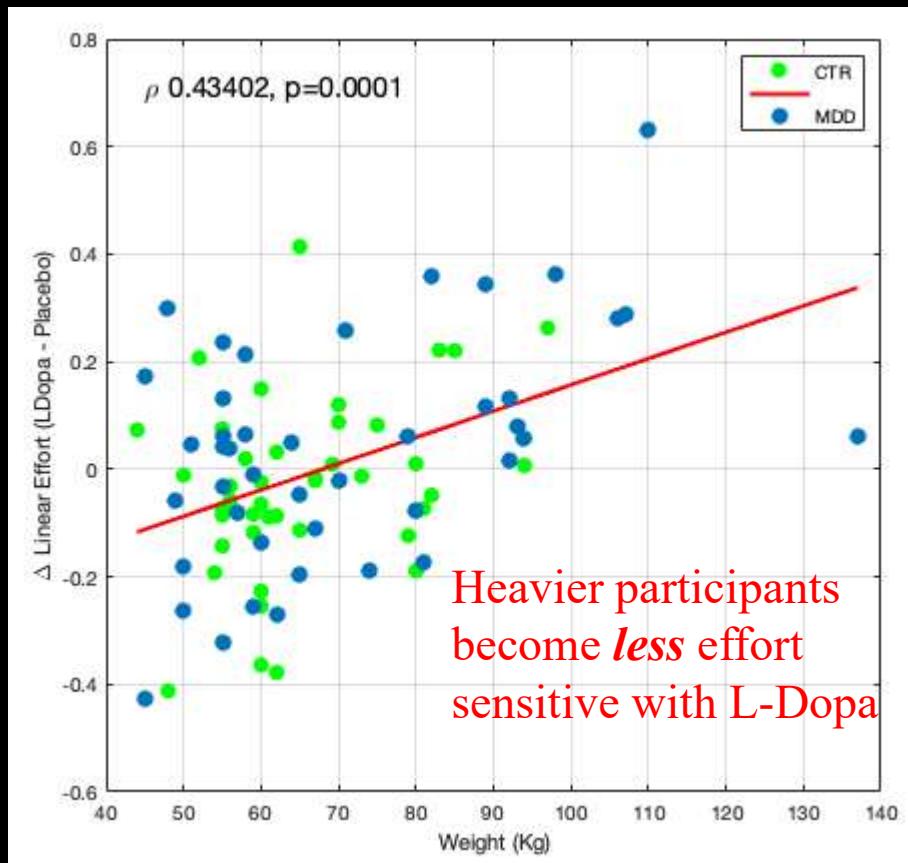
Reward

Effort



Effort^{^2}

L-Dopa: Weight dependency



Conclusions

- Depression is associated with *lower willingness to engage in effort, independent of reward or effort level*
- Unclear whether disrupted effort processing is a *risk-factor for or consequence* of depression
- Symptoms reveal a more nuanced picture
 - Mood disturbance associated with low *reward sensitivity*
 - Anhedonia associated with high *effort sensitivity*
 - However this was not consistent across studies
- L-Dopa did not appear to affect reward sensitivity, whereas it altered *effort sensitivity in a weight-dependent fashion*