

The computational psychiatry of major depressive disorder

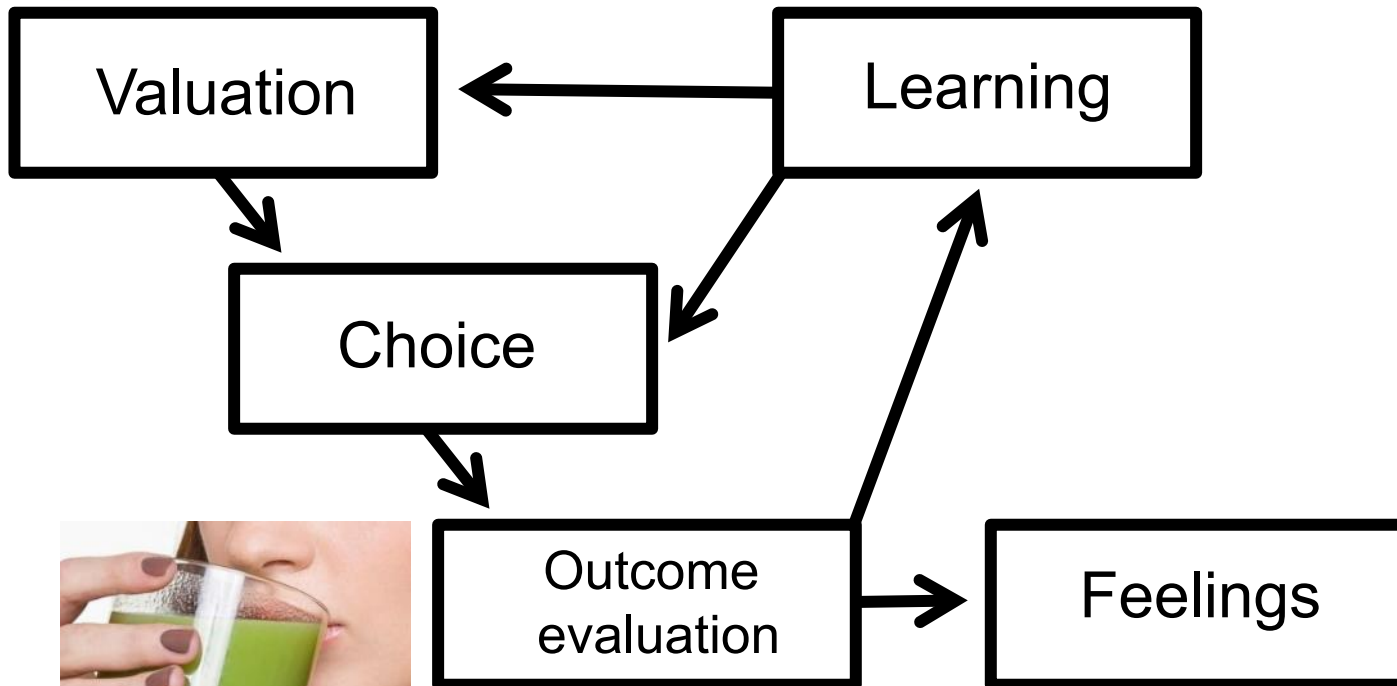
Robb Rutledge

MRC Career Development Fellow

Max Planck UCL Centre for Computational Psychiatry and
Ageing Research

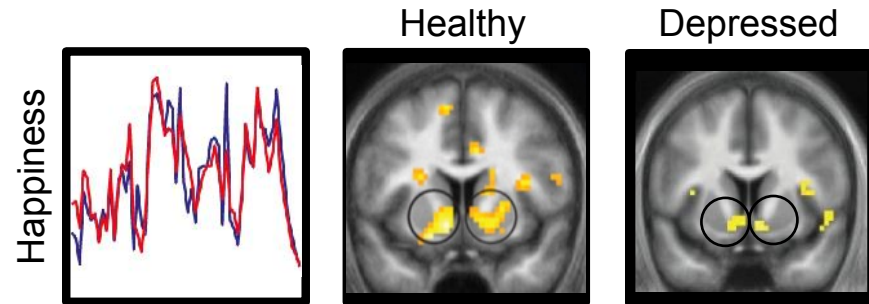
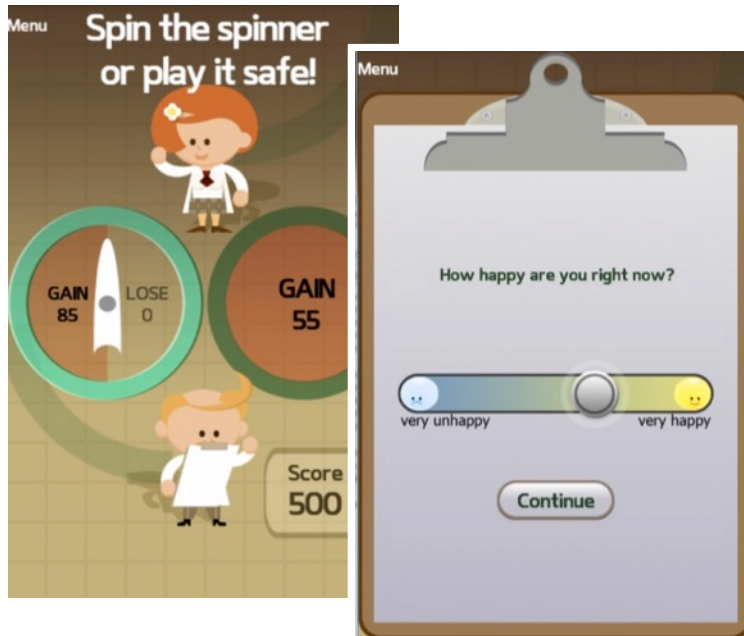
Symposium and Advanced Course on Computational
Psychiatry and Ageing Research
Ringberg Castle
25 September 2018

How does mood relate to behaviour?



Rutledge et al. (2014) PNAS
Rutledge et al. (2015) J Neurosci
Rutledge et al. (2016) Nature Comm
Rutledge et al. (2017) JAMA Psychiatry

Does depression affect mood and behaviour?



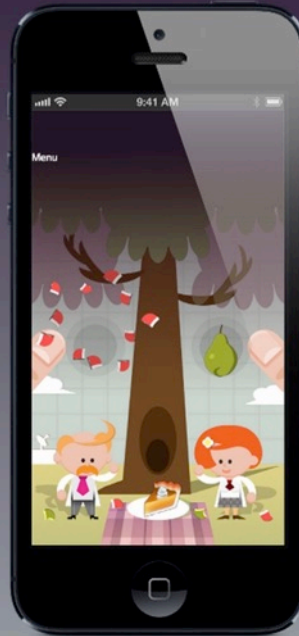
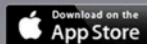
$$Happiness(t) = w_0 + w_1 \sum_{j=1}^t \gamma^{t-j} CR_j + w_2 \sum_{j=1}^t \gamma^{t-j} EV_j + w_3 \sum_{j=1}^t \gamma^{t-j} RPE_j$$

↑
Certain Reward
↑
Expected Value
↑
Reward Prediction Error
(reward – expectation)

The Great Brain Experiment

Be part of a unique scientific experiment by playing games on your phone.

Test your memory, your impulsivity, your attention and decision making. Learn about the neuroscience of every day life.



www.thegreatbrainexperiment.com

Core team

Robb Rutledge

Peter Zeidman

Peter Smittenaar

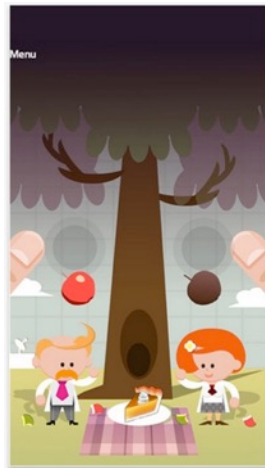
Harriet Brown

Rick Adams

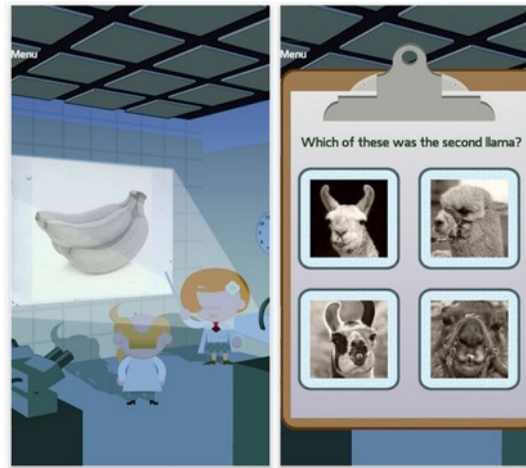
working memory



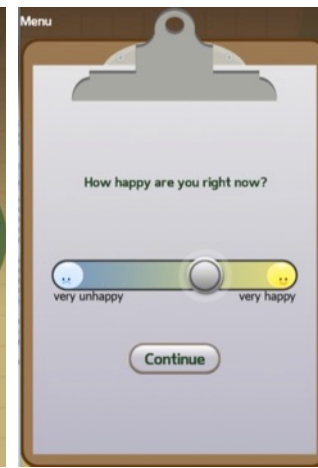
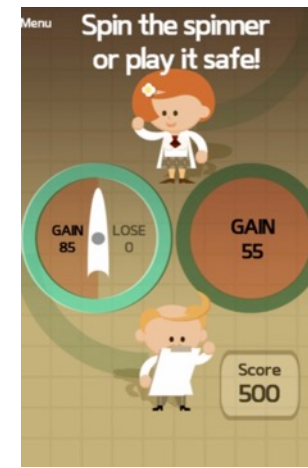
impulsivity



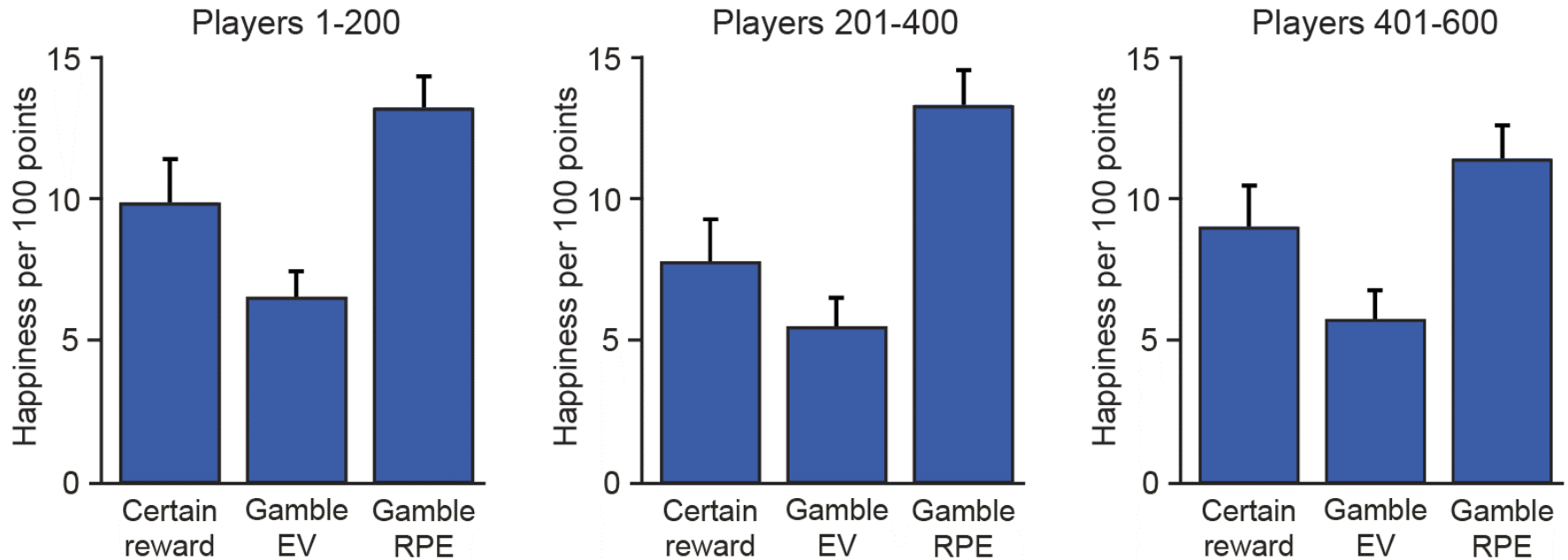
attentional blink



decisions and happiness



The Great Brain Experiment



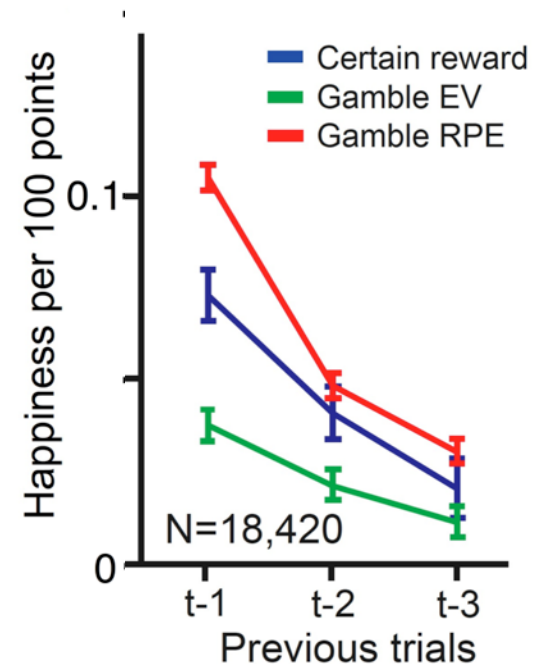
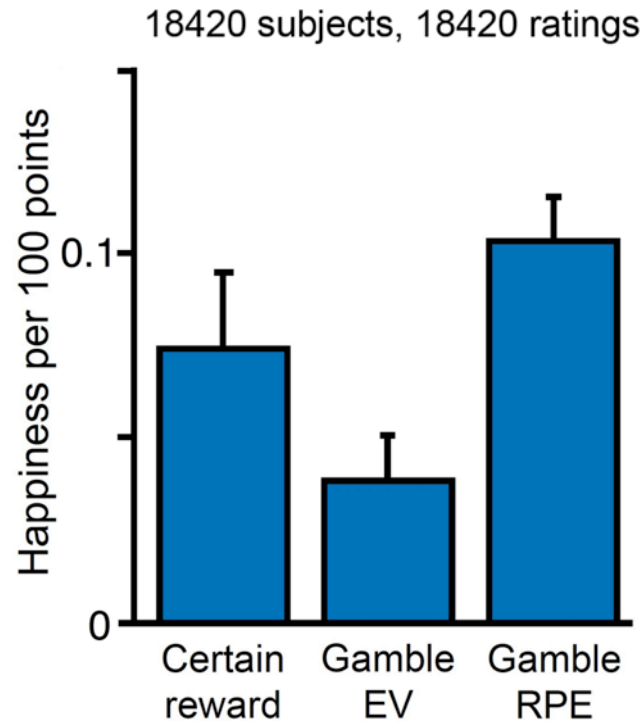
$$Happiness(t) = w_0 + w_1 \sum_{j=1}^t \gamma^{t-j} CR_j + w_2 \sum_{j=1}^t \gamma^{t-j} EV_j + w_3 \sum_{j=1}^t \gamma^{t-j} RPE_j$$

Rutledge, Skandali, Dayan & Dolan (2014) PNAS

The Great Brain Experiment

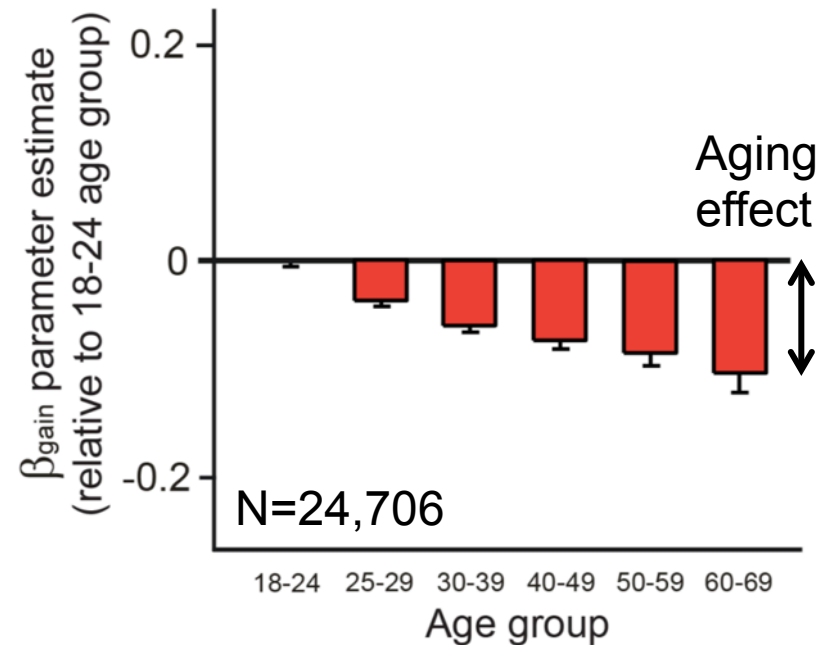
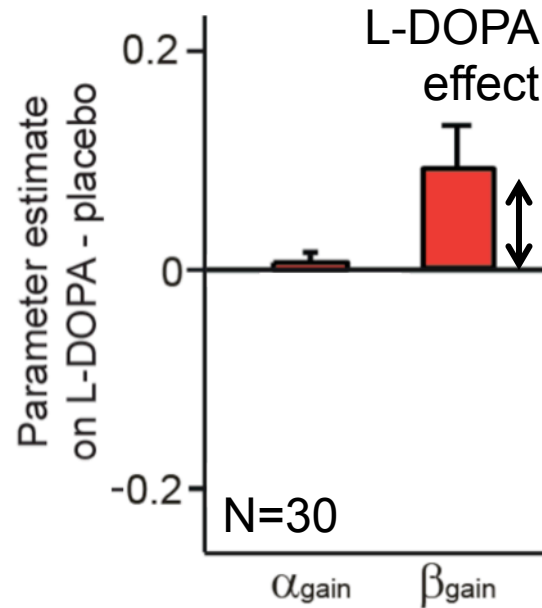
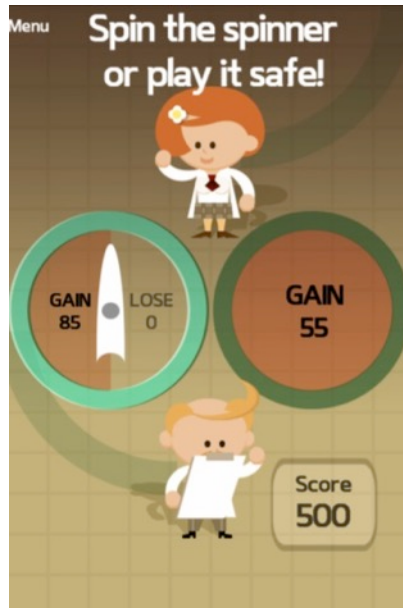


1 happiness rating
per subject
2-3 trials per subject



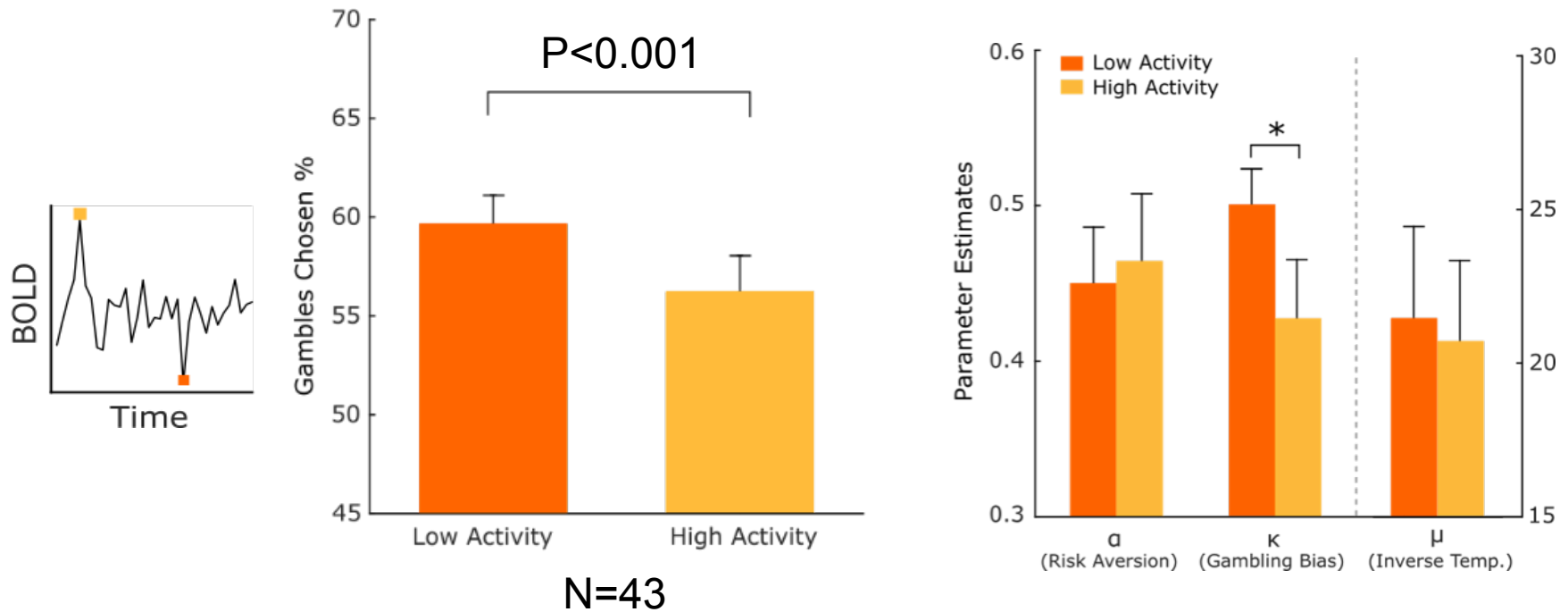
$$Happiness(t) = w_0 + w_1 \sum_{j=1}^t \gamma^{t-j} CR_j + w_2 \sum_{j=1}^t \gamma^{t-j} EV_j + w_3 \sum_{j=1}^t \gamma^{t-j} RPE_j$$

L-DOPA and aging have opposite effects on Pavlovian approach behaviour



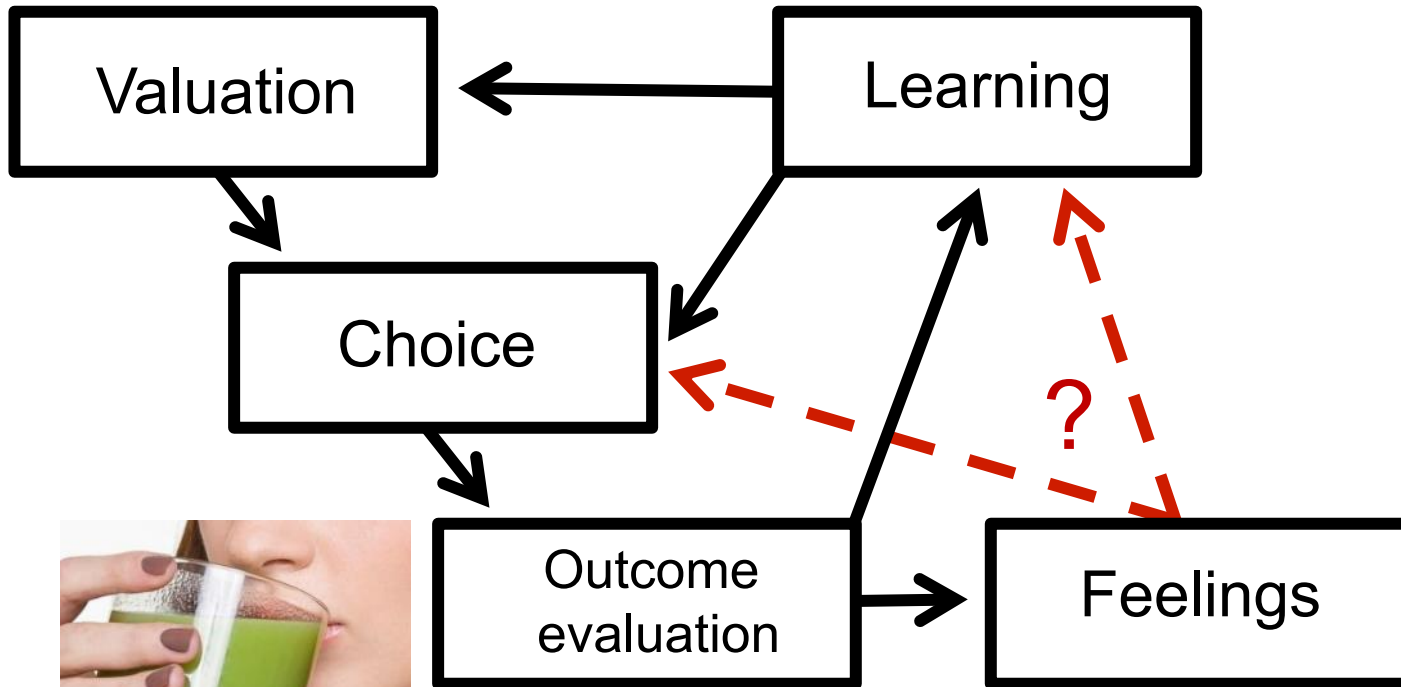
Rutledge et al. (2015) *J Neurosci*
Rutledge et al. (2016) *Current Biology*

Risk taking increases when endogenous dopaminergic midbrain activity is low



Chew, Hauser* ... Dolan & Rutledge (Submitted)*

How does mood relate to behaviour?



Rutledge et al. (2014) PNAS
Rutledge et al. (2015) J Neurosci
Rutledge et al. (2016) Nature Comm
Rutledge et al. (2017) JAMA Psychiatry

Does inequality impact happiness?

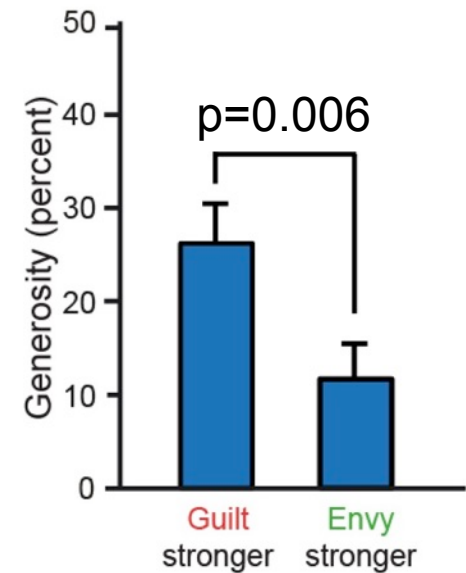
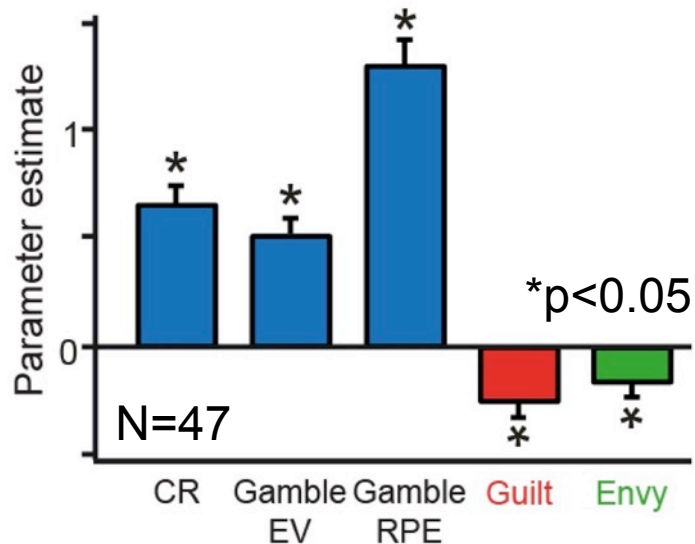


$$\text{Happiness}(t) = w_0 + w_1 \sum_{j=1}^t \gamma^{t-j} \text{CR}_j + w_2 \sum_{j=1}^t \gamma^{t-j} \text{EV}_j + w_3 \sum_{j=1}^t \gamma^{t-j} \text{RPE}_j$$

$$+ w_4 \sum_{j=1}^t \gamma^{t-j} \max(\text{R}_j - \text{O}_j, 0) + w_5 \sum_{j=1}^t \gamma^{t-j} \max(\text{O}_j - \text{R}_j, 0)$$

Guilt

Envy



Rutledge*, de Berker*, et al. (2016) Nature Comm

Understanding depression

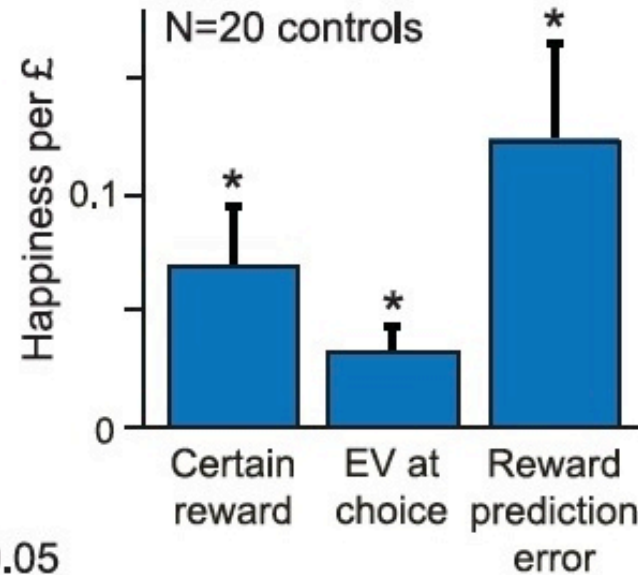
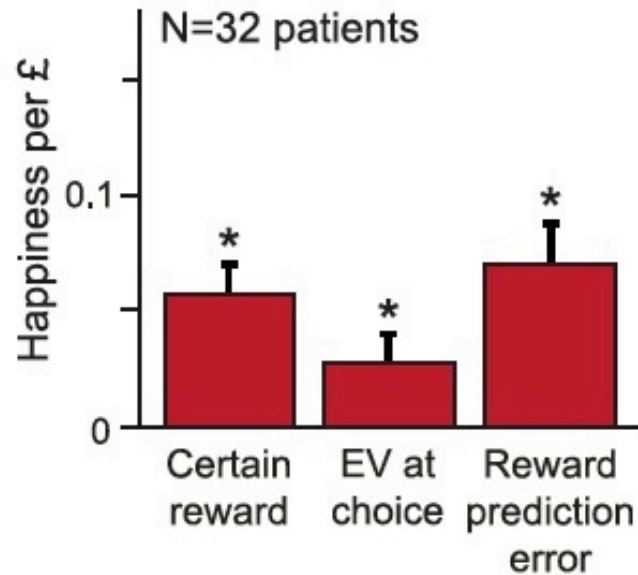


350 million worldwide suffer from depression

Major clinical symptoms

- 1) Depressed mood as indicated by subjective report
- 2) Diminished interest or pleasure as indicated by subjective report

Understanding depression



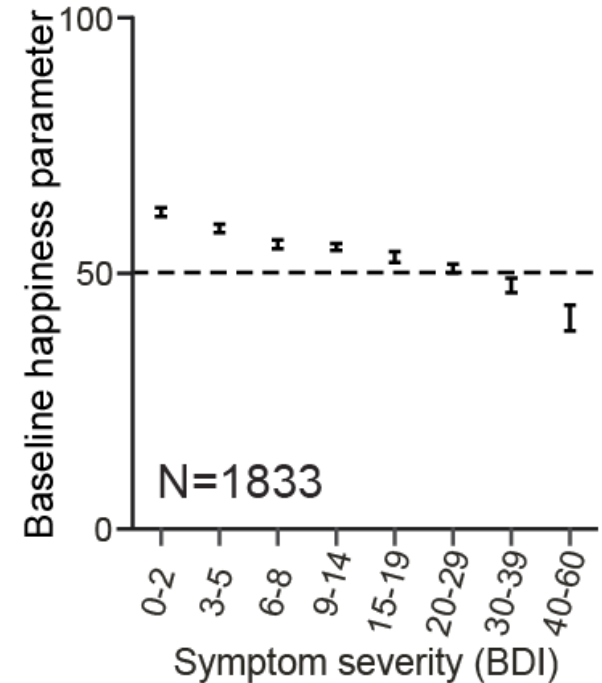
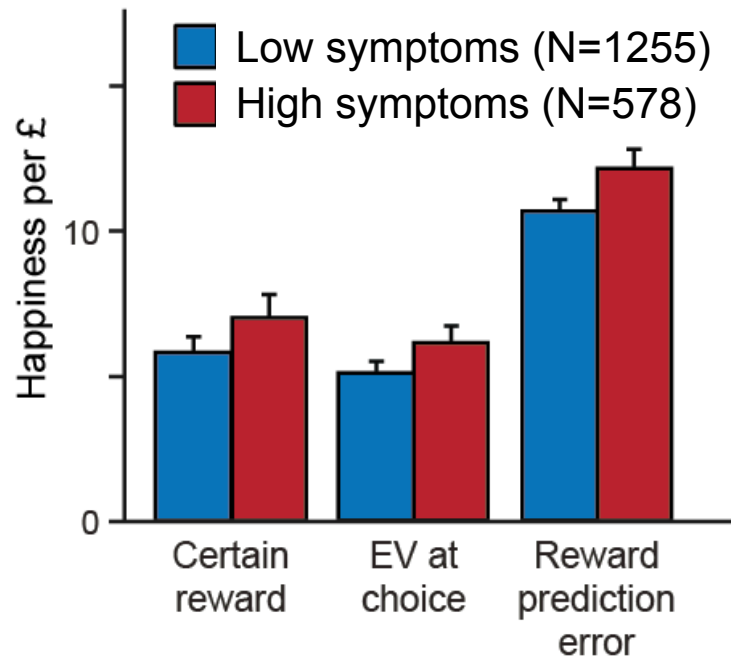
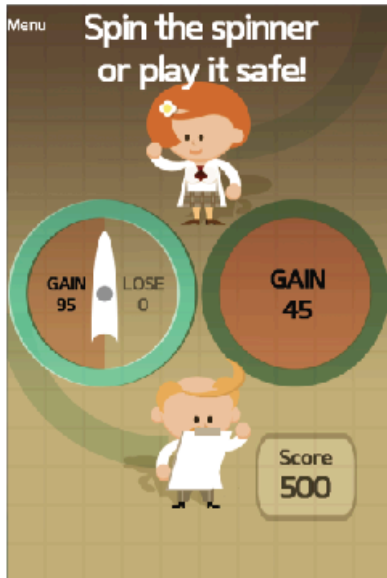
$$Happiness(t) = w_0 + w_1 \sum_{j=1}^t \gamma^{t-j} CR_j + w_2 \sum_{j=1}^t \gamma^{t-j} EV_j + w_3 \sum_{j=1}^t \gamma^{t-j} RPE_j$$

↑
↑
↑

Certain reward
 Expected value
Reward prediction error (reward – expectation)

Rutledge et al. (2017) JAMA Psychiatry

Depression does not reduce RPE mood impacts



$$Happiness(t) = \textcircled{w_0} + w_1 \sum_{j=1}^t \gamma^{t-j} CR_j + w_2 \sum_{j=1}^t \gamma^{t-j} EV_j + w_3 \sum_{j=1}^t \gamma^{t-j} RPE_j$$

Smartphones for longitudinal clinical data



Control



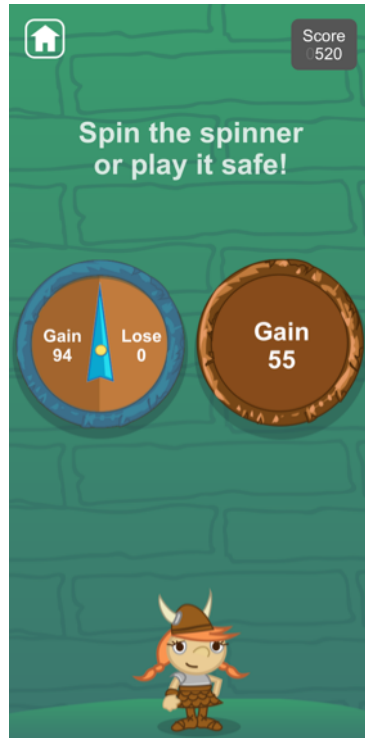
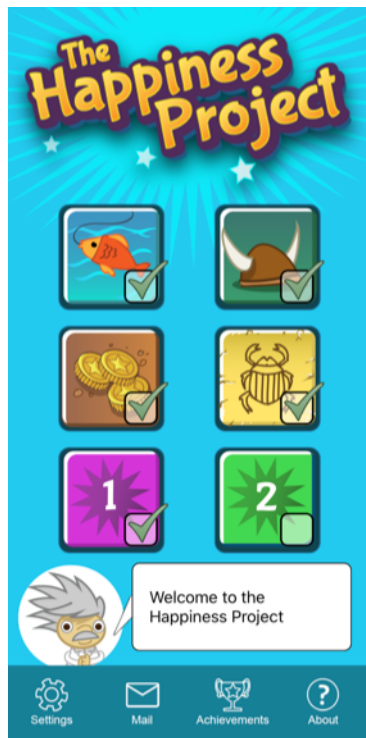
Future bias



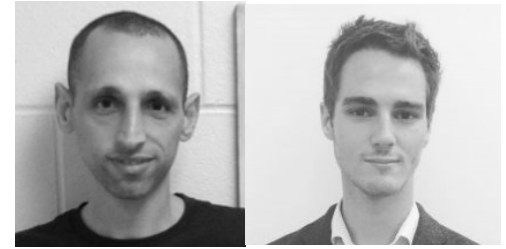
Learning



Effort



Mood as reward momentum

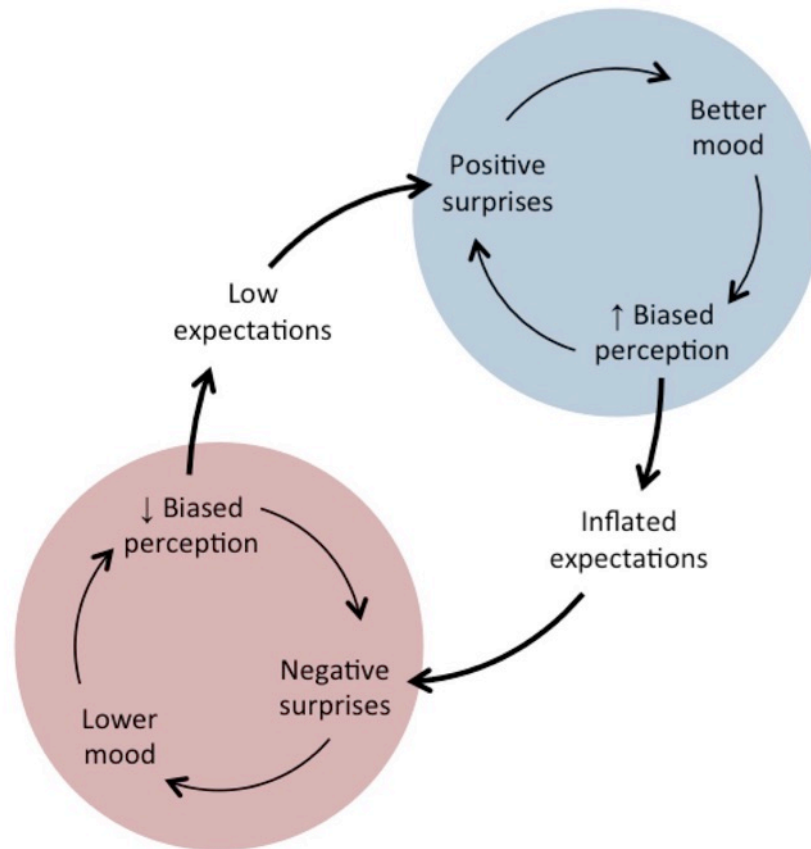


Mood represents whether an environment is getting better

Mood biases reward perception, speeding up learning

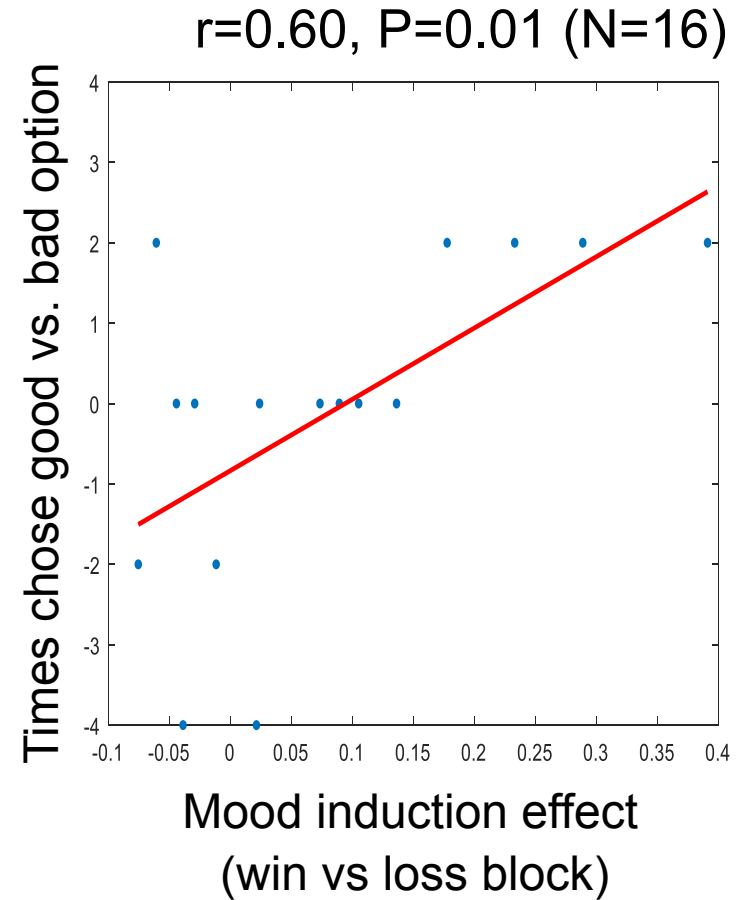
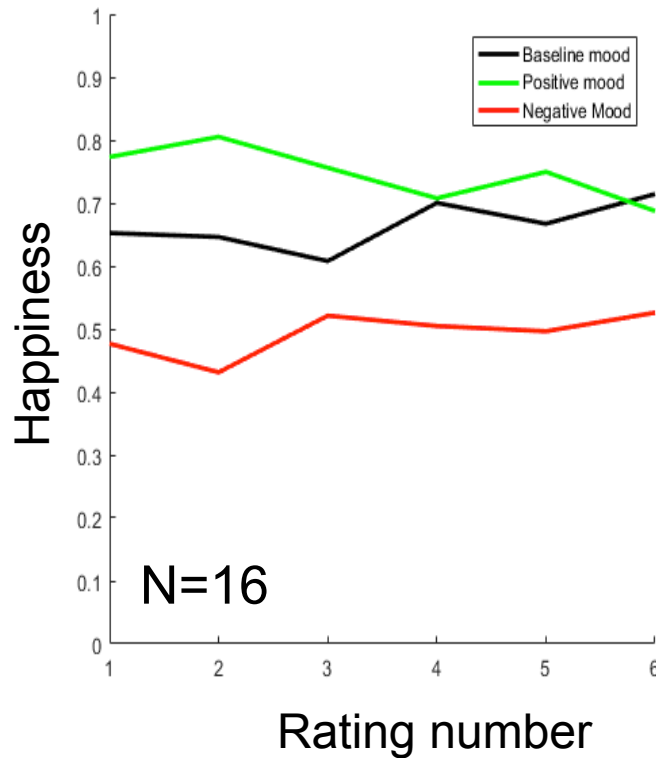
This can lead to inflated expectations

Positive feedback cycles could contribute to mood disorders like bipolar disorder



*Mason, Eldar & Rutledge (2017) JAMA Psychiatry
Eldar*, Rutledge*, Dolan & Niv (2016) TICS*

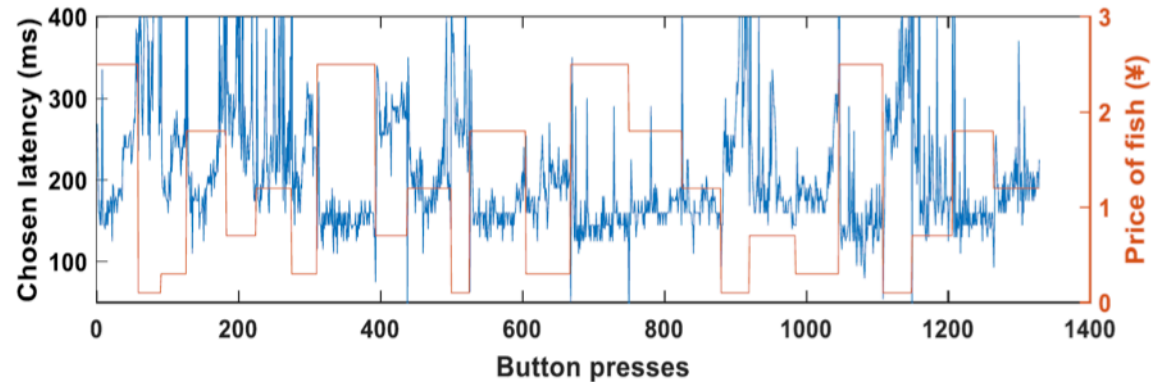
Mood as reward momentum



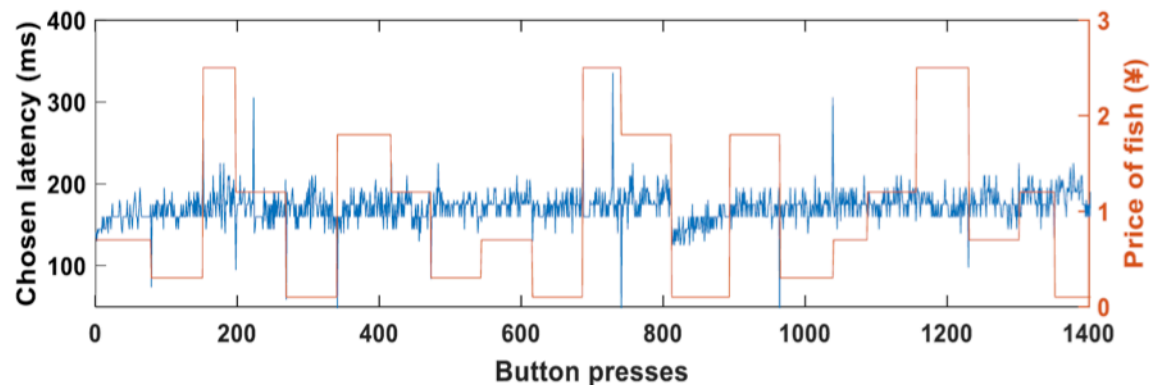
Reward rates predict action latencies



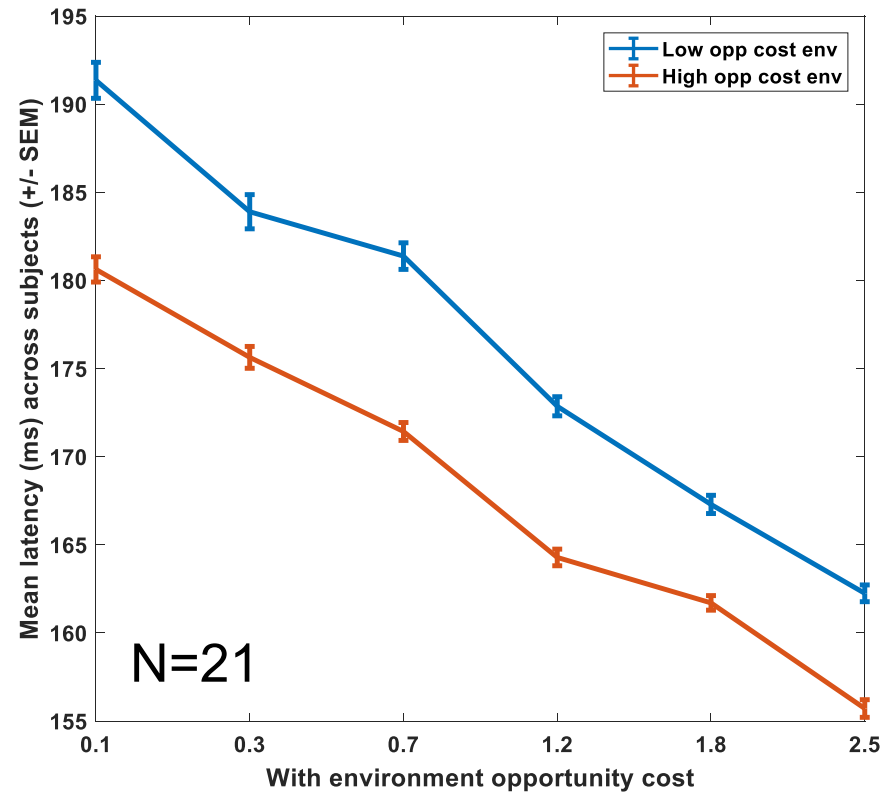
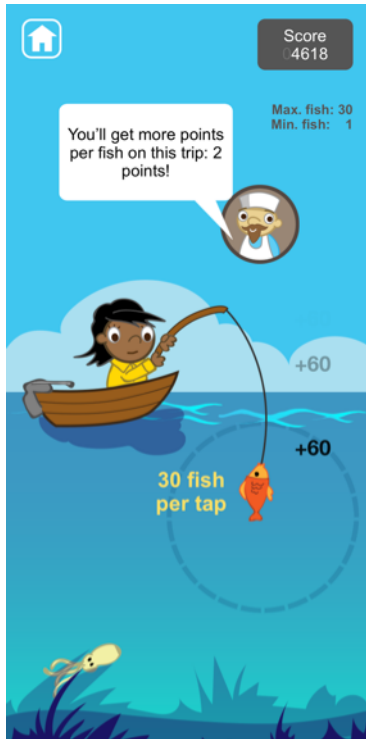
High apathy participant (bAMI = 21)



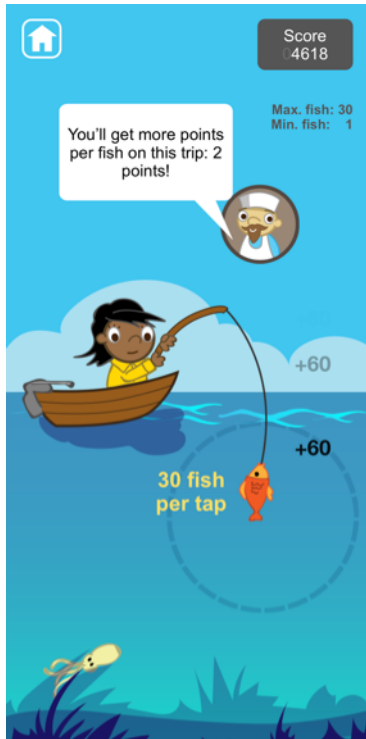
Low apathy participant (bAMI = 5)



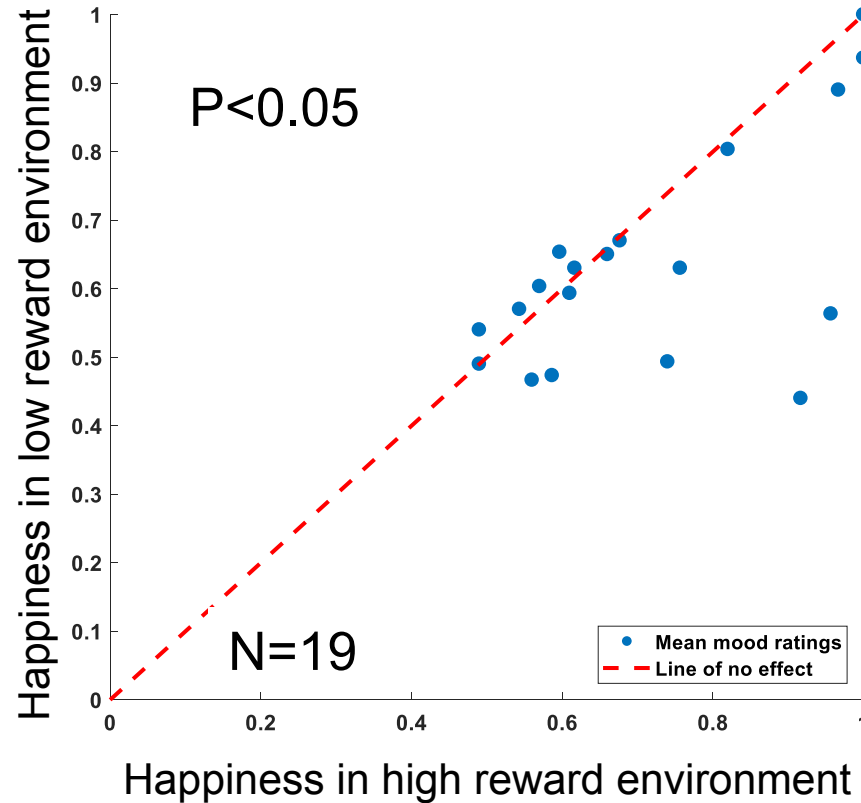
Reward rates predict action latencies



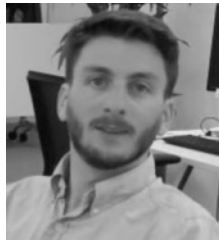
Reward rates predict action latencies



Smartphone data



Smartphones for longitudinal clinical data



Control



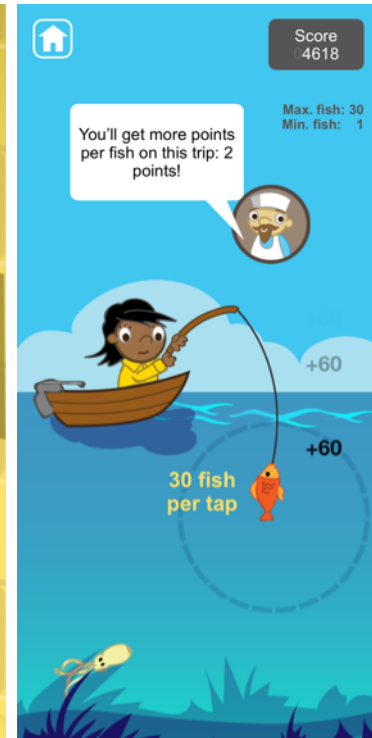
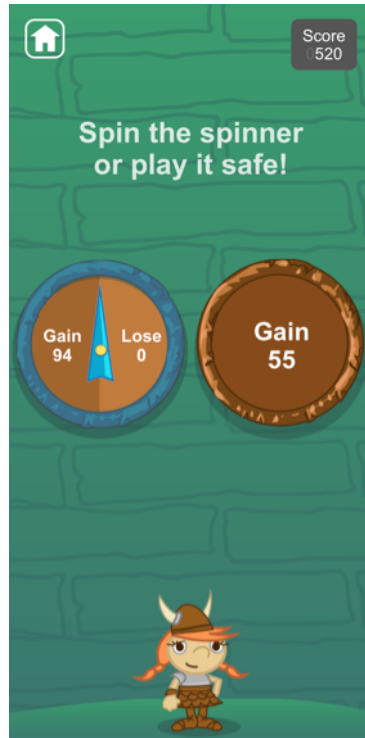
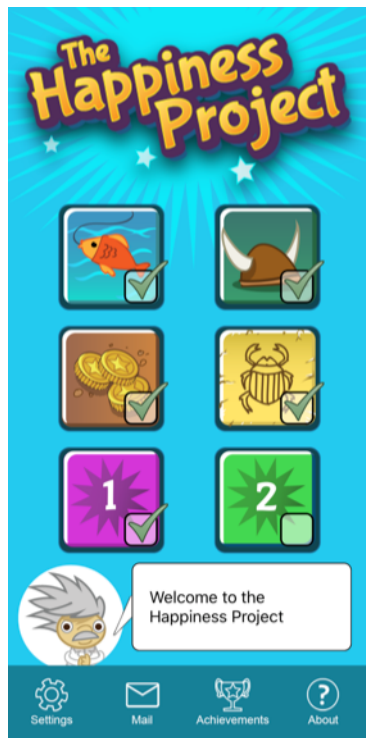
Future bias



Learning

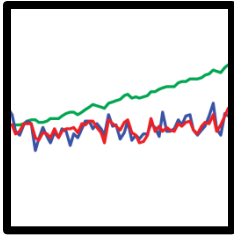


Effort



How do **antidepressants** affect mood and behaviour?

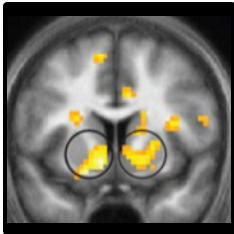
Can we **predict** when symptoms will **worsen**?



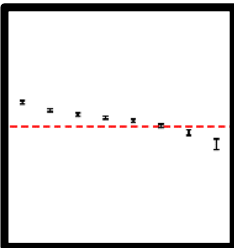
A computational model explains happiness from past expectations and reward prediction errors



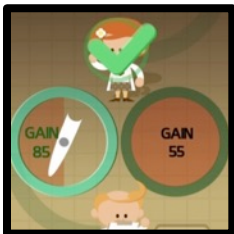
MAX-PLANCK-GESELLSCHAFT



Striatal activity predicts future happiness ratings and boosting dopamine increases happiness for small rewards



Depression reduces baseline happiness parameters but does not affect the impact of rewards on happiness



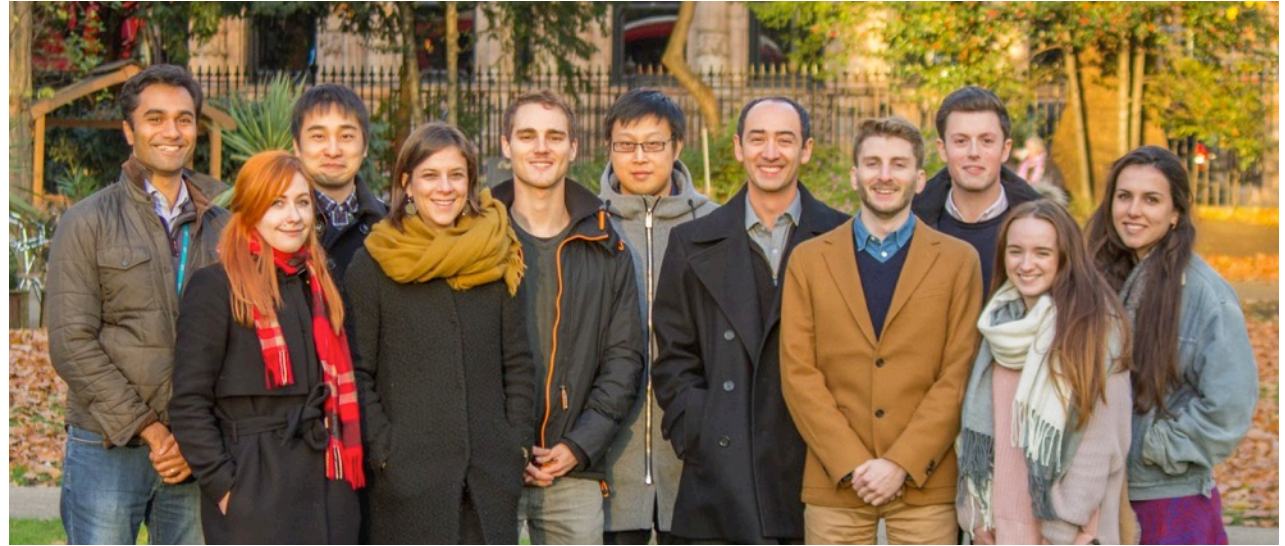
New tasks and models can be used for remote longitudinal testing with smartphones in psychiatric patients

Thank you

Ray Dolan
Peter Dayan

Rutledge lab

Rachel Bedder
Archy de Berker
Bastien Blain
Benjamin Chew
Liam Mason
Akshay Nair
Ritwik Niyogi
Yuki Shimura
Nikolina Skandali
Matilde Vaghi



MAX-PLANCK-GESELLSCHAFT



Web: rutledgelab.org
Twitter: @robbrutledge
Email: robb.rutledge@ucl.ac.uk

Supported by
wellcometrust