The role of dopamine in learning about effort

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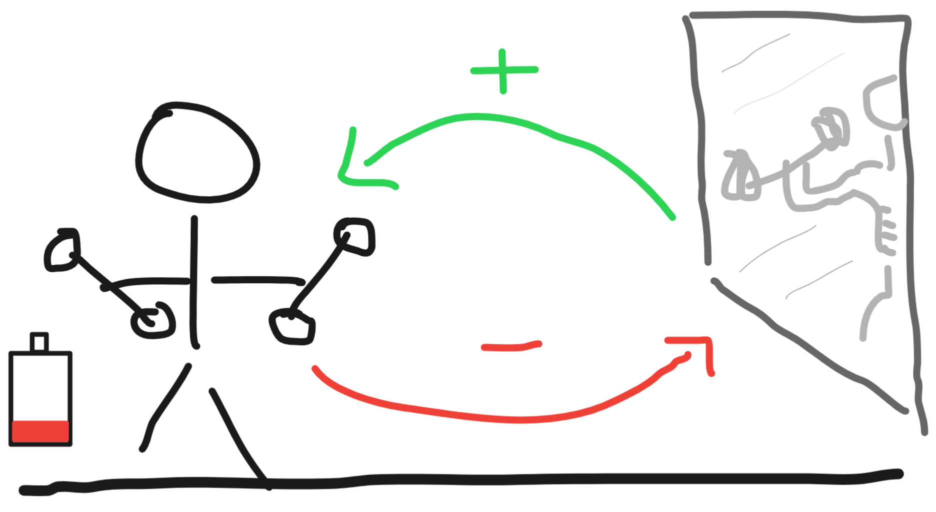
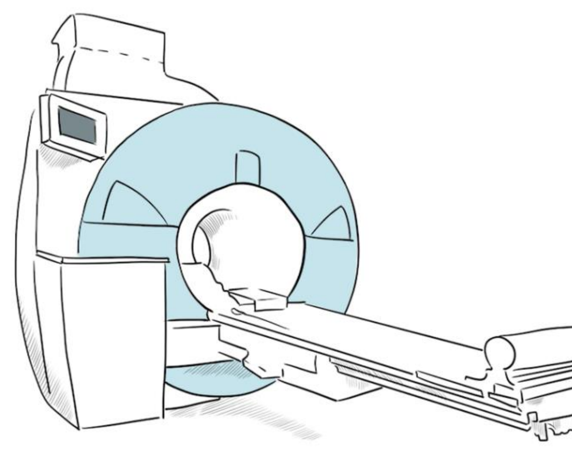
L-dopa increased effort after failure (not reward)

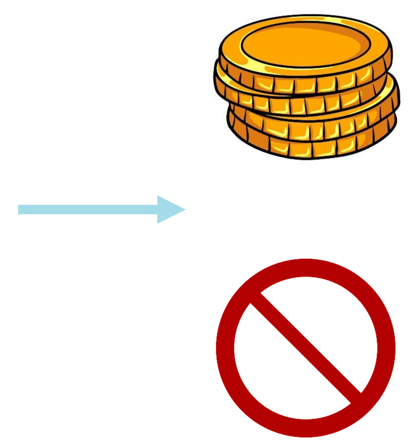
Effort (like rewards) must be learned



"Gosh, this was a breeze"

Double-blind placebo-controlled fMRI study of effort learning

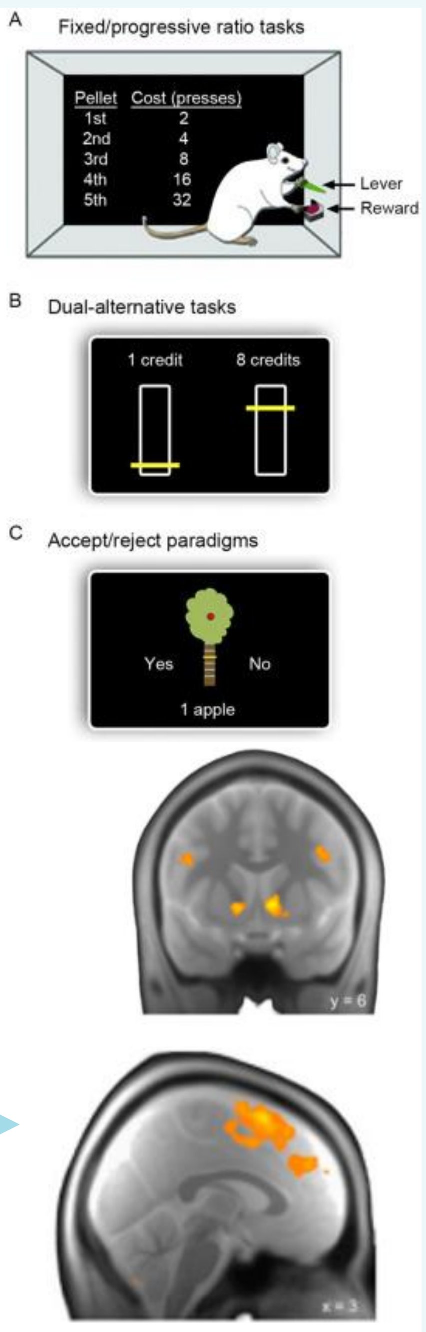




L-dopa invigorated response after failure

Background

- Dopamine enhances willingness to exert effort for reward (Chong et al., 2015; Bogdanov et al., 2022) and response vigour (Niv et al., 2007; Zenon et al., 2016)
- Tetrabenazine (VMAT2 inhibitor) depletes dopamine, causes fatigue/apathy in humans (Frank, 2009) and reduces work for reward in animals (Salamone, *unpublished*)
- Reward learning is implemented with prediction-error signals which are encoded by dopaminergic neurons (Glimcher, 2011)
- Previous work (with this task) found dissociable mesolimbic and mesocortical learning (PE) signals during reward-effort learning which strongly implicates dopamine (Hauser et al., 2017)
- How does increased dopamine transmission (L-dopa) impact human learning about effort?



Methods

- 60 healthy men included (mean age: 25.6 ± 0.88)
- Double-blind placebo-controlled between-subjects study
- Task-based fMRI and structural imaging (not included here)
- Bespoke reward-effort learning task (Hauser et al., 2017, PNAS)

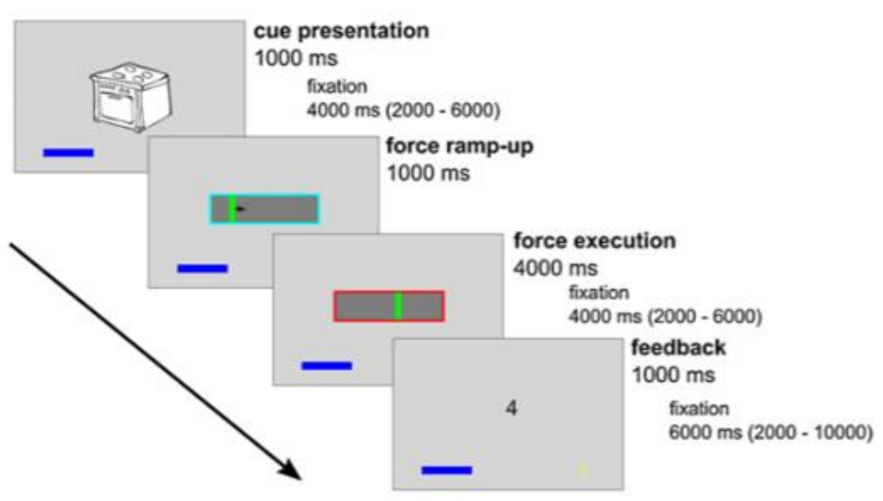


Fig 1. Participants learn fluctuating reward and effort contingencies by exerting effort and receiving feedback.

- 4 blocks of 40 trials
- 2 stimuli with fluctuating reward and effort
- Effort calibrated to participant maximum voluntary contraction during practice (and updated after blocks)
- reward and effort decorrelated (mean *rho*=0.01, *p* = 0.55)

Fig 2. Example participant attempting to approximate force (orange) minimally greater than the required threshold (green).

Successful blinding: medication guesses not better than chance (X^2 = 1.67, *p* = 0.24)

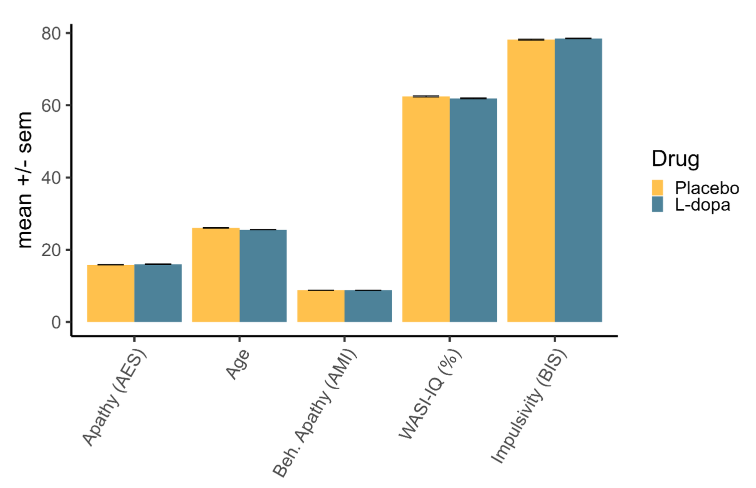
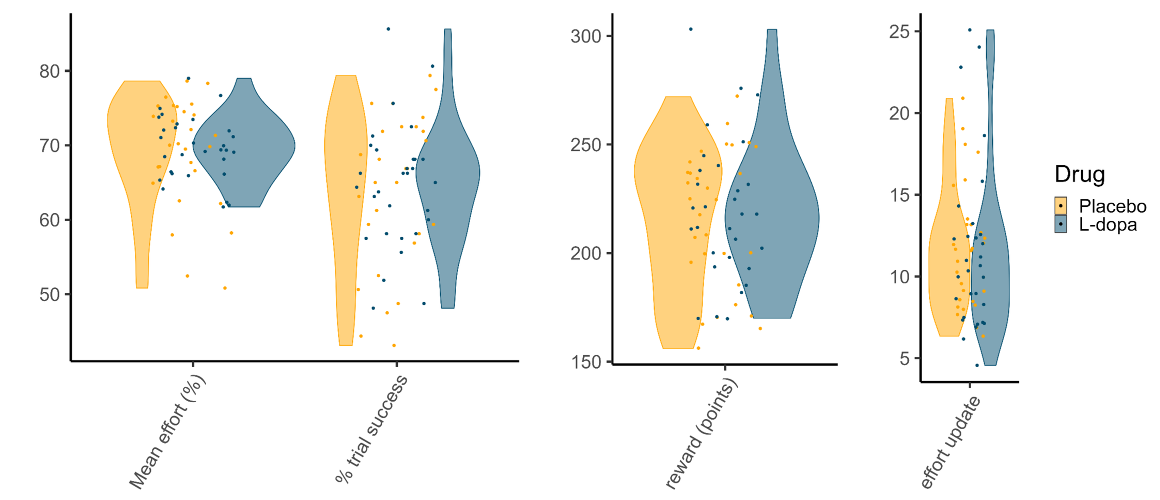


Fig 3. Groups matched for age, IQ and trait psychopathology.

Behavioural results



No effect of L-dopa on mean effort exertion *t*(58) = -0.61, *p* = 0.54 (Fig. 4 & 5).

Fig 4. Groups matched for overall performance (effort, success and reward).

Linear mixed effects model:
*Effort(t) ~ effort(t-1)*drug + reward(t-1)*drug + failure(t-1)*drug + (1|subject)*

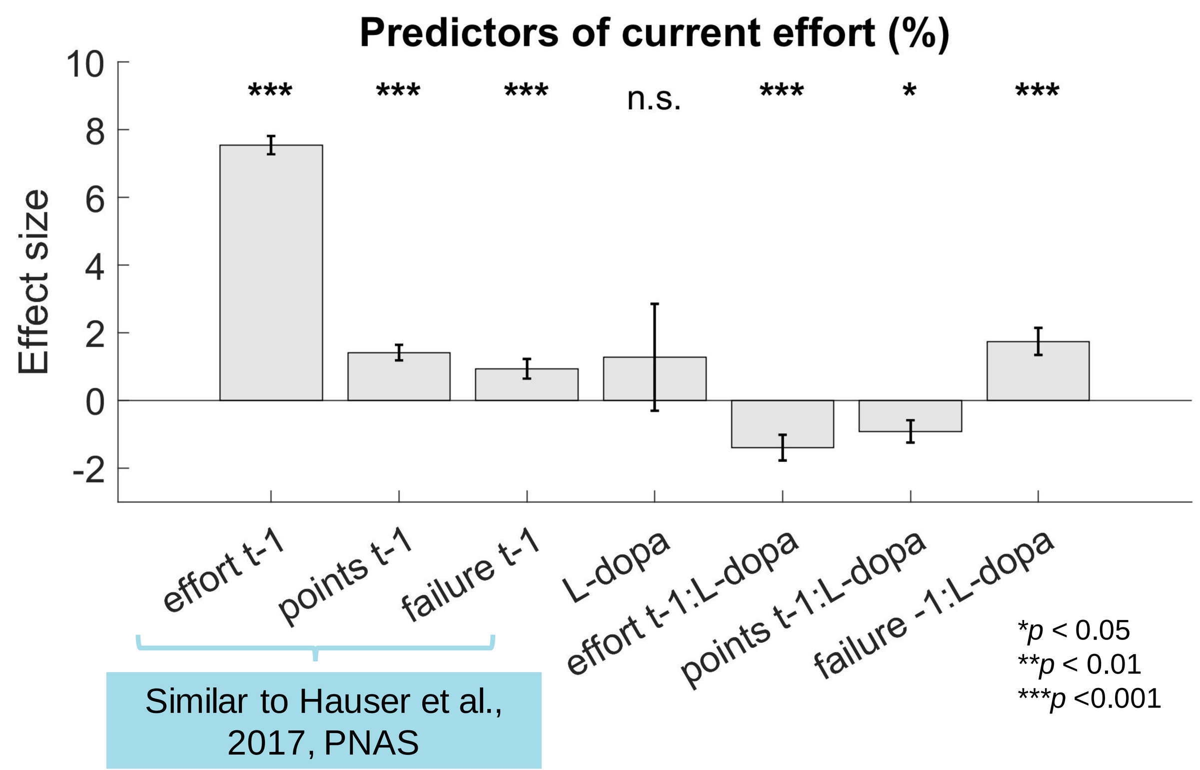


Fig 5. Effort on a given trial was predicted by previous effort, previous points (reward) and previous failure (for that stimulus).

L-dopa **increased** the impact of **failure** and **decreased** the impact of **reward**

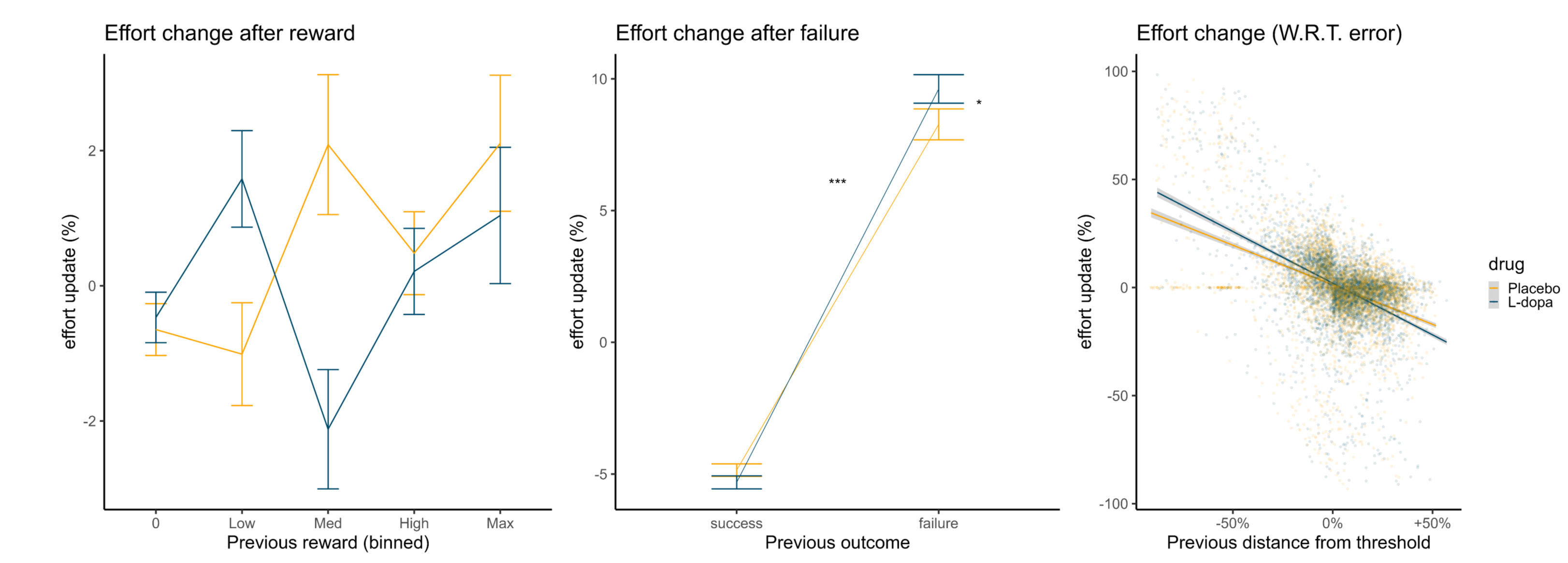


Fig 6. Effort change (mean ± SEM) after feedback and change relative to distance from required effort (threshold)

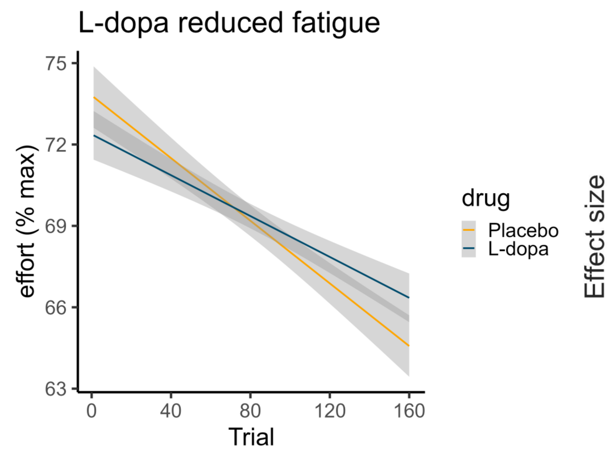


Fig 7. L-dopa sustained effort for longer (β_{fixed} = 0.88, 95%CI [0.22, 1.54], *p* = 0.01)

Interactions with behavioural apathy (AMI)

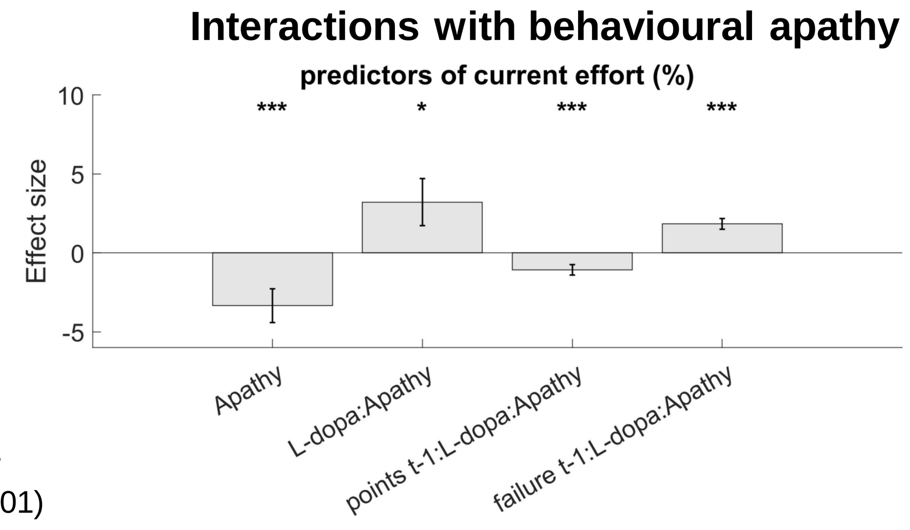


Fig 8. Apathy is associated with reduced effort but a stronger effect of L-dopa.

Next

- Learning model fitting and selection
- fMRI analysis with parametric modulation by learning parameters
- Model derived reward and effort-learning PEs underlined by similar or distinct circuitry? How does L-dopa modulate?

Image source credits
Hauser et al., 2017, PNAS 114 (35), E7395-E7404)
Chong et al., 2016, Progress in brain research (229), 71-100
https://rb.gy/g8hni; https://rb.gy/ukcq8; https://rb.gy/d5pvg

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