Science

NEUROSCIENCE

Dopamine promotes cognitive effort by biasing the benefits versus costs of cognitive work

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2020.04.23

Jihyun Hur

Introduction

ADHD and Psychostimulant

Impulsivity

Hyperactivity

Inattentiveness

+

Psychostimulants

→

Improved Cognitive Control

Introduction

Psychostimulant

: stimulates the central nervous system and enhances mood, cognitive control, or motor activity

Chemical	Brand name(s)	Mechanism of action	Neurotransmitters systems affected
Methylphenidate	Concerta© and Ritalin©	NET and DAT inhibitor	Norepinephrine and dopamine
Amphetamine	Adderall© and Adzenys XR-ODT	NET, DAT, and SET inhibitor	Norepinephrine, dopamine, and serotonin
Atomoxetine	Strattera©	NET inhibitor	Norepinephrine (potentially serotonin)
AHN 2-005	N/A	DAT inhibitor	Dopamine

DAT, dopamine transporter; NET, norepinephrine transporter; SET, serotonin transporter.

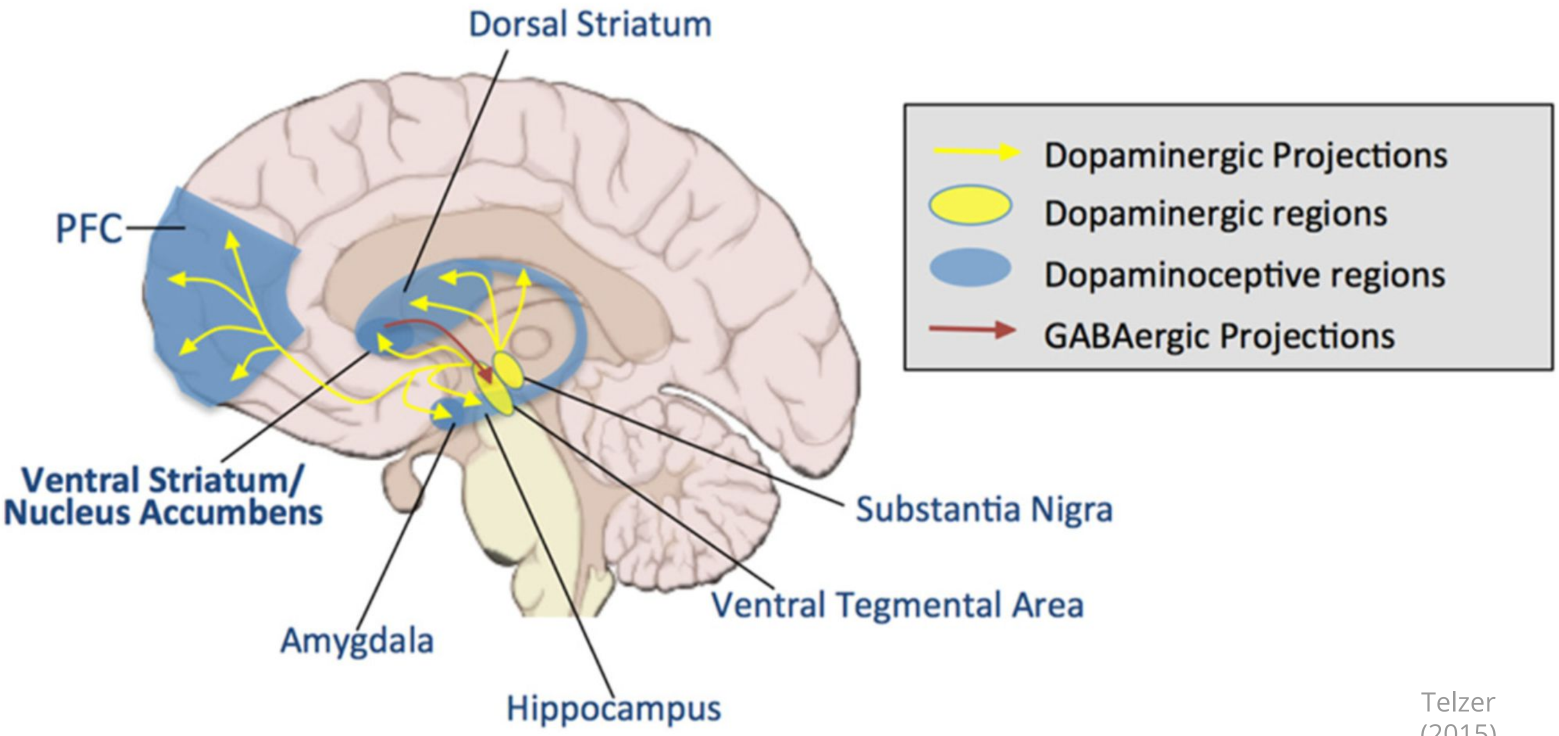
*Dopamine transporter: responsible for dopamine reuptake

Urban & Gao (2017)

Introduction

Dopamine Pathways

: a catecholamine neurotransmitter in the brain



Telzer (2015)

Introduction

Hypotheses on Psychostimulant Effect

Hyp. 1: Direct cortical effect

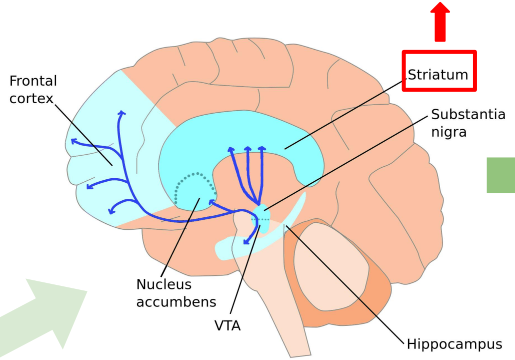
- Psychostimulants directly involve in cognitive-enhancing effect in the PFC - Spencer et al. (2015)

Hyp. 2: Indirect effect: sensitivity modulation

- Striatum dopamine modulates sensitivity to the benefits versus costs - Collins et al. (2014)
- “Dopamine restores cognitive motivation in Parkinson’s disease” - McGuigan et al. (2019)
- Psychostimulants modulate whether or not to avoid cognitive control in humans - Froböse et al. (2018)

Introduction

Hypothesis



Psychostimulants

"Psychostimulant **boosts cognitive control** by **increasing striatal dopamine** and **sensitivity to the benefits versus costs of cognitive effort.**"

Improved Cognitive Control

Methods

Methods

Participants & Study Design

	Broader study	This study
Participants	100	50 (25 men)
Demographics	18-43 (ages), healthy, neurologically normal, right-handed	

Study Design

1st day: Screening

2nd: **Placebo** + Tasks

3rd: **Sulpiride** + Tasks

4th: **Methylphenidate** + Tasks

5th: PET (Dopamine Synthesis Capacity)

Total: 5 visits

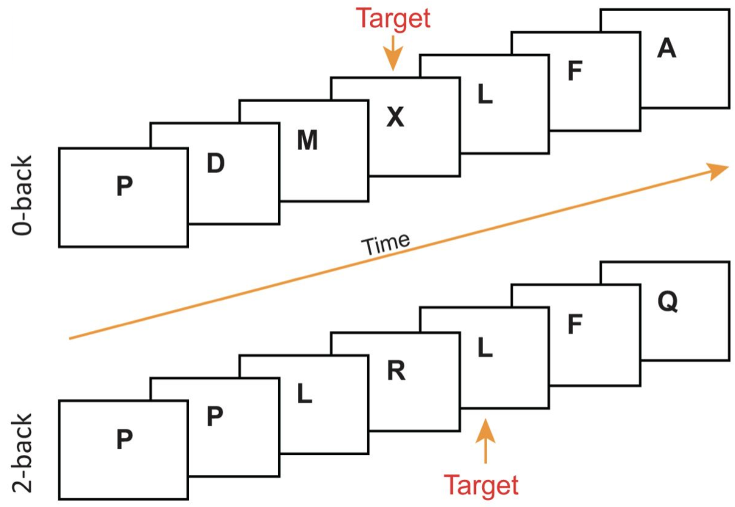
Methods

Tasks

Level	Label
1	a
2	e
3	i
4	o

Base offer for the high-effort option:
€2.00 or €4.00

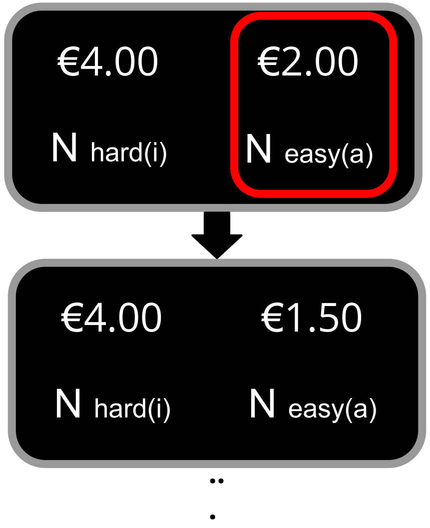
1) N-back task (Level: 1-4)



Varga et al. (2015)

2) Discounting task

(50 trials)

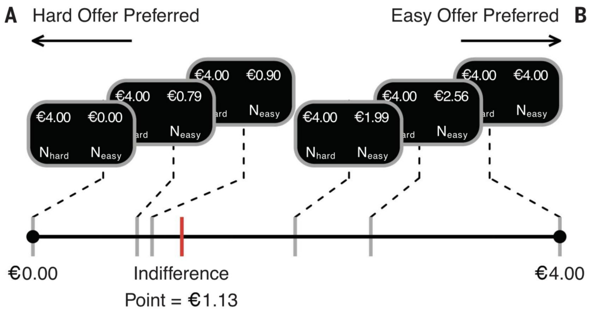


1. Indifference Point

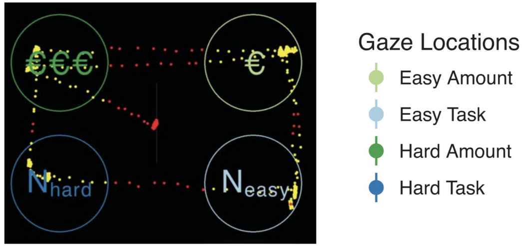
2. Subjective Value

3) Gaze-Decision task

(168 trials)



With eye-tracking



Westbrook et al. (2020)

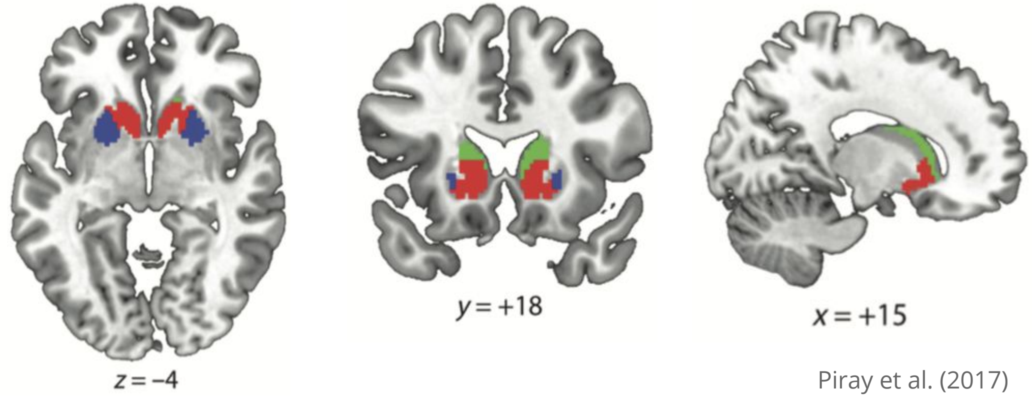
Methods

Dopamine Synthesis Capacity

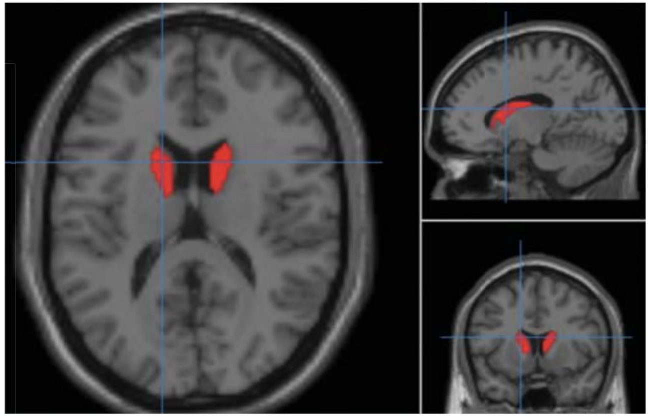
: the rate of dopamine synthesis (indexed as influx rate)

Functional Parcellation of the Striatum

Ventral striatum | Dorsal caudate nucleus | Dorsal anterior-putamen



Piray et al. (2017)



Westbrook et al. (2020)

Methods

Models

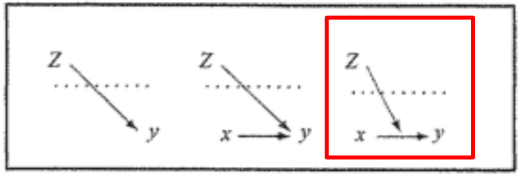


Figure 2.5: The structure of macro–micro propositions.

Discounting task

- Multilevel / Hierarchical linear regression ➡ includes a **predictor** at the **group level**
  - Cross-level interaction ➡ y is dependent on the relationship x and Z

- Model: $SV_{ij} = \beta_{0j} + \beta_{1j} amt_i + \beta_{2j} drug_i + \beta_{3j} ldiff_i + \beta_{4j} S_{2i} + \beta_{5j} S_{3i} + \varepsilon_{ij}$

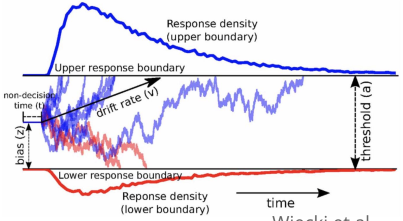
  High-offer amount | Load difference | Session factors | i - trial, j - subject

  Subjective Value(SV) of the High-effort offer | Drug (dummy coded) | Caudate dopamine

  - Group-level: **Dopamine** $\beta_{0j} = \alpha_{00} + \alpha_{01} cDA + u_{0j}$

    $\beta_{1j} = \alpha_{10} + \alpha_{11} cDA + u_{1j}$ 1 → 2*

Gaze-Decision Task



Wiecki et al. (2013)

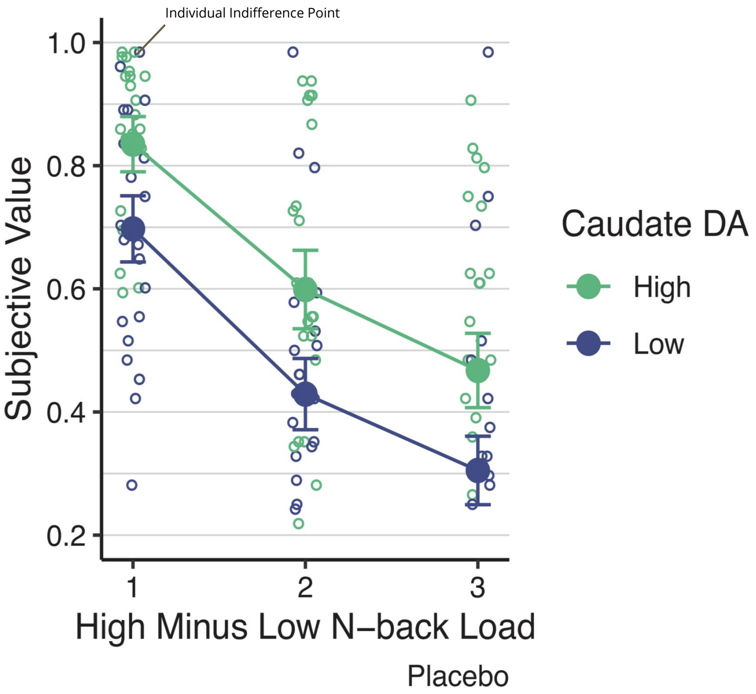
- Hierarchical logistic regression ➡ **binary-choice of the high-effort offer** as y
- Hierarchical **Attentional Drift Diffusion Model**
  - More gaze leads to more selection (drift rate ↑) $V_t = V_{t-1} + d\left(r_{fixated} - \theta * r_{non-fixated}\right) + \varepsilon$
  - Compared 6 models based on DIC scores

Results

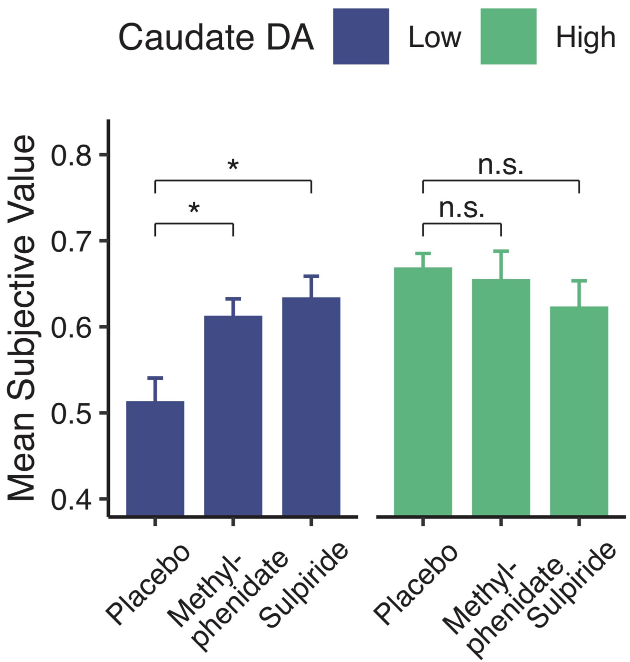
Results

Discounting Task

1) Load Difference and Subjective Value by DA Group



2) Effect of Drugs on SV by DA Group



3) Significant Predictors of SV

***Predictor* (beta)**

- Intercept (0.57)
- Offer Amount (0.018)
- Caudate DA (0.068)
- Load Difference (-0.14)
- MPH*Caudate DA (-0.067)
- SUL*Caudate DA (-0.10)

Westbrook et al. (2020)

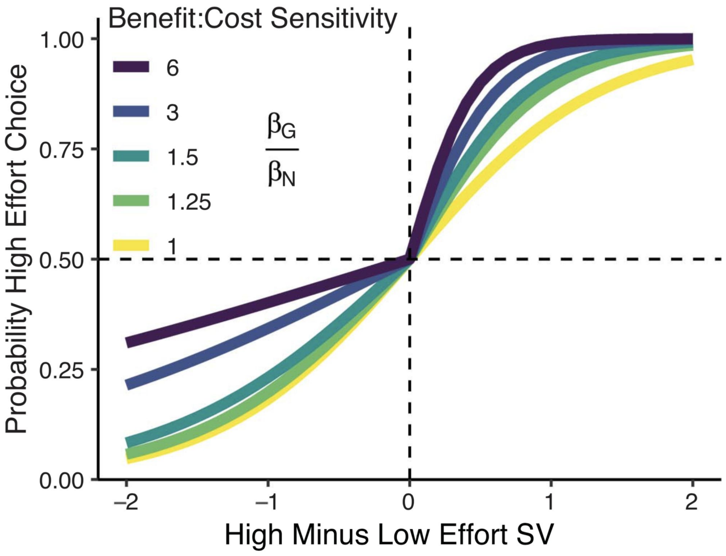
Result 1: Dopamine increases motivation (SV of harder task).

Results

Dopamine & Benefits vs Costs Sensitivity

Hypothesis: Striatum Dopamine ↑ **Sensitivity to Benefits versus Costs**

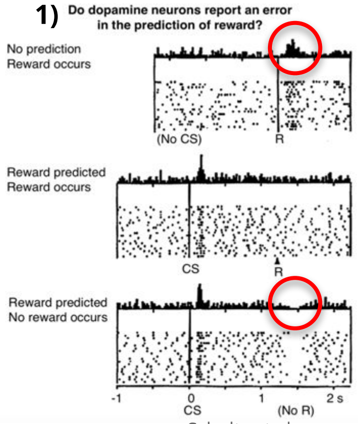
1) Simulation



Opponent Actor Learning Model

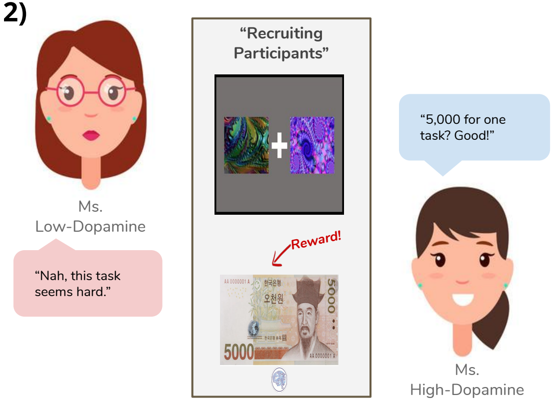
- Goal: to integrate the **1)reinforcement learning** and **2)incentive theories** of dopamine into one model

1)



Schultz et al. (1997)

2)



Results

Opponent Actor Learning (OpAL) Model

- Base: **actor - critic** architecture
  - critic: evaluates the values ➡ Delta rule
  - actor: selects actions

1) Critic Learning Model:

Prediction error

$$\delta(t) = r(t) - V(t)$$

$$V(t+1) = V(t) + \alpha_C \times \delta(t).$$

t: time

Estimated value

Learning rate

2) Actor Learning Model:

Go actor

$$G_a(t+1) = G_a(t) + \boxed{[\alpha_G G_a(t)]} \times \delta(t)$$

NoGo actor

$$N_a(t+1) = N_a(t) + \boxed{[\alpha_N N_a(t)]} \times \boxed{[-\delta(t)]}$$

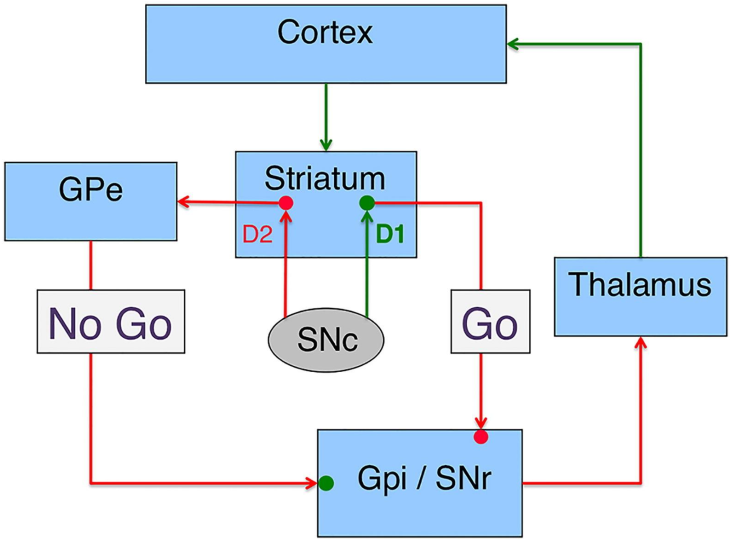
3) Policy:

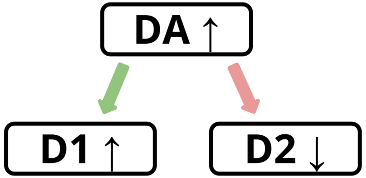
$$Act_a(t) = \beta_G G_a(t) - \beta_N N_a(t)\,, \quad p(a) = \frac{e^{Act_a(t)}}{\sum_i e^{Act_{a_i}(t)}}$$

Sensitivity to Go & NoGo Activity

Collins et al. (2014)

Action values modulated by D1 & D2 Stimulation





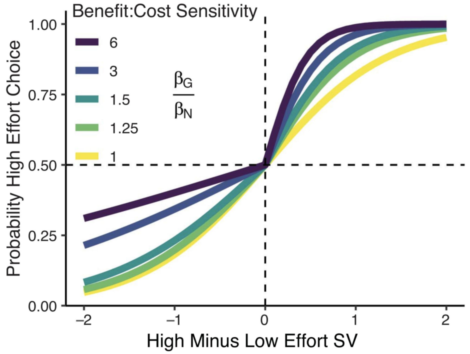
Cox et al. (2015)

Results

Dopamine & Benefits vs Costs Sensitivity

Westbrook et al. (2020)

Modification: $V_p = \beta_G \boxed{ben_p} - \beta_N \boxed{cos_p}$

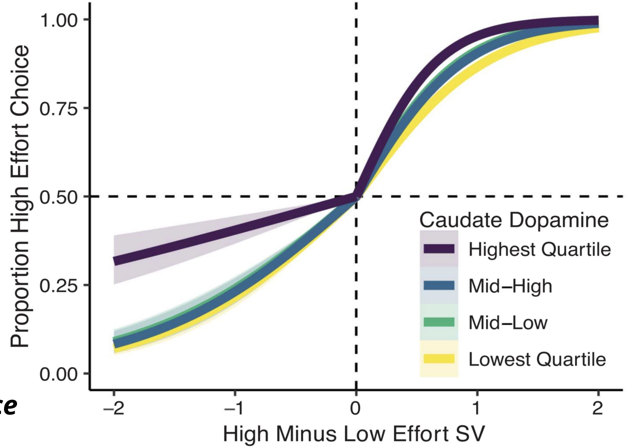


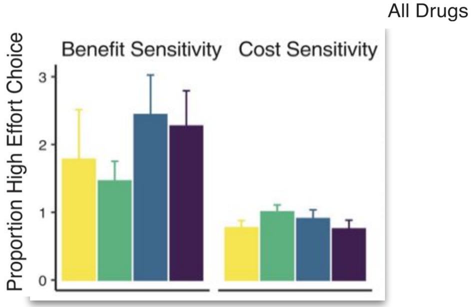
Significant Predictors of High Effort Choice

Predictor **(beta)**

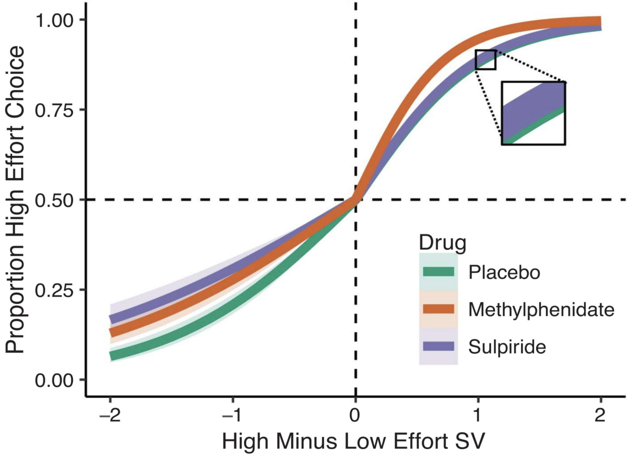
- Costs (-1.07)
- Benefits (2.30)
- Caudate DA (1.02)
- Benefits*MPH (1.34)
- Benefits*cDA (0.65)

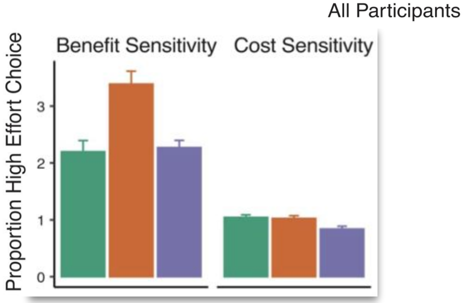
Effect of Dopamine on Sensitivity (All Drugs)





Effect of Dopamine on Sensitivity (All Subjects)





Result 2: Dopamine increases sensitivity to benefits.

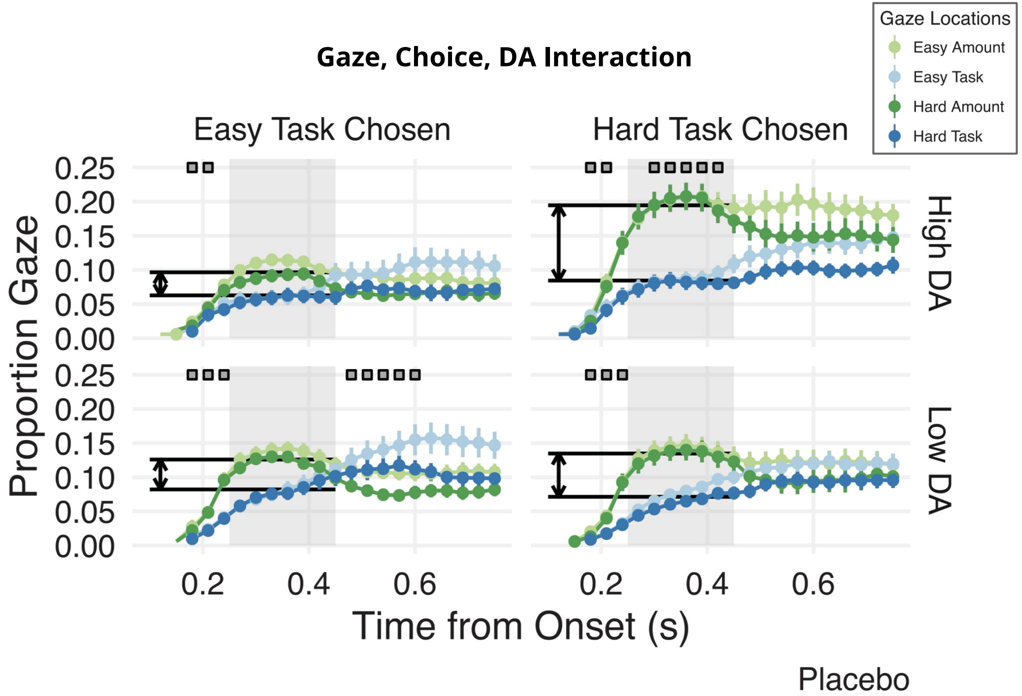
HOW?

1) Attention: higher DA increases gaze at benefits vs. costs

2) Impact but no Attention

Results

Gaze-Decision Task



Westbrook et al. (2020)

Significant Predictors of Gaze at Ben vs. Cost

Predictor **(beta)**

Choice type (high vs. low) (0.42)

Choice * Caudate DA (0.37)

Choice*MPH*Caudate DA (-0.067)

Non-significant Predictors of Gaze at Ben vs. Cost

Predictor

Caudate DA

SUL vs. PBO

MPH vs. PBO

Gaze amplified the attended offer?

or

People just gazed more at the offers that they already chose?

Results

Choice- and Attention-biased Models

Six aDDM Models

1. Additive Model (Choice-biased)	DIC	2. Additive Model with Ben & Cost Attributes
3. Multiplicative Model (Attention-biased)	>	4. Multiplicative Model with Ben & Cost Attributes
5. Multiplicative + Additive Model	>	6. Multiplicative + Additive Model with Ben & Cost Attributes ✓

Model 1 vs. Model 2: >

1. Additive Model (Choice-biased)

$$v_{ij} \sim \beta_{0j} + \beta_{1j}\boxed{(g_A - g_B)}_i + \beta_{2j}(V_A - V_B)_i$$

Gaze difference between A and B offers

2. Additive Model with Ben & Cost Attributes

V_A: Ben_A, $Cost_A$

g_A: g_{BenA}, g_{CostA}

$$v_{ij} \sim \beta_{0j} + \beta_{1j}(Ben_A - Ben_B)_i + \beta_{2j}(Cost_A - Cost_B)_i + \cdots$$
$$\beta_{3j}(g_{BenA} - g_{BenB})_i + \beta_{4j}(g_{CostA} - g_{CostB})_i$$

3. Multiplicative Model (Attention-biased)

$$v_{ij} \sim \beta_{0j} + \beta_{1j}\boxed{(g_A V_A - g_B V_B)}_i + \beta_{2j}\boxed{(g_B V_A - g_A V_B)}_i$$

4. Multiplicative Model with Ben & Cost Attributes

5. Multiplicative + Additive Model

$$v_{ij} \sim \beta_{0j} + \beta_{1j}(g_A V_A - g_B V_B)_i + \beta_{2j}(g_B V_A - g_A V_B)_i + \beta_{3j}(g_A - g_B)_i$$

6. Multiplicative + Additive Model with Ben & Cost Attributes ✓

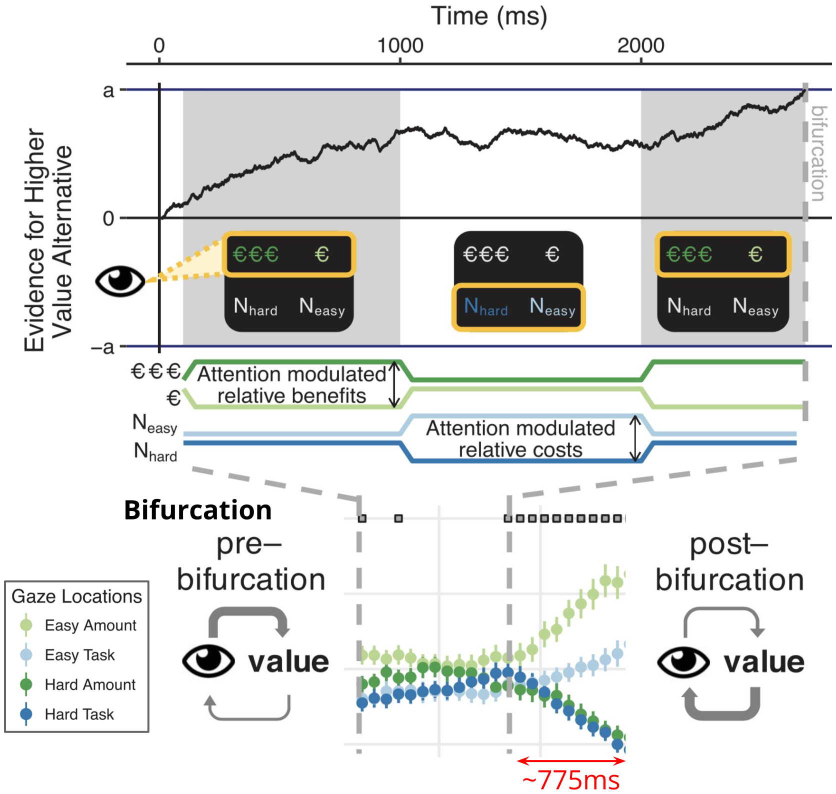
Supports both explanations

Would this gaze-value interactions change dynamically within a trial?

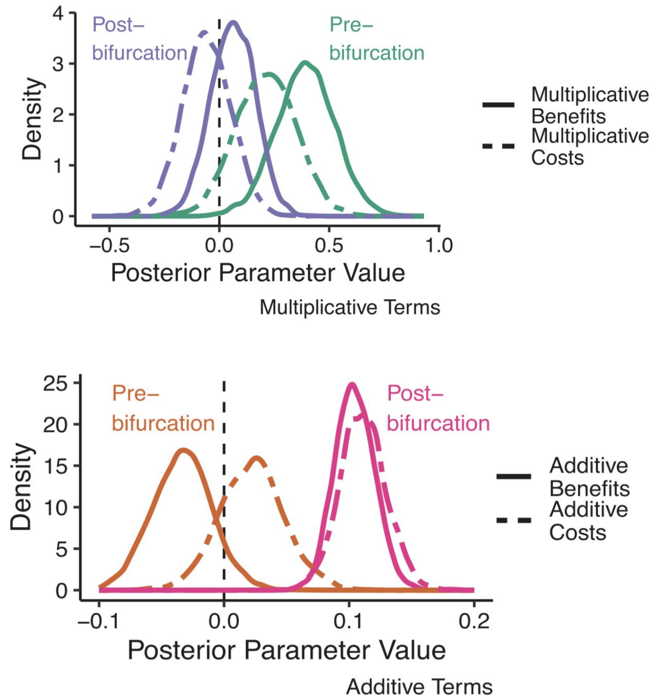
Results

Bifurcation & Refitting

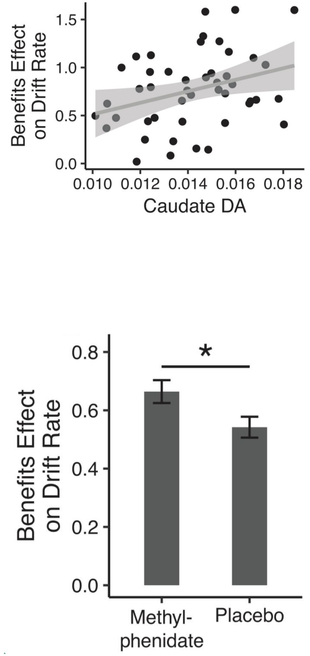
Gaze Attribute Model



Bifurcated Posterior Parameter Values

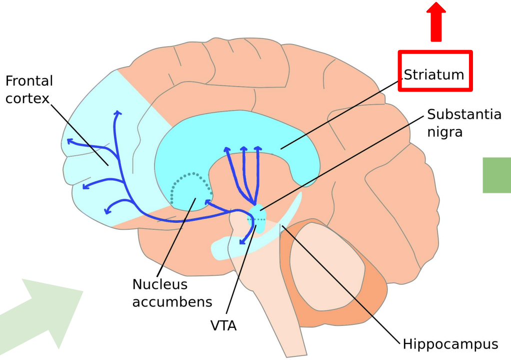


Ben Effects on Drift Rate & DA



Conclusion

Psychostimulants



"Psychostimulant **boosts cognitive control** by **increasing striatal dopamine** and accordingly, **sensitivity to the benefits versus costs of cognitive effort.**"

Improved Cognitive Control

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Thank you for listening!