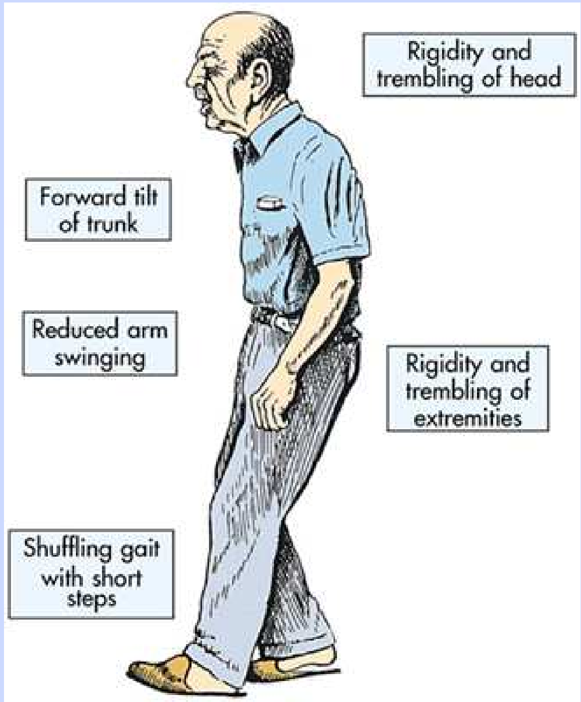
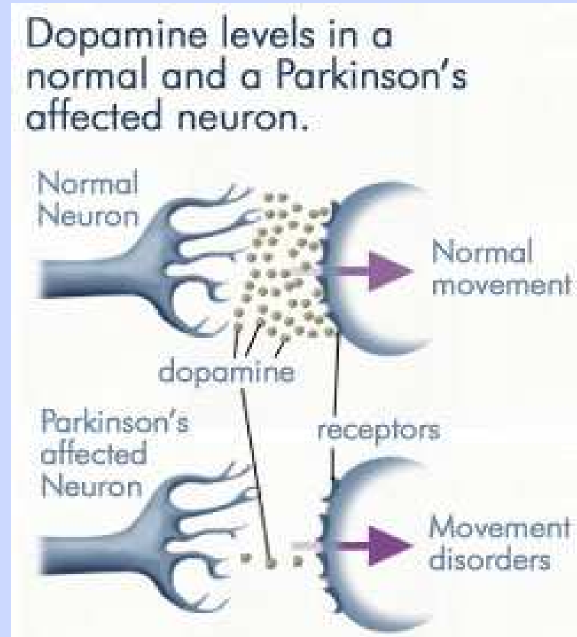
Parkinson's disease and dopamine (DA) control of movement



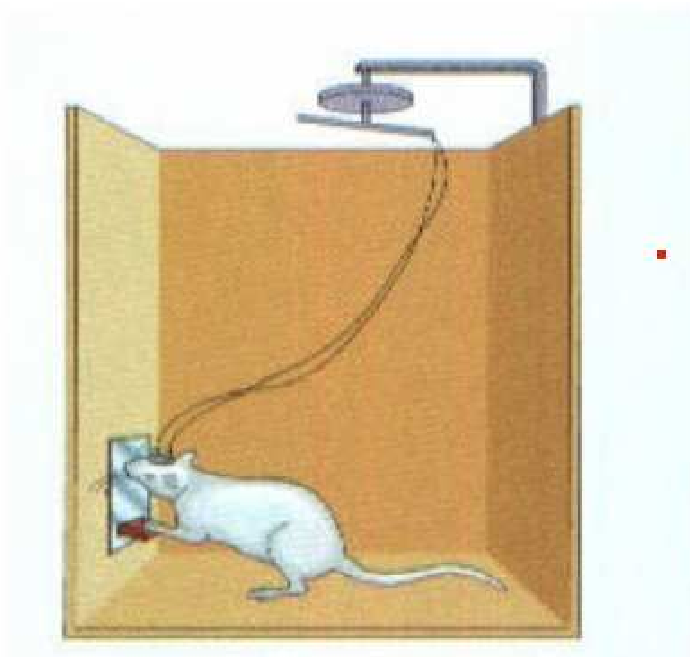


- Standard account is that DA directly boosts movement *performance*
- Models suggest that DA modulates motivational *incentive* and *learning*, too

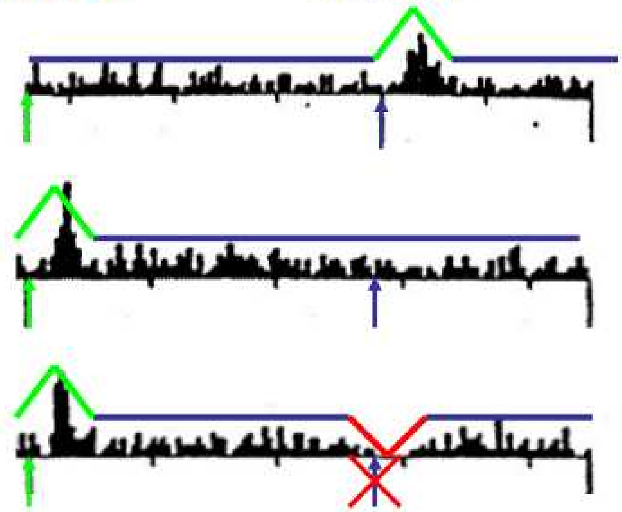

sundance
CHANNEL
HOME ENTERTAINMENT
LOVE.
REAL OR JUST A CHEMICAL REACTION?
John Livingston Sabrina Lloyd
DOPAMINE
"A sweet, smart romance."
- Kevin Crust, Los Angeles Times

What is Dopamine Doing?

Dopamine carries the brain's ~~reward~~ signal
reward prediction error



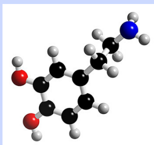
Wise & Romper, 89



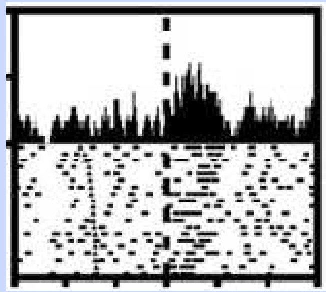
Schultz et. al, 98

Reinforcement learning and dopamine: prediction errors

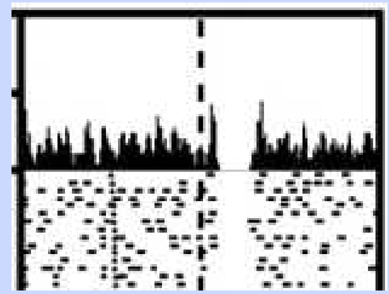
dopamine:



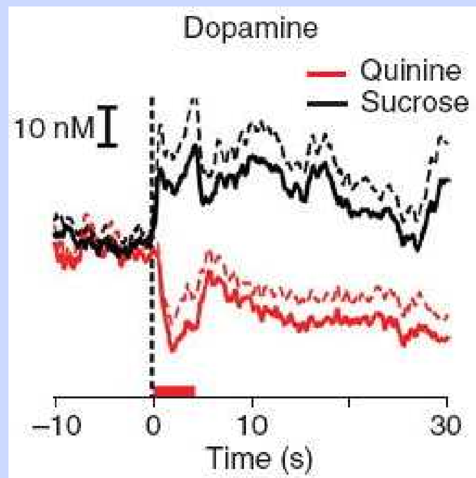
Positive PE:



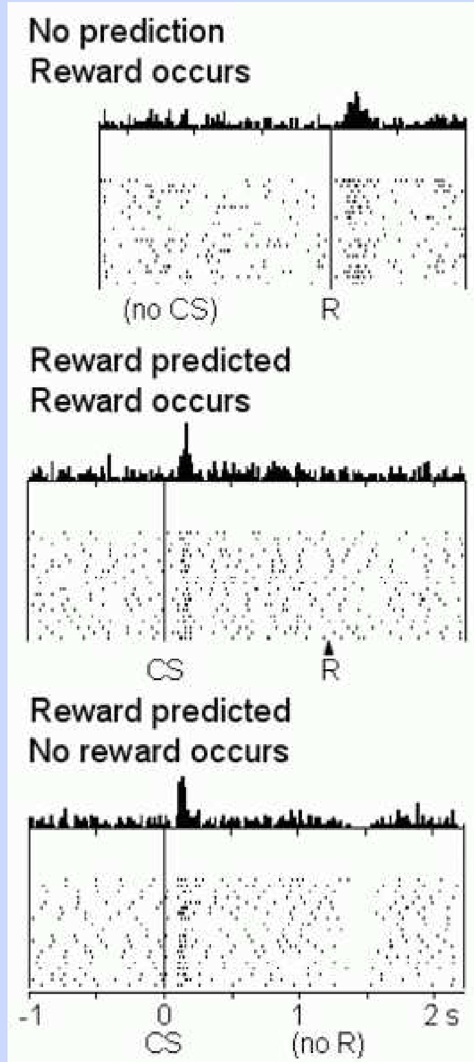
Negative PE:



Schultz, Satoh, Roesch, Zaghoul, Glimcher, Hyland.. and many more



Basic Data: VTA dopamine firing in Conditioning



Schultz, Montague & Dayan, 2007

Temporal Difference Learning: Equations

Value function, sum of discounted future rewards:

$$V(t) = \langle \gamma^0 r(t) + \gamma^1 r(t+1) + \gamma^2 r(t+2) ... \rangle \tag{1}$$

Temporal Difference Learning: Equations

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Recursive definition:

$$V(t) = \langle r(t) + \gamma V(t+1) \rangle \tag{2}$$

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Error in predicted reward (from previous to next time-step):

$$\delta(t) = \left(r(t) + \gamma \widehat{V}(t+1) \right) - \widehat{V}(t) \tag{3}$$

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Error in predicted reward (from previous to next time-step):

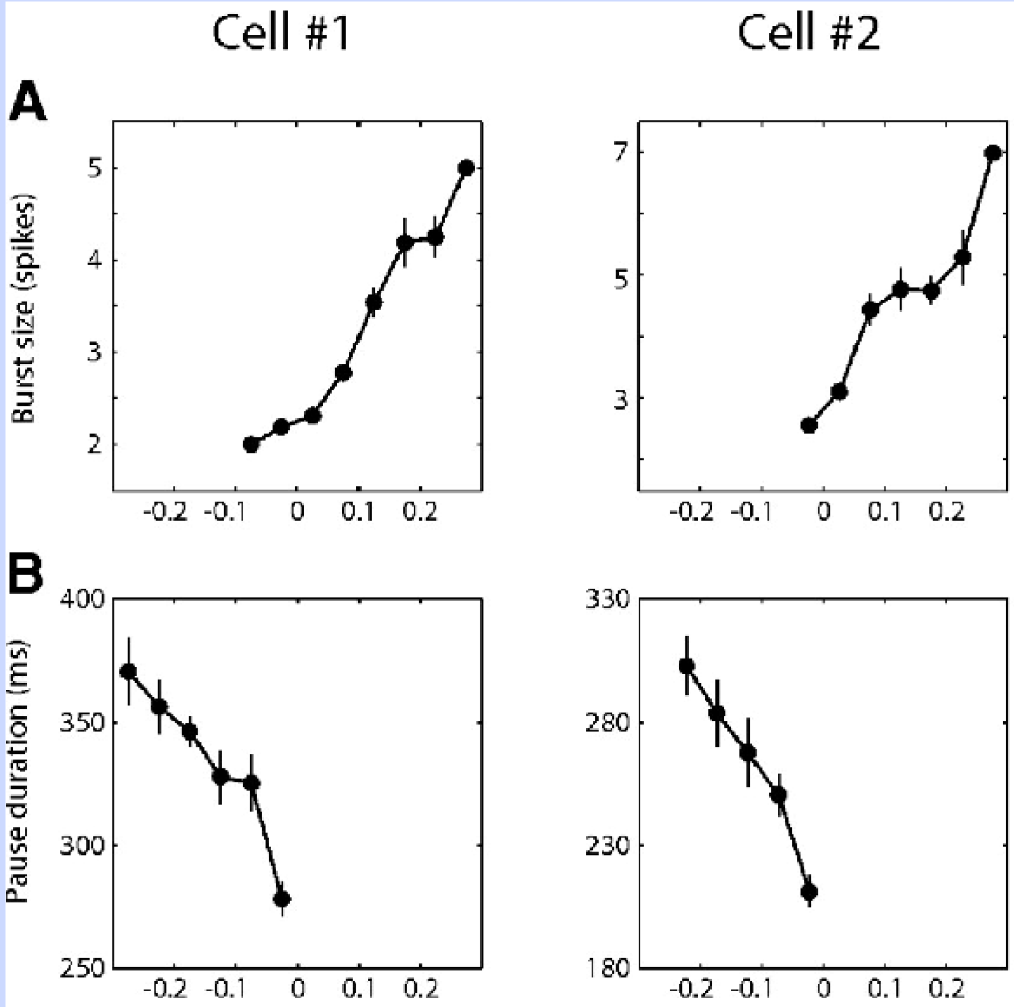
$$\delta(t) = \Big(r(t) + \gamma \widehat{V}(t+1) \Big) - \widehat{V}(t) \tag{3}$$

Update value estimate:

$$\widehat{V}(t) \leftarrow \widehat{V}(t) + \alpha \delta(t) \tag{4}$$

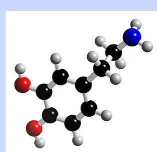
α = learning rate

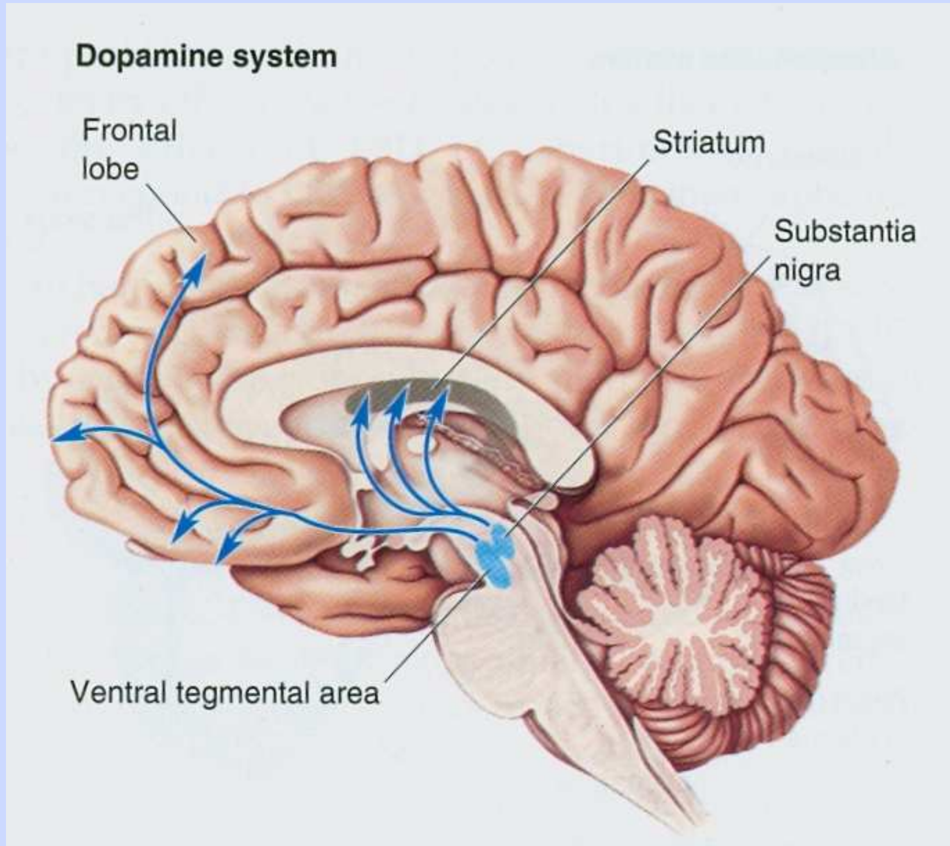
Burst/Pause correlations with Rew Prediction Errors



Bayer et al, 2007 JNeurophys

How are dopamine-based RPE signals used to select *actions*?





What Do the Basal Ganglia Do?

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  BG do not directly implement any cognitive (or motor) process.

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  BG **modulate** activity in multiple cortical areas: affects motor, implicit learning, motivation, decision making and executive function processes.

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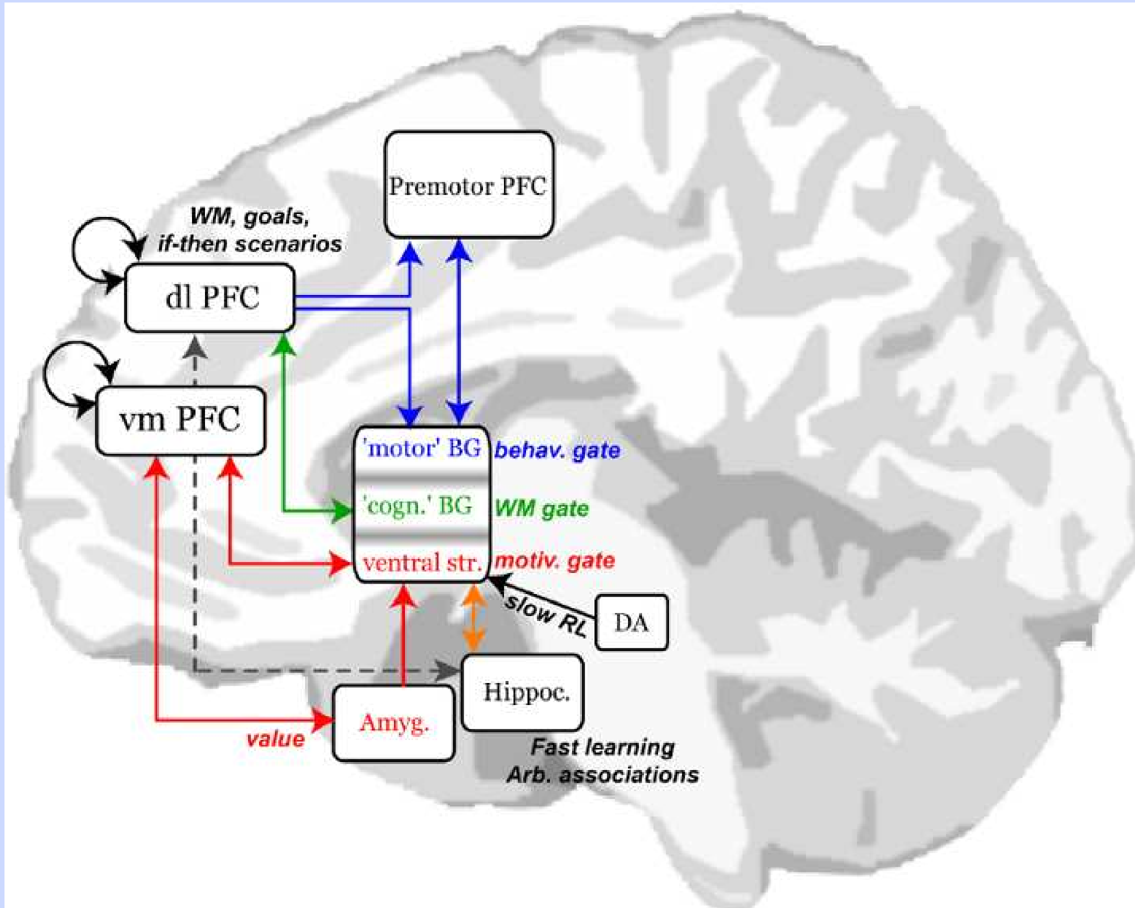
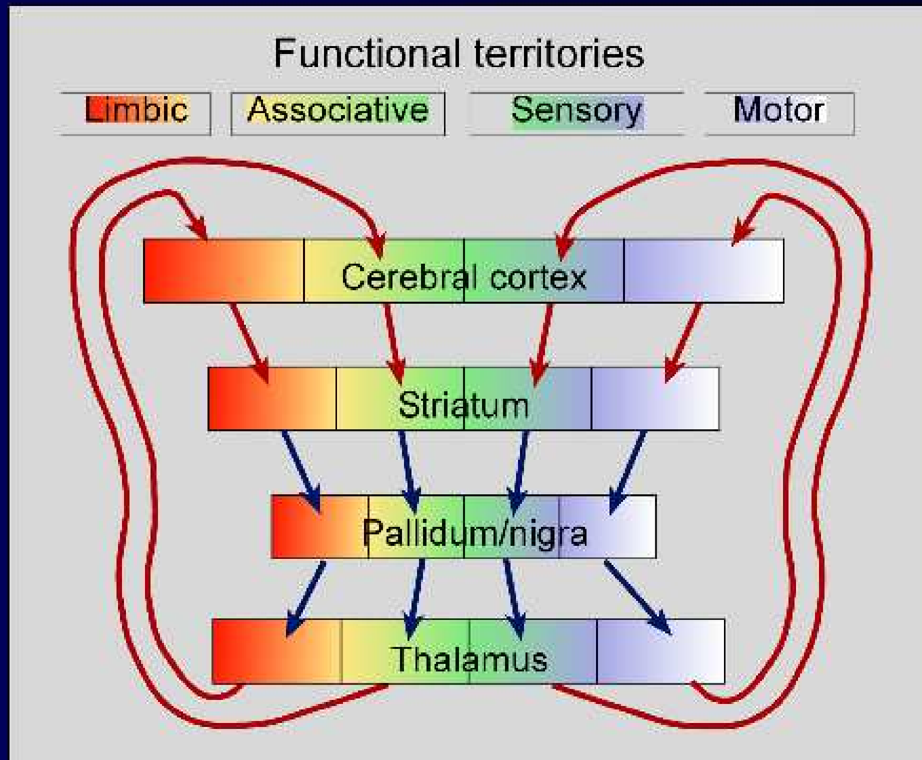
- *Also: excess BG DA can induce impulsivity, e.g. pathological gambling, compulsive shopping (for review Dagher & Robbins, 2009)*

Fronto-basal ganglia circuits in motivation, action, cognition



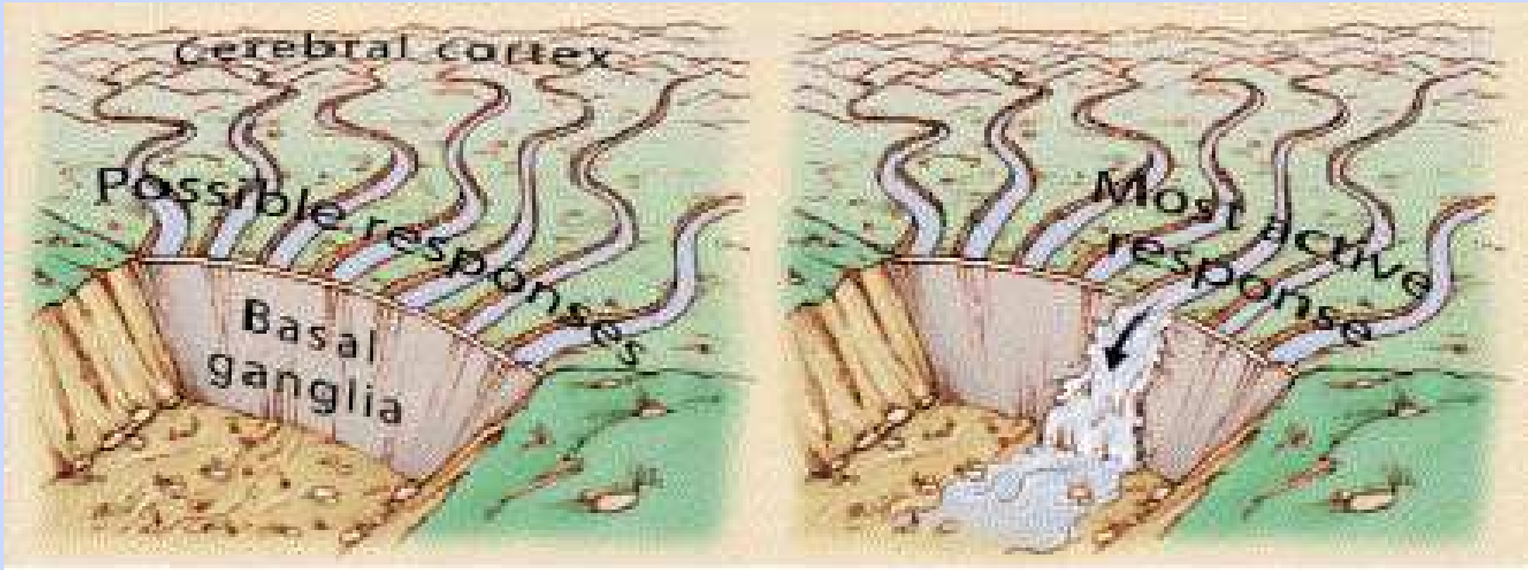
Basal Ganglia Architecture: Cortically based loops



Alexander, G. E., et al. (1986). "Parallel organization of functionally segregated circuits linking basal ganglia and cortex." Ann. Rev. Neurosci. **9**: 357-381.

BG damage $\Rightarrow$ deficits in motor, learning, motivation, working memory, cognitive control

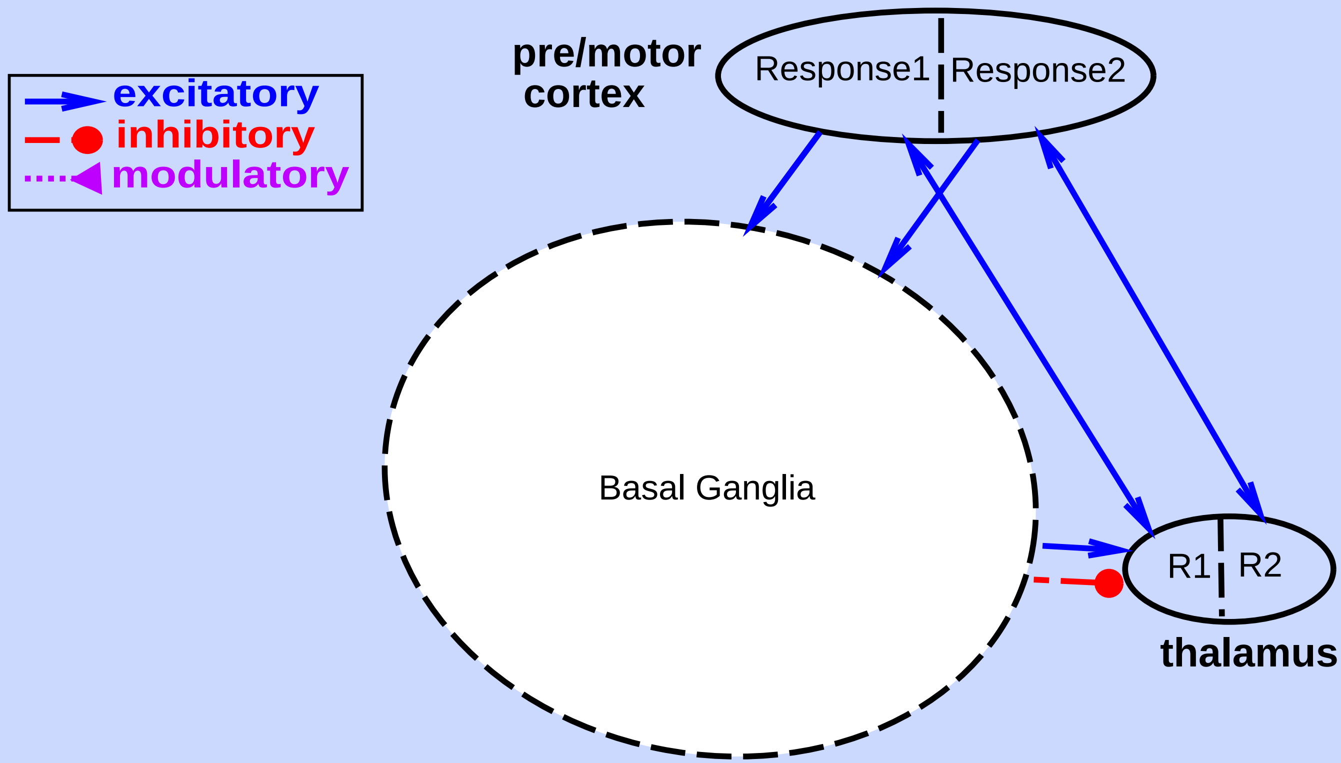
The Basal Ganglia as a Gate: Action Selection



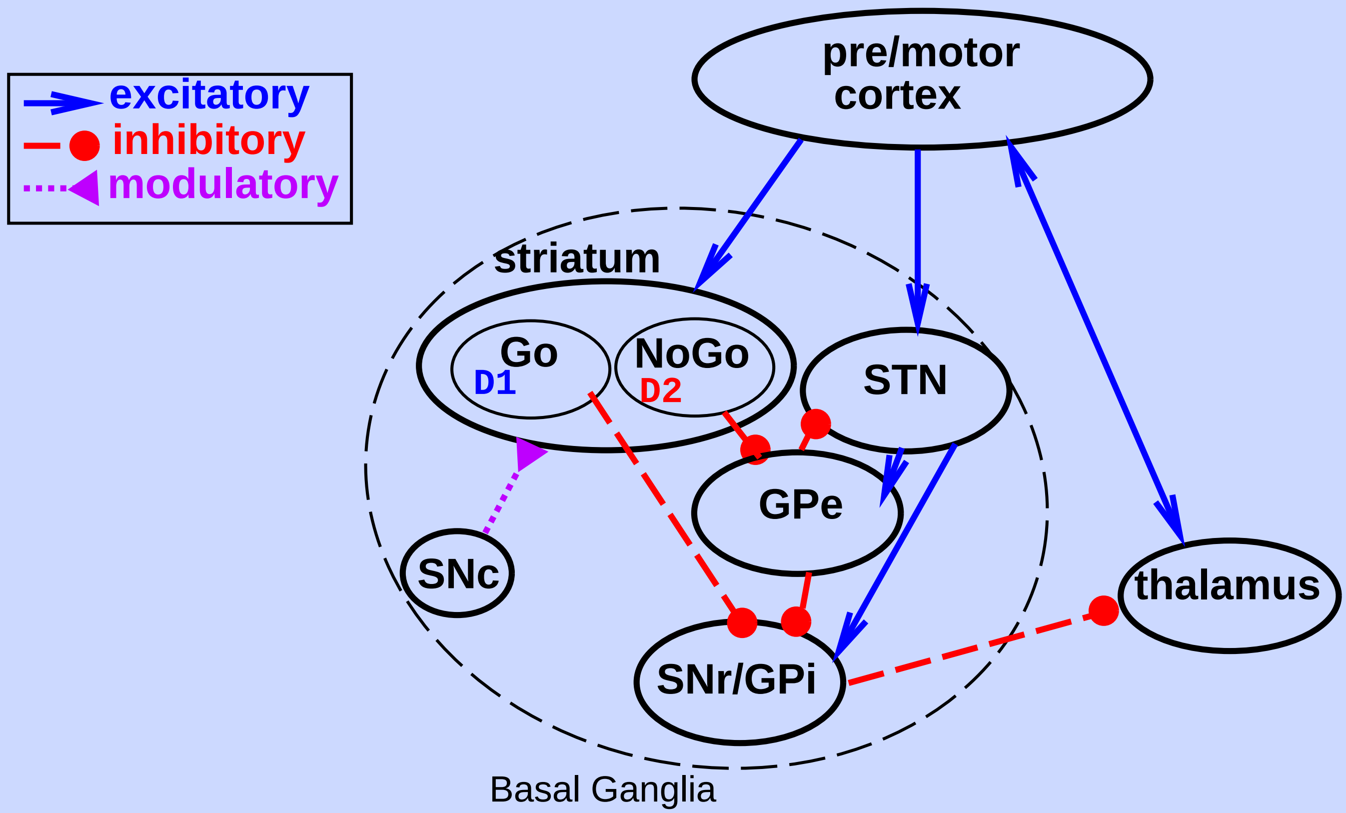
(figure borrowed from Ivry & Spencer, 2004)

- BG selectively facilitates (gates) one action while suppressing others (Mink, 1996; Frank et al, 2001; Gurney et al, 2001; Brown et al, 2004...)
- Gating occurs in proportion to relative probability of positive-negative outcomes for each action, learned via dopamine...

Striato-Cortical Functional Circuitry

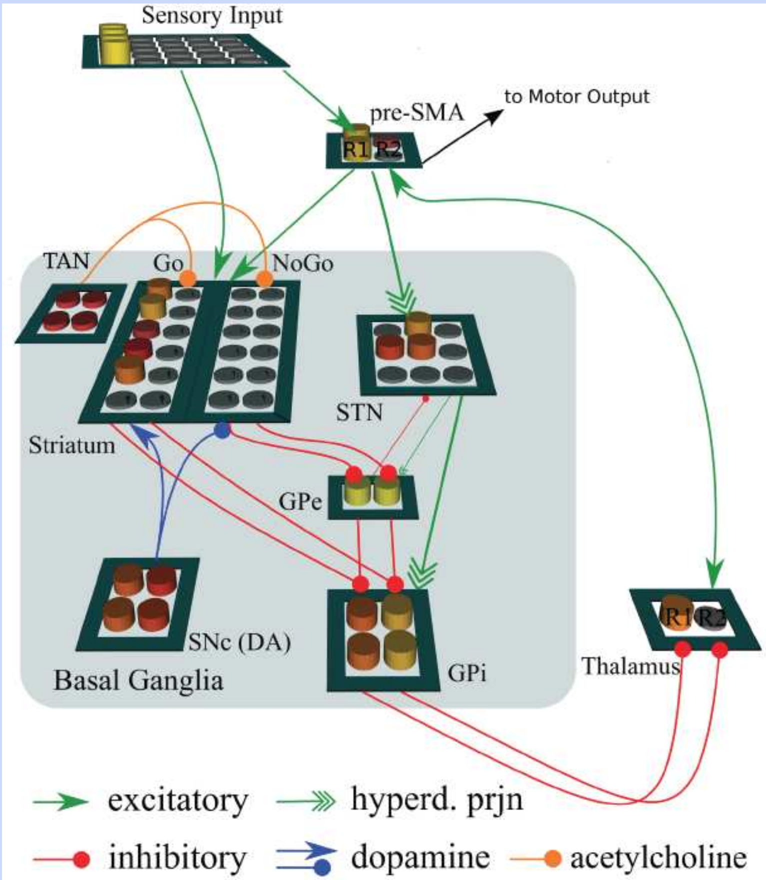


Striato-Cortical Functional Circuitry



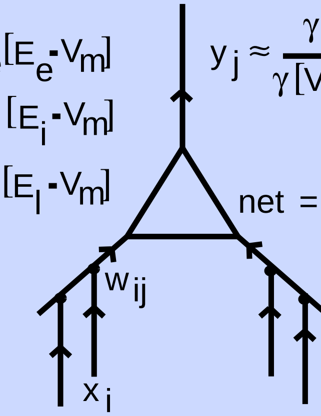
Neural circuit model of BG in learning / decision making

Integrates a wide range of physiological data into a single coherent framework



$$c\dot{V}_m = g_e \bar{g}_e [E_e - V_m] + g_i \bar{g}_i [E_i - V_m] + g_l \bar{g}_l [E_l - V_m] + \ldots$$

$$y_j \approx \frac{\gamma [V_m - \Theta]_+}{\gamma [V_m - \Theta]_+ + 1}$$

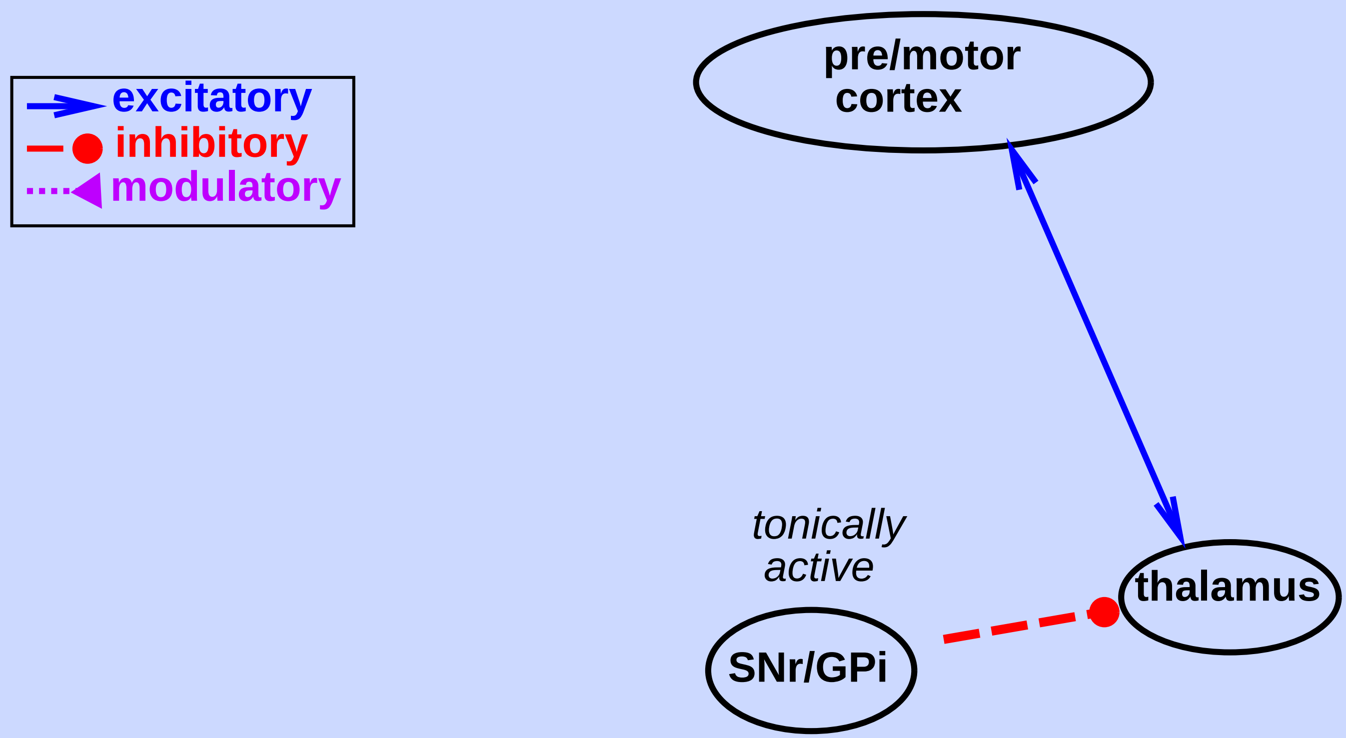


$$net = g_e \approx \langle x_i w_{ij} \rangle + \frac{\beta}{N}$$

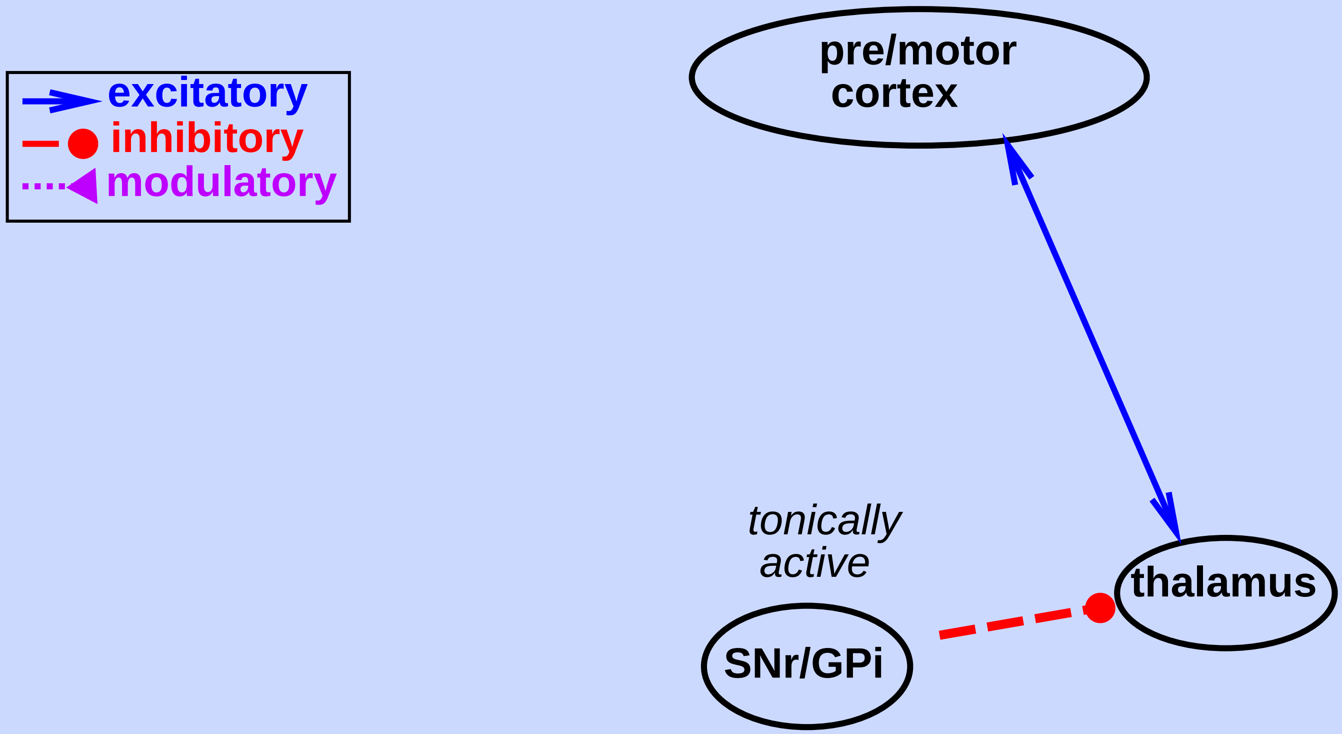
$$\Delta w_{ij} \approx (x_i^p y_j^p) - (x_i^t y_j^t)$$

Frank, 2005, 2006; Franklin & Frank, 2016

Striato-Cortical Functional Circuitry

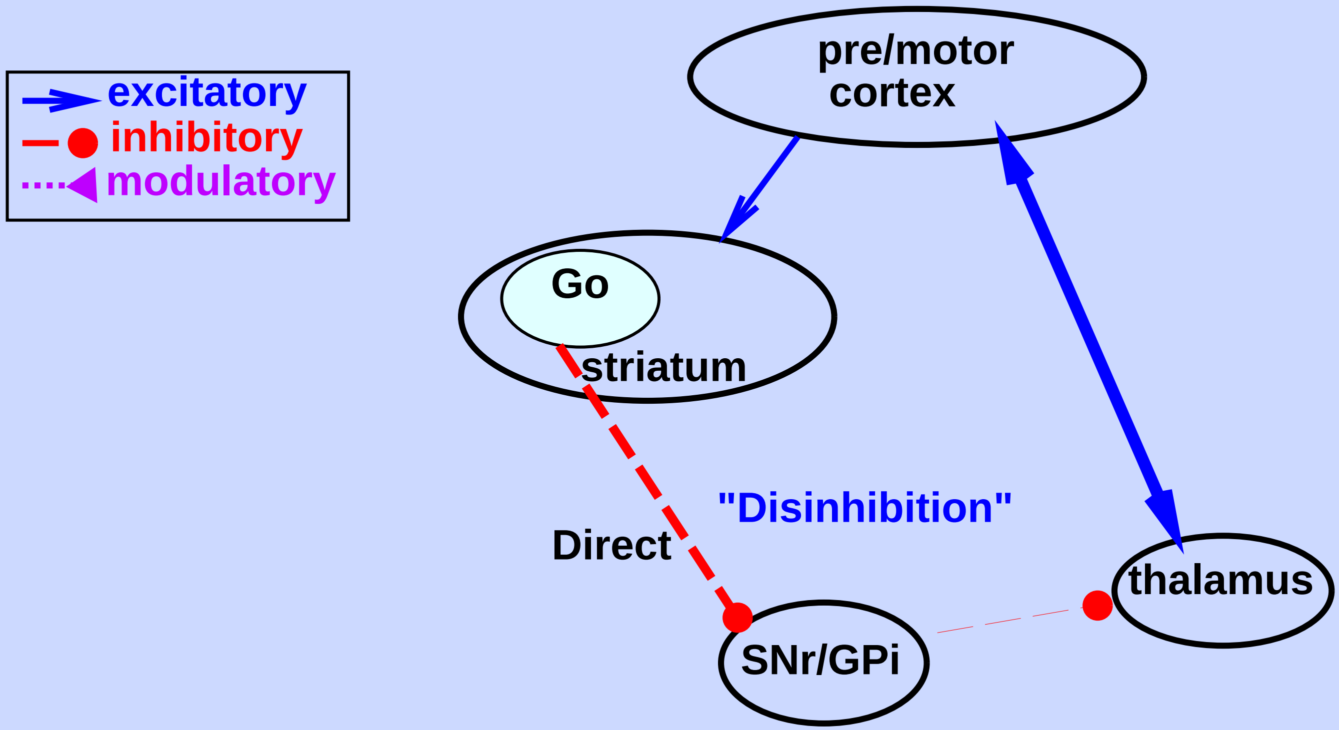


Striato-Cortical Functional Circuitry

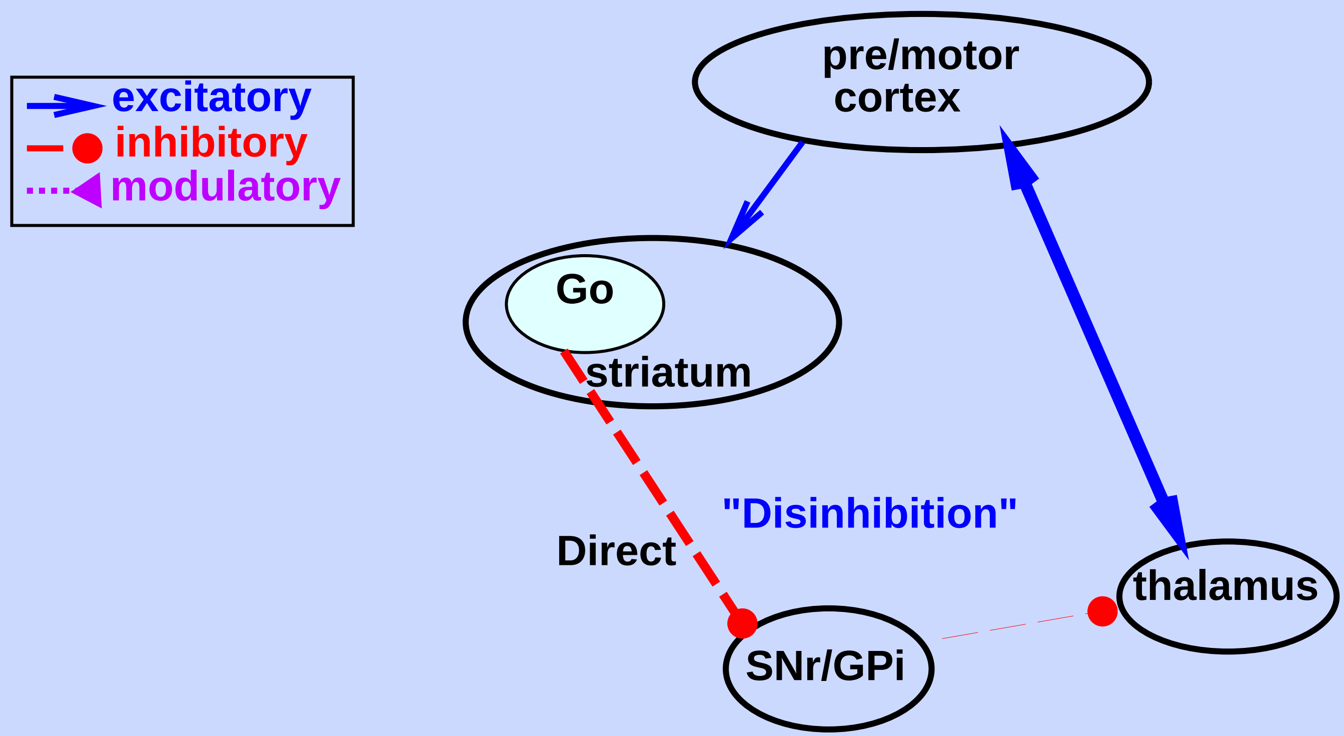


Simulation

Striato-Cortical Functional Circuitry

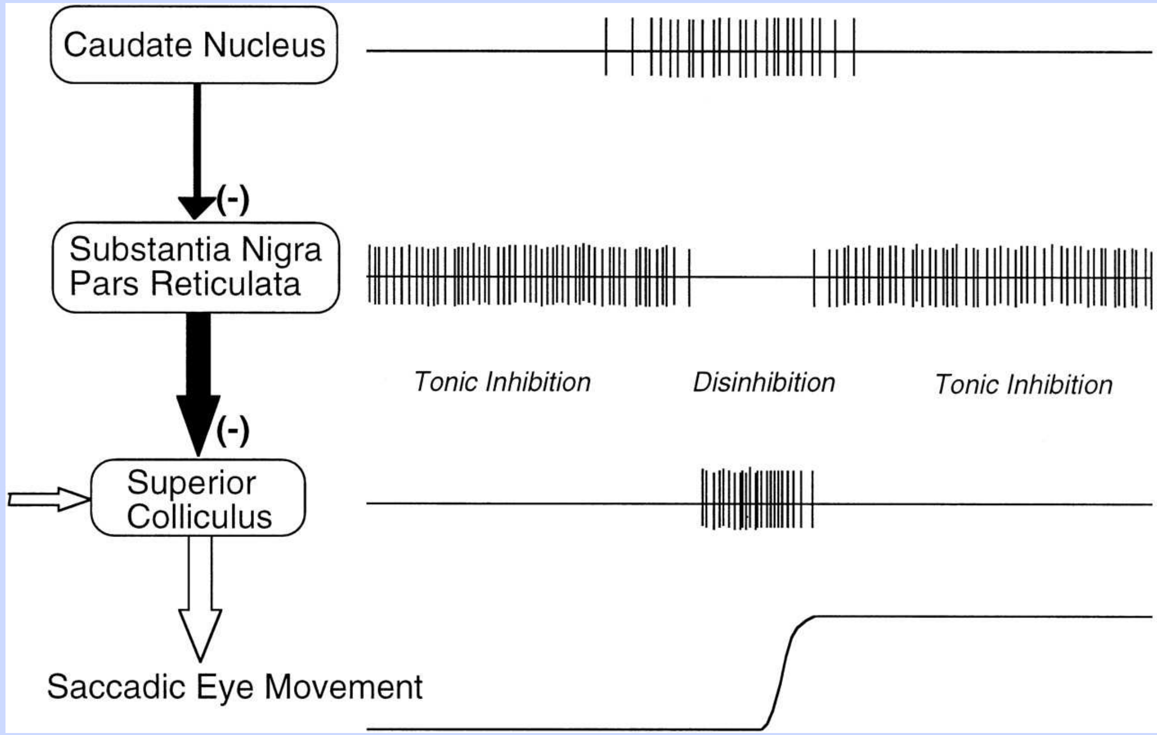


Striato-Cortical Functional Circuitry



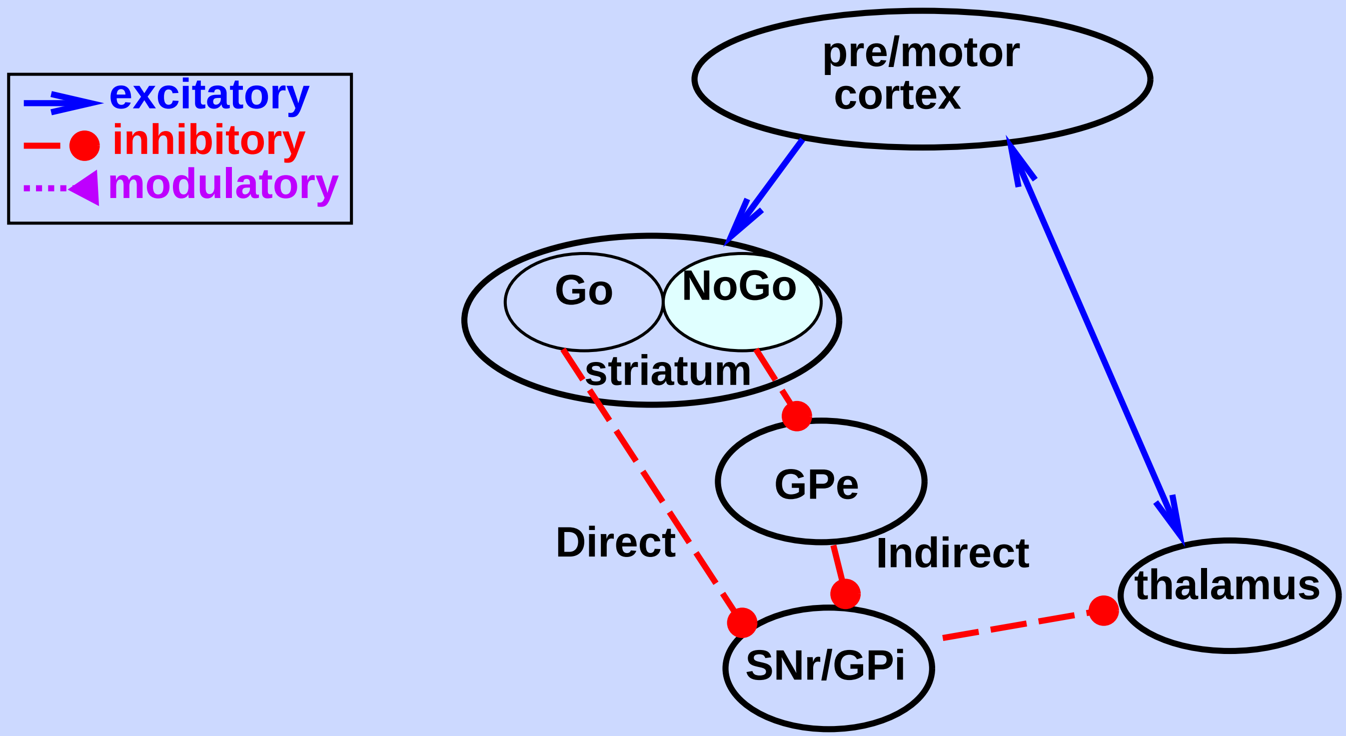
Simulation

Disinhibition as a gating mechanism

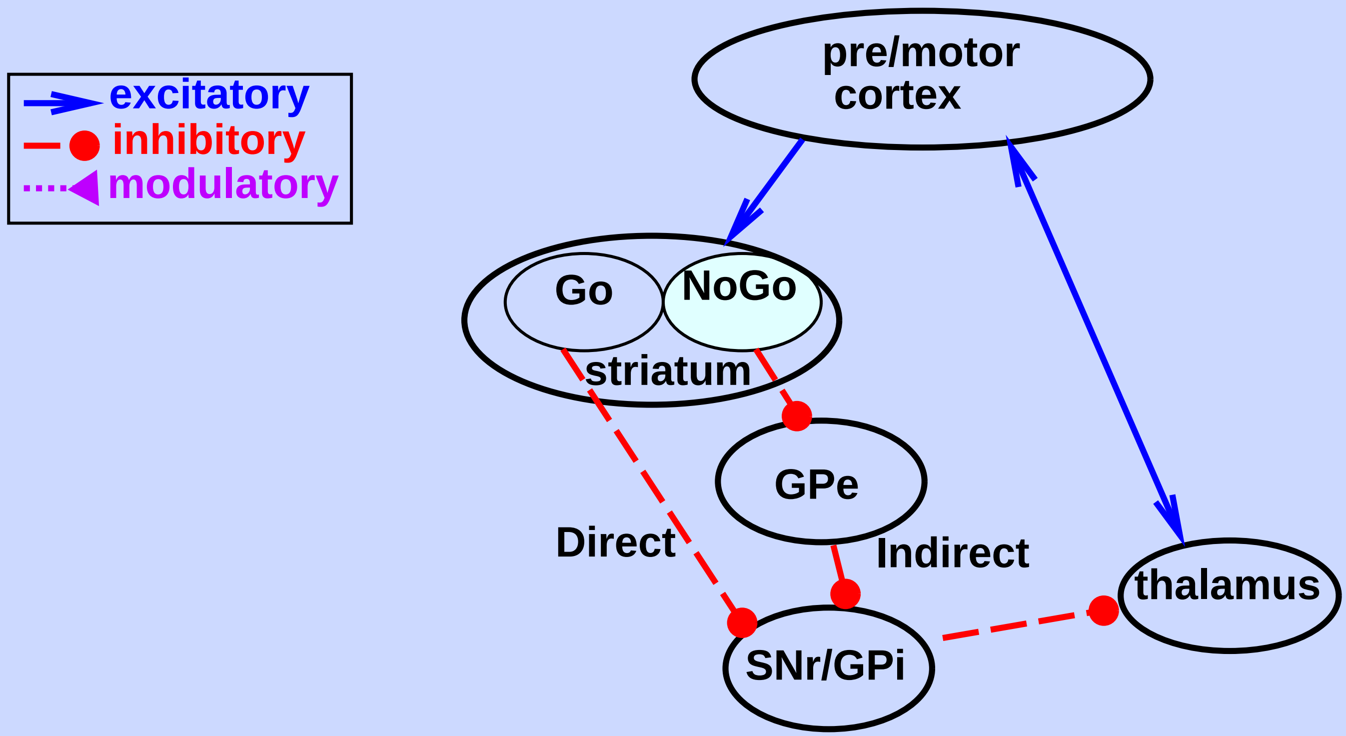


Hikosaka and colleagues; Chevalier & Deniau, 90 etc

Striato-Cortical Functional Circuitry

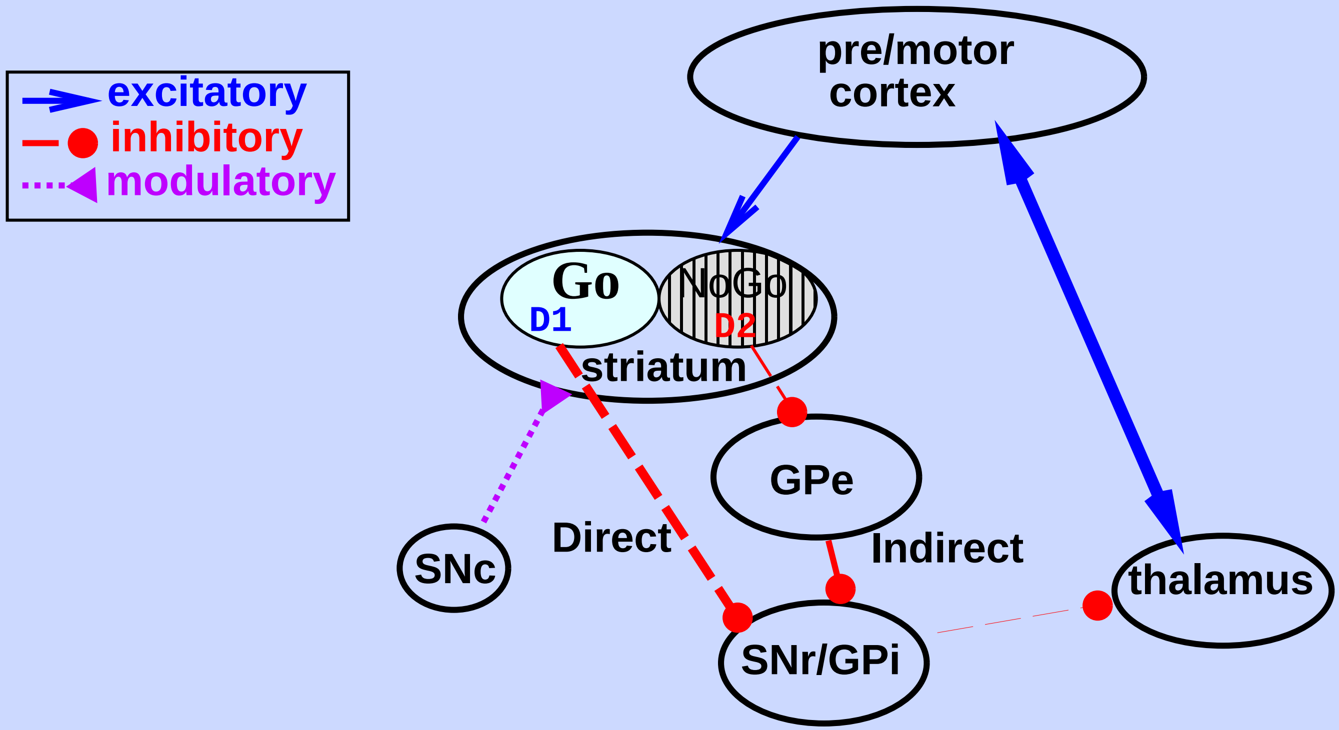


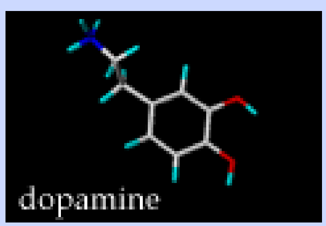
Striato-Cortical Functional Circuitry



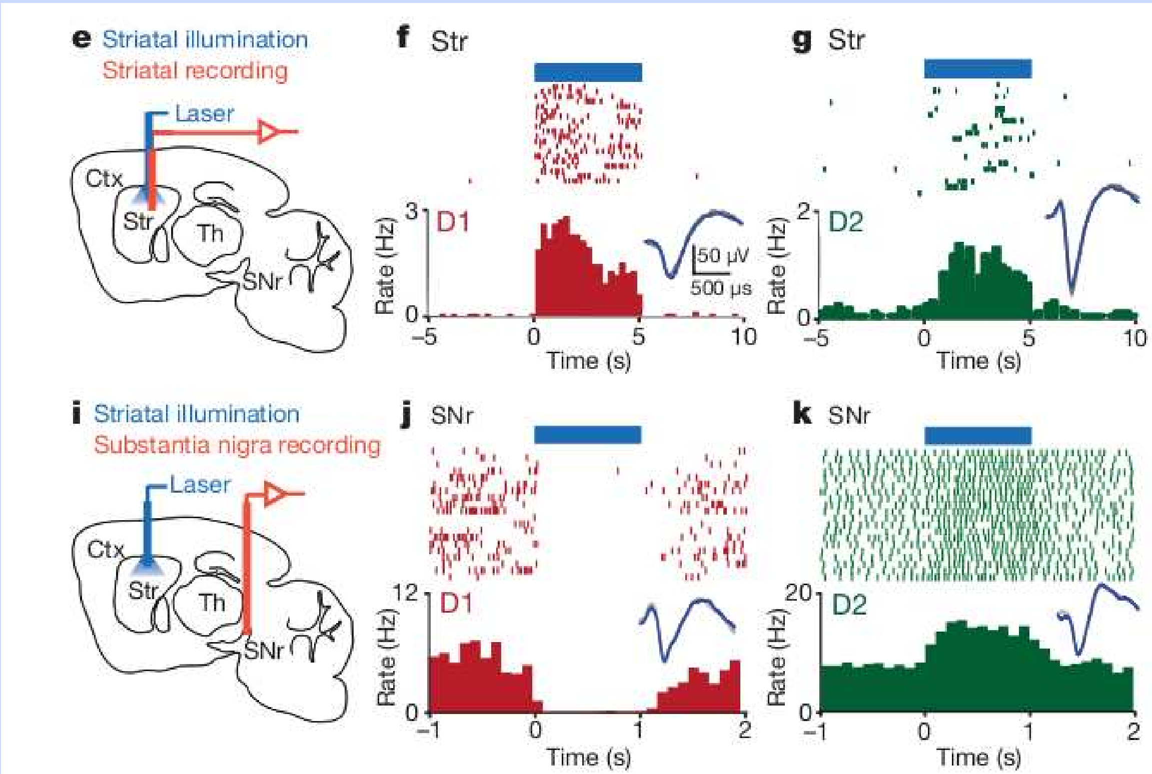
Simulation

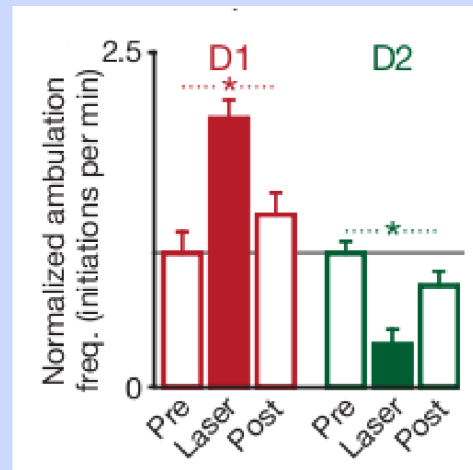
Striato-Cortical Functional Circuitry





Evidence for go/nogo mechanism:
Optogenetic stimulation of direct and indirect pathways

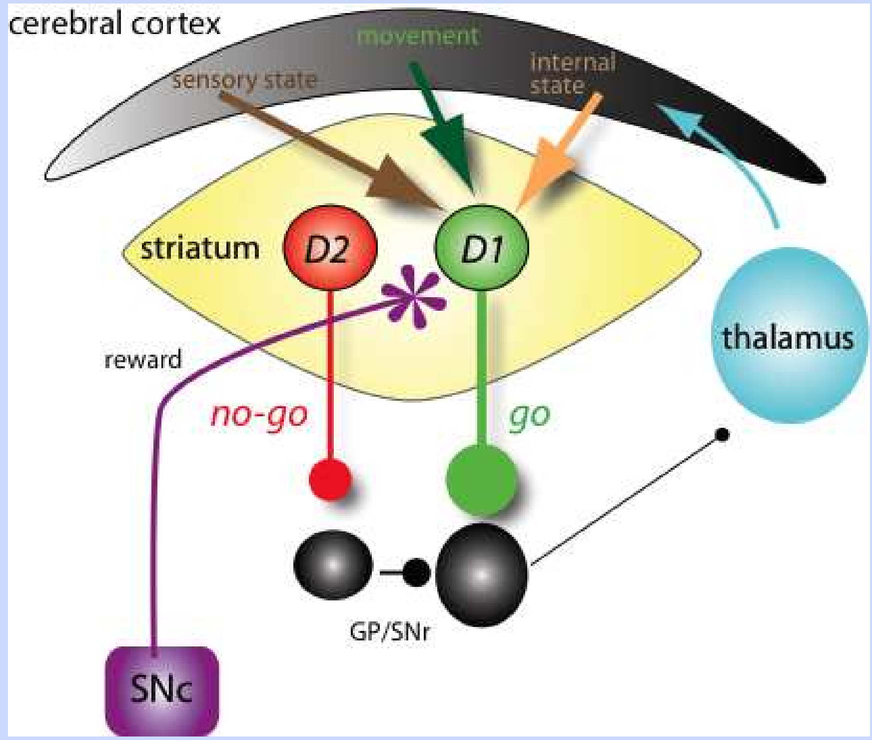




Go $\rightarrow$ inhibits SNr; NoGo $\rightarrow$ excites SNr ...and induces/inhibits movement

Kravitz et al, 2010, Nature

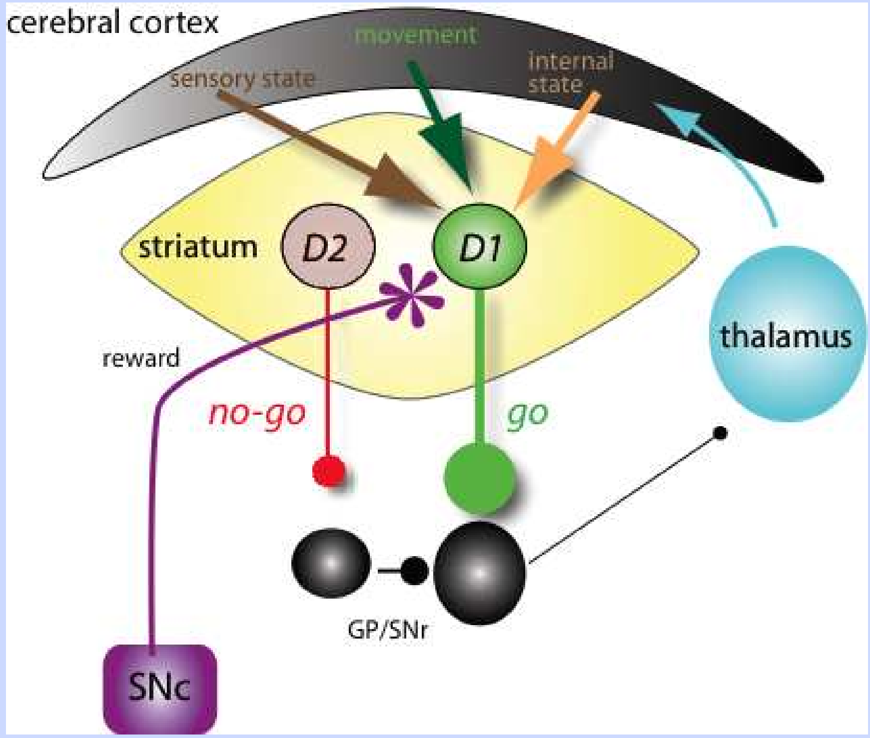
Dual pathways in the BG: Cartoon version

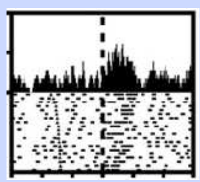


- Go/NoGo terminology is misleading (implies “act” vs. “not act”)
- Benefit vs. cost of alternative actions (both at the same time!)
- Phasic DA signals drive learning via modulation of activation dynamics

D1 effects on BG learning: Positive PE

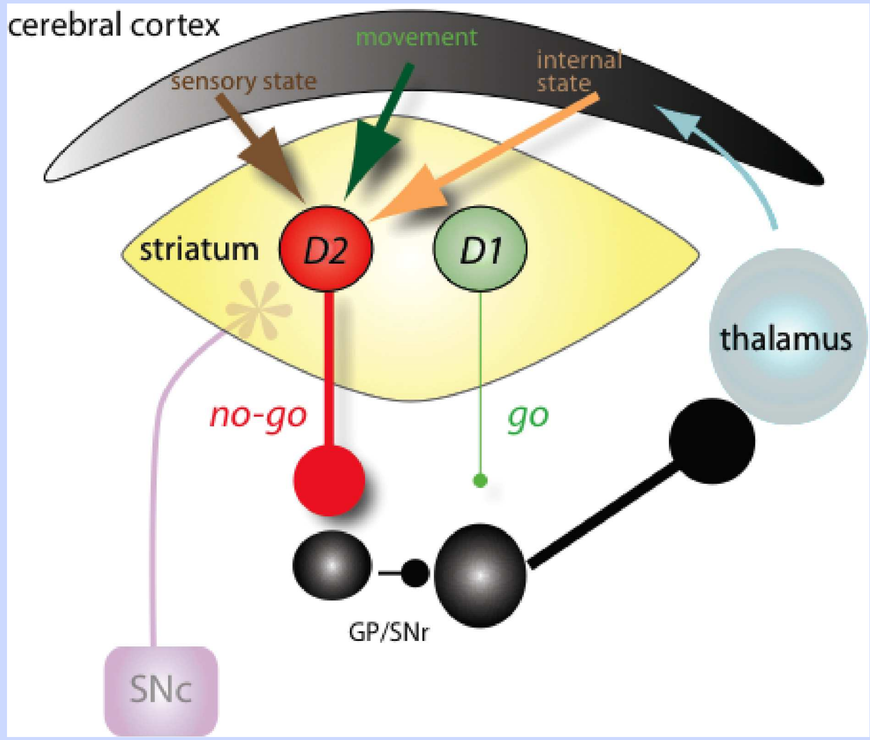
D1 effects on BG learning: Positive PE

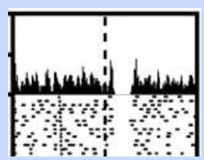




Three factor learning: presynaptic, postsynaptic and DA

D2 effects on BG learning: Negative PE

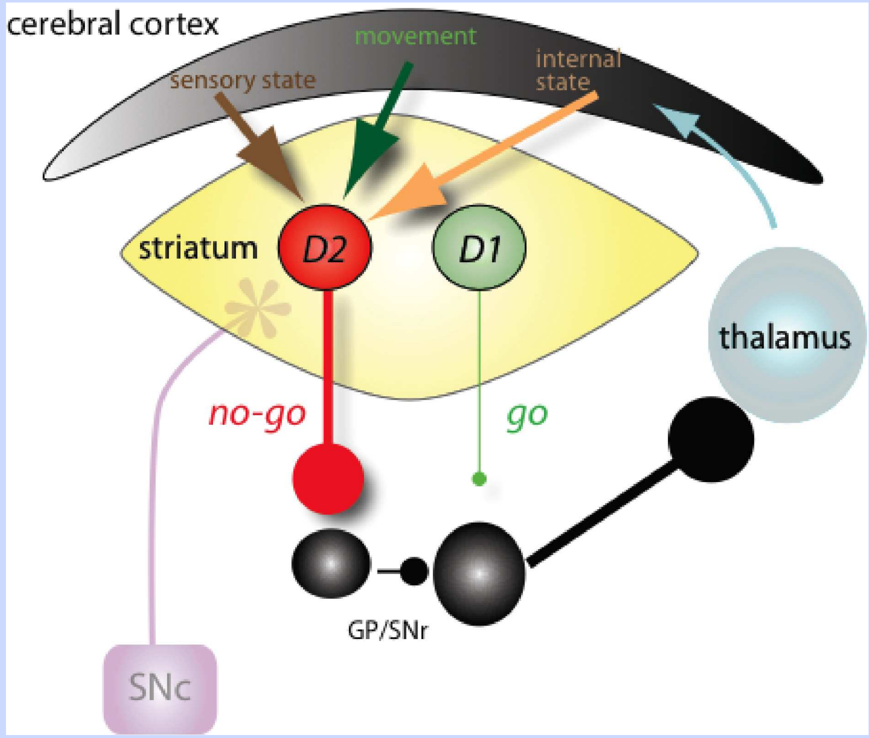


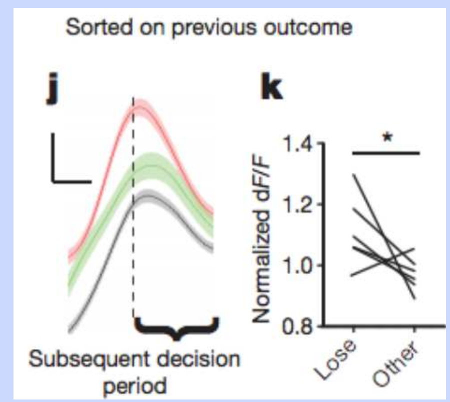


- originally: prediction based on computation (function) and circumstantial data
- D2 weights accumulate with experience - learned Parkinsonism

Frank et al, 2004; 2005

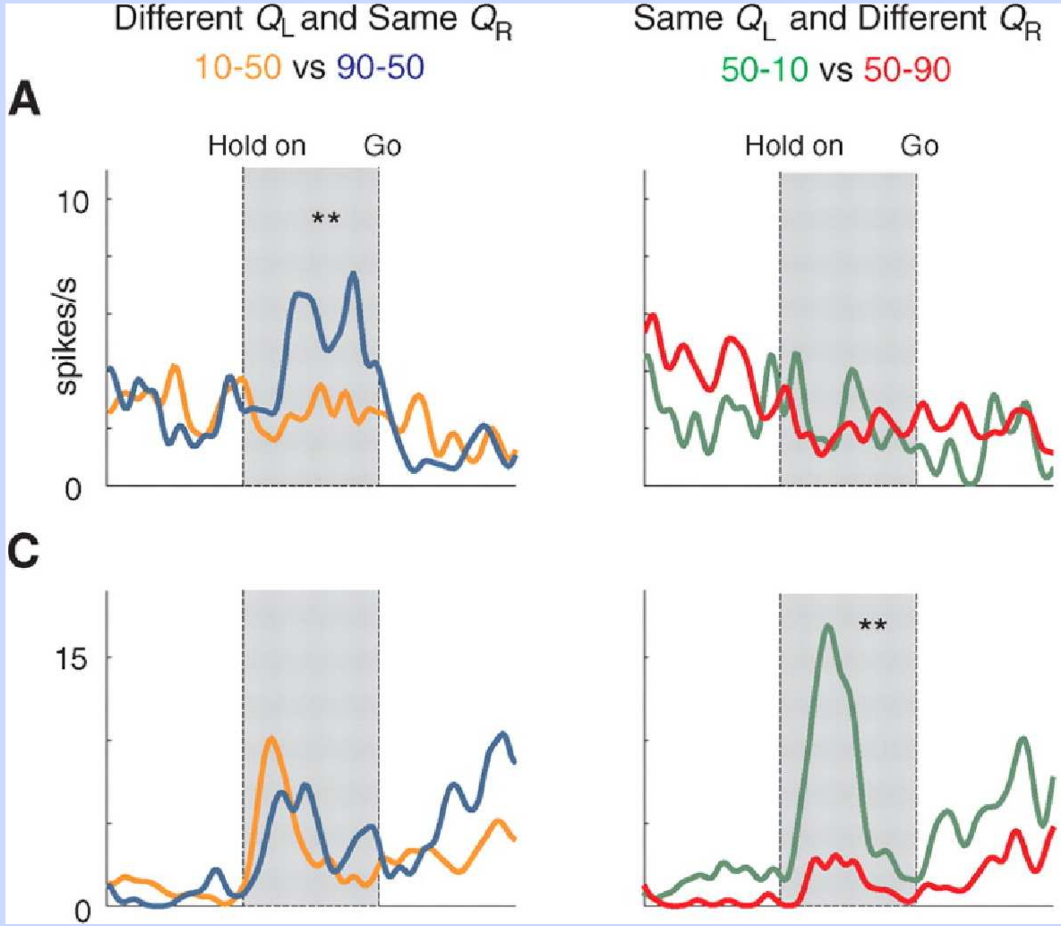
D2 effects on BG learning: Negative PE





Zalocusky et al, 2016

Separate striatal populations code for pos/neg action values

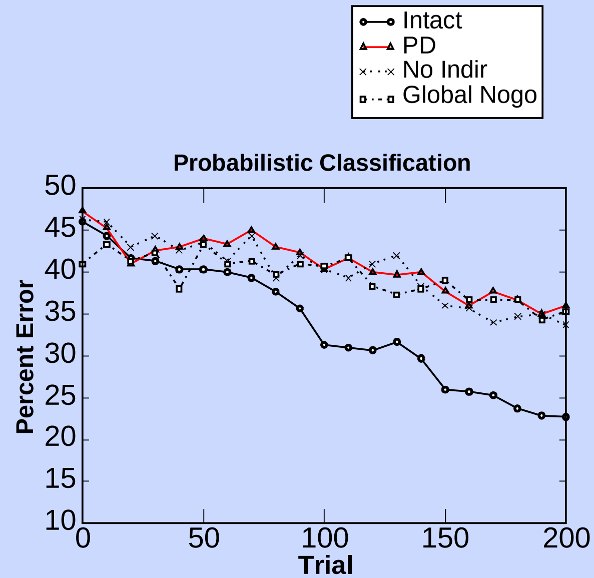


Samejima et al., 2005 *Science*

BG.proj

- uses DA RPE to drive contrastive Hebbian learning signal
- No supervised target; just reward-DA driven learning
- But still XCAL / CHL at level of synapse - activity dependent learning.
- Note: wiki version is yet more simplified for demo

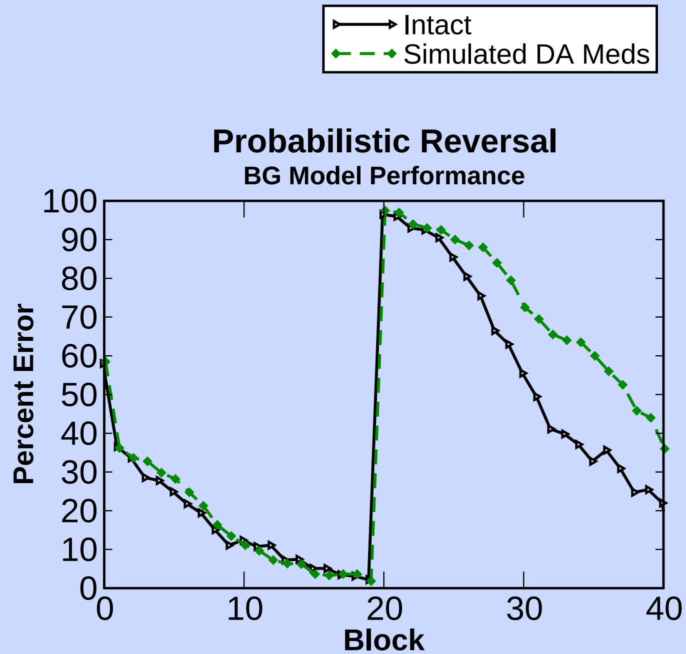
Simulating Probabilistic Classification



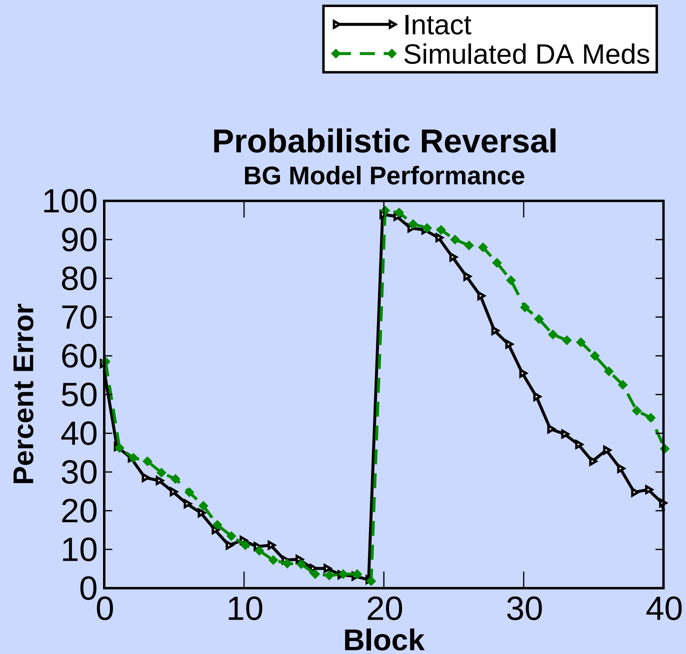
- Intact nets extracted probabilistic structure by resolving differences in Go/NoGo representations.
- PD nets were impaired due to reduced dynamic range of DA, capturing experimental data in same task.

Frank, 2005, *J Cog Neurosci*

Simulating human learning and DA meds



Simulating human learning and DA meds



- *Medication: ↑ DA levels, but tonic stimulation of D2 receptors prevents DA dips from inducing NoGo learning*.

Cools et al, 2001; Frank, 2005

Model predictions supported by rodent D1/D2 manips

DISTINCT DOPAMINERGIC CONTROL OF THE DIRECT AND INDIRECT PATHWAYS IN REWARD-BASED AND AVOIDANCE LEARNING BEHAVIORS

Distinct Roles of Synaptic Transmission in Direct and Indirect Striatal Pathways to Reward and Aversive Behavior

Takatoshi Hikida,[1,2] Kensuke Kimura,[1,3] Norio Wada,[1] Kazuo Funabiki,[1] and Shigetada Nakanishi[1,*]

Distinct roles for direct and indirect pathway striatal neurons in reinforcement

Alexxai V Kravitz[1,4], Lynne D Tye[1,2,4] & Anatol C Kreitzer[1–3]

Transient stimulation of distinct subpopulations of striatal neurons mimics changes in action value

Lung-Hao Tai[1,7], A Moses Lee[1,2,7], Nora Benavidez[1,3], Antonello Bonci[4–6] & Linda Wilbrecht[1,4]

Nucleus accumbens D2R cells signal prior outcomes and control risky decision-making

Kelly A. Zalocusky[1,2,3], Charu Ramakrishnan[1,3], Talia N. Lerner[1,3], Thomas J. Davidson[1,3], Brian Knutson[4] & Karl Deisseroth[1,3,5]

Dichotomous Dopaminergic Control of Striatal Synaptic Plasticity

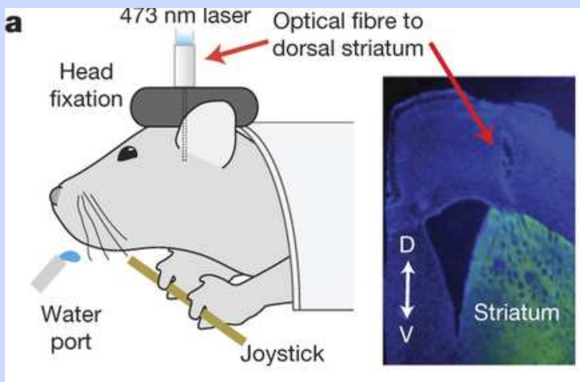
Weixing Shen,[1] Marc Flajolet,[2] Paul Greengard,[2] D. James Surmeier[1]*

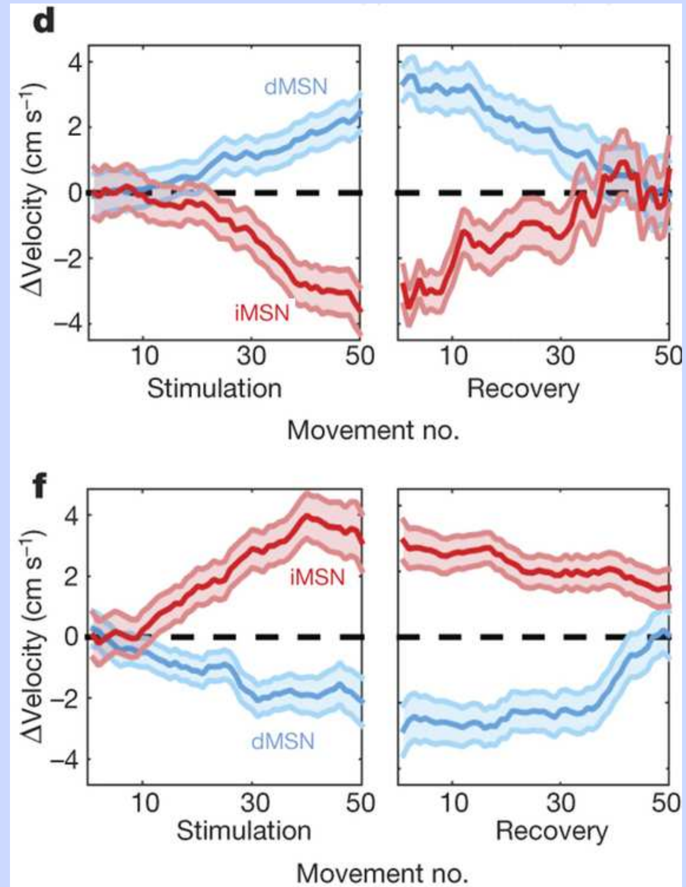
Phasic Firing in Dopaminergic Neurons Is Sufficient for Behavioral Conditioning

Hsing-Chen Tsai,[1,2]* Feng Zhang,[2]* Antoine Adamantidis,[3] Garret D. Stuber,[4] Antonello Bonci,[4] Luis de Lecea,[3] Karl Deisseroth[2,3]†

also monkey d1/d2 pharmacology, e.g. Nakamura & Hikosaka 06

Pitting action against RL accounts of D1/D2





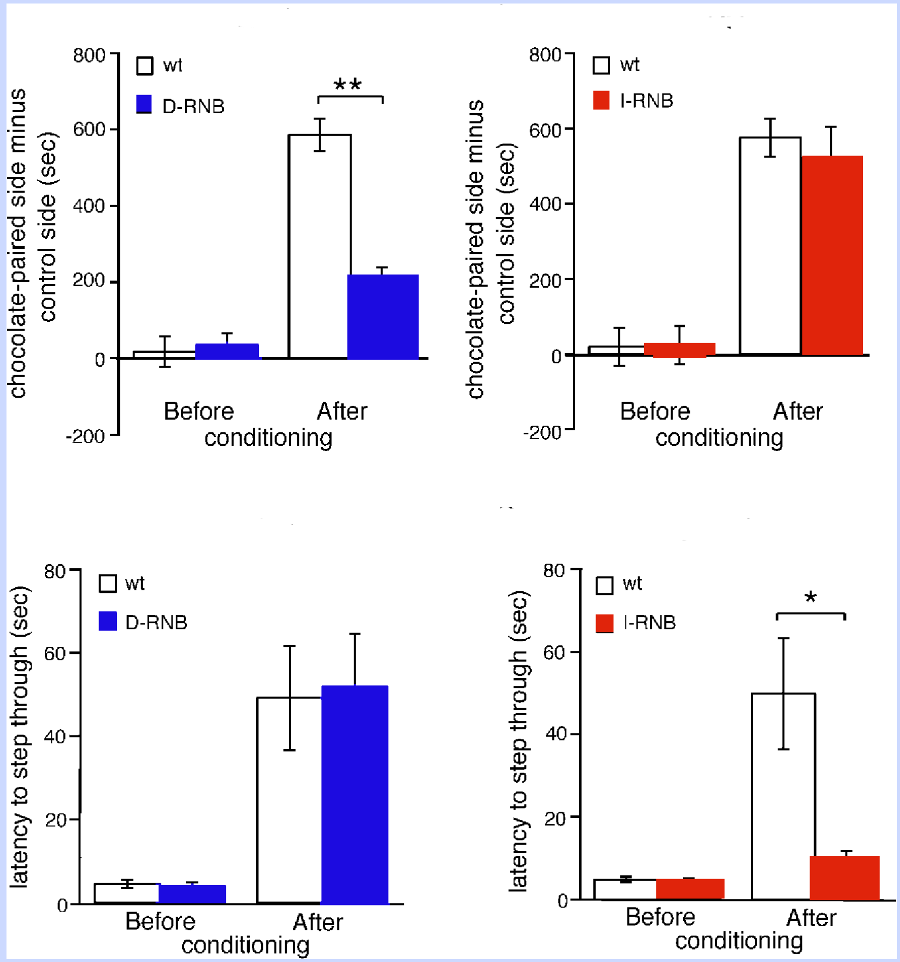
Yttri & Dudman, 2016, *Nature*

Blocking neurotransmission in mouse Go/NoGo pathways

Direct pathway *Indirect pathway*

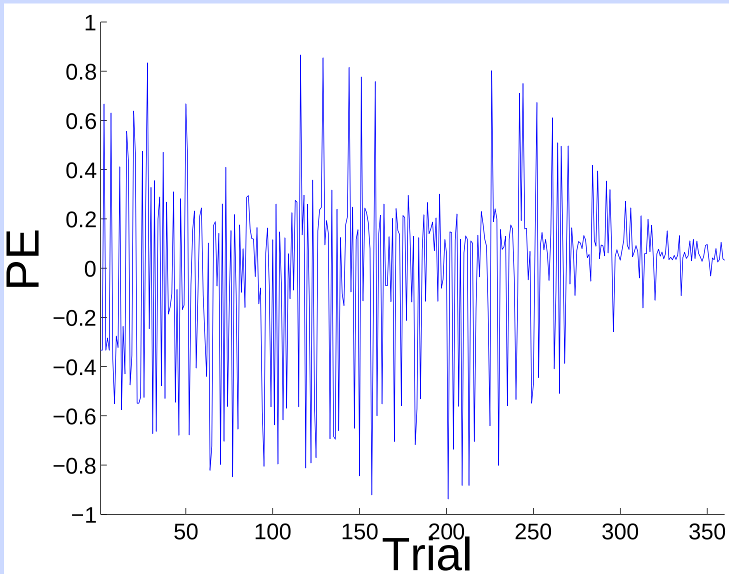
Reward/
approach

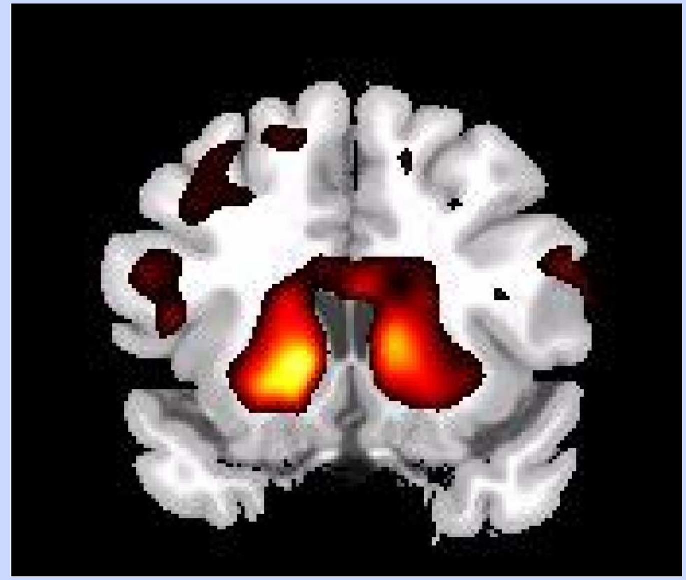
Avoid/
punishment



Hikida et al, 2010, *Neuron*

Reward prediction error and human functional imaging

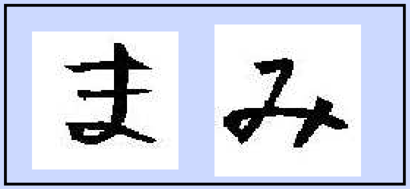




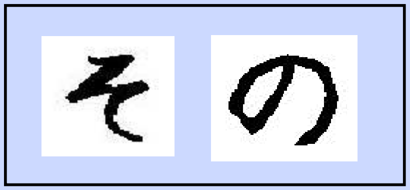
McClure et al, 2003; O’Doherty et al, 2004; Daw et al, 2006; Caplin et al, 2010; Badre & Frank, 2011 etc

Human probabilistic reinforcement learning

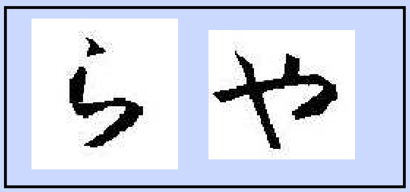
Train



A (80/20) B (20/80)



C (70/30) D (30/70)



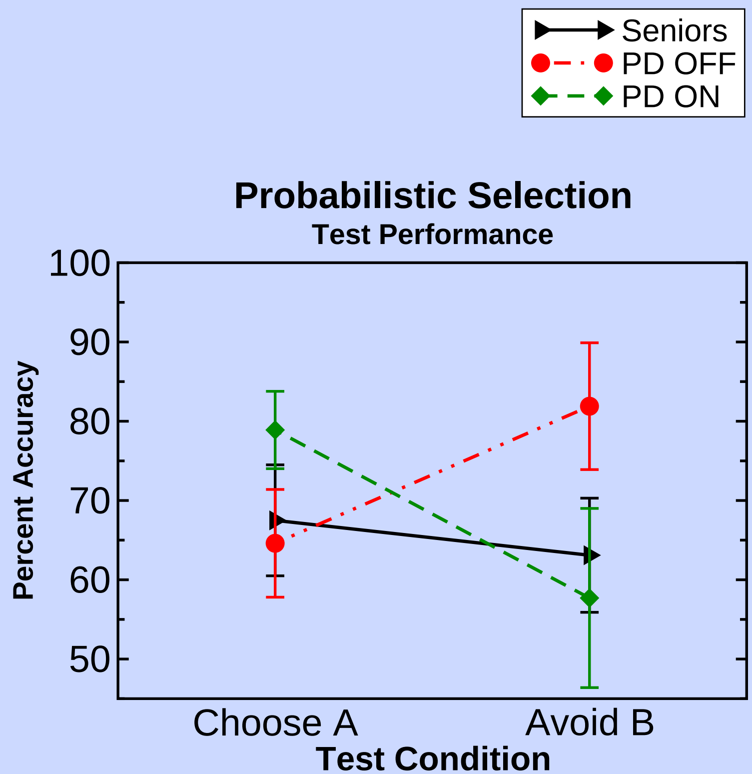
E (60/40) F (40/60)

Test

A > CDEF **Choose A?**

B < CDEF **Avoid B?**

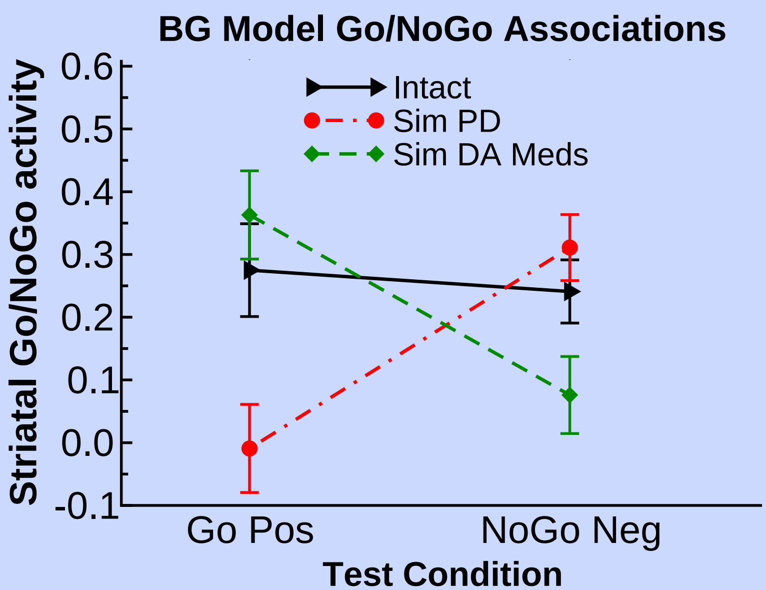
Testing the model:
Parkinson's and medication effects



Frank, Seeberger & O'Reilly (2004)

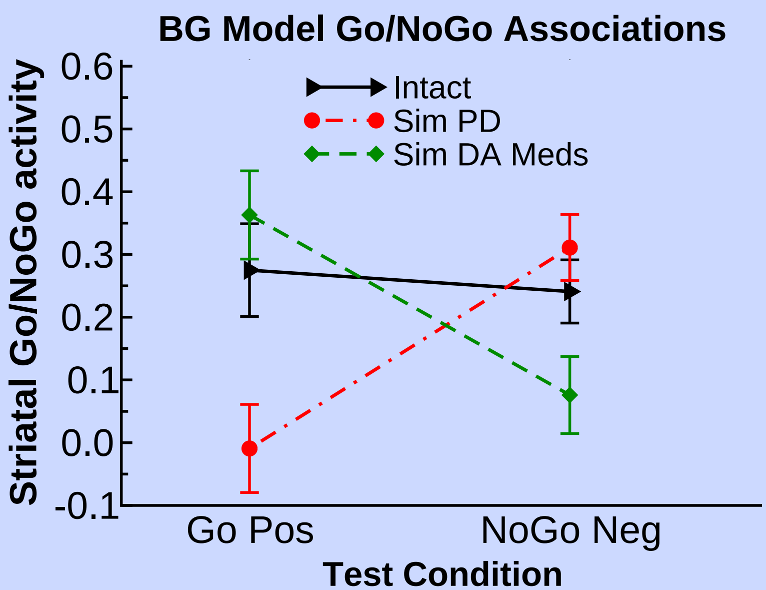
(See also: Cools et al, 06, Frank et al 07, Moustafa et al 08, Bódi et al 09, Palminteri et al, 09, Voon et al 10, etc)

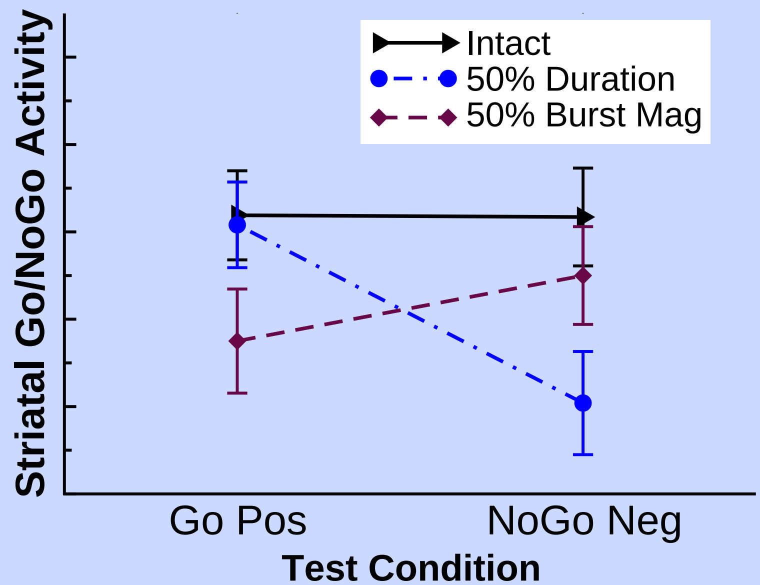
BG model: DA modulates learning from pos/neg PE's



- Go learning to positive S-R requires sufficient phasic DA bursts
- NoGo learning to negative S-R requires sufficiently low DA during pauses

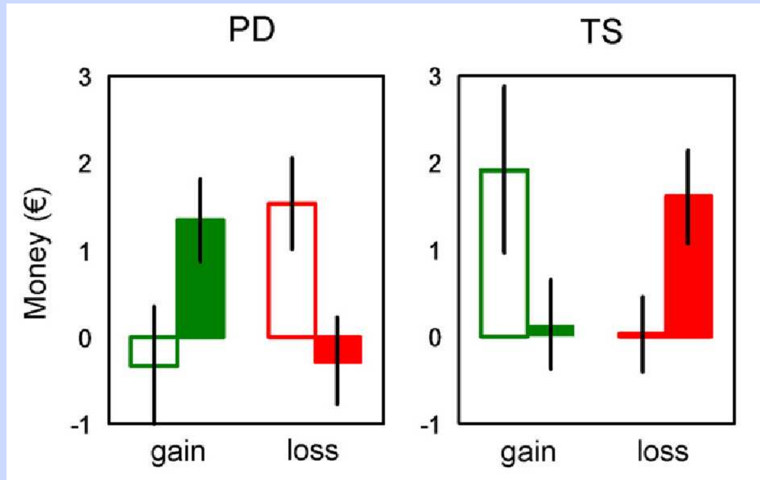
BG model: DA modulates learning from pos/neg PE's





- Burst magnitude facilitates Go learning (D1)
- Pause duration facilitates NoGo learning (D2)

DA stimulation vs. D2 blockade on go/nogo learning



Filled bars = medicated (l-dopa or D2 blockade)

Open bars = unmedicated

Palminteri et al, 2009

see Wiecki et al, 2009 for model of D2 blockade effects on NoGo learning in rats

Genetics of striatal dopamine function and model-based predictions

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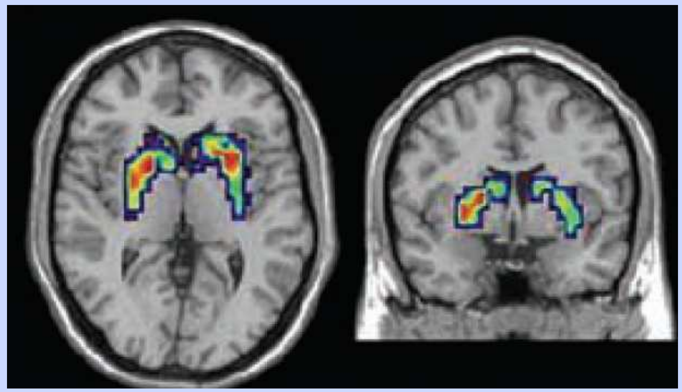
- *DARPP-32*: protein concentrated in striatum, required for *D1*-dependent plasticity (Calabresi et al 00, Stipanovich et al 08)



Meyer-Lindenberg et al, 2007

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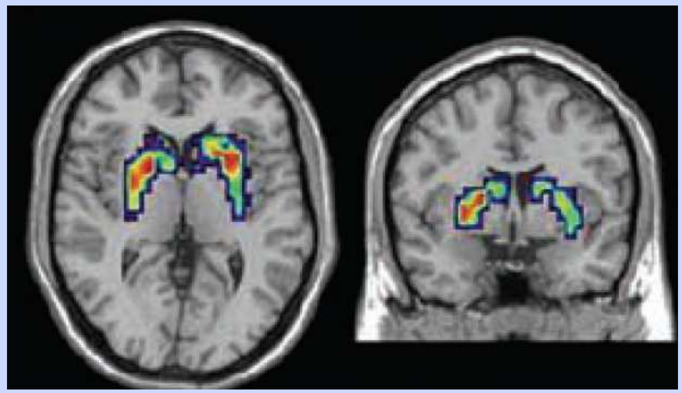

Meyer-Lindenberg et al, 2007

Dylan quotes Aristotle quotes Plato on DARPP-32!

Genetics of striatal dopamine function and model-based predictions

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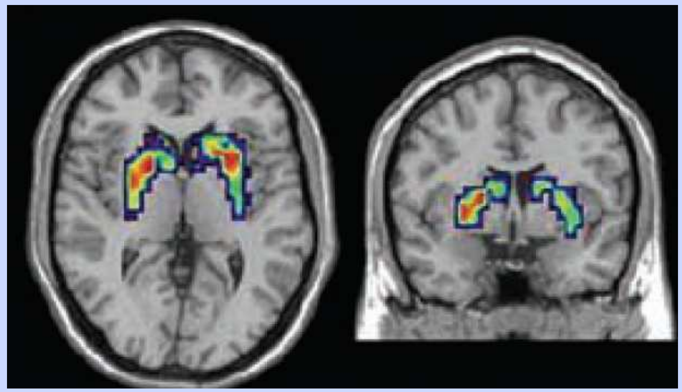
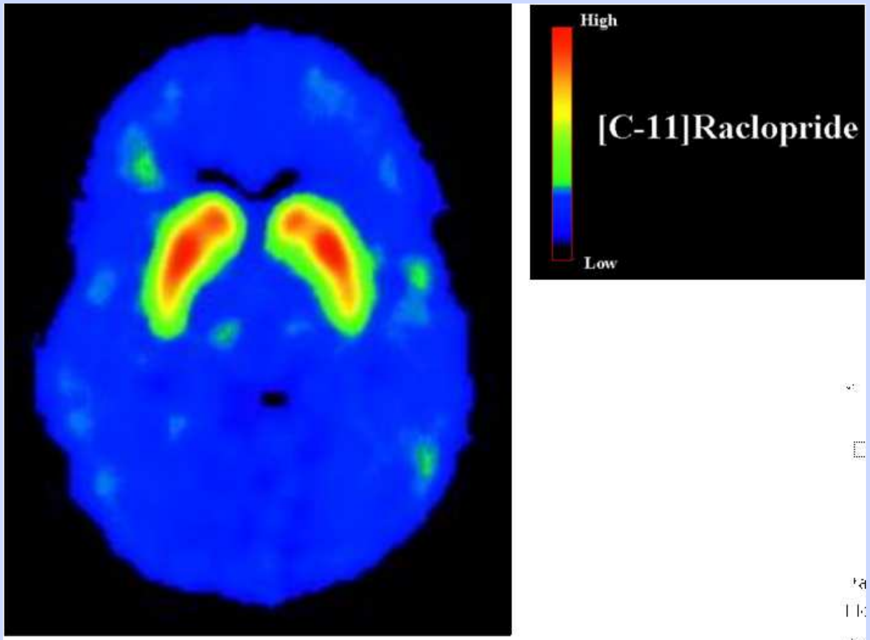


Meyer-Lindenberg et al, 2007

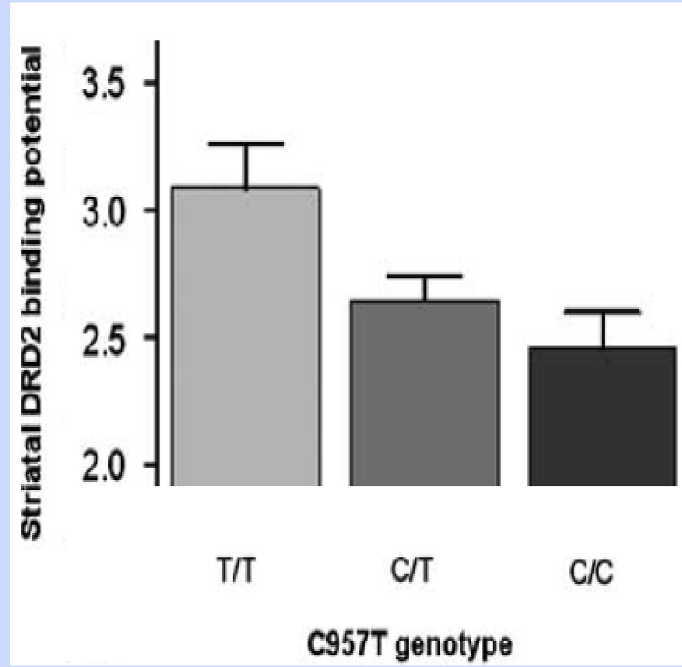
Dylan quotes Aristotle quotes Plato on DARPP-32!

⇒ *Model: D1= probabilistic Go learning*

DRD2 gene: affects striatal D2 receptor function



Wang *et al*, 2004



Hirvonen et al, 2009

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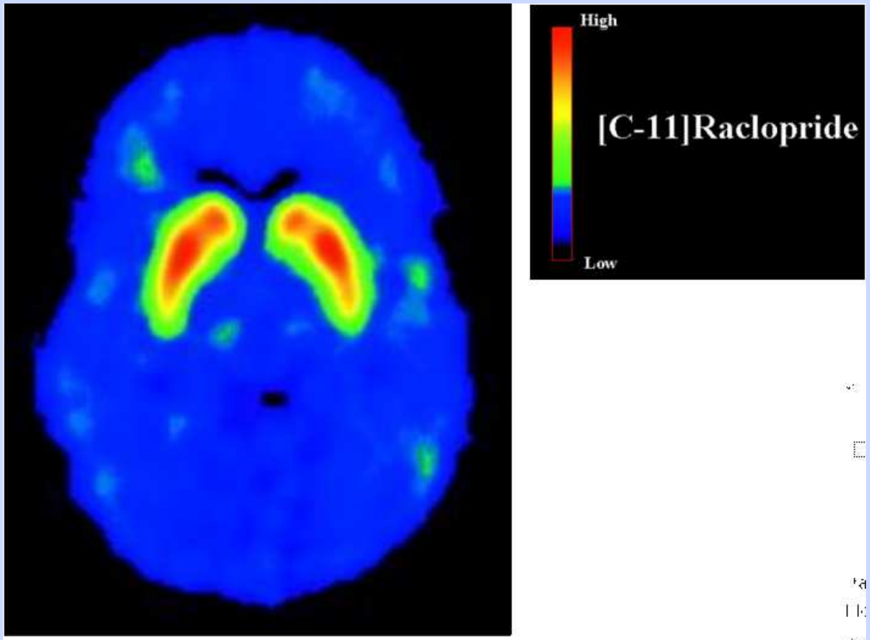
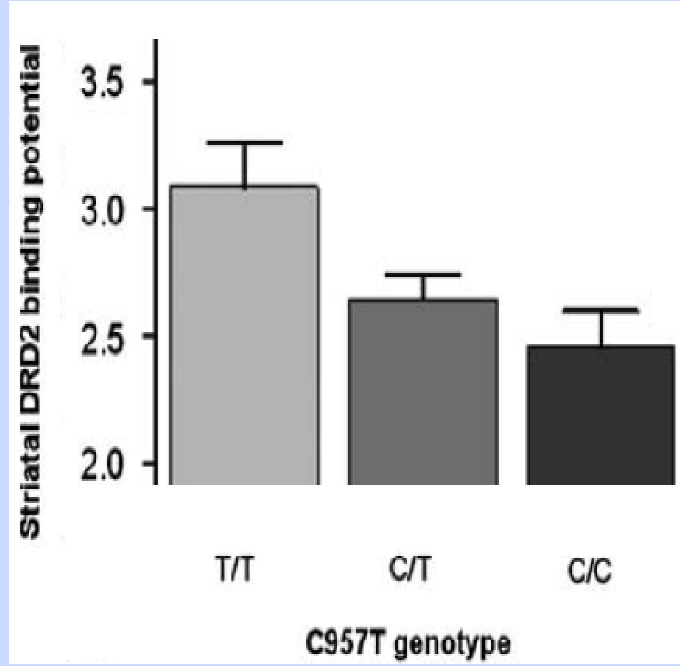


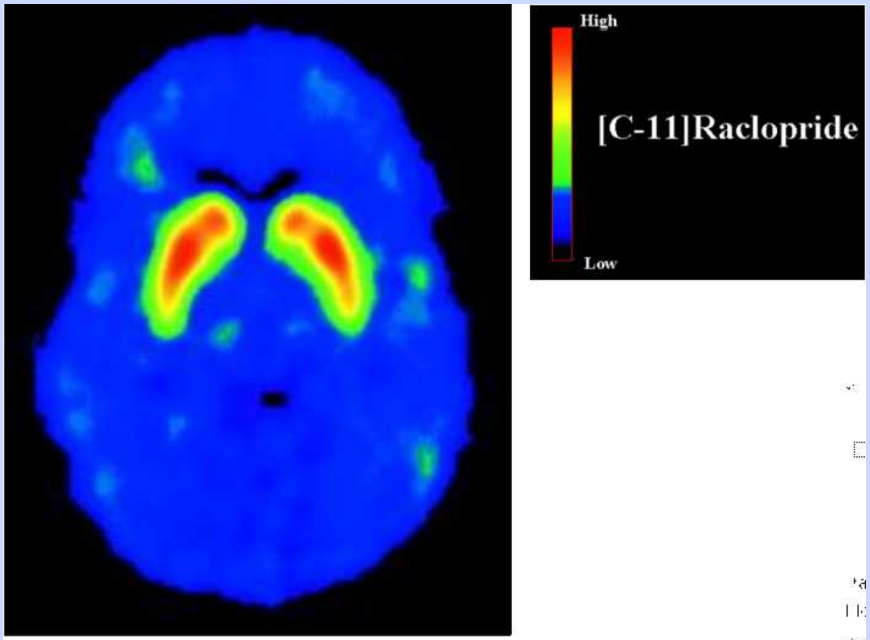
Wang *et al*, 2004



Hirvonen et al, 2009

and heres what the red hot chilli peppers have to say about this gene

DRD2 gene: affects striatal D2 receptor function



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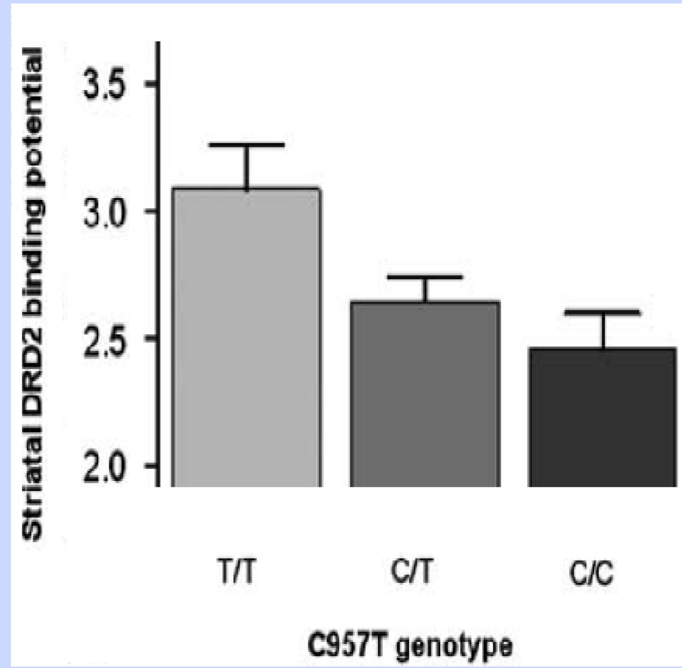


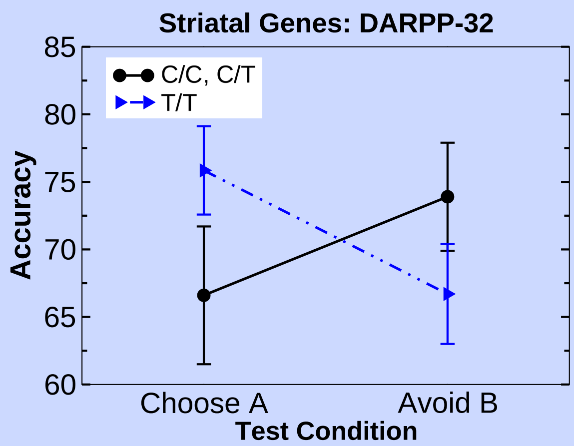
Hirvonen et al, 2009

and heres what the red hot chilli peppers have to say about this gene

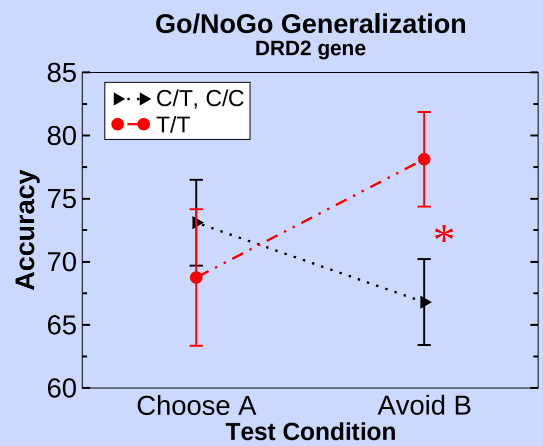
⇒ Model: D2 = probabilistic NoGo learning

DA genes and probabilistic learning

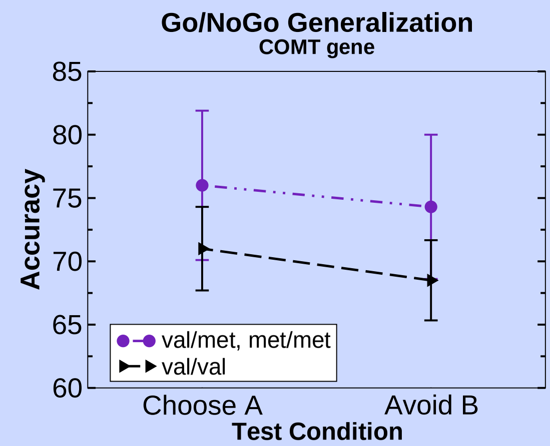
“D1”



“D2”

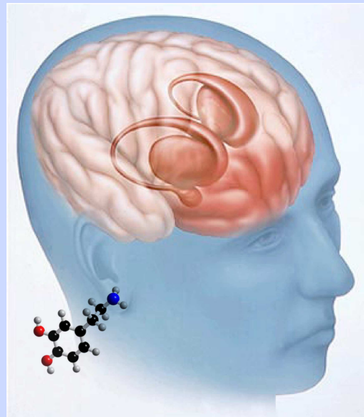


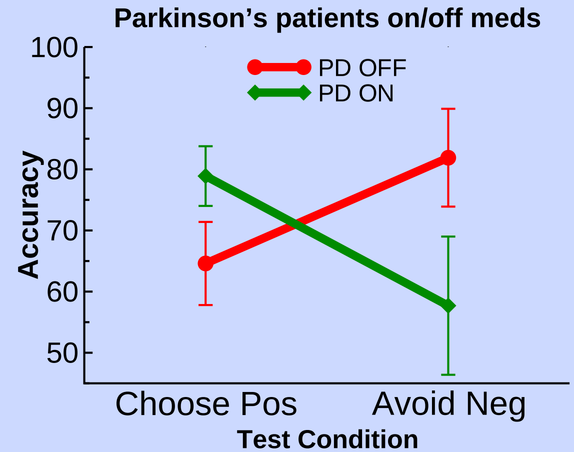
“PFC”

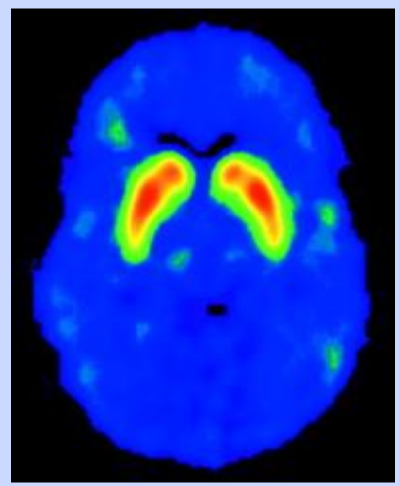


Frank et al 07, *PNAS*

In humans: probabilistic reinforcement learning

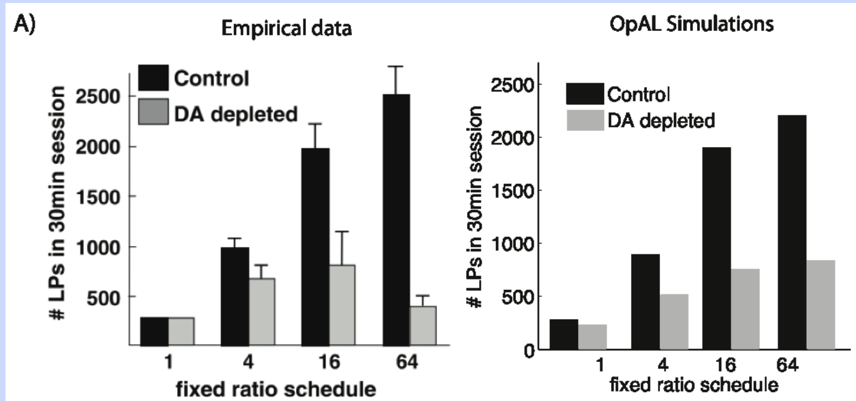






Frank et al (04, 06 , 07), Cockburn et al 14, Cox et al 2015...

Not just learning: striatal DA modulates “incentive salience” (influence of value on choice)



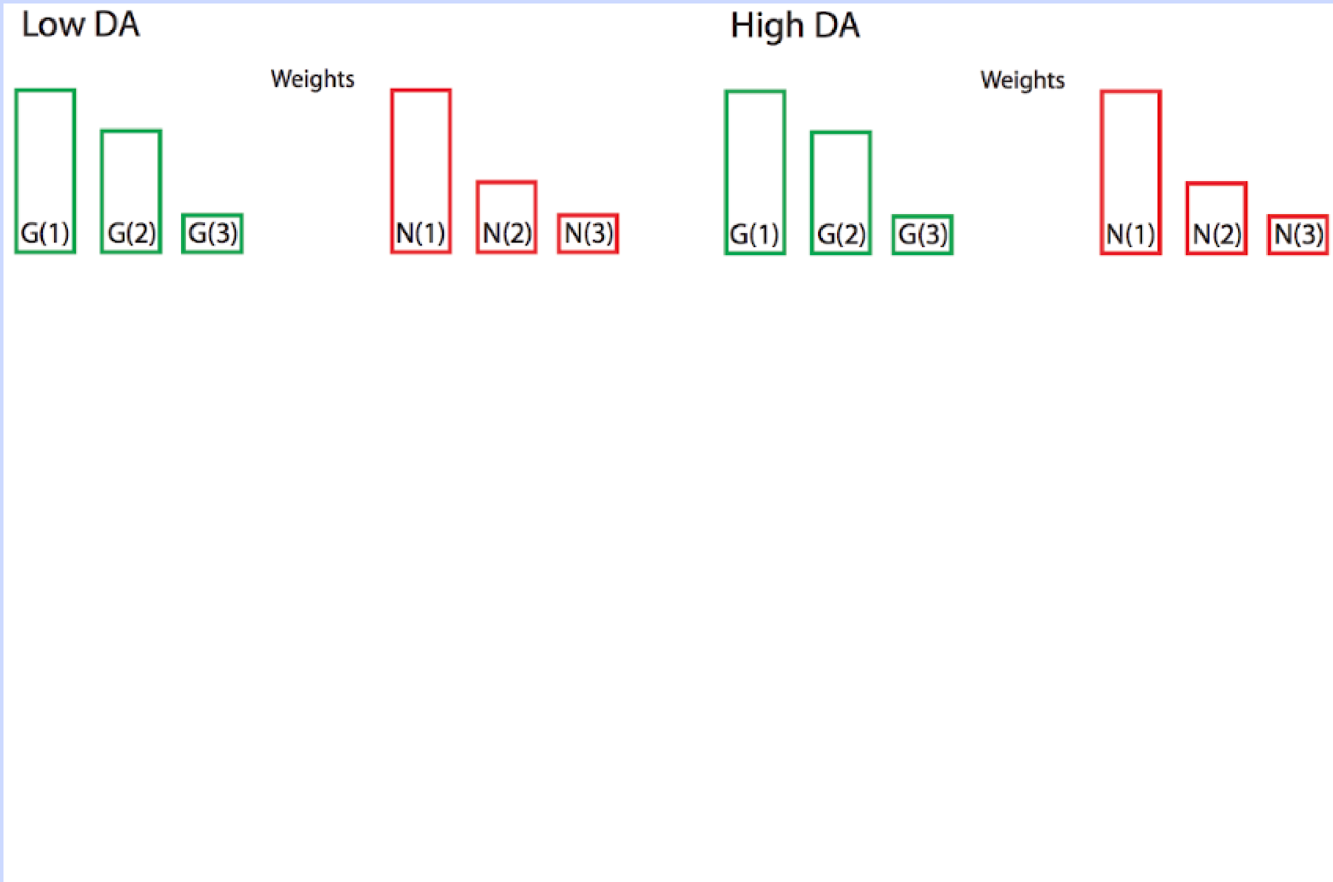
Opponent Actor Learning (OpAL): Modeling Interactive Effects of Striatal Dopamine on Reinforcement Learning and Choice Incentive

Anne G. E. Collins and Michael J. Frank

Salamone et al, 2003

also: risky decision making; Floresco, Rutledge etc; effort/reward choice tasks T-maze etc.

Dissecting DA contributions to learning vs. choice incentive (OpAL model)



Collins & Frank, *Psych Rev*, 2014

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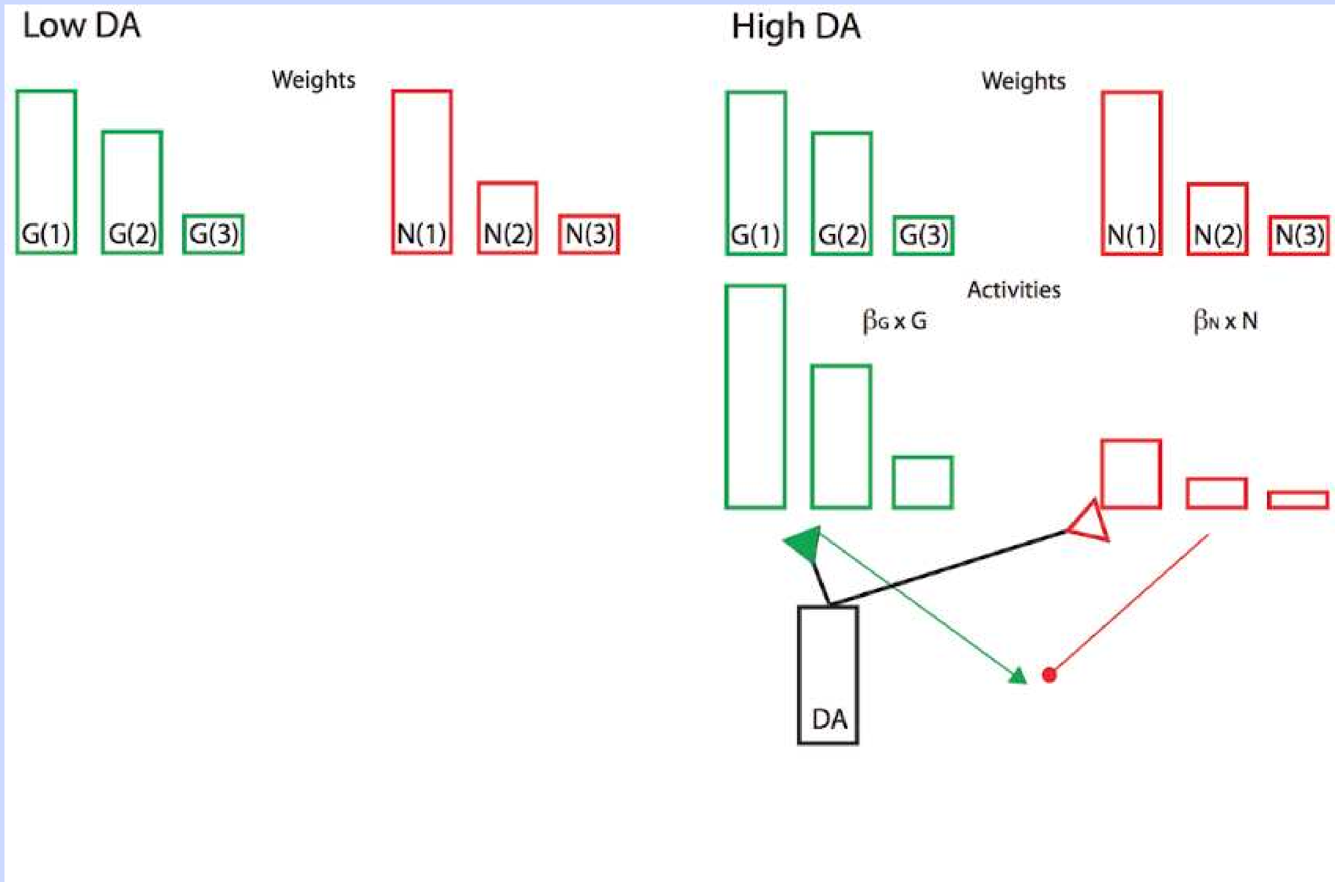

Collins & Frank, *Psych Rev*, 2014

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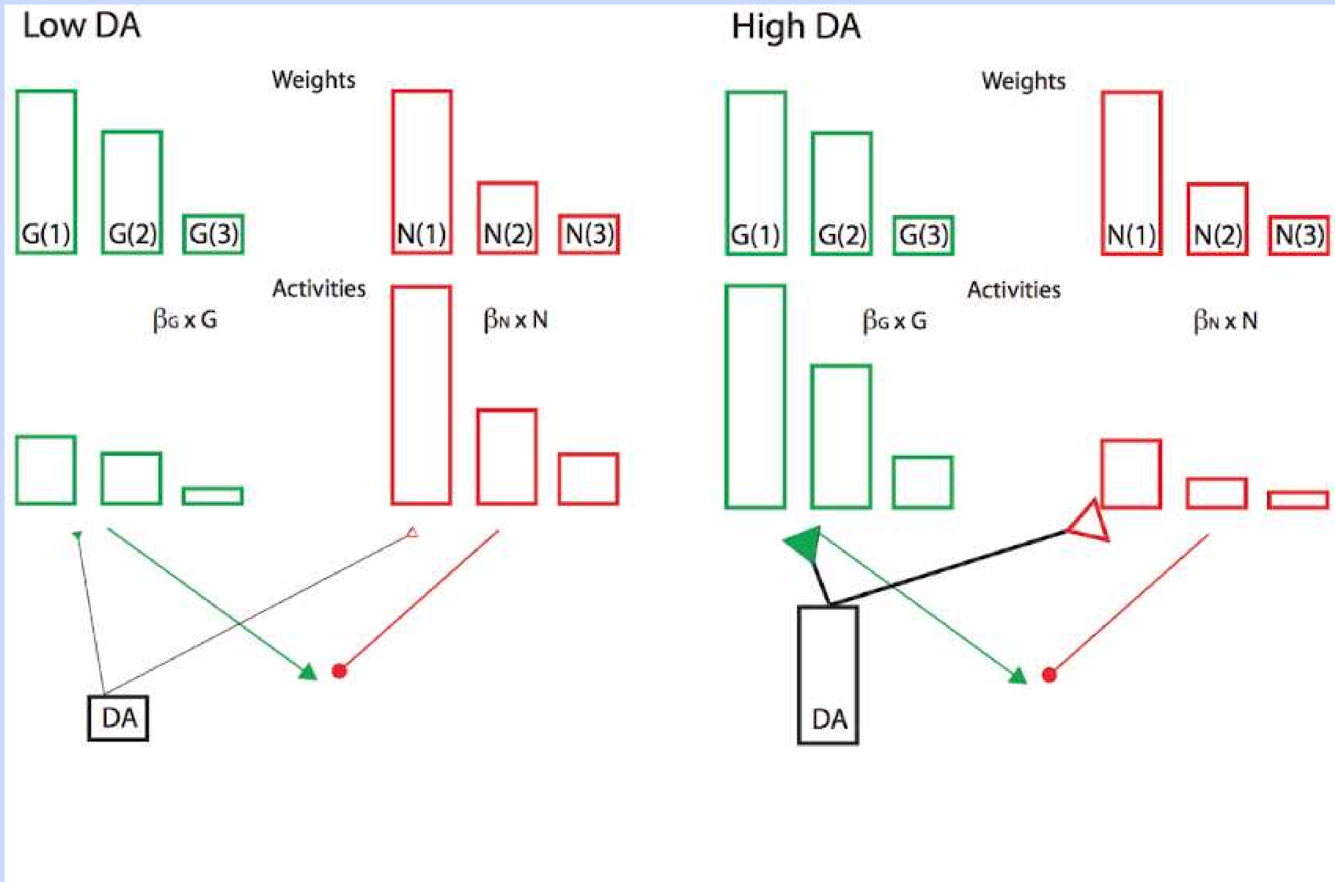

Collins & Frank, *Psych Rev*, 2014

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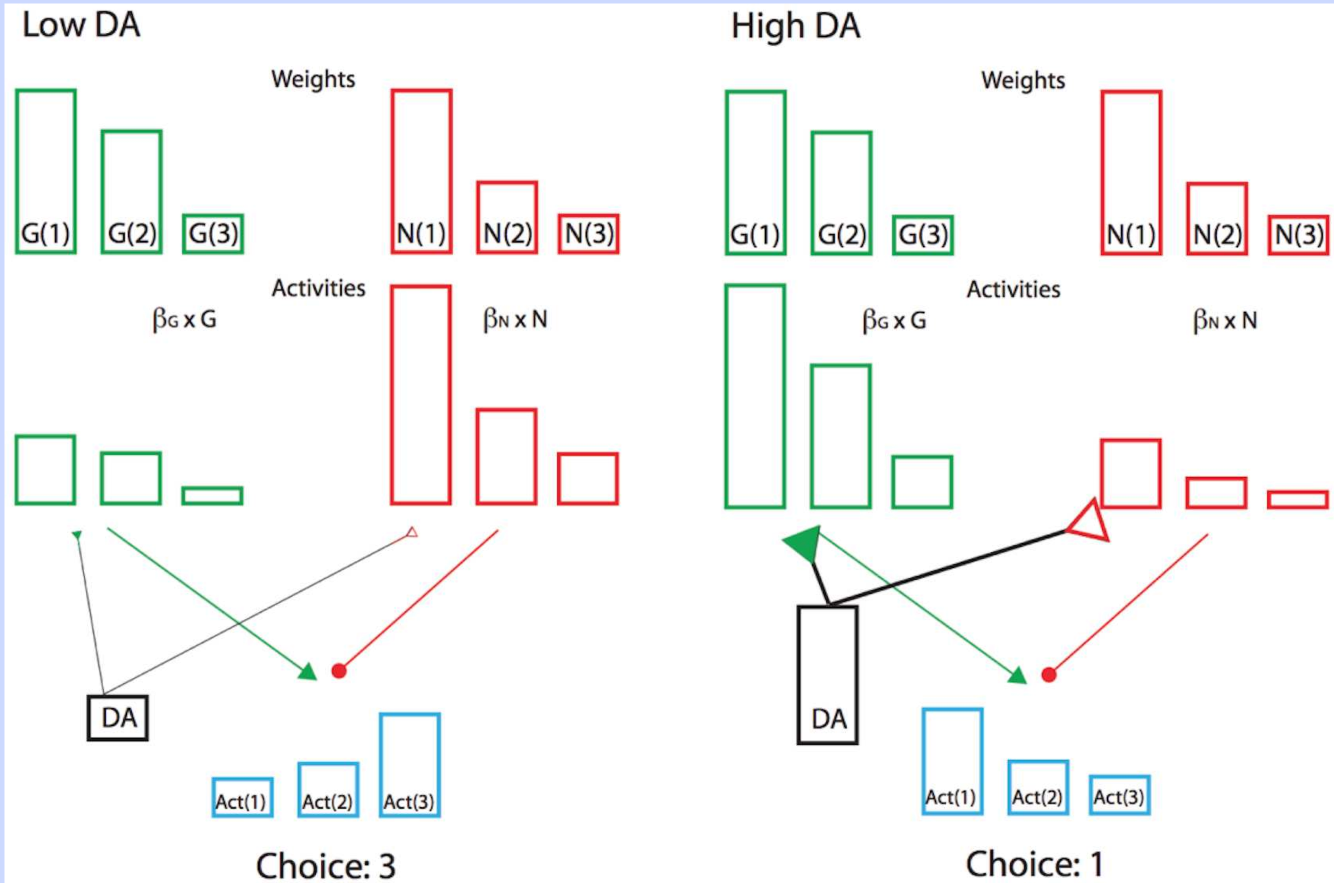

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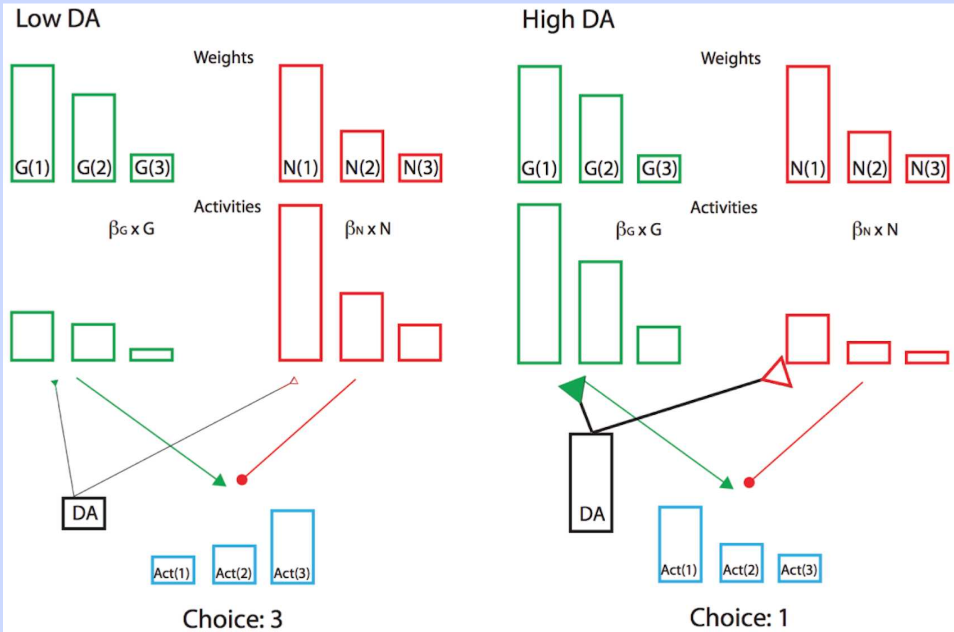
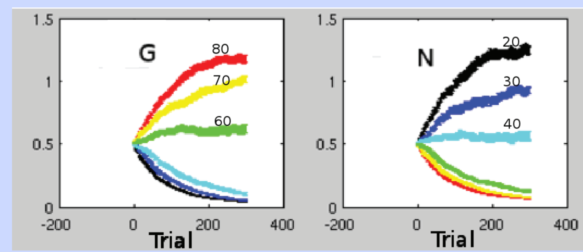
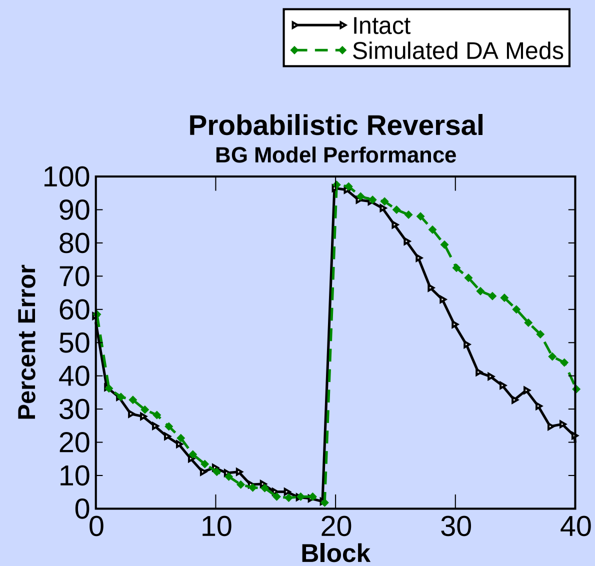




Collins & Frank, *Psych Rev*, 2014

Back to reversal learning: DA-mediated Go/NoGo learning alone is limited

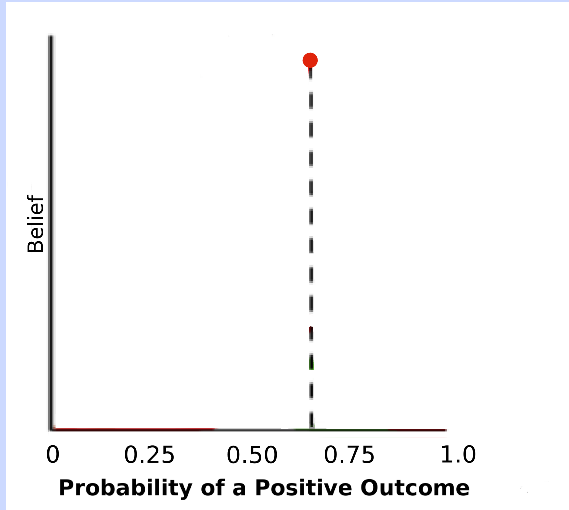


- Simulated D2 agonists prevent learning in D2 MSNs

- intact BG model learns probabilistic reversal, but not optimally ⇒ motivates need for dynamic learning rate...

Cools et al, 2001; Frank, 2005

Bayesian approach to dynamic learning



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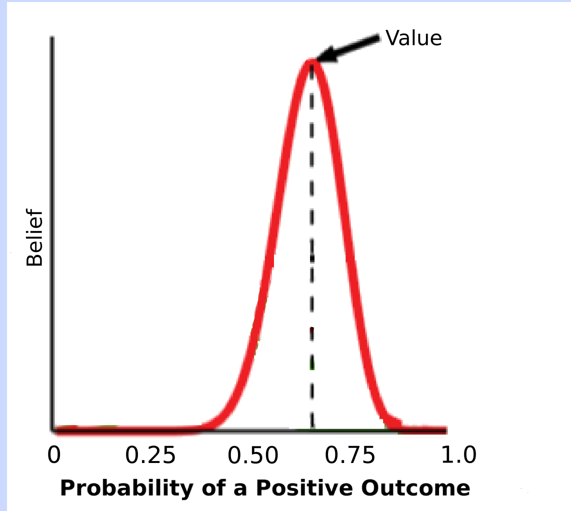

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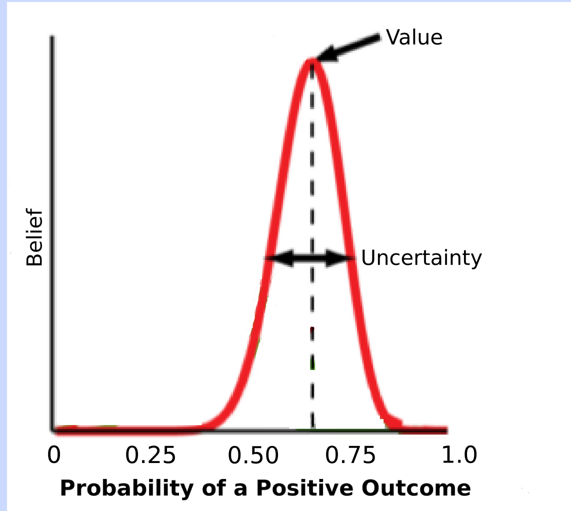

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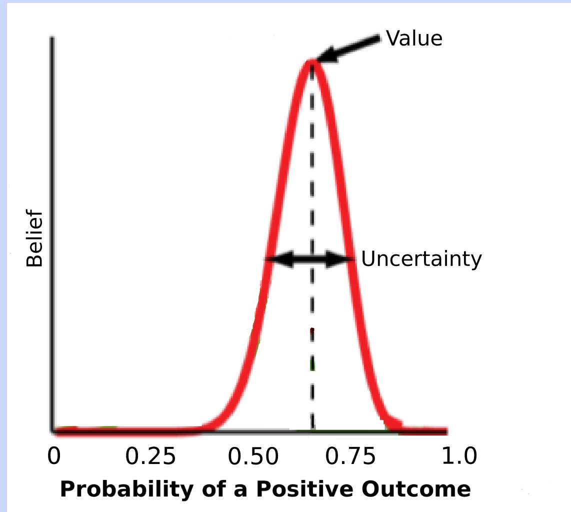
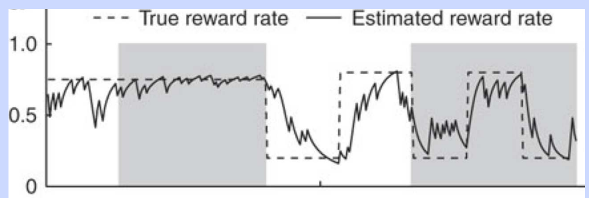
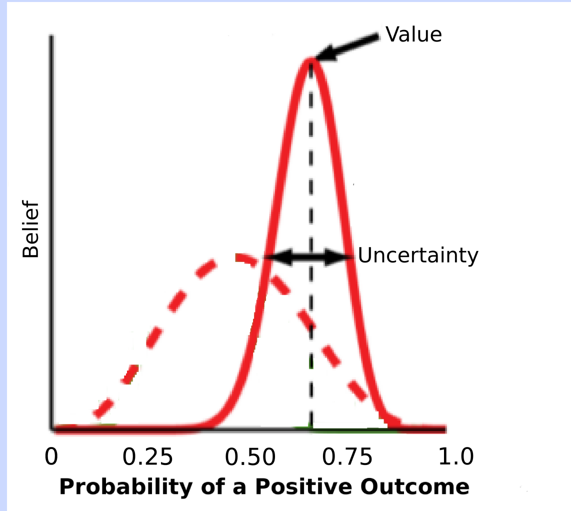


- Learning from individual noisy outcomes should depend on uncertainty (cf Kalman filter).



e.g., Yu & Dayan 05; Behrens et al 2007; Nassar et al 2010; Mathys et al 2011

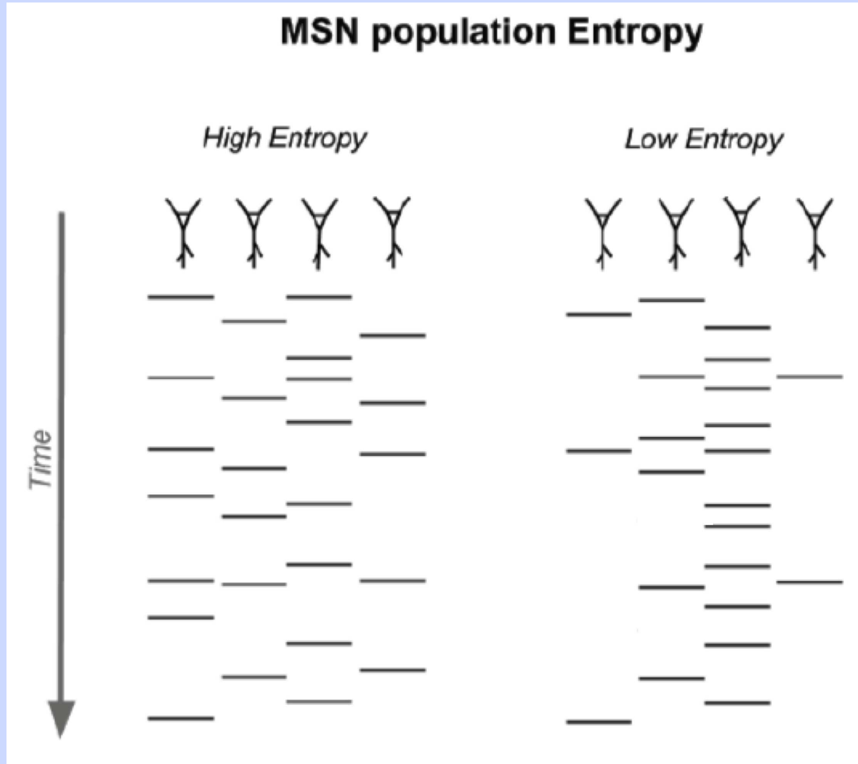
Bayesian approach to dynamic learning



- Learning from individual noisy outcomes should depend on uncertainty
- For choice tasks, uncertainty in A>B (overlap)

e.g., Yu & Dayan 05; Behrens et al 2007; Nassar et al 2010; Mathys et al 2011

MSN population entropy indexes choice uncertainty



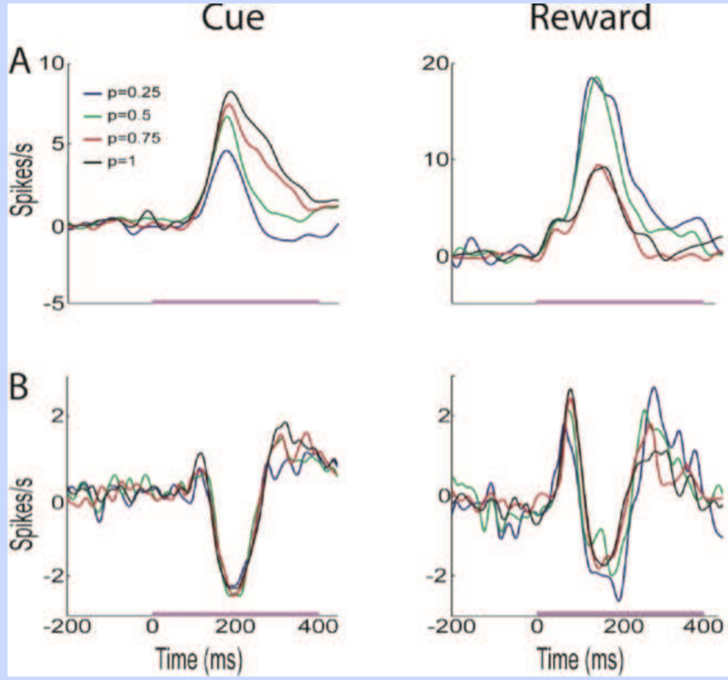
$$p_a(t) = \sum_i y_i^a(t) / \sum_{MSN} y$$

$$H = -\sum_t \sum_a p_a(t) log_2 p_a(t)$$

Role for cholinergic intereurons in modulating learning?

DA

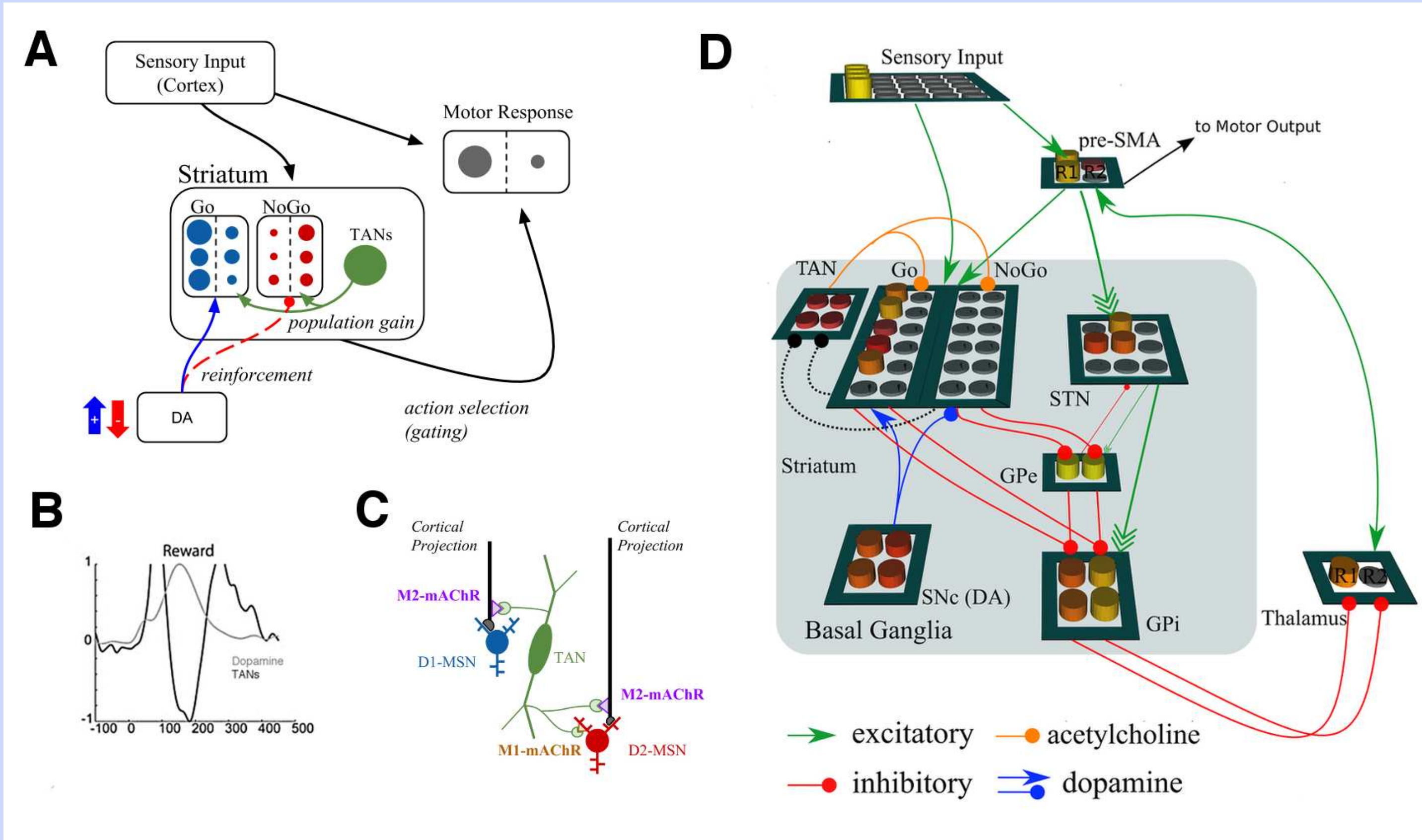
TAN



- TANs gate plasticity (e.g., Graybiel, Bergman, Cragg etc)
- TAN ablations impair reversal learning (e.g,. Witten et al 2010)
- striatal M1 blockade impairs reversal learning (McCool et al 08)

Morris et al., 2004

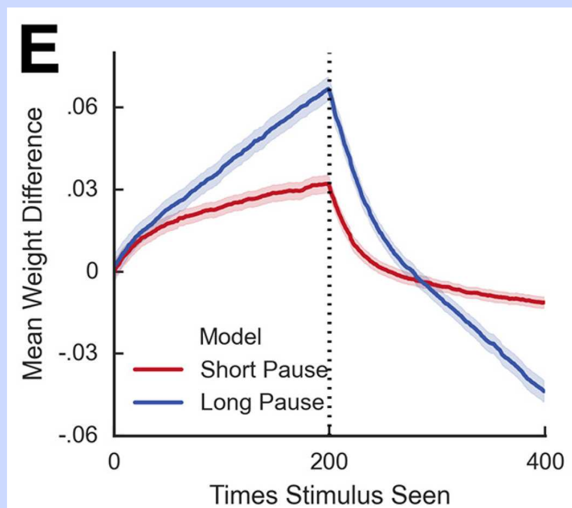
TAN effects on network learning

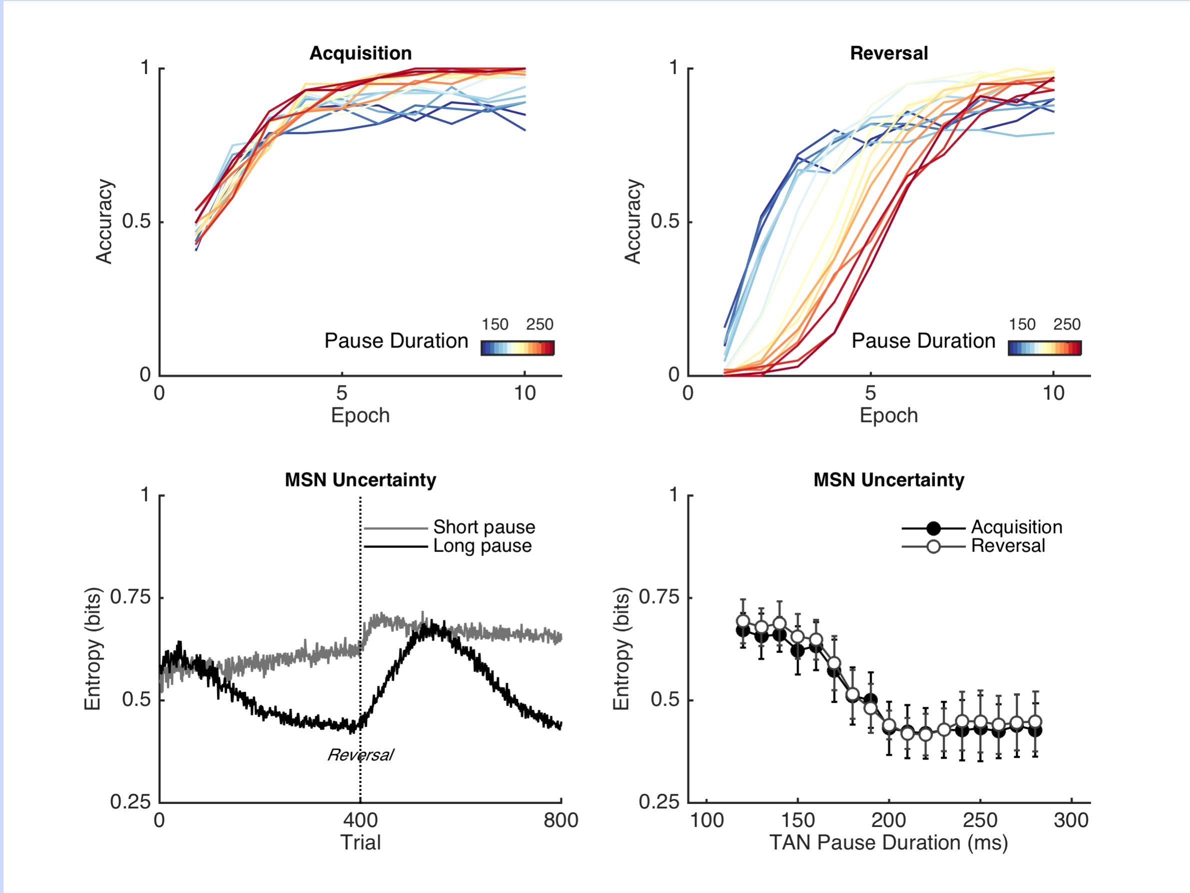


- TANs modulate MSN excitability during phasic DA signal (e.g., Koos)
- Long pause → disinhibit corticostriatal input across population, more learning

TANs moderate divergence in MSN weights with learning and population entropy

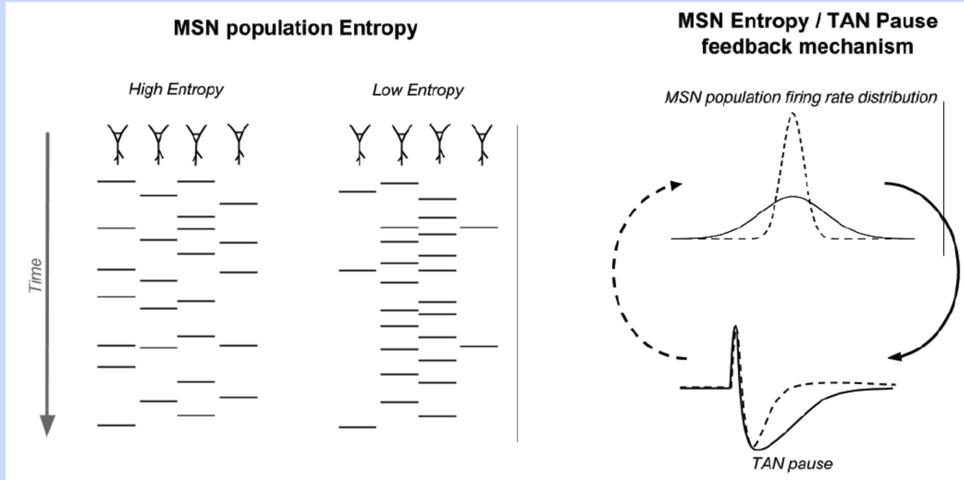
- TAN pauses modulate MSN excitability during phasic DA (via M1, presynaptic M2 and nicotinic effects on GABA-internerons)
- Long pause → larger population of MSNs learn from DA
- Short pause → learning focused on sparse population
- ⇒ TAN pause modulates effective learning rate

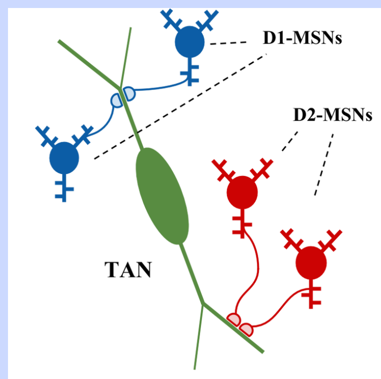




Franklin & Frank, 2015, *eLife*

MSN-TAN feedback circuit for adaptive learning rates

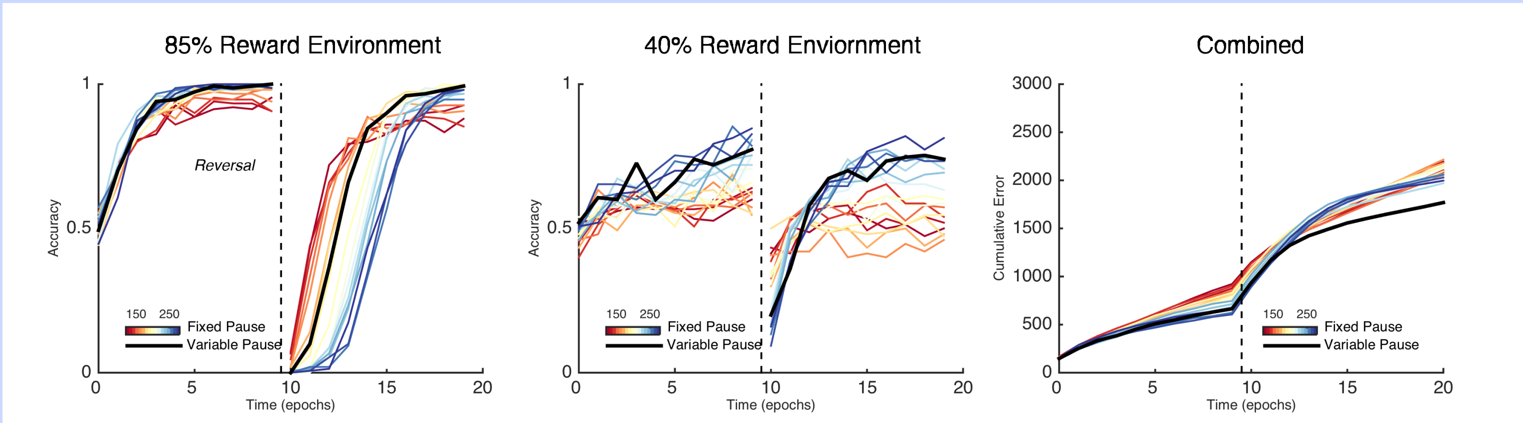




MSN-TAN collaterals: Bolam et al ’86; Chuhma et al 11; Gonzalez et al 13

MSN entropy $\rightarrow$ longer TAN pauses

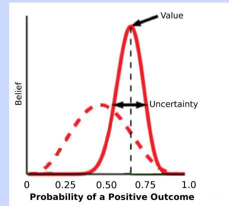
TAN/MSN/DA interactions optimize learning across levels of stochasticity & volatility



- benefit of long/short pause depends on level of stochasticity
- 85/15 vs 40/10 environments
- Self-regulating pause optimizes learning/reversal overall

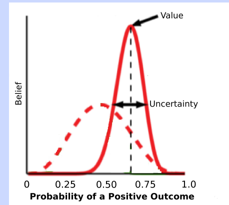
Franklin & Frank, 2015, *eLife*

Bayesian approach to dynamic learning



- How do deal with volatility?

Bayesian approach to dynamic learning



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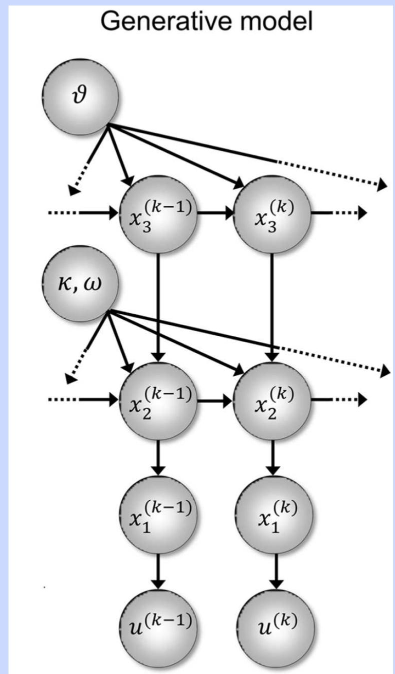
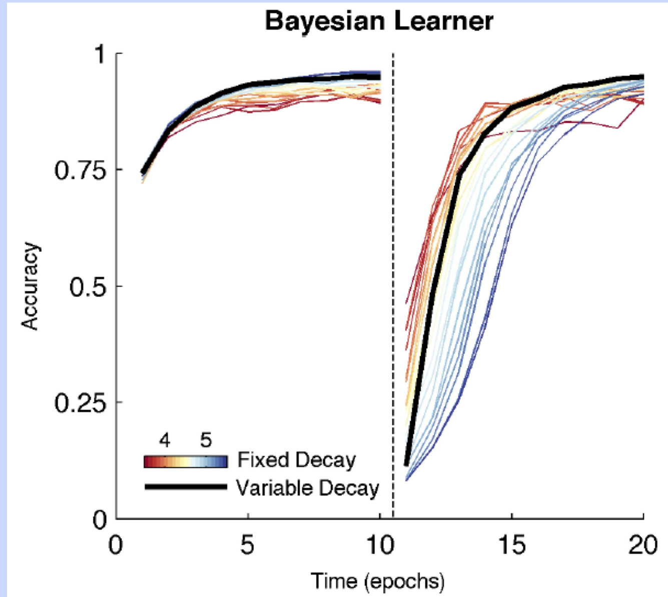


e.g., Yu & Dayan 05; Behrens et al 2007; Nassar et al 2010; Mathys et al 2011

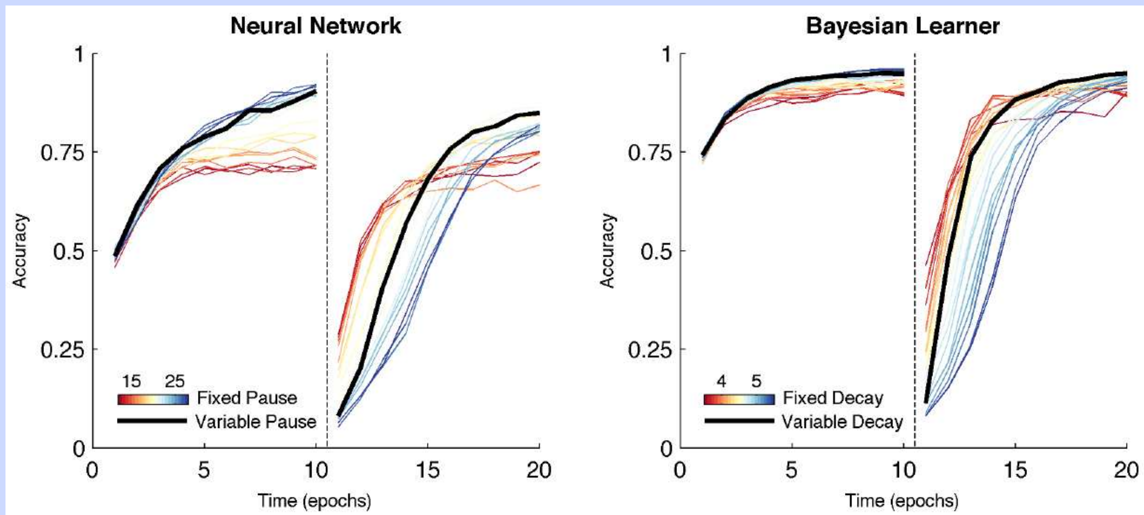
approximate Bayesian approach to dynamic learning

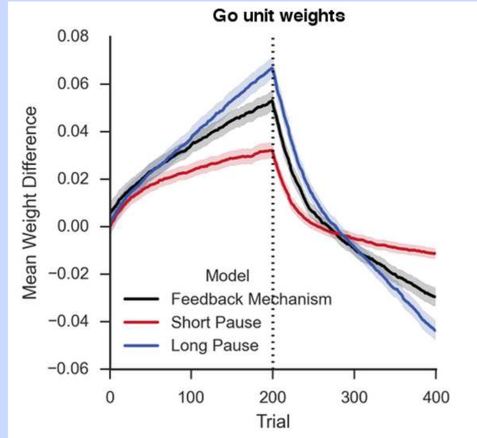


- add uncertainty to belief distributions (decay counts)
- regulate trade off by dynamically changing decay according to changes in choice uncertainty

Franklin & Frank 2015, eLife

BG-TAN net is analogous to Bayesian uncertainty-driven learner

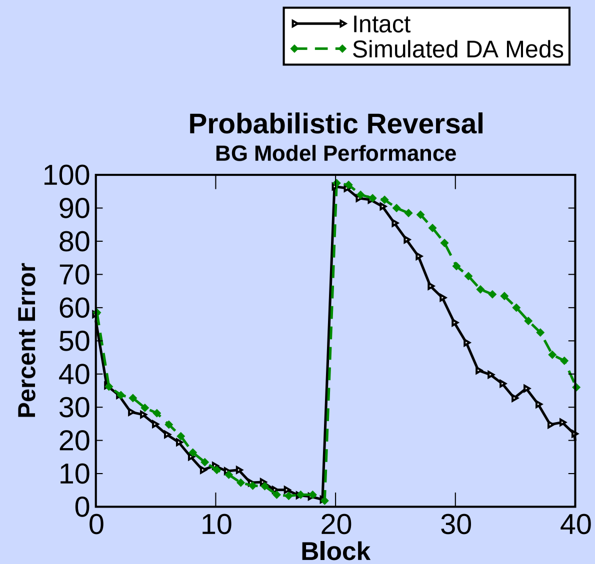




same result in OpAL formulation

Franklin & Frank, 2015, *eLife*

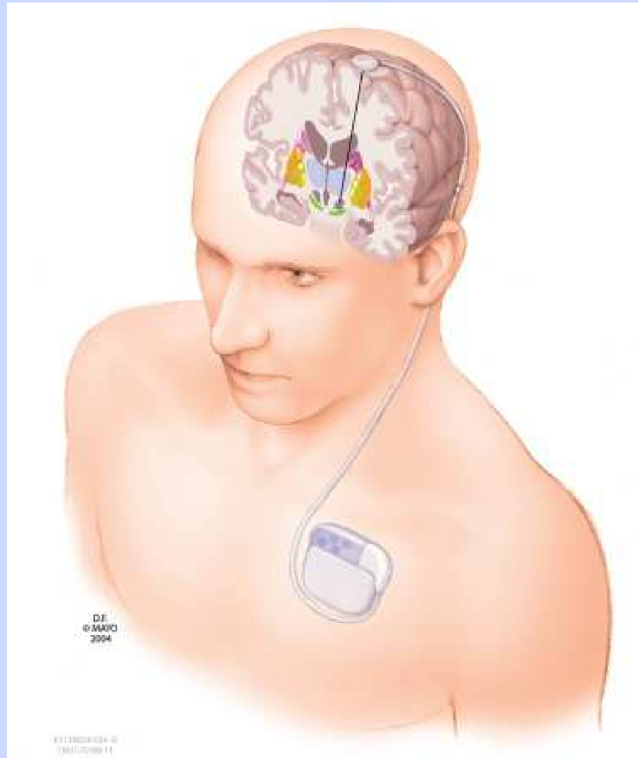
DA-mediated Go/NoGo learning alone is limited: Probabilistic reversal learning



- Simulated D2 agonists prevent learning in D2 MSNs
- intact BG model learns probabilistic reversal, but not optimally $\Rightarrow$ motivates need for dynamic learning rate...

Cools et al, 2001; Frank, 2005

Deep Brain Stimulation of the Subthalamic Nucleus (STN) for treatment of Parkinson’s disease



Video #1: http://ski.clps.brown.edu/dbs2.mp4

Video #2: http://ski.clps.brown.edu/dbs.mp4

But not all is grand in the world of DBS...

But not all is grand in the world of DBS...

hi, i found your email address in an article i was reading about dbs surgery for parkinsons. my dad had the surgery last may and we have a mess on our hands. two months following the surgery we began to notice some personality changes. he became impulsive, cocky, oblivious to his surroundings, forgetful, has lied, he has no empathy, he uses foul language ... canceled his 2 follow up dr appointments, he was always very detailed oriented and now he is sloppy, and he is spending a lot of money. he has NOT gone one day without buying something. he can't sit still, he's always on the move. going somewhere and buying something...

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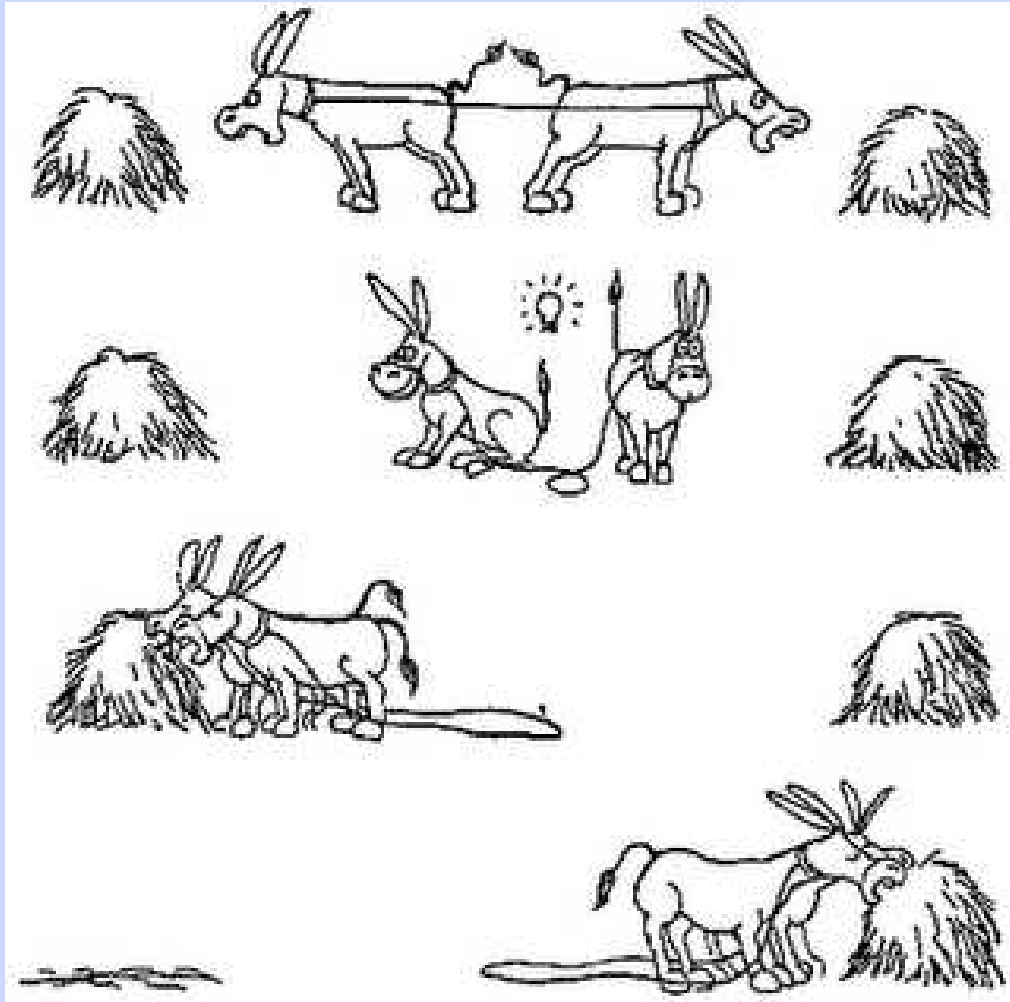
STN-DBS dramatically improves PD motor symptoms, but can induce impulsivity

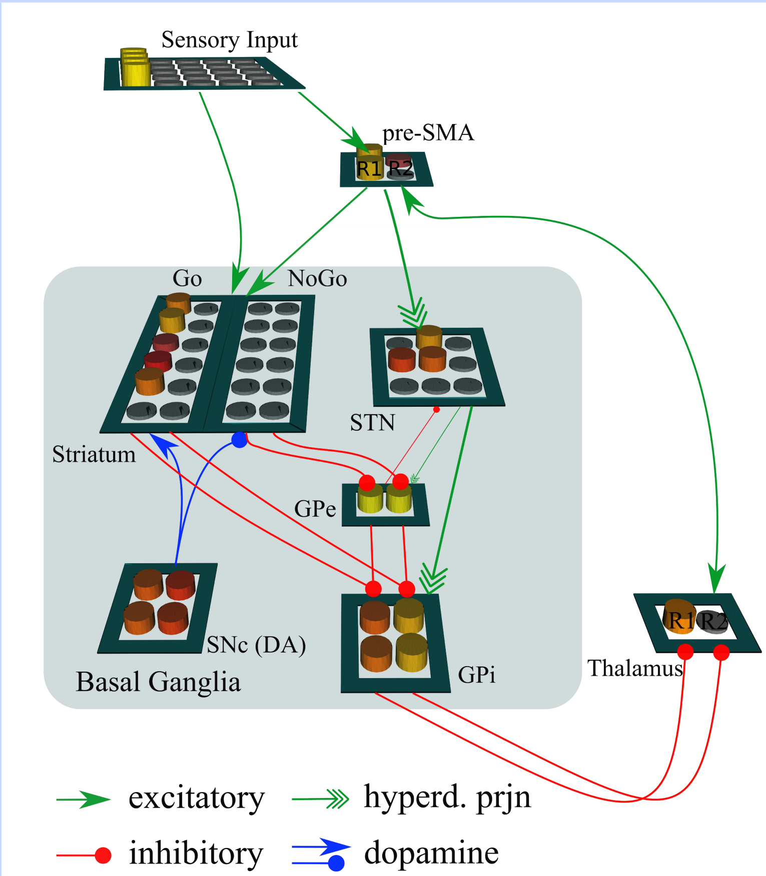
(Saint-Cyr et al 06, Frank et al, 07; Wylie et al 10; Hälbig et al 09)

From reinforcement learning...

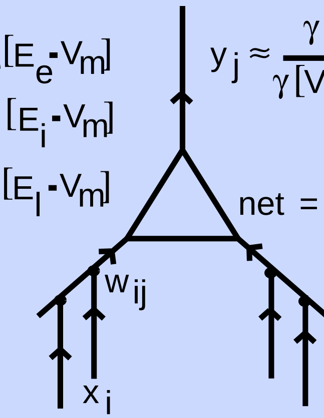
...to reinforcement conflict-based decision making



Neural circuit model of BG in learning / decision making



$$c\dot{V}_m = g_e \bar{g}_e [E_e - V_m] + g_i \bar{g}_i [E_i - V_m] + g_l \bar{g}_l [E_l - V_m] + \ldots$$



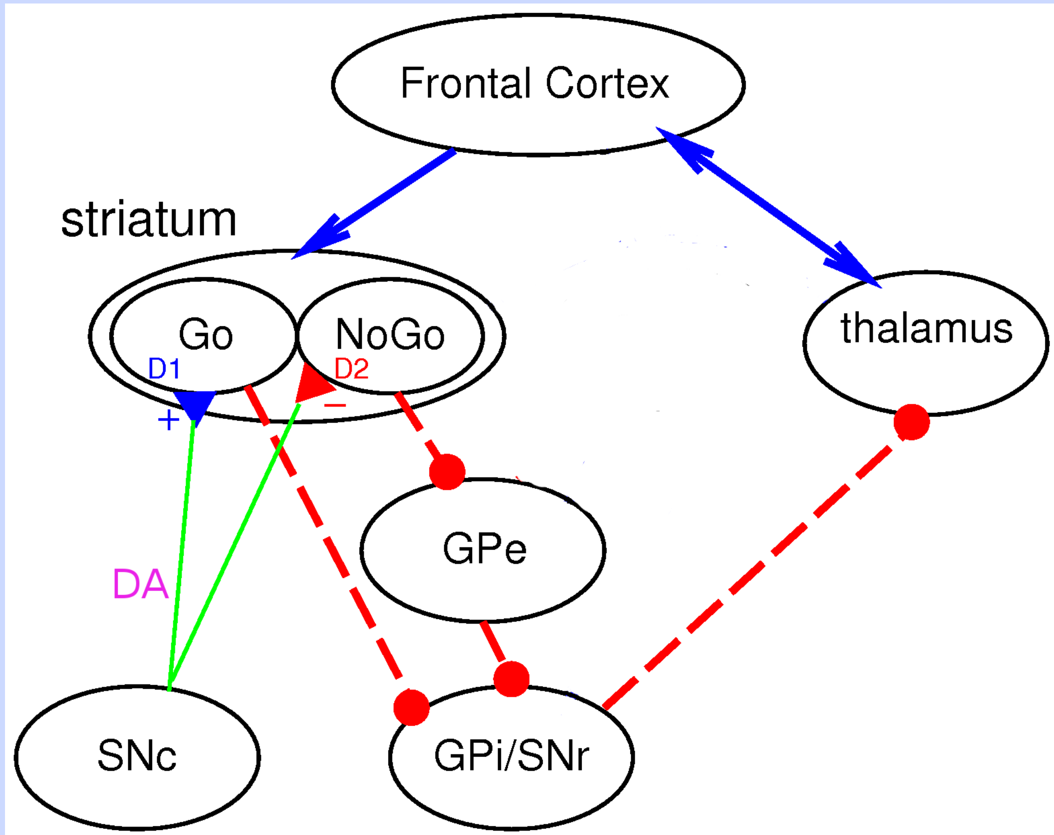
$$y_j \approx \frac{\gamma [V_m - \Theta]_+}{\gamma [V_m - \Theta]_+ + 1}$$

$$net = g_e \approx \langle x_i w_{ij} \rangle + \frac{\beta}{N}$$

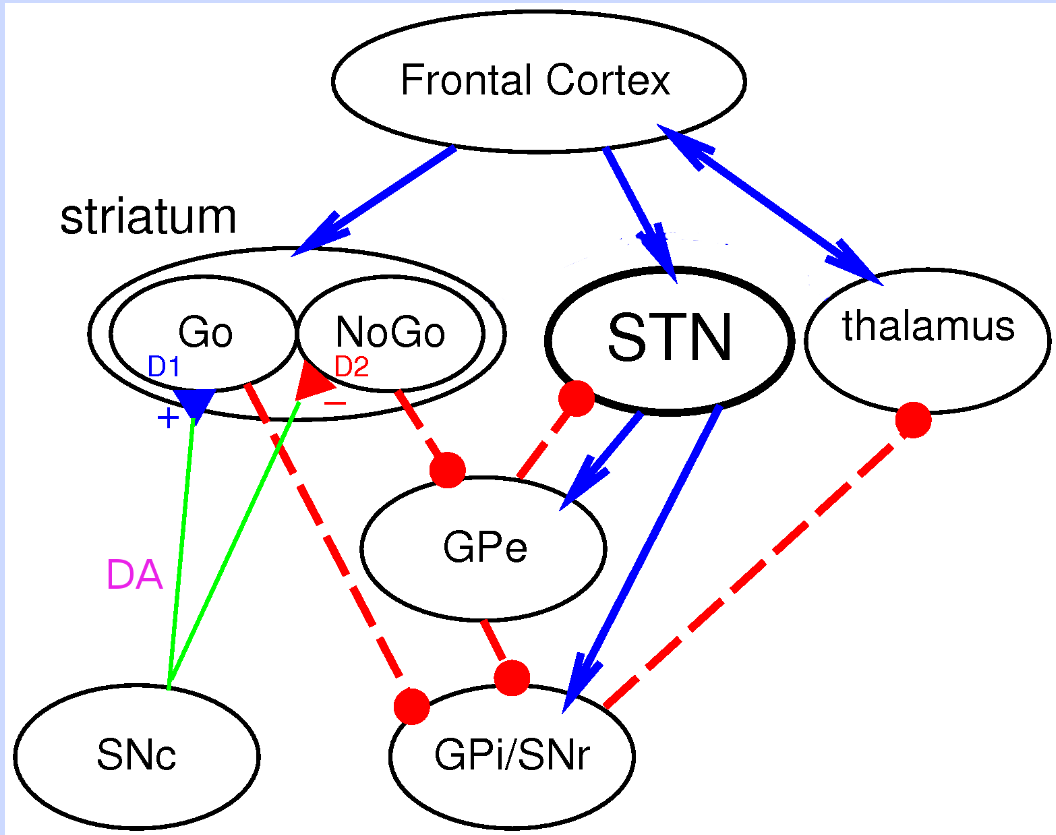
$$\Delta w_{ij} \approx (x_i^p y_j^p) - (x_i^t y_j^t)$$

Frank, 2005, 2006 *J Cog Neurosci, Neural Networks*

Anatomy of BG gating: without STN

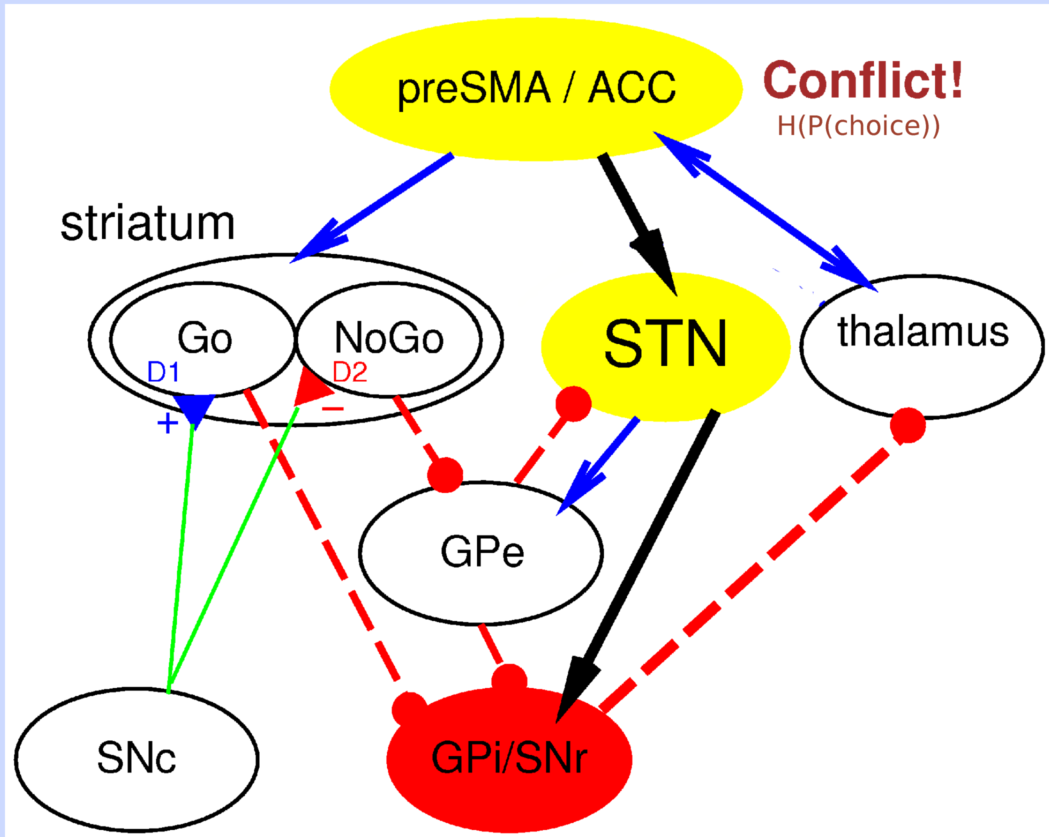


Anatomy of BG gating: with subthalamic nucleus (STN)



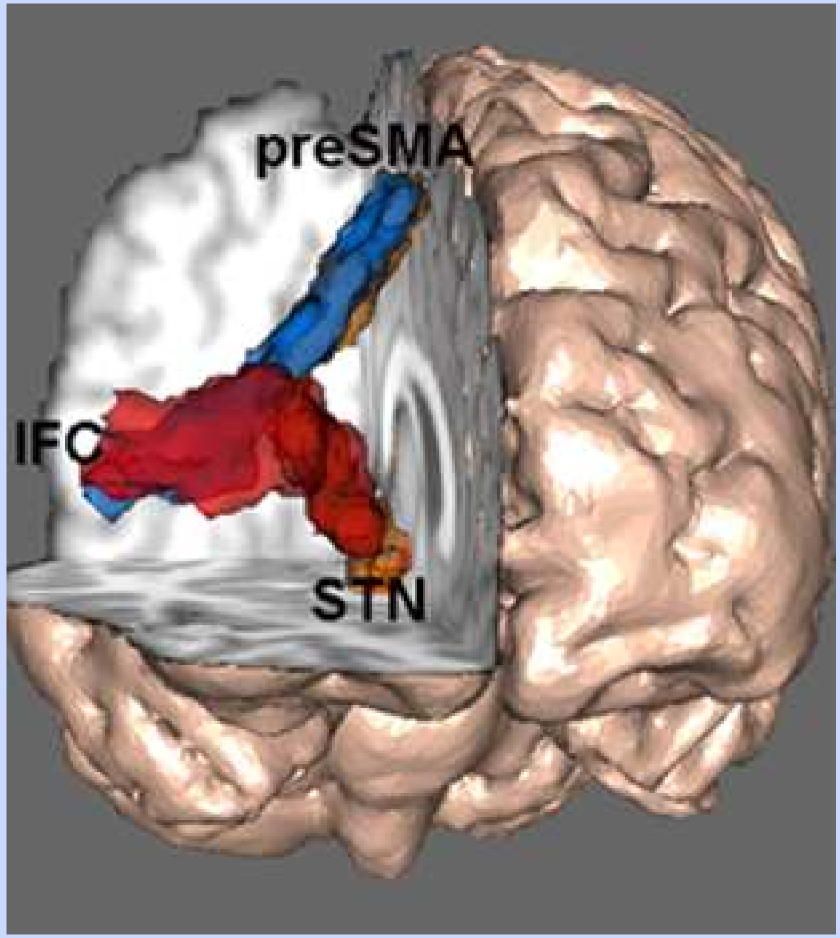
- PFC-STN provides an override mechanism

Subthalamic Nucleus:
Dynamic modulation of decision threshold



- Conflict (entropy) in choice prob: $\Rightarrow$ *Hold Your Horses!*

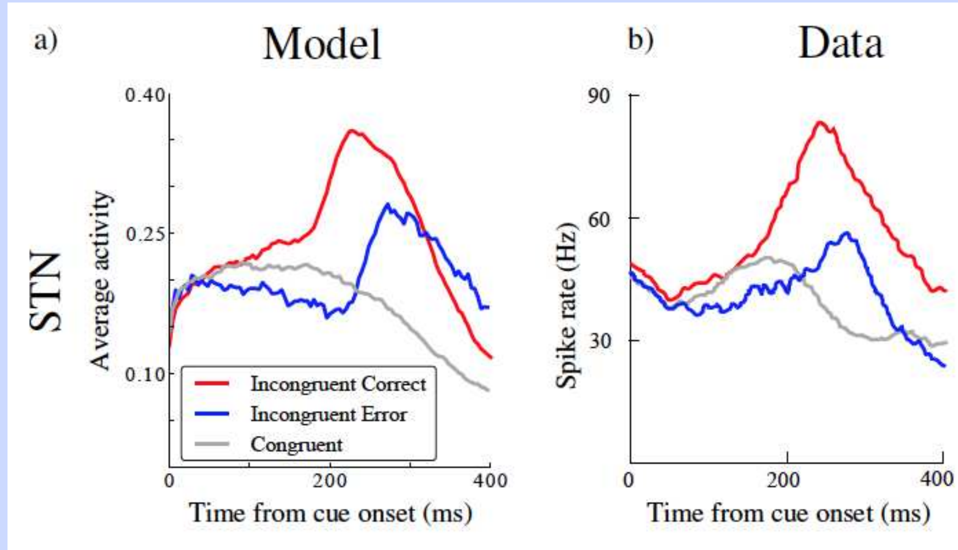
STN and frontal cortex are directly connected via white matter



Aron et al (2007), J Neurosci

Neural model and STN ephys: decision conflict

spike rate:



data from Isoda & Hikosaka 2008

Wiecki & Frank, 2013 *Psych Review*

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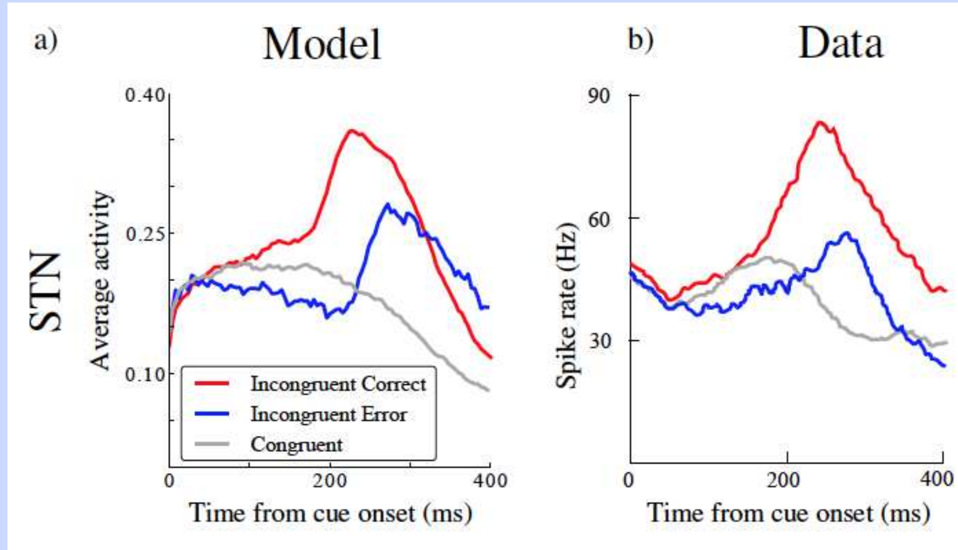
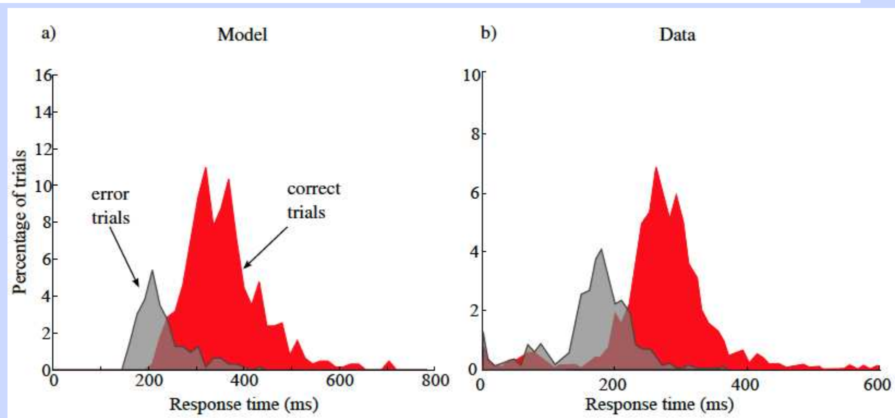


behavior:



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Human probabilistic reward/choice conflict

A (80%) B (20%) C (70%) D (30%) E (60%) F (40%)

Low Conflict: e.g., 80 vs 30% $H(P_{softmax}) = .06$

High Conflict: e.g., 80 vs 70% $H(P_{softmax}) = .84$

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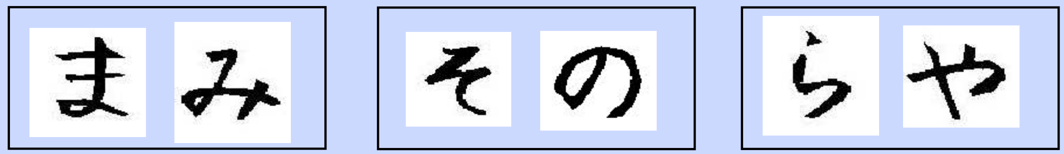

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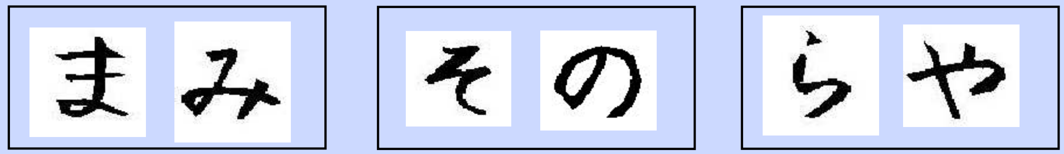

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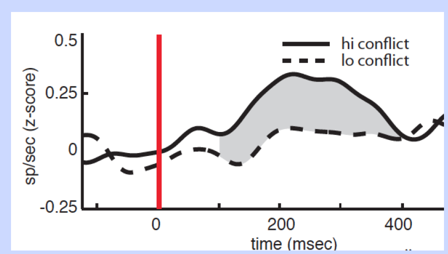
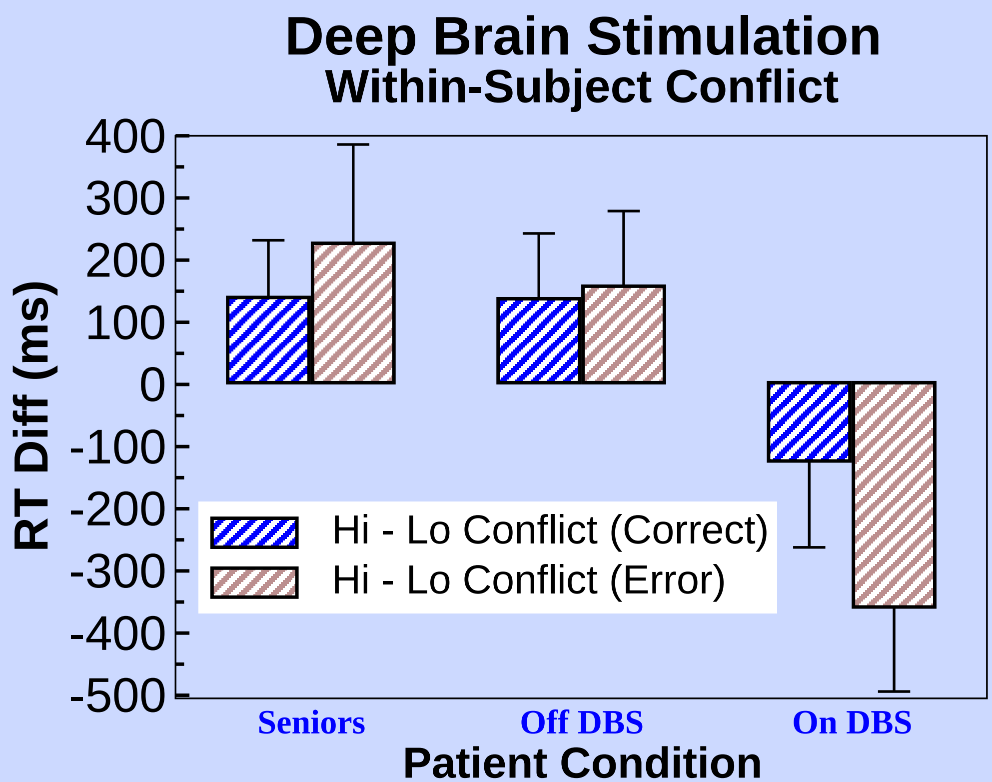


human STN spiking, Zaghloul et al., 2012

STN-DBS reverses conflict RT adjustments



Frank, Samanta, Moustafa & Sherman (2007)

see also Wylie et al 10; Hälbig et al 09; Cavanagh et al 11; Coulthard et al 12; Green et al 13

Interim Summary

- DBS induces speeded responding in conflict conditions
- Simulations: STN modulates decision threshold $\propto$ cortical conflict

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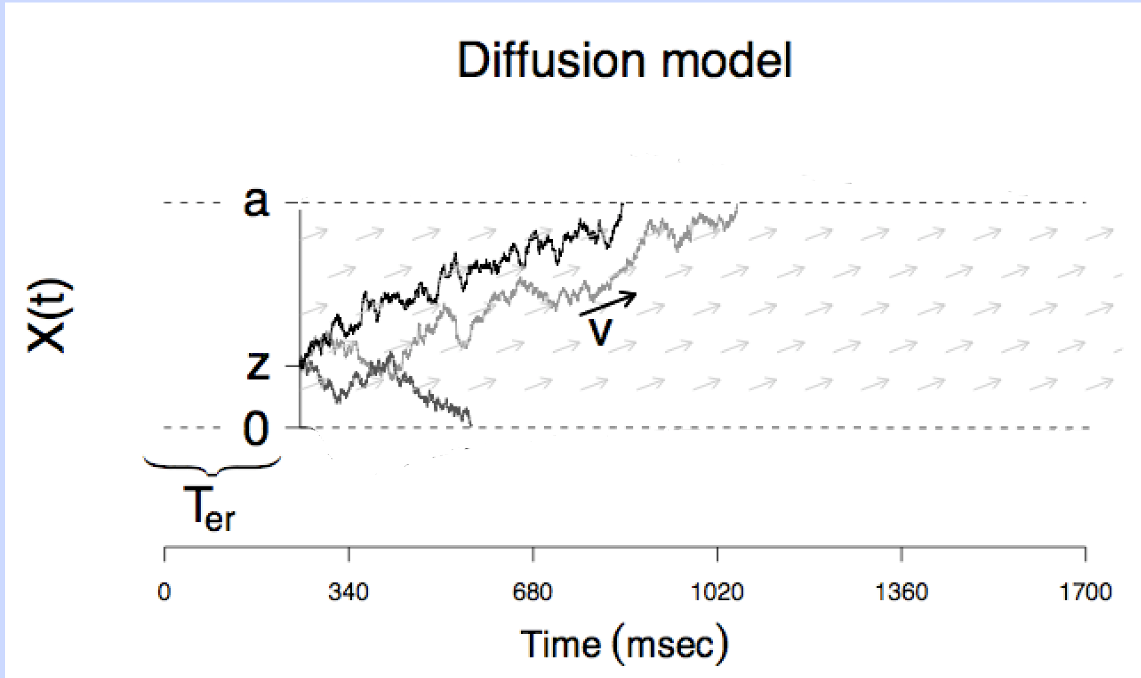
- DBS induces speeded responding in conflict conditions
- Simulations: STN modulates decision threshold $\propto$ cortical conflict
- **More precise predictions to be tested:**
  - Does mediofrontal cortex and STN represent reinforcement conflict?
  - Does decision threshold vary as a function of mediofrontal conflict?
  - Does STN-DBS alter this relationship?

Abstraction: the drift diffusion model



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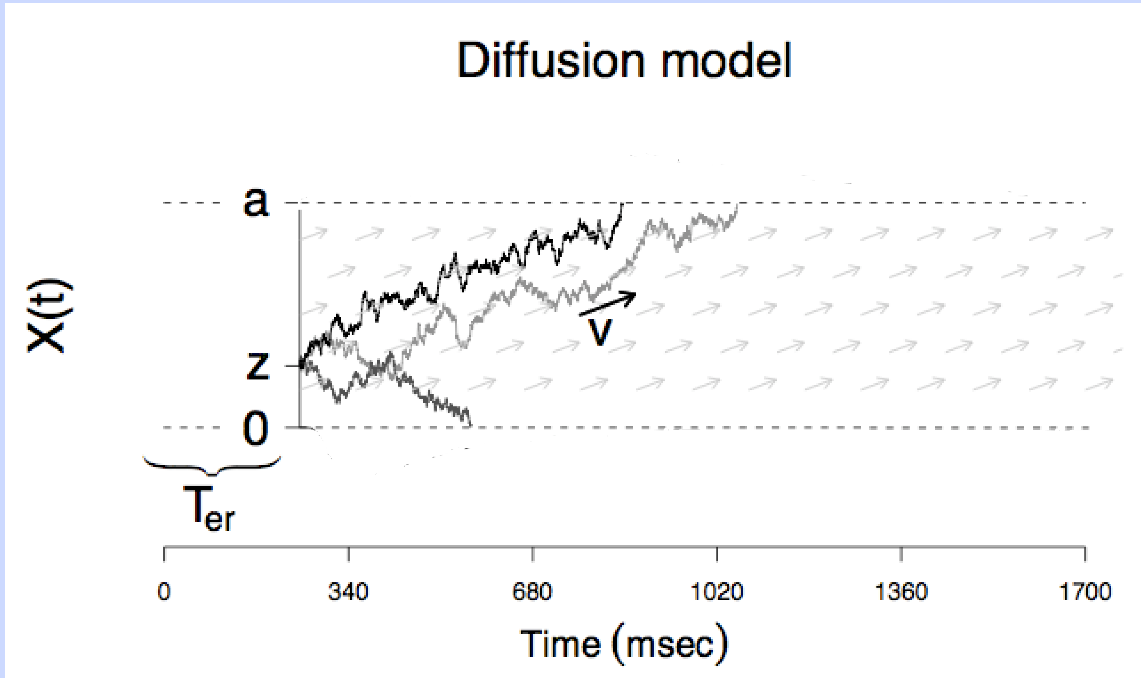

- Provides quantitative fits to error rates and RT distributions in many tasks
- Allows estimation of decision threshold (a), separately from other factors (v, z, Ter)

e.g. Ratcliff & McKoon, 2008

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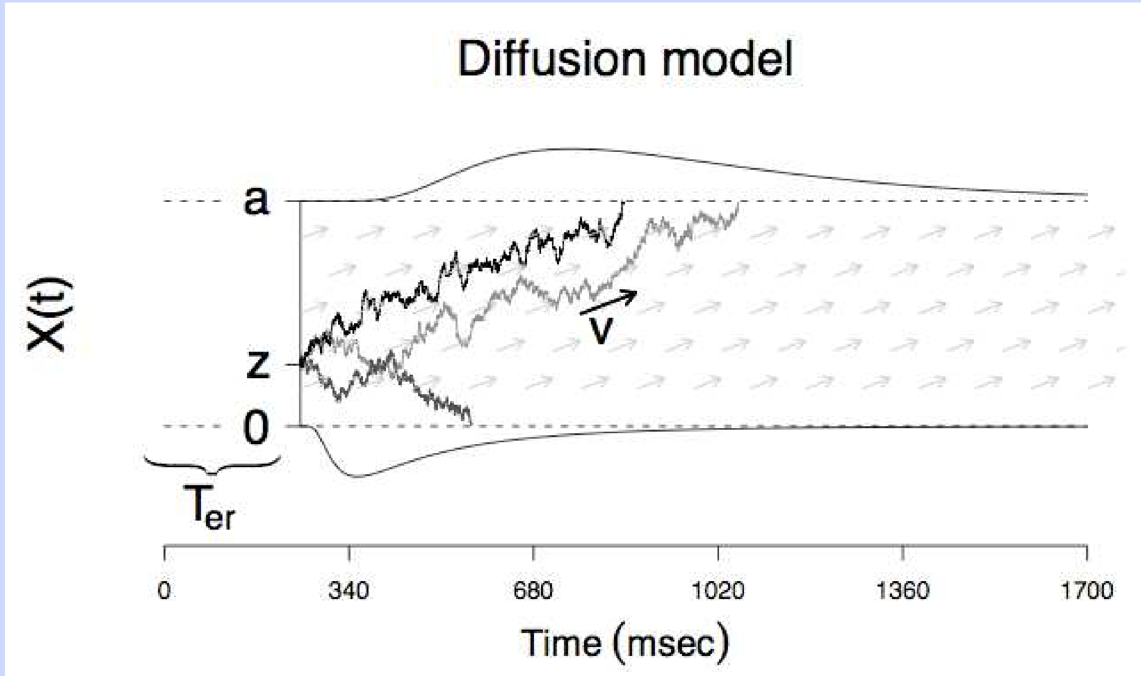

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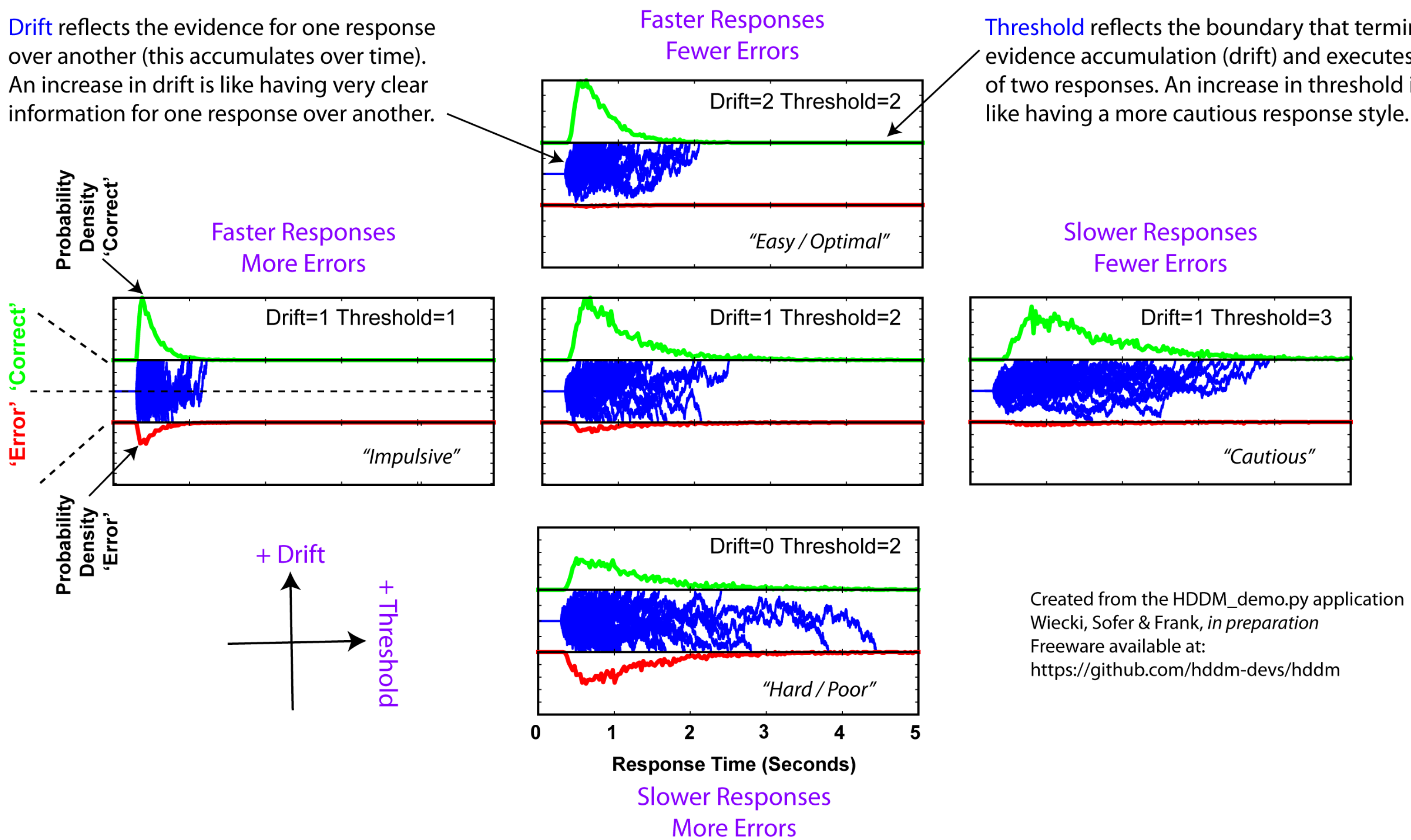
Contrasting drift rate vs threshold

Drift reflects the evidence for one response over another (this accumulates over time). An increase in drift is like having very clear information for one response over another.

Threshold reflects the boundary that terminates evidence accumulation (drift) and executes one of two responses. An increase in threshold is like having a more cautious response style.



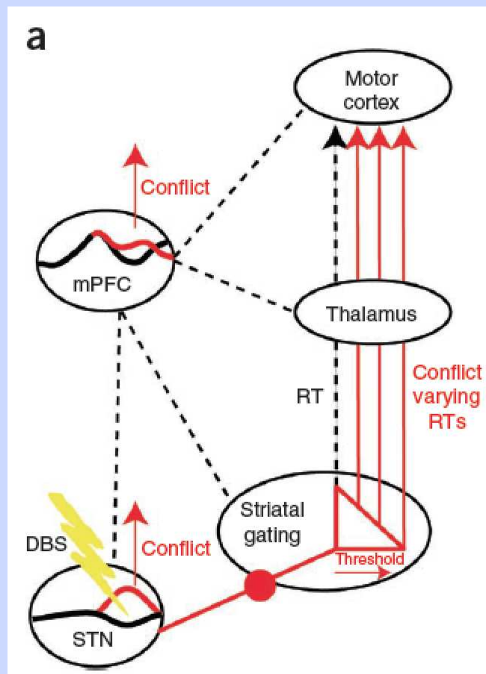
Created from the HDDM_demo.py application
Wiecki, Sofer & Frank, *in preparation*
Freeware available at:
https://github.com/hddm-devs/hddm

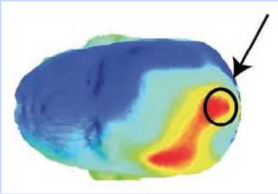
Mechanism

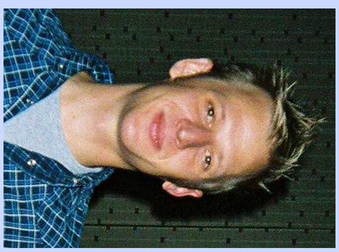
nature neuroscience

Subthalamic nucleus stimulation reverses mediofrontal influence over decision threshold

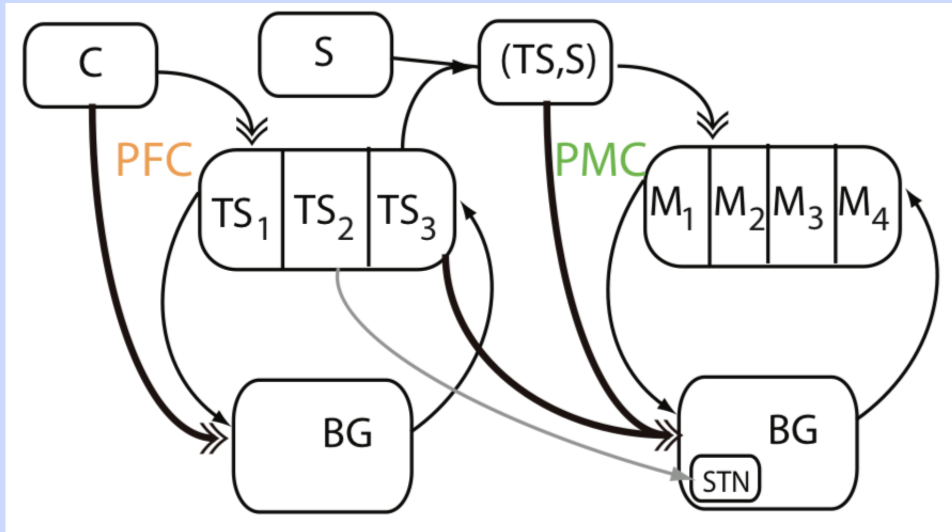
James F Cavanagh[1], Thomas V Wiecki[1], Michael X Cohen[2,3], Christina M Figueroa[1], Johan Samanta[4,5], Scott J Sherman[4] & Michael J Frank[1,6,7]







Hierarchical interactions in BG-FC circuits: PFC & cognitive control influences on learning



Collins & Frank 2013, *Psych Rev*; Frank & Badre 2012

Broader speculations:
Why does motor control develop so slowly in humans??

- Standard story: infants born early due to large head, small birth canal
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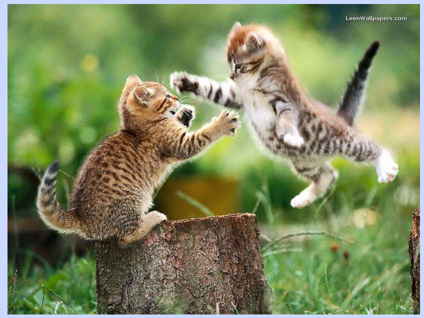

- Standard story: infants born early due to large head, small birth canal
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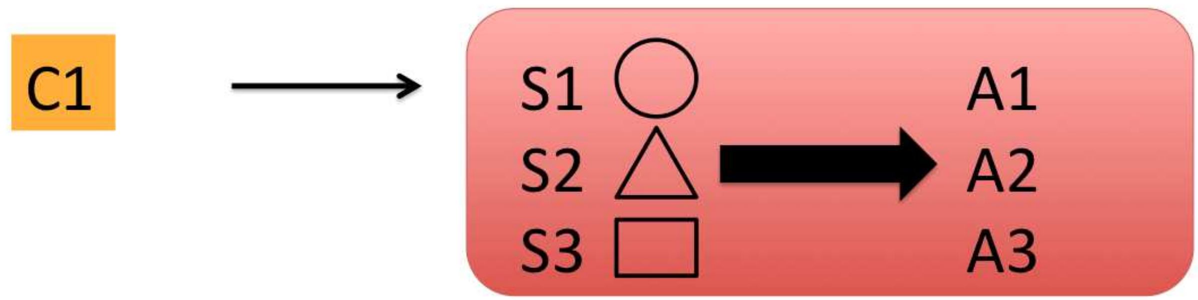
- But 3 month old infants still pretty incompetent (from *babycenter.com*):

  “You no longer need to support his head. When he’s on his stomach, he can lift his head and chest. He can open and close his hands..”
- Hypothesis: human brain is wired to discover generalizable structure....

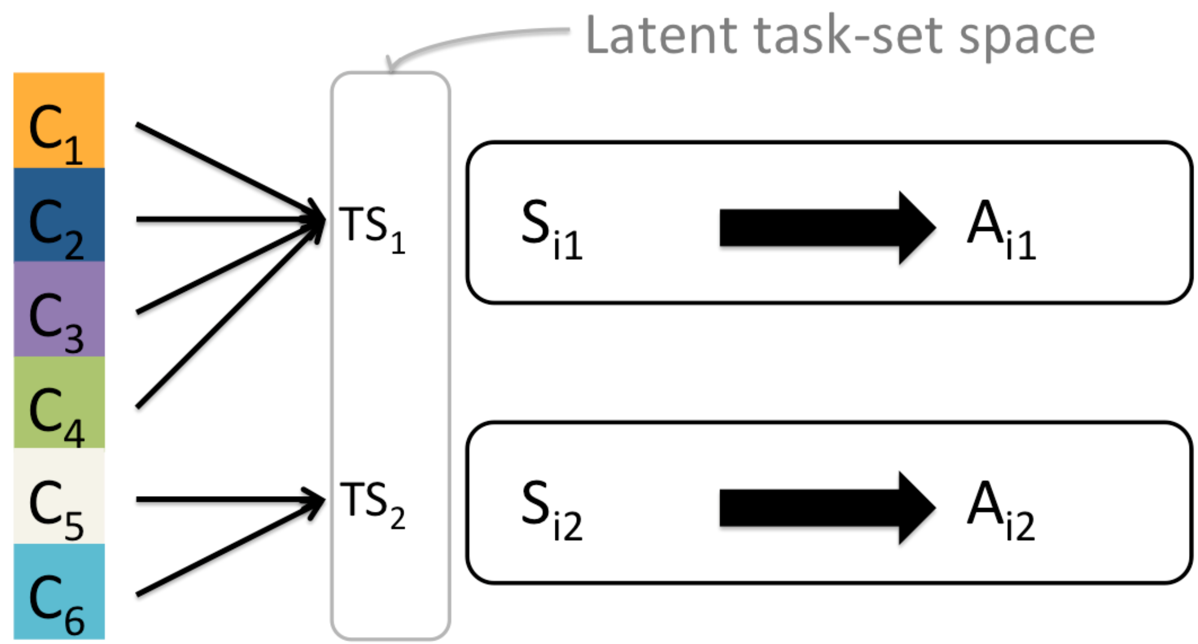
which is initially inefficient.

Task-sets (TS)



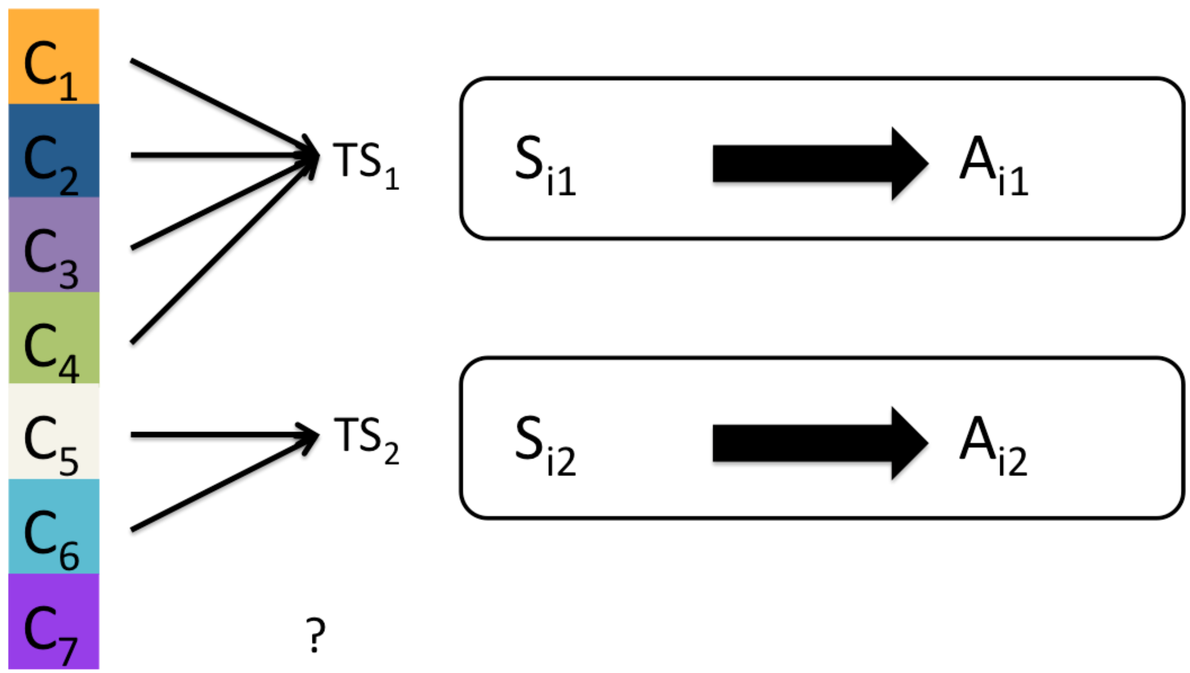
Task-sets (TS)

Abstracting Task-set rules



TS as abstract rule objects
Reverberi et al 2011
Woolgar et al 2011

Abstracting Task-sets rules



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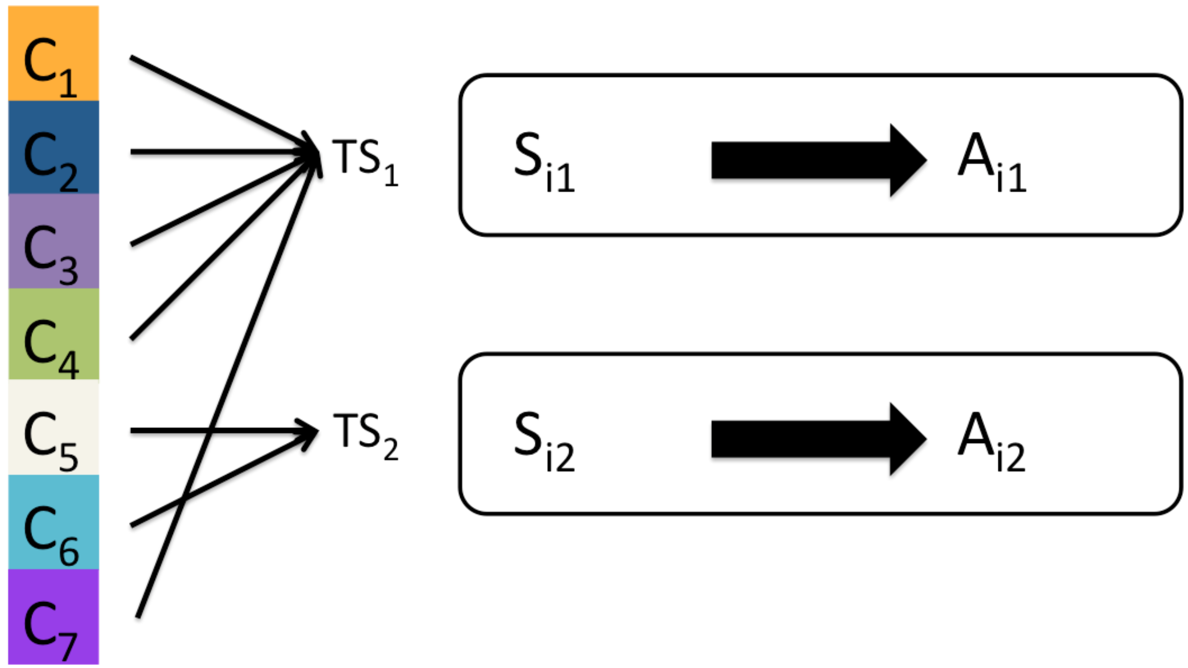

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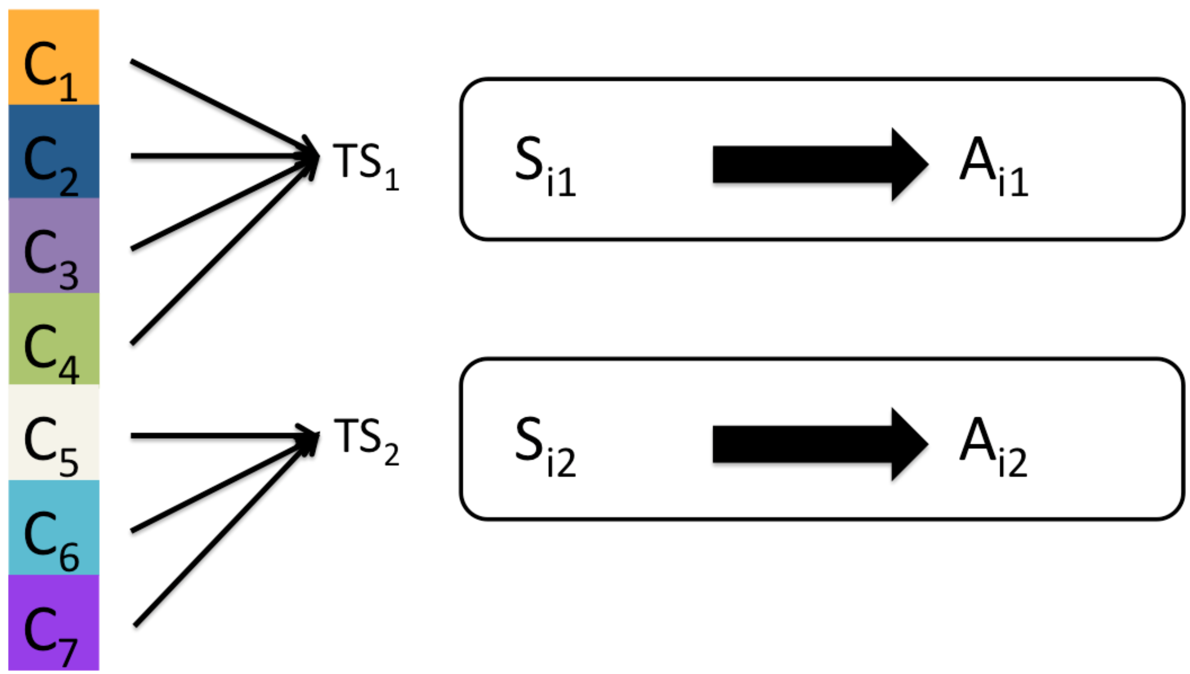

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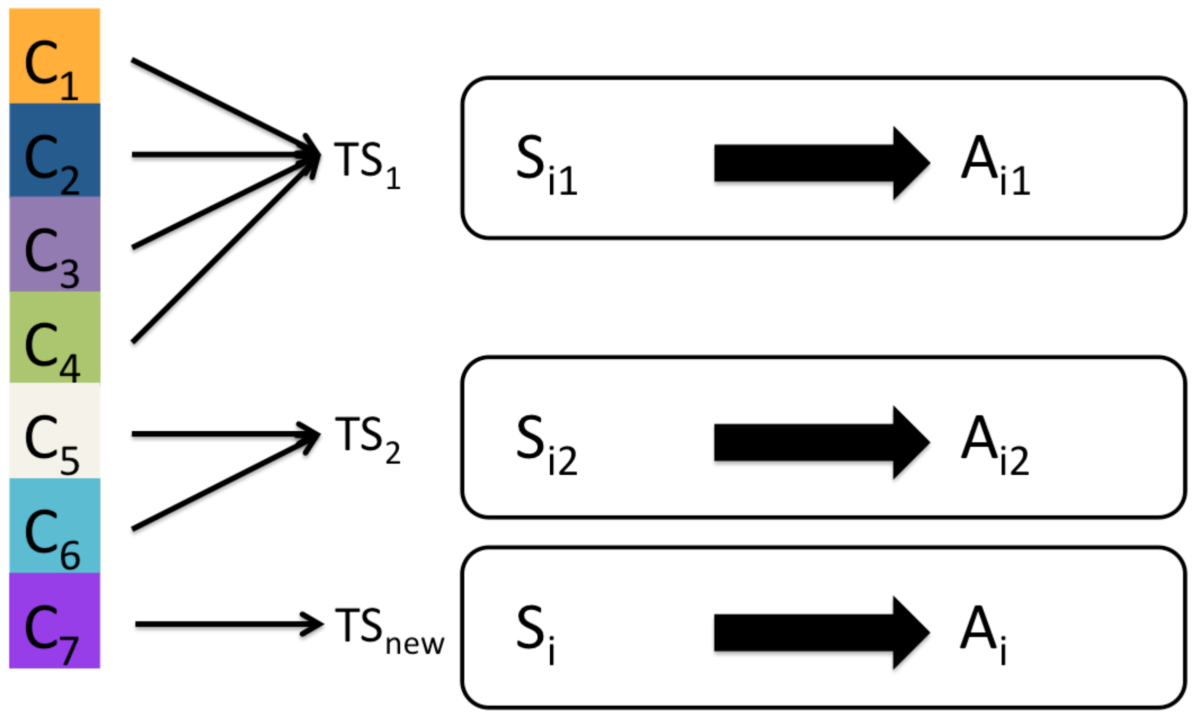

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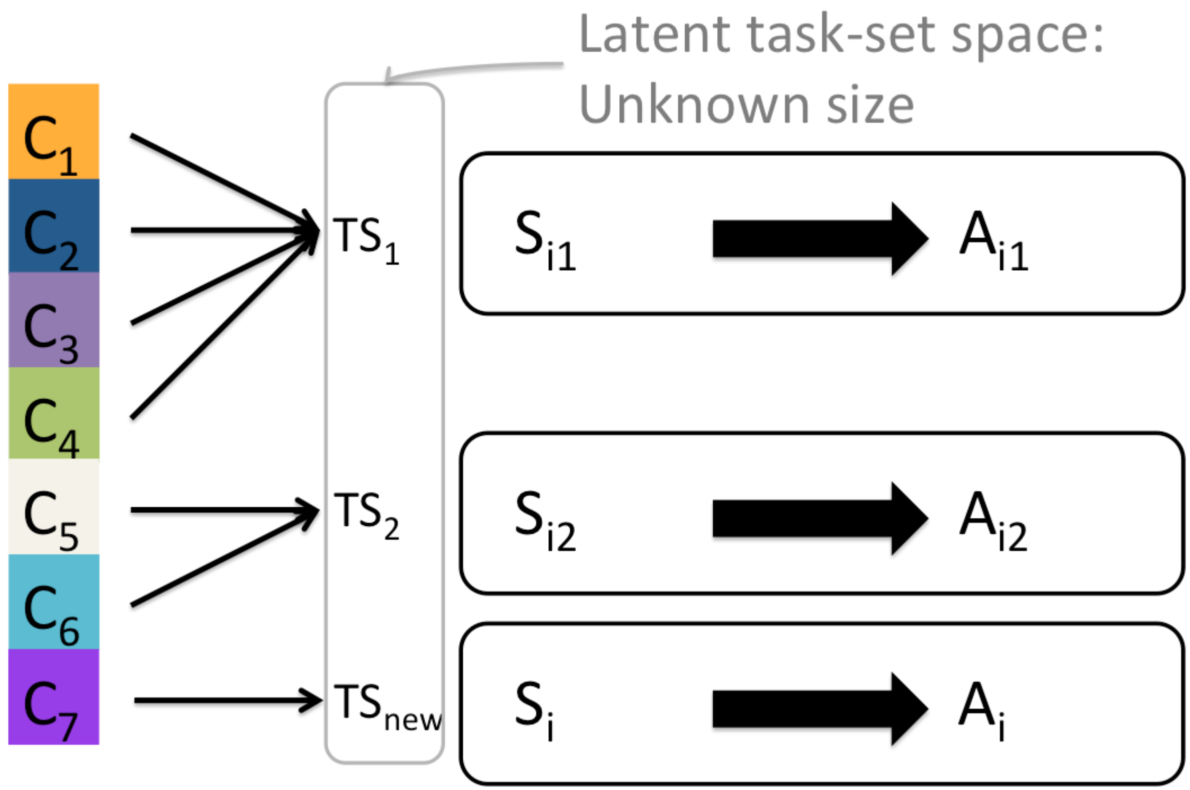
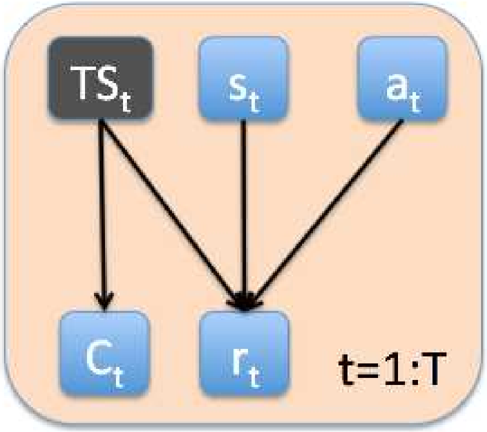


C-TS model



Task-sets are clustered across contexts and can be revisited in new contexts

- Prior prob on TS space given a new C:

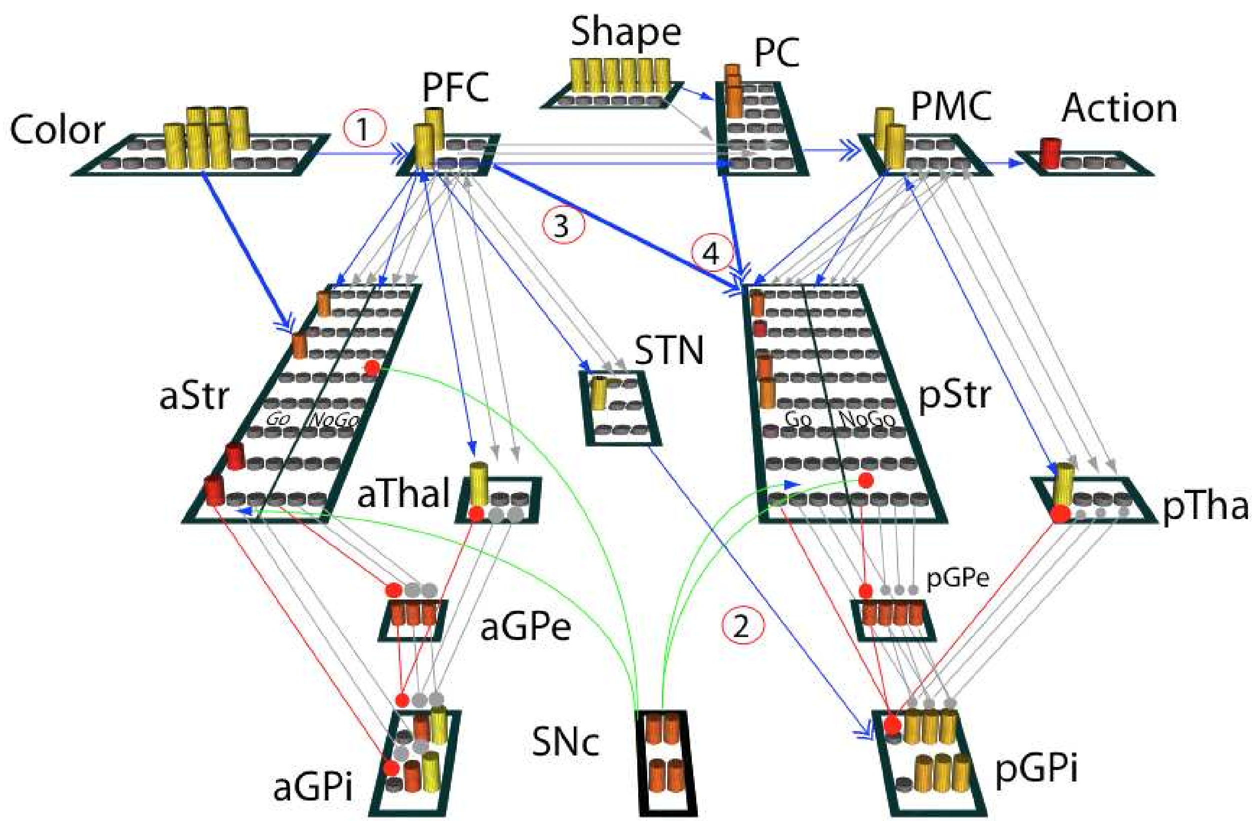
$$P(TS^* = . \,|c_{n+1}) = \begin{cases} P(TS^* = TS_{new}|c_{n+1}) & = & \alpha/A \\ \forall i \neq new,\ P(TS^* = TS_i|c_{n+1}) & = & \sum_j P(TS_i|c_j)/A \end{cases}$$

- α> 0: Clustering parameter

- Chinese restaurant process Jordan, Blei Teh 2005

see also Gershman et al 2010

Neurobiologically plausible implementation



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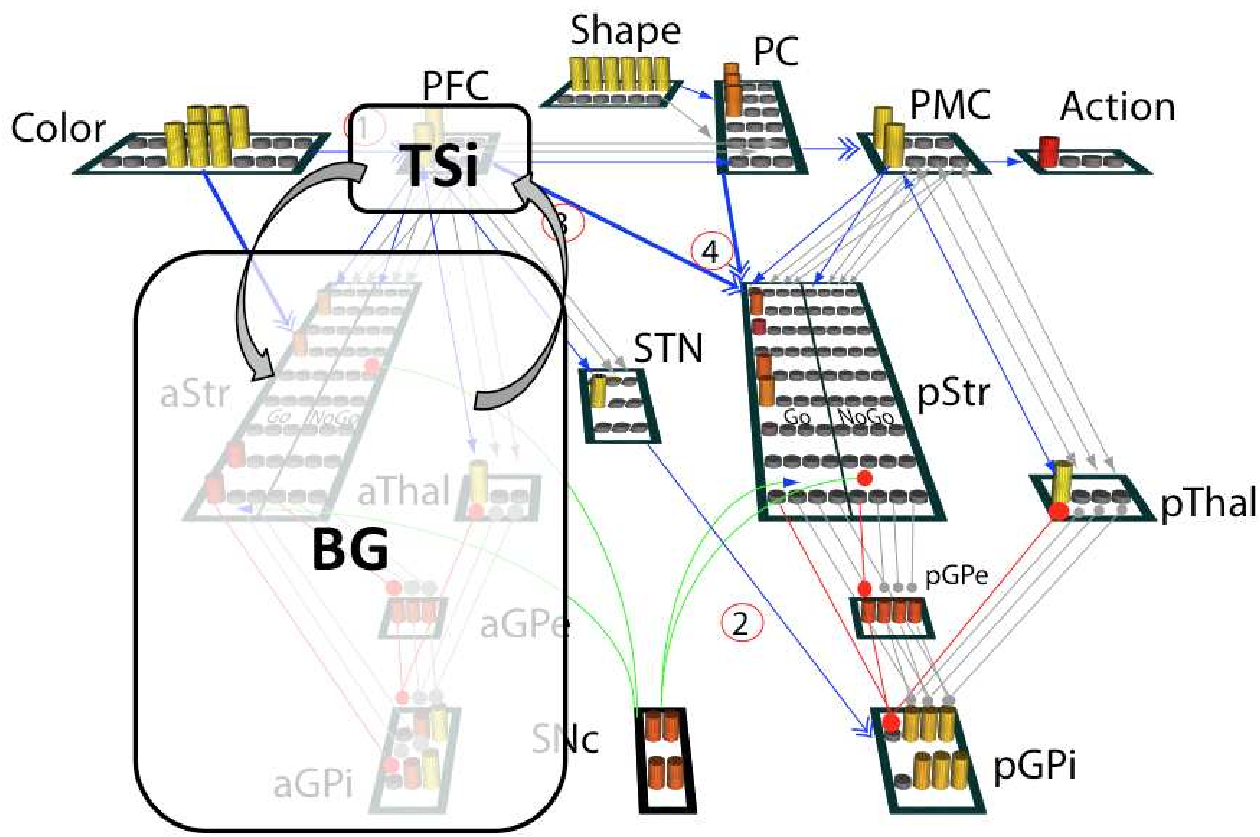

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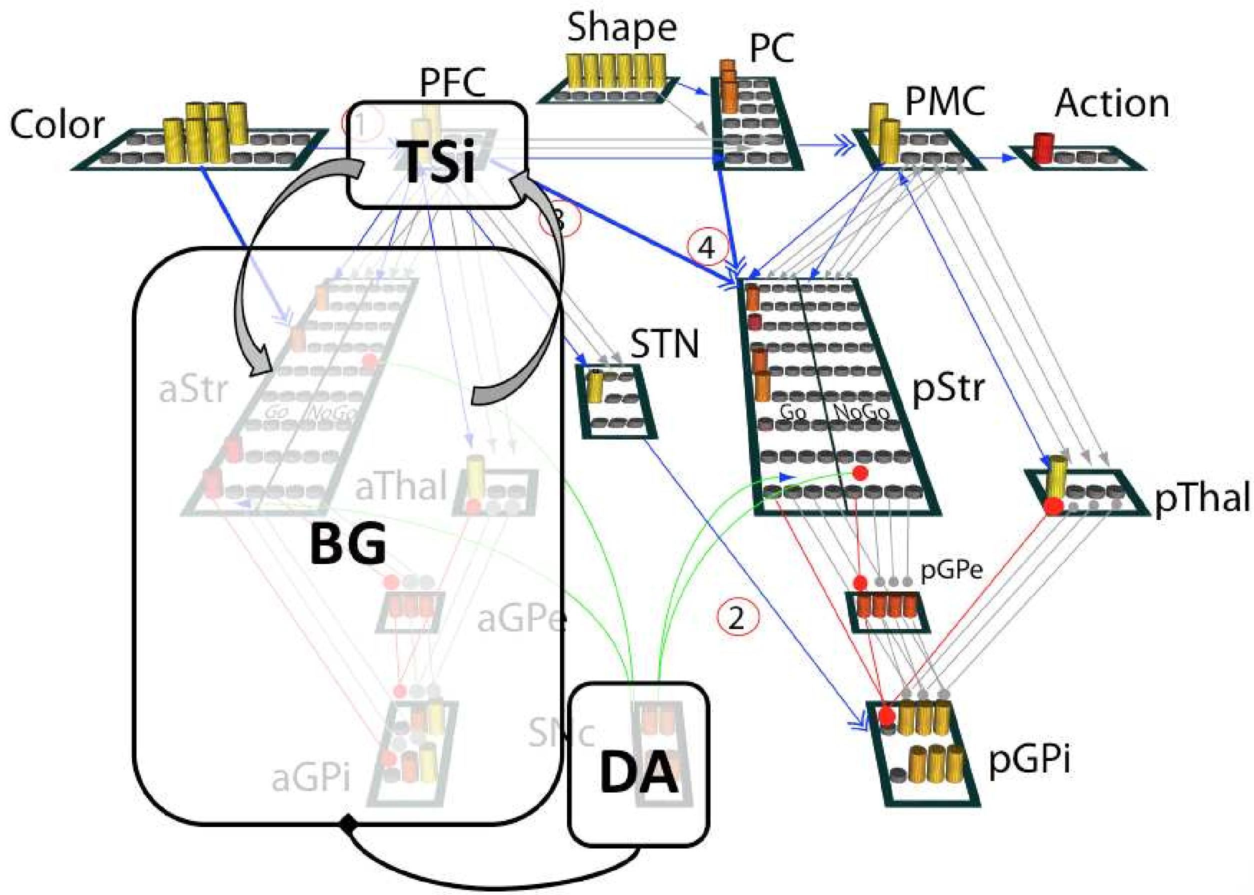

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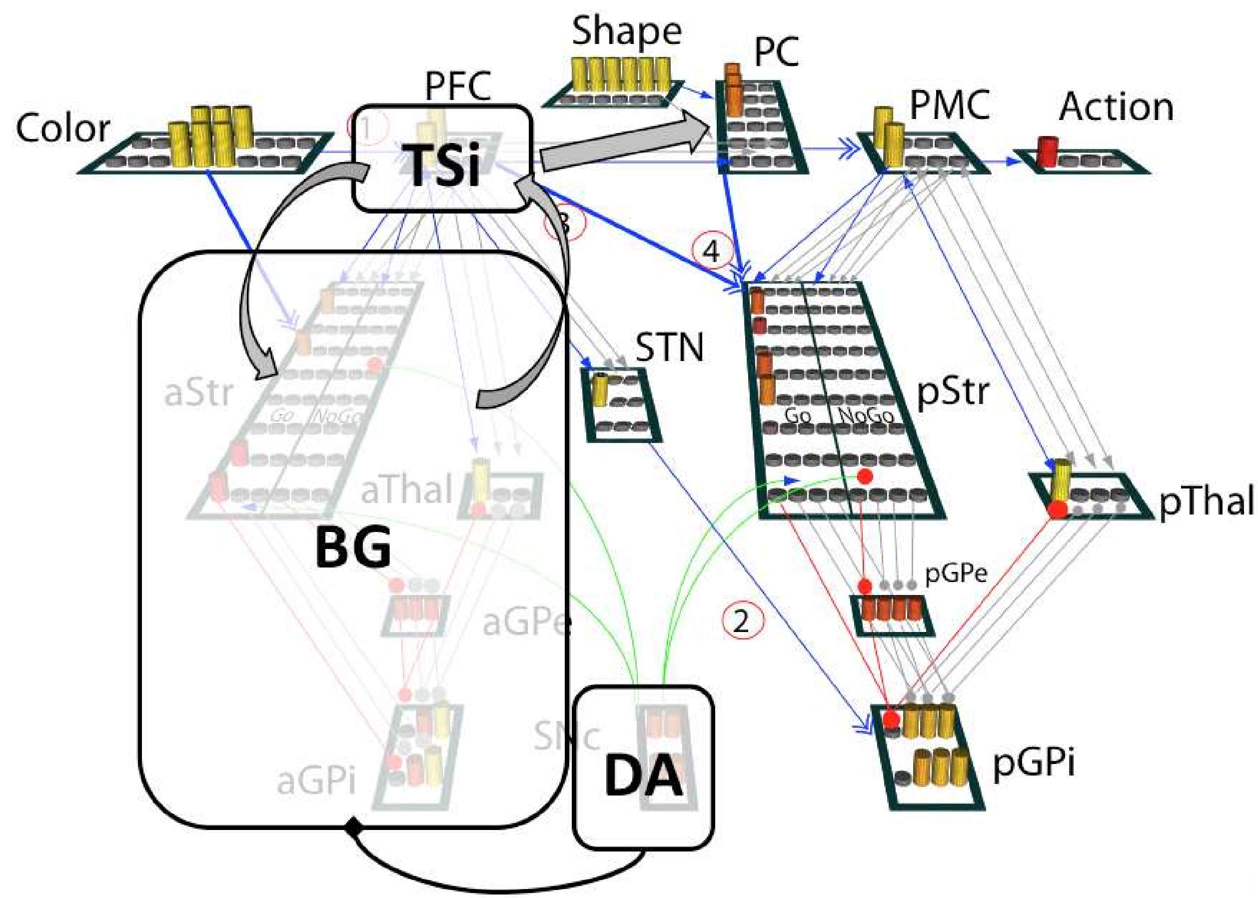

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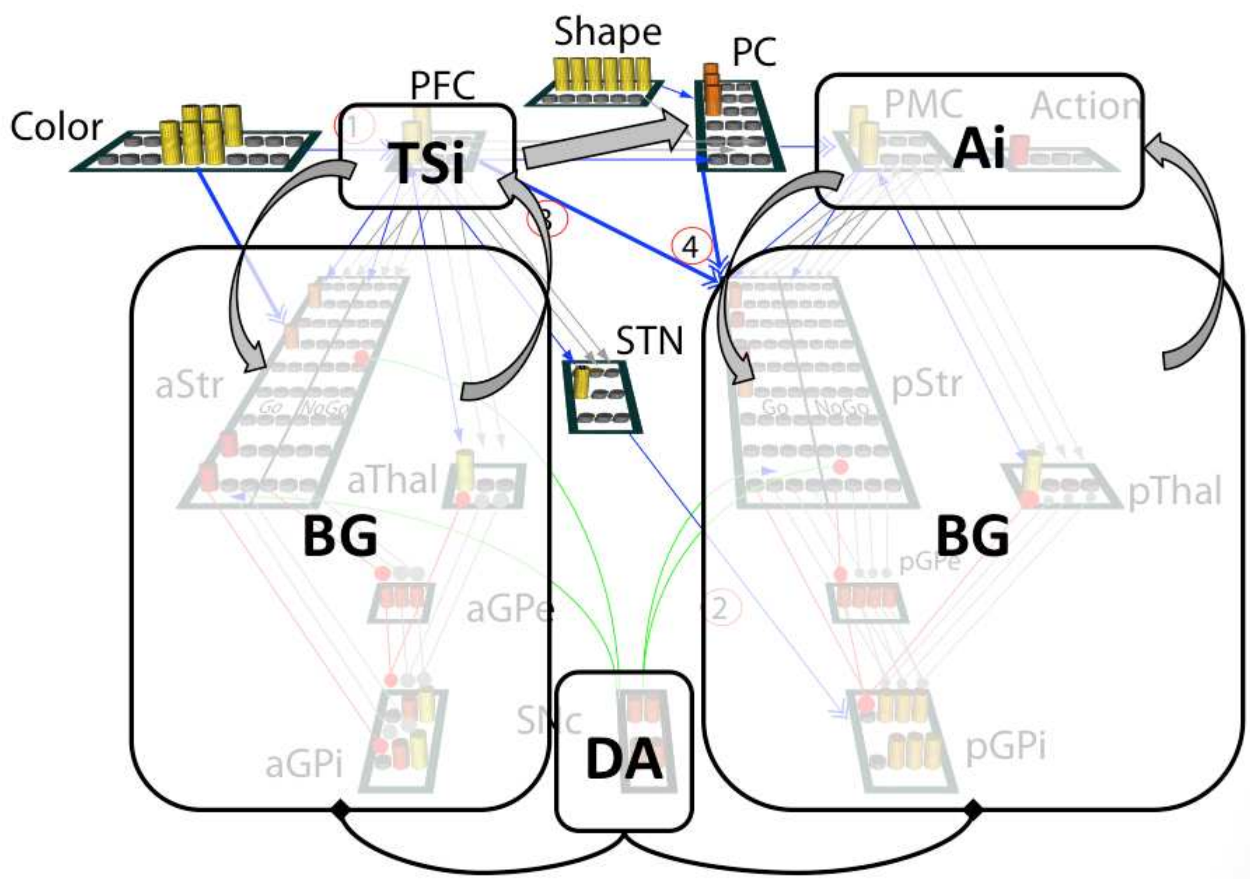
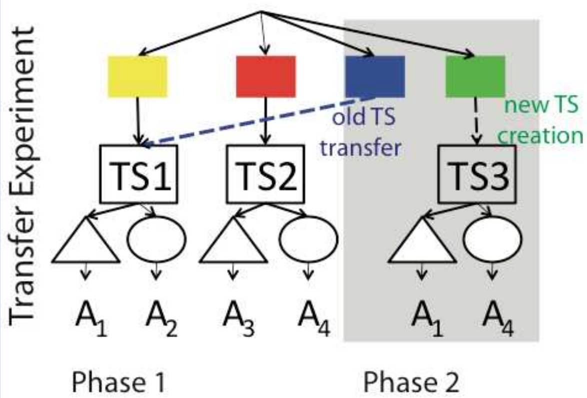
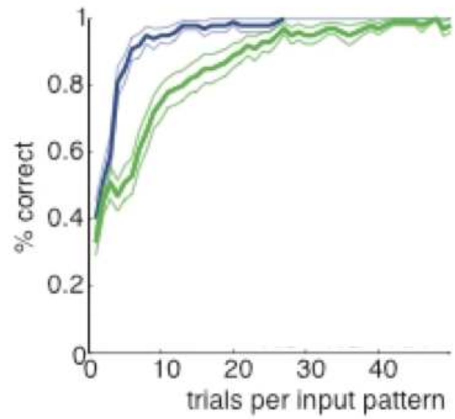


Neural Network – Results



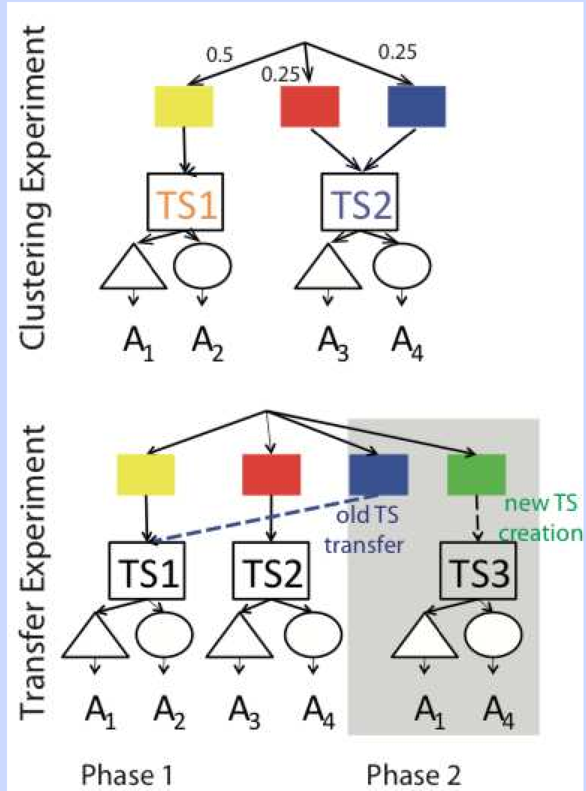


Phase 2
new contexts:
Old TS
New TS

The network learns efficiently unsupervised,
Predicts positive, negative transfer

Collins & Frank, Psych Review, 2013

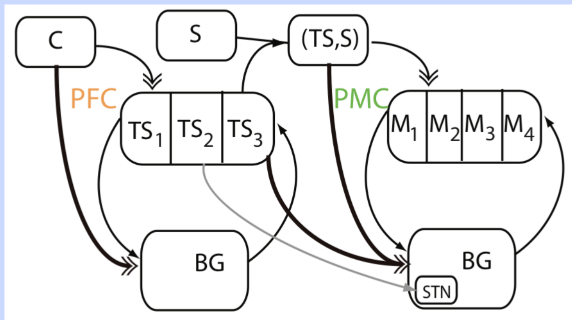
Re-using and creating task-sets

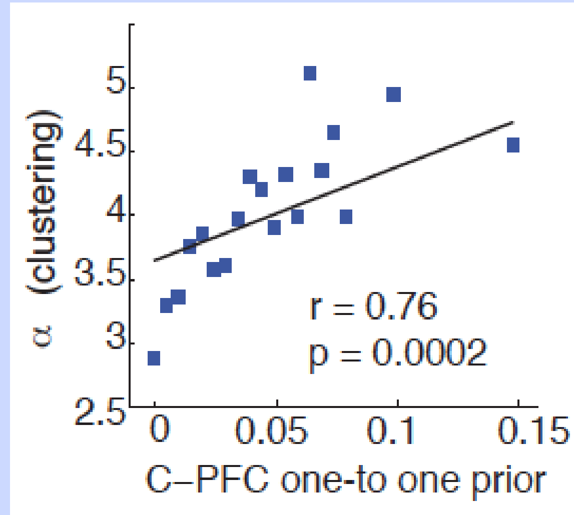


Collins & Frank 2013, *Psych Rev*; Collins et al, 2014 *J Neurosci*; Collins & Frank, in review

fMRI evidence: Badre & Frank 2012

Model mimicry: C-TS and hierarchical BG-PFC network





- Sparseness of context-PFC connectivity matrix is linked to α clustering
- *Both models are approximations of the same process: building TS structure*
- fMRI evidence for hierarchical PFC-BG mechanisms Badre & Frank 2012

Collins & Frank 2013 *Psych Rev*