Theories about Dopamine

Reinforcement learning signals in biological organisms

(Talk by Michael Pfeiffer)

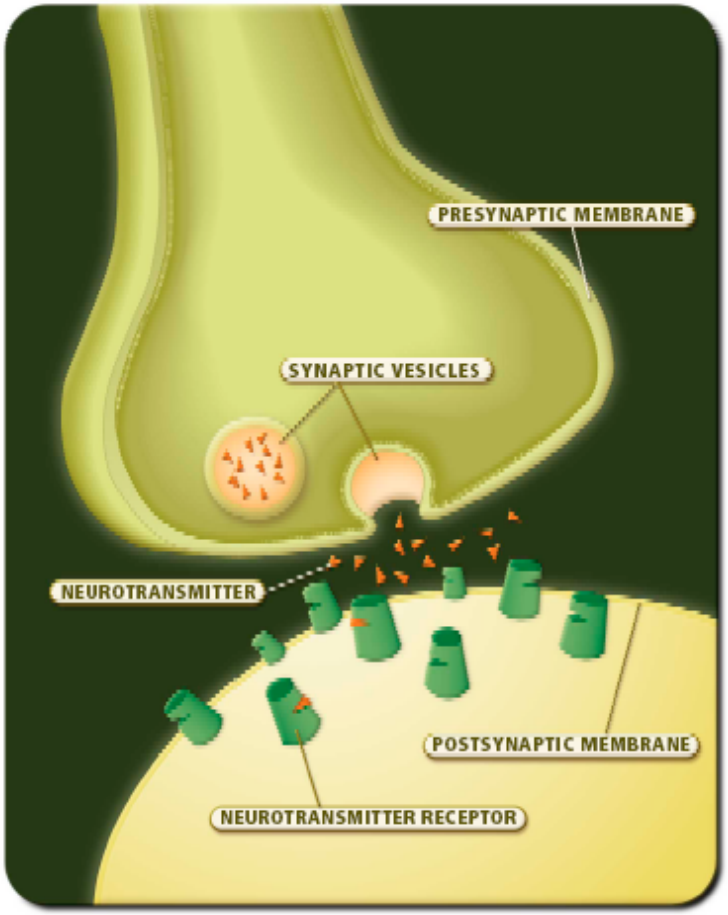
Outline

- Neuromodulators
- Dopamine System
- Dopamine, Rewards and Learning
- Dopamine and Drug Addiction

Neurotransmission

- Signal arrives at presynaptic terminal
- Neurotransmitters are released into synaptic cleft
- Receptors at postsynaptic cause excitatory or inhibitory response

- ~ 50 Neurotransmitters:
  - Glutamate, GABA
  - Dopamine, Serotonine
  - Acetylcholine
  - Endorphines
  - …



Neuromodulators

- Substances that modulate neurotransmission pre- or postsynaptically
  - Release of transmitters
  - Sensitivity of receptors
  - Reuptake
- Effects are slower, but longer lasting
- Involved in control of general arousal
- Substances can be both neurotransmitters and neuromodulators at the same time

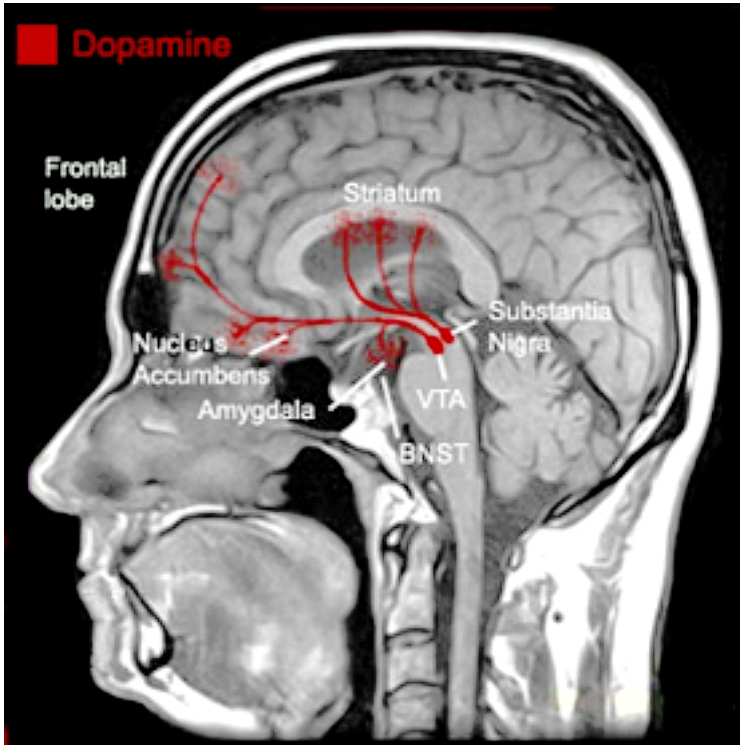
- Neuromodulators
  - Natural modulators
    - **Dopamine**
    - Serotonine
    - Acetylcholine
    - Norepinephrine
    - ...
  - Therapeutic psychoactive drugs
    - Prozac, anaesthetics, pain killers, ...
  - *Recreational* drugs
    - Cocaine, opiates, alcohol, nicotine, ...

Special Role of Dopamine

- Transmitter & Modulator

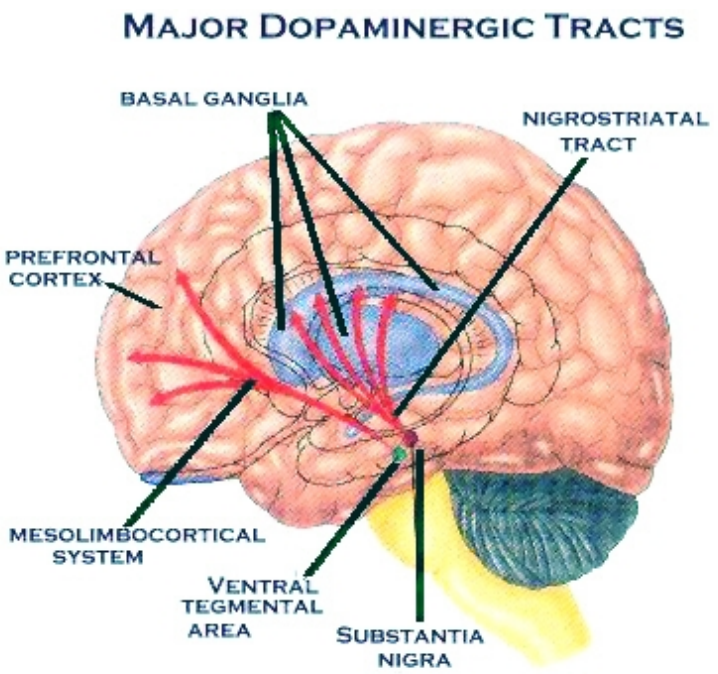
- Motor Processes
- Motivational Processes
- Learning

- Clinical significance
  - Parkinson's disease
  - Schizophrenia
  - Drug addiction



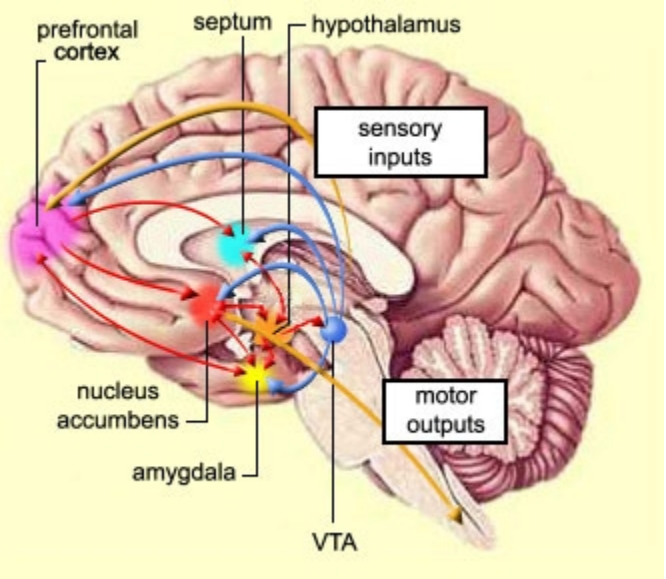
The Dopamine System

- Dopamine (DA) Neurons
  - Substantia Nigra pars compacta (SNc)
  - Ventral Tegmental Area (VTA)
- Nigrostriatal Pathway
  - SNc → Striatum
  - Movements
- Mesolimbic Pathway
  - VTA → Nucleus Accumbens
  - Pleasure
- Mesocortical Pathway
  - VTA → Frontal Cortex
  - Motivation and Emotions



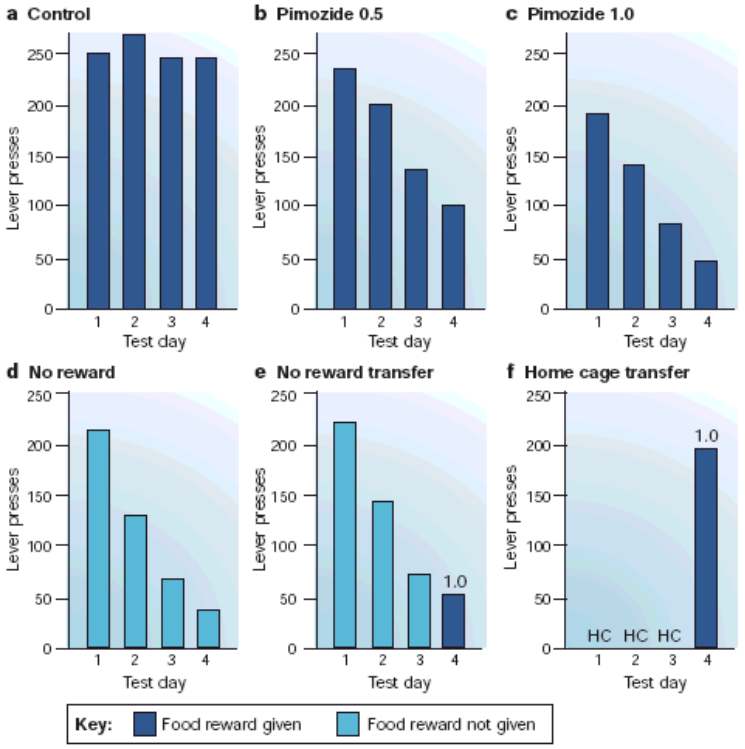
Dopamine and Rewards

- Positive reward circuit
  - VTA
- Early hypothesis: DA directly indicates pleasure
- Newer hypothesis: DA facilitates learning
  - DA level prior to behavior is proportional to potential for providing pleasure
- Punishment circuit is different
  - acetylcholine



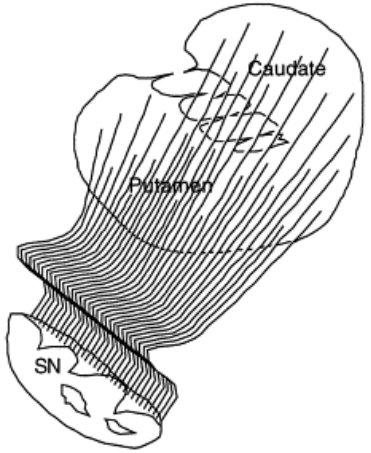
Effects of DA Receptor Blockade

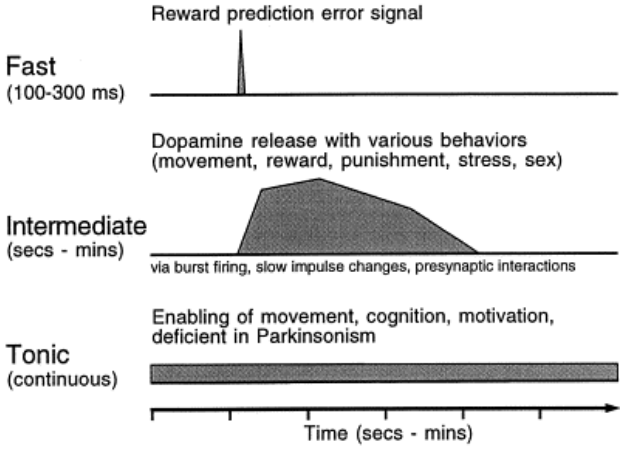
- Animals trained to lever-press for food-reward
- When reward is still given, animals keep on lever-pressing (a)
- When DA is blocked (Pimozide), animals unlearn behavior, although reward is given (b-c)
  - Same as in extinction(d-e)
  - Drug did not attenuate performance capacity
- If animals have no chance to unlearn, drug does not influence the behavior (f)



Dopamine Activation by Rewarding Stimuli

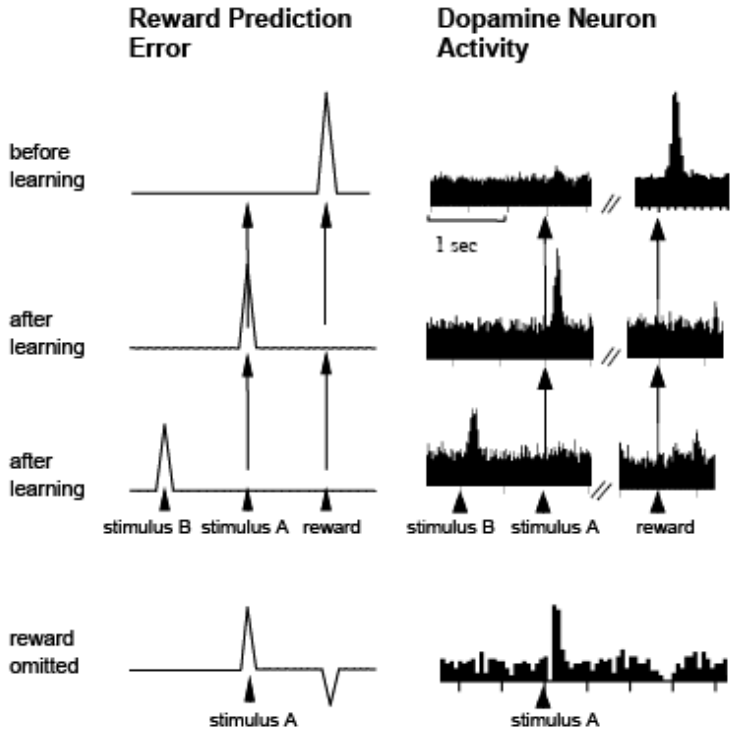
- Most DA neurons show **phasic** (~ 200 ms) activations to rewarding and reward-predicting stimuli
  - Only 14% to aversive stimuli
- DA neurons do not discriminate between sources of reward
- DA reward signal is a relatively homogeneous population signal
  - **Global** reinforcement signal
  - High divergence
- Different time courses of different DA functions





Shift of DA Response

- Before learning:
  - No response to neutral stimulus A
  - DA neurons are activated by reward
- After training, DA response shifts to time of conditioned stimulus
  - If another stimulus B is trained to predict reward, stimulus A becomes neutral again
- Depression of DA activity if reward is omitted
  - DA neuron still sensitive to delivery of reward



Learning with Rewards

- Pavlov: Pairing of stimuli with rewards and punishments guide learning
- Newer animal learning theories argue that reward prediction errors trigger learning

- **Rescorla-Wagner** learning rule:
  - Linear model for expected reward: $V = w \cdot s$
  - Update $w \leftarrow w + \varepsilon \cdot \delta \cdot s$
  - Where $\delta = r - V$ … r = actual reward

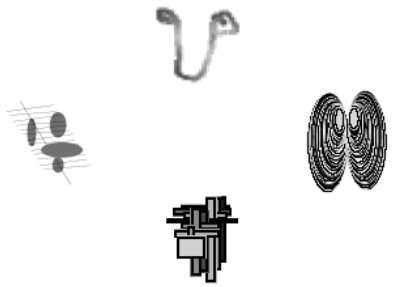
- Similar to TD-rule in Reinforcement Learning
- Activity of dopamine neurons is similar to δ

Dopamine as Reward Predictor

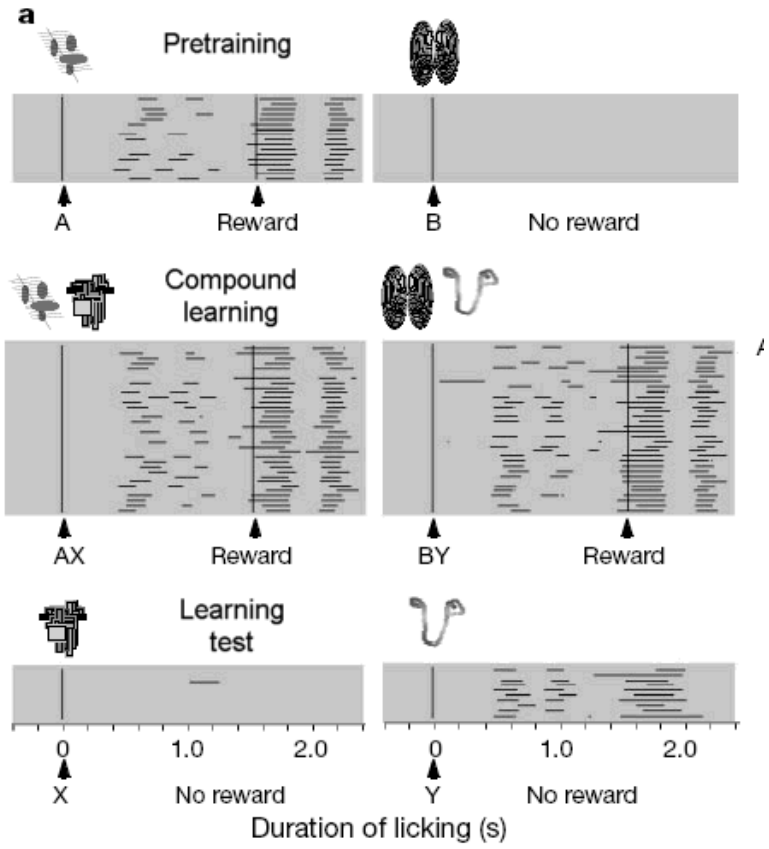
Waelti, Dickinson & Schultz, 2001

- Phasic DA response to rewards compatible with prediction errors
- Formal test with blocking paradigm

- Classical / Pavlovian conditioning experiment
  - Monkey receives juice rewards
  - Visual stimuli (fractals) before reward delivery become conditioned stimuli
  - Anticipatory licking is conditioned reponse

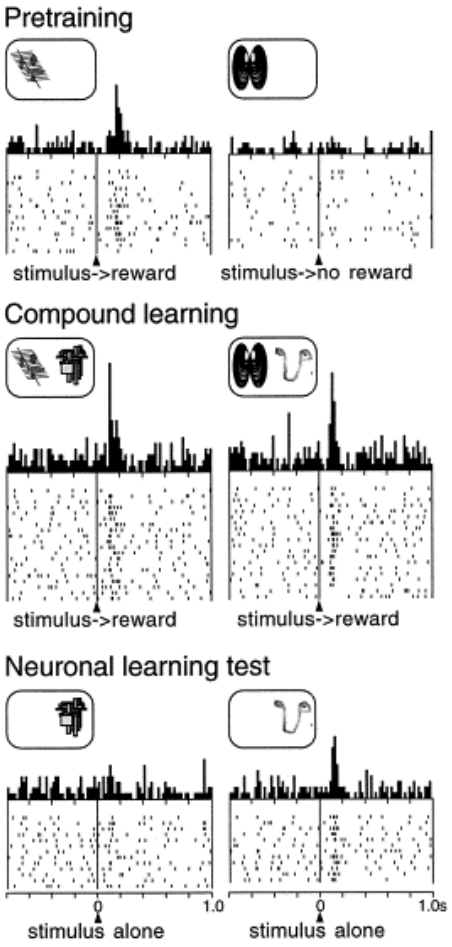


Blocking Test: Behavioral Response



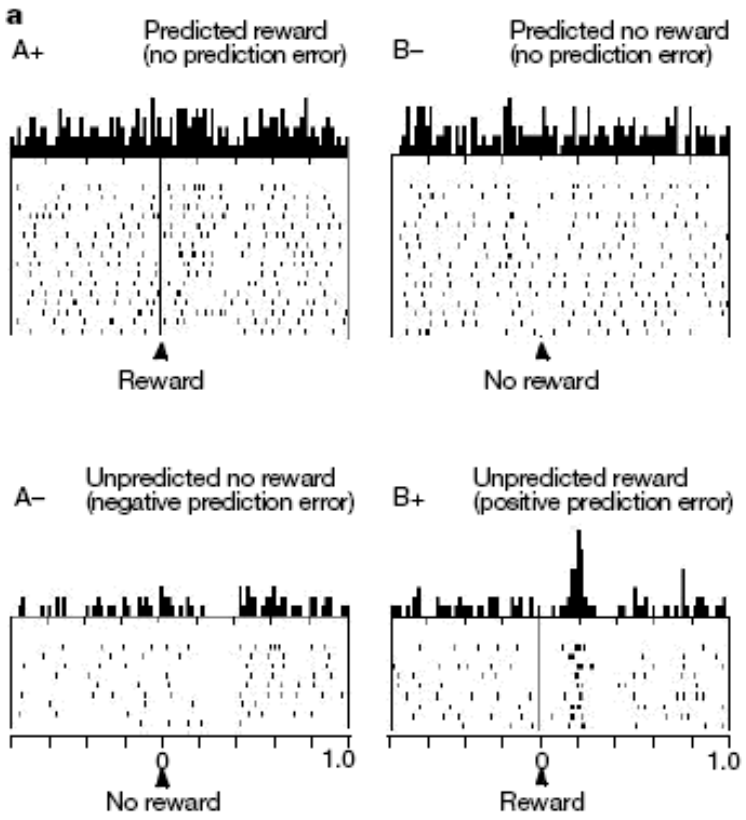
- Pretraining
  - A+ (A→r), B- (B→'.') trials
- Compound learning
  - Additional novel stimuli X and Y
  - AX+, BY+ trials
  - Anticipatory licking is observed in both cases
- Learning test
  - Response to X and Y?
  - X is blocked by A
  - Y becomes reward predictor

Neuronal Response



- Response of DA neurons to stimuli
  - Activated by reward-predicting stimulus A
  - No reaction to unrewarded stimulus B
  - Same activation caused by AX and BY
  - Blocked neuronal response to redundant stimulus X
  - Learned response to Y

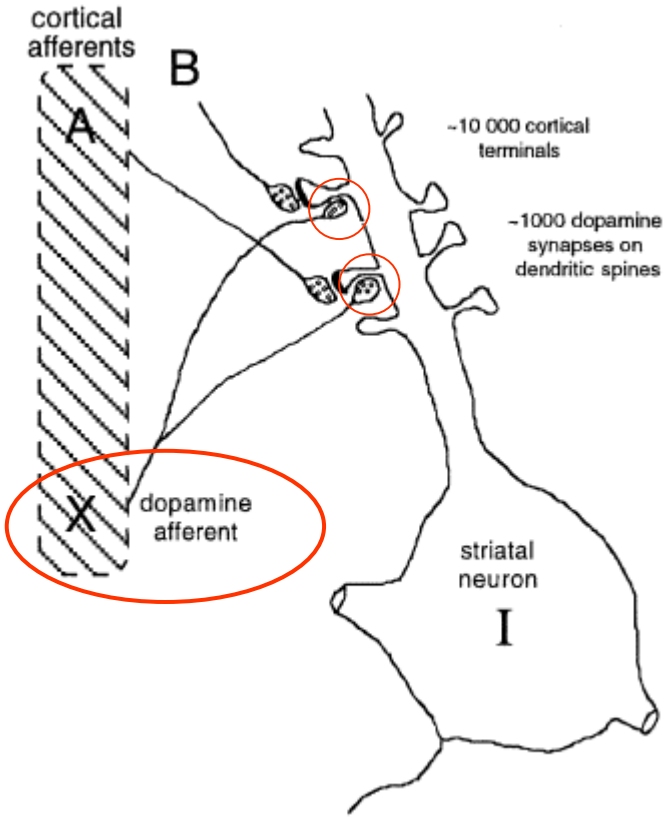
Response at Time of Reward



- Responses during pretraining
  - Expected reward generates no DA response
  - Surprising reward creates positive DA response
  - Omission of reward creates DA depression

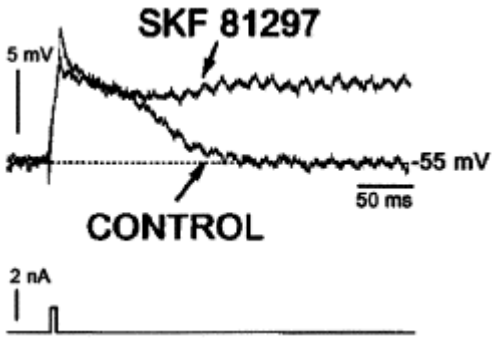
Influence of DA on postsynaptic Structures

- DA signal is broadcast as **global reinforcement signal**
- DA and cortical inputs often converge on same dendritic spine in striatum
- Cortical input signals information about stimulus
- Concurrent DA and cortical input leads to synaptic change
  - Sign and Amplitude of DA signal affect plasticity
  - Effect depends on DA receptor type
- Heterogeneous learning through different cortical inputs



Possible Effects of DA Signal

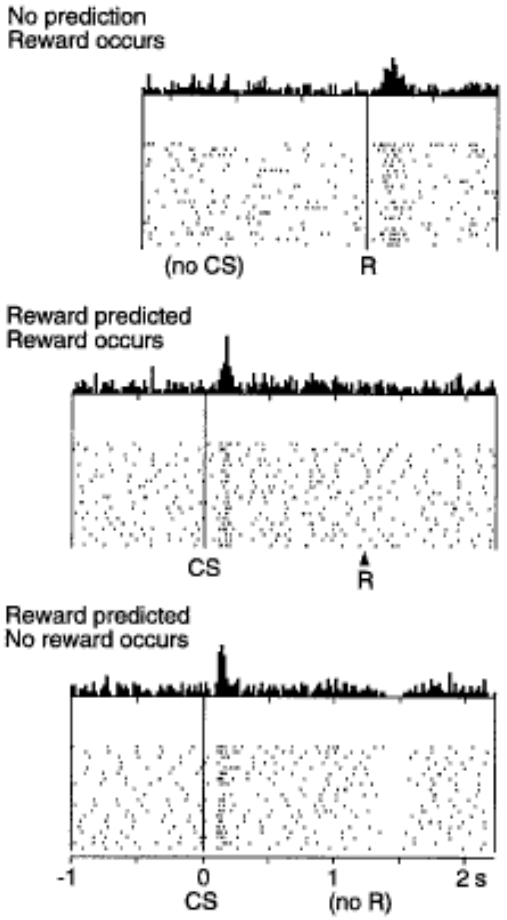
- Transient enhancement of neurotransmission
  - D1 agonist SKF 81297
- Enabling of postsynaptic plasticity
  - Allow plasticity to take place
- Enhancement of postsynaptic plasticity
  - DA antagonists disrupt plasticity
- Induction of postsynaptic plasticity
  - DA application leads to LTP



See W. Schultz: “Getting formal with dopamine and reward”, Neuron, 2002, for an overview

Summary: DA as Prediction Error

- Acquisition of DA responses and behavioral reactions is governed by **prediction errors**, not simple stimulus-reinforcer pairings
- Responses of DA neurons follow theory of blocking paradigm
- Behavioral and neuronal learning is correlated with activations of DA neurons by rewards
- DA responses gives error signal for modifying synaptic processing
  - Similar to Rescorla-Wagner rule and TD-Learning



More Hypotheses about DA

- Role of dopamine remains controversial

- Drug Addiction
- Attention and Novelty
- Motivation
- Motor Hypothesis

Sources

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