Simulation of the neuromodulatory pathways responsible for incrementing and decrementing attention during reversal learning and set-shifting

Nicolas Oros[a], Andrea A. Chiba[b], Douglas A. Nitz[b], Michael C. Avery[a], and Jeffrey L. Krichmar[a]

[a] Department of Cognitive Sciences, University of California, Irvine
[b] Department of Cognitive Sciences, University of California, San Diego

INTRODUCTION

The cholinergic, dopaminergic, and noradrenergic systems regulate attention in distinct, but complementary ways.

ACh projections from the substantia innominata / nucleus basalis region (SI/nBM) to the neocortex are necessary to increase attention to relevant stimuli [1].

ACh projections from the medial septum / vertical limb of the diagonal band (MS/VDB) to the hippocampus and medial frontal cortex are crucial to reduce attention to irrelevant stimuli [2].

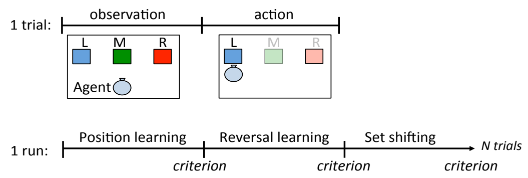
The noradrenergic system, which is driven by activity in the locus coeruleus (LC), is thought to shift attention when facing uncertainty and novelty in an environment [3].

Dopamine originating from the ventral tegmental area (VTA) and substantia nigra, is necessary for reinforcement learning and reward prediction [4].

We developed a neural simulation to provide insight into how ACh can decrement or increment attention using two distinct pathways, and how dopamine and noradrenaline influence these pathways.

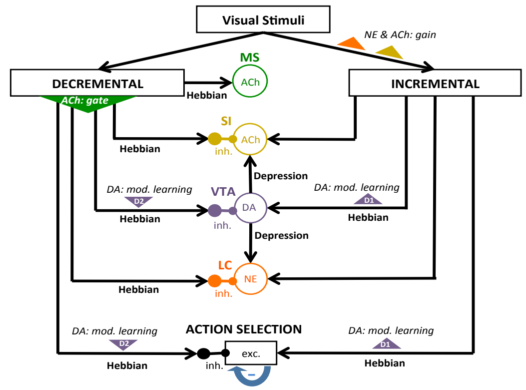
METHODS

Experimental Setup



Criterion: 8 consecutive correct trials

Neural Architecture



Neural and Synaptic Dynamics

Firing rate neuron model: $s_i(t) = \rho_i s_i(t-1) + (1-\rho_i)\left(\frac{1}{1+\exp((\theta_i - I_i(t))G_i)}\right)$

Input: $I_i(t+1) = \sum_j nm_{ij}(t) w_{ij}(t) s_j(t)$ Nm MS: $nm_{ij}^{ACh}(t+1) = K_1 s_i^{MS}(t)$

Nm LC & SI: $nm_{ij}^{NE\_ACh}(t+1) = 1 + \left[\left(s^{LC}(t) + s_i^{SI}(t)\right)/K_2\right]$

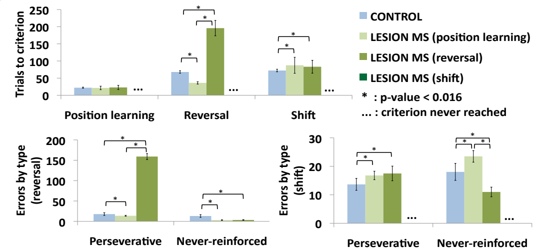
Plasticity: **Hebb.** $\Delta w_{ij}(t+1) = \varepsilon\, nm_{ij}^{D2}(t)(w_{ij}(0) - w_{ij}(t)) + \delta\, nm_{ij}^{D1} s_j(t) w_{ij}(t)$

Depres. $\Delta w_{ij}(t+1) = \varepsilon(w_{ij}(0) - w_{ij}(t)) - d\, s_j(t) w_{ij}(t)$

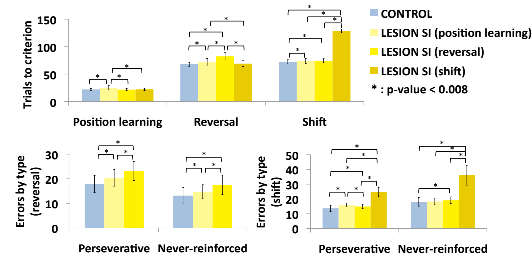
Nm VTA: $nm_{ij}^{D1}(t+1) = s_j^{VTA}(t)$ $nm_{ij}^{D2}(t+1) = s_j^{VTA}(t)$

RESULTS

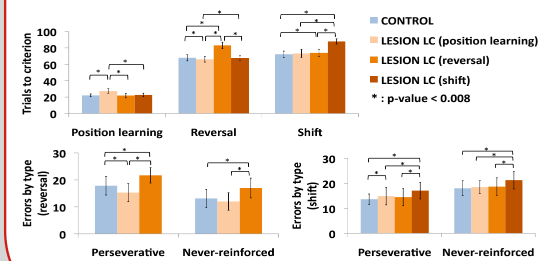
Lesion MS



Lesion SI

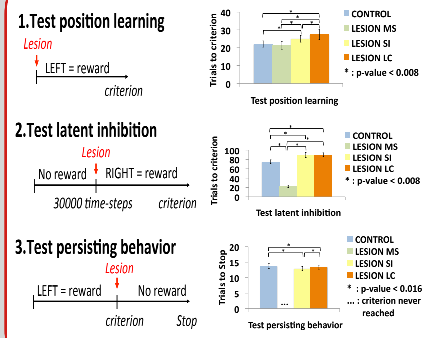


Lesion LC



Mean and standard deviation recorded over 100 runs for each experiment.

Latent Inhibition and Persisting Behavior



Criterion: *8 consecutive correct trials.*
Stop: *no selected actions for 8 consecutive trials.*

CONCLUSIONS

We developed a behavioral paradigm that dissociates decremental and incremental attention.

The model exhibits latent inhibition, persisting behavior, habituation to stimuli, and increased learning when facing novel or unexpected stimuli and reward associations.

Lesioning the MS disrupts latent inhibition, and increases drastically perseverative behavior.

Lesioning the SI disrupts increments in conditioned stimulus processing.

Lesioning the LC results in difficulty learning novel reward associations.

1. Chiba, A. A., et. al., J Neurosci 15 (1995)
2. Baxter, M.G., et. al., J Neurosci 17 (1997)
3. Yu, A., et. al., Neuron 46 (2005)
4. Schultz, W., Curr Opin Neurobiol 7 (1997)

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Contact: Nicolas Oros at *noros@uci.edu*