Reliable Transmission of Visual Inputs into Cortex Depends on Thalamic Synchrony

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Introduction

Visual information enters the cerebral cortex through thalamocortical connections, partly on the basis of synchronized neuronal firing.

How many synchronous synapses are necessary for reliable thalamocortical transmission to occur?

Difficult to quantify experimentally: Would require the simultaneous monitoring of many synaptic inputs.

We used a biophysical multi-compartment model of a layer 4 cortical spiny stellate cell contacted by stochastic synapses exhibiting short term dynamics.

We used simultaneous recordings from LGN and V1 obtained in anesthetized cats during visual stimulation with drifting gratings[1].

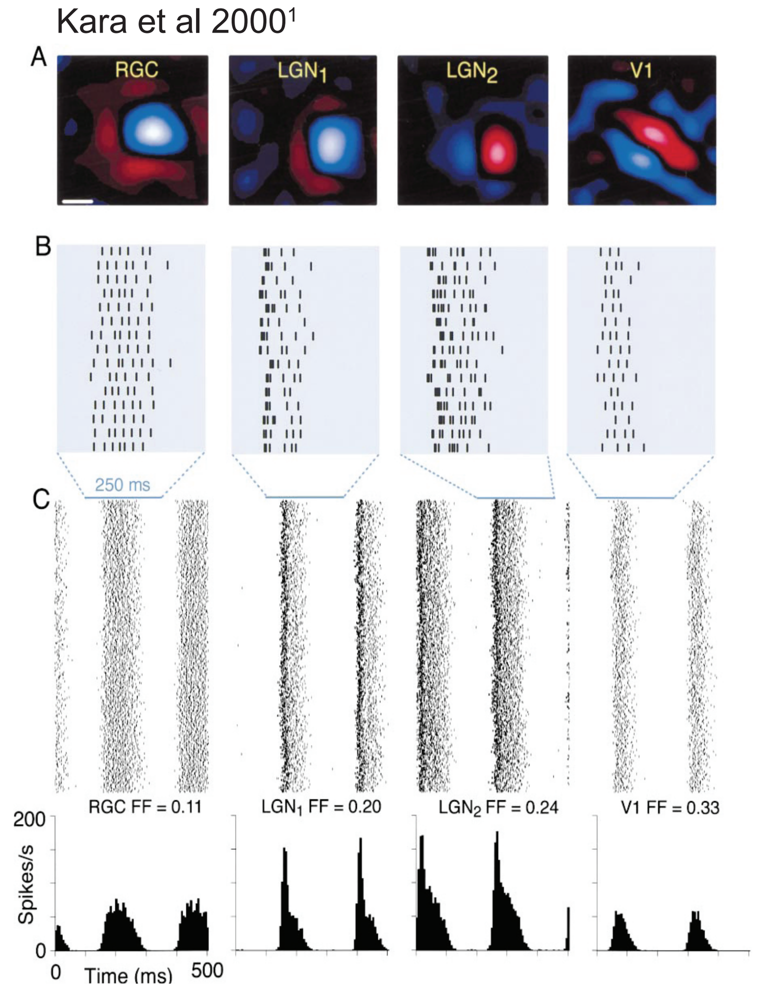
The model synapses were stimulated with the experimental LGN data and the output of the model cell was compared to the experimental V1 recordings.

We used the reliability of firing patterns as a measure of

Found that thalamic inputs operate in a regime of around 20-40 synapses that optimizes efficient information transfer by synchronous population coding.

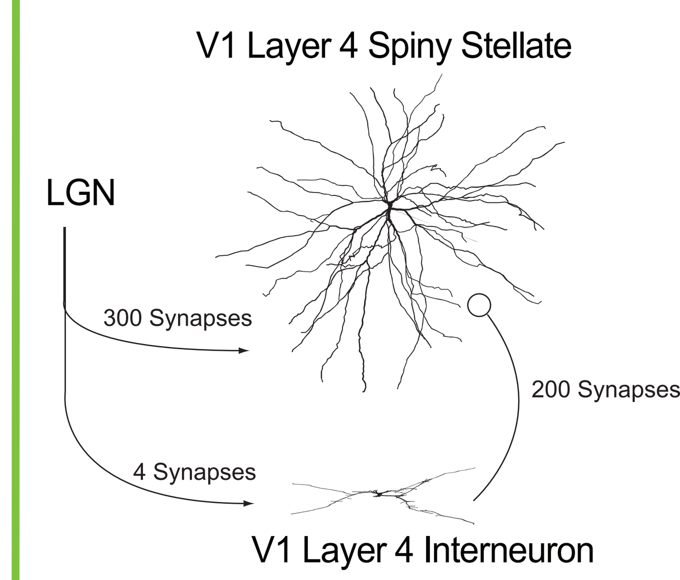
Figure 1 - Experimental[1] triple recordings in anesthetized cat

Kara et al 2000[1]



Stimulus: 4 Hz drifting gaussian grating at 50% contrast (effective for all cell types). Orientation was matched to the tuning of V1 cells. (A) receptive fields, (B) rastergrams, (C) expanded rastergrams and their corresponding histograms.

Figure 2 - Model Morphology & Setup

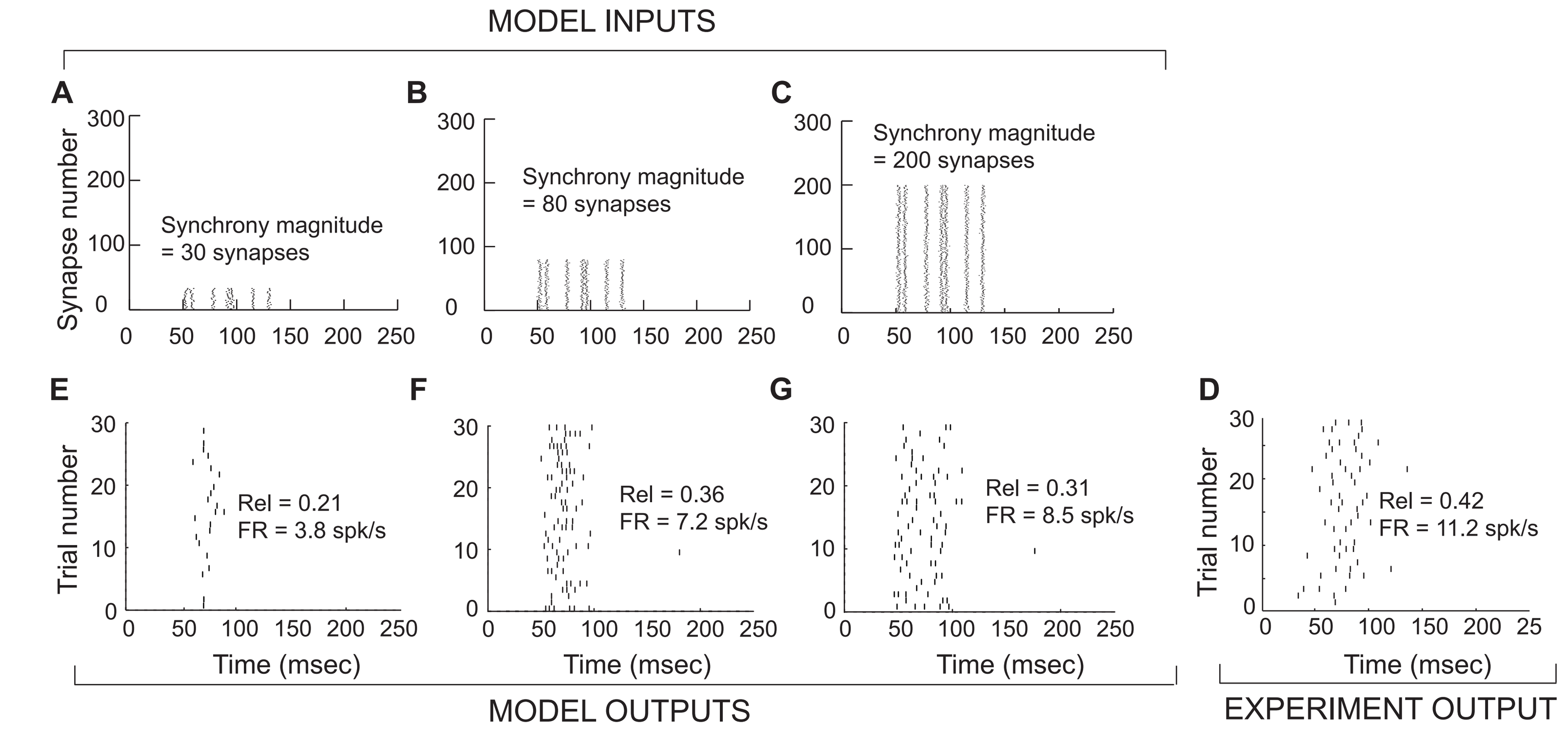


Morphology and interconnections of the reconstructed V1 layer 4 spiny stellate cell and feedforward inhibitory interneuron.

Stellate cell: 744 compartments, 1000 GABA and 4500 dynamics excitatory synapses.

Interneuron: 5 compartments, 4 excitatory inputs and 200 GABA outputs to SC.

Figure 3 - Varying synchrony of input events affects output reliability and firing rates



(A-C) Rastergrams of all 300 thalamocortical synaptic inputs into the model cell for one trial for synchrony magnitude 30, 80 and 200 respectively. Input spike train from in vivo LGN recordings was duplicated for the number of inputs. Spikes jittered by 1 msec and 10% randomly deleted.
(D) Thirty trials from in vivo cat V1 cortical cell recordings.
(E-G) Rastergrams and statistics of outputs from 30 trials of inputs each using different LGN spike trains. Synchrony magnitude 30, 80, 200 respectively.

Conclusions

Firing pattern reliability in V1 simple cells is a highly non-linear function of thalamic synchrony magnitude

Reliable cortical response begins at about 20 synchronous synapses, with a temporal integration window of less than 5 ms

An optimal synchrony magnitude (OSM) is achieved for about 30 synapses to match the data of Kara et. al.

Spike count variability (Fano Factor) is low: 0.2-0.4 if 20-80 synchronous input synapses are used

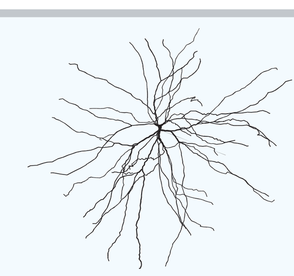
OSM depends on the balance between cortical excitatory and inhibitory background inputs.

Feedforward inhibition gradually increases OSM and decreases reliability

In vivo recordings (4 animals) predict OSM in the range of 20-60 synapses

As few as 6-10 dLGN cells may be effective at driving a V1 simple cell and at transmitting temporal spike information reliably.

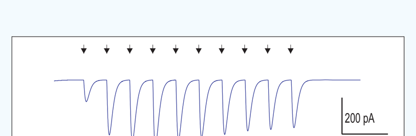
Methods



Multi-compartment (744) model of V1 spiny stellate cell (SC) with feedforward inhibition (model basket cell)

Separate LGN inputs and excitatory and inhibitory cortical synapses.

Dynamic synapses with low initial probability of release (0.2) endowed with short term facilitation and depression dynamics.

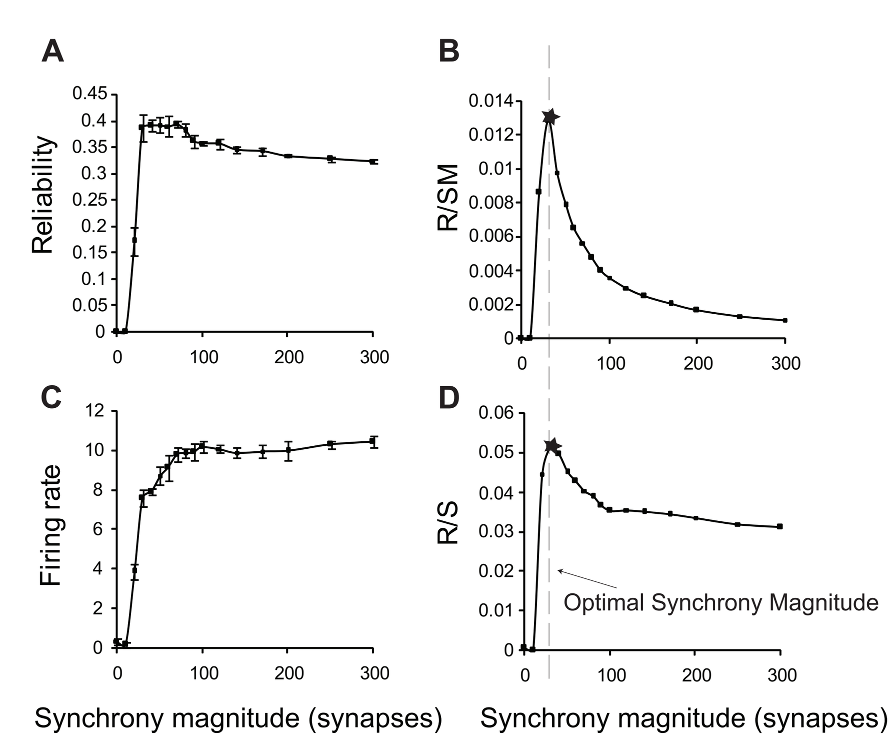


Input spike trains were taken from experimental recordings of Kara et al. with added jitter and noise. We used recent anatomical data[3] to estimate LGN convergence.

200 repeated trials with identical drifting pattern inputs to establish reliable statistics.

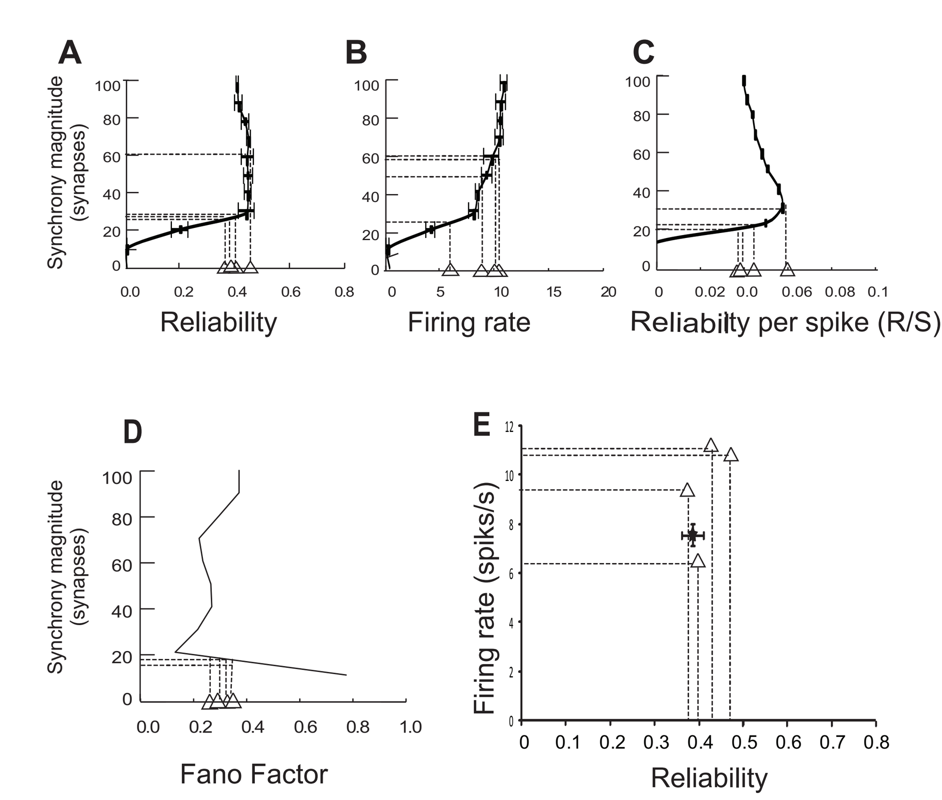
Developed new analysis tools to assess model output, and compared the model outputs with recorded data to derive the number of synchronous LGN synapses required for efficient

Figure 4 - Synchrony magnitude controls reliability



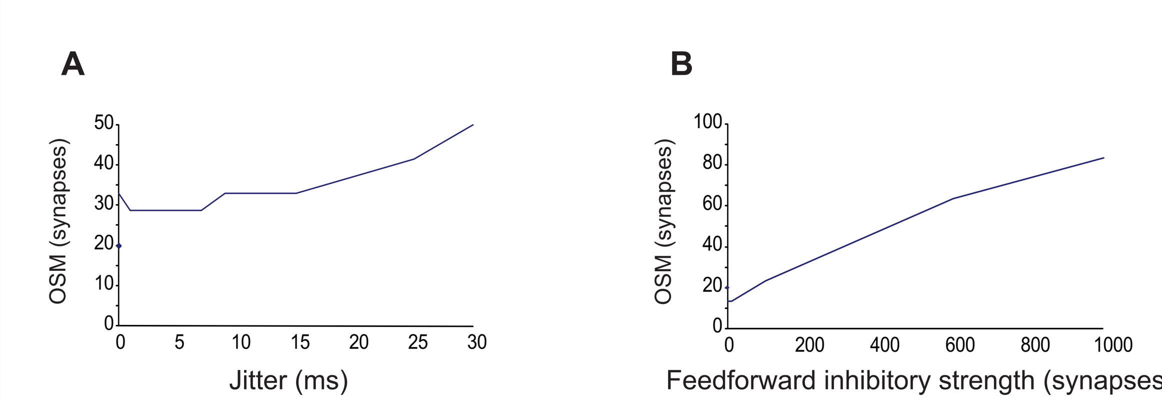
SC response with 1 ms jitter and 200 synapse feed forward inhibition.
(A) Average spike-time reliability.
(B) Firing rate response.
(C) Reliability per synchrony magnitude (RPSM). Optimum Synchrony Magnitude
(OSM) is maximum RPSM.
(D) Reliability-per-spike (RPS) efficiency (reliability/firing rate).
Standard deviation bars from 10 data points using 30 independent trials each.

Figure 5 - Predicted input synchrony ranges from experimental data

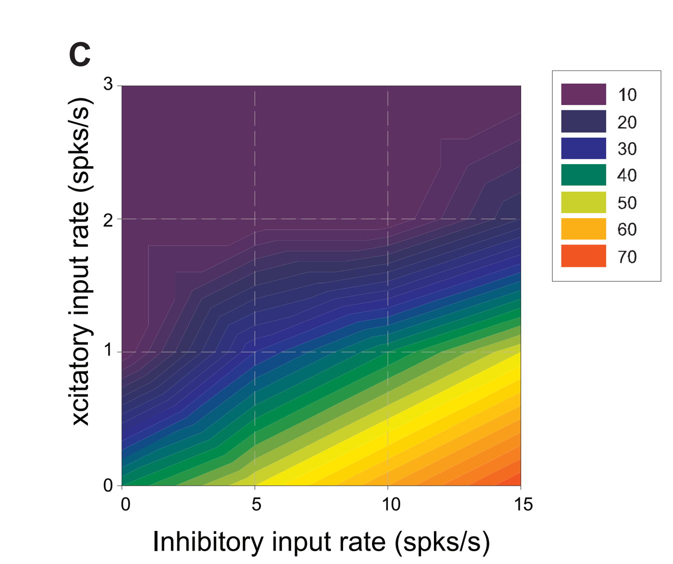


Graphs from Figure 2 were inverted to make synchrony magnitude the dependent variable. Triangles correspond to in vivo experimentally measured values from separate animals. Dashed lines are inferred output synchrony magnitude for:
(A) Reliability,
(B) Firing rates,
(C) Reliability-per-spike (RPS),
(D) Fano Factor,
(E) Predicted firing rate and reliability at SM = 30.

Figure 6 - Influence of key model parameters on Optimum Synchrony Magnitude (OSM)



(A) Varying input spike jitter from 0 to 30 msec.
(B) Varying strength of feedforward inhibitory interneuron from 0 to 1000 synapses.



(C) Effect of covarying background (Poisson) intra-cortical balance from 1 to 3 spikes/s excitatory rate and 1 to 15 spikes/s inhibitory rate. Feedforward inhibition 200 synapses, jitter 1 msec.

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Learning to give up! The contribution of the dopaminergic system to extinction

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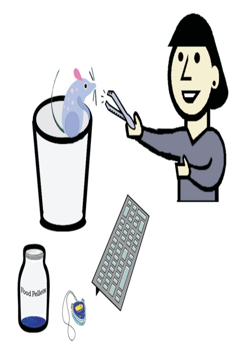
INTRODUCTION

- The rate of extinction learning depends on the probability of getting the reward [1].
- The potential neural substrate that could account for this phenomenon is the ventral tegmental area (VTA) of the midbrain. Prior studies have shown that dopamine neurons in the VTA are involved in coding values of rewards with different probabilities, expectation of rewards, and reward related motivation [2,3].
- We hypothesize that VTA may play a role in this probability-dependent "resistance to extinction" phenomenon.

METHODS

Behavioral experiment

	Training session			Extinction session
	Trial # constant	Pellet # constant		
25%	20	80	No time gap	Until the rat makes no attempt for 7 consecutive trials
50%	20	40		
75%	20	27		
100%	20	20		



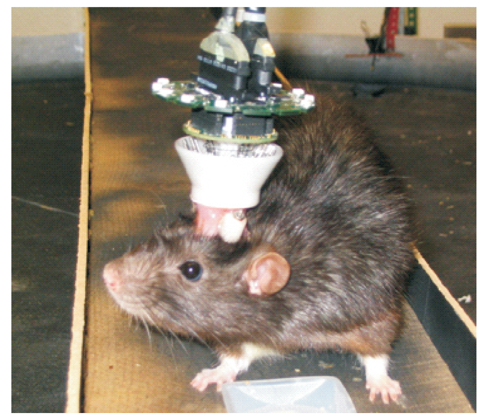
Modulation of VTA dopamine neural activity

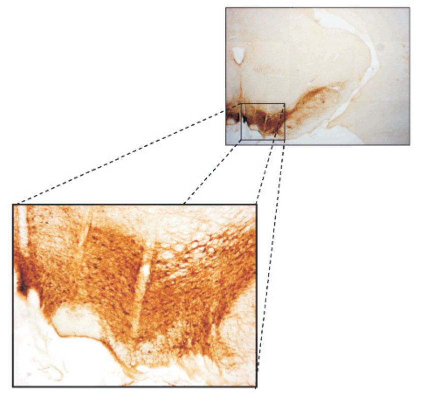
Day	saline		bupivacaine or WIN-2
1	100%	1 hour	50%
2	75%		25%
3	50%		100%
4	25%		75%

Bupivacaine (2.5%, 0.5μL), WIN-55212-2 mesylate (2.5%, 0.5μL) or saline (5μL) was injected into the bilateral VTA just before the experiment.

High density electrophysiology

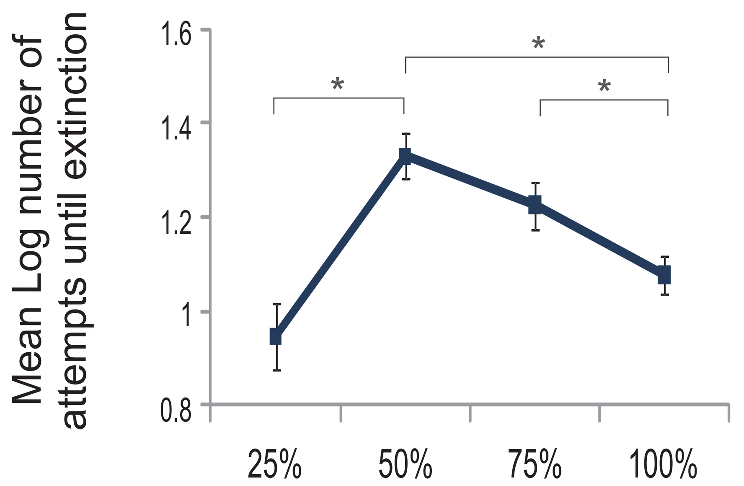
Each rat was implated a hyperdrive consisting of 12 independently movable tetrodes. We recorded neuronal activity in the VTA in awake and freely moving animals.



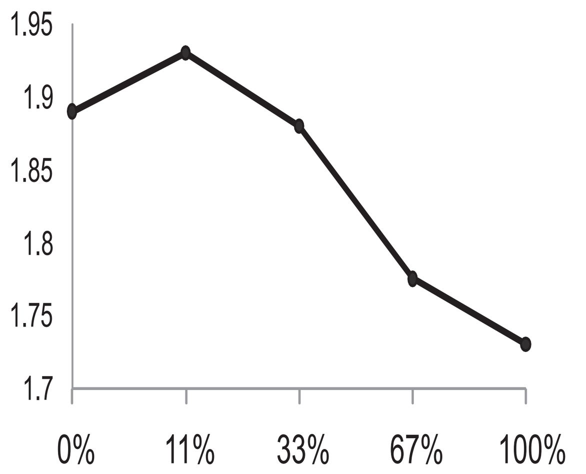


RESULTS

Rat behavior experiment gave consistent result with the human behavior study

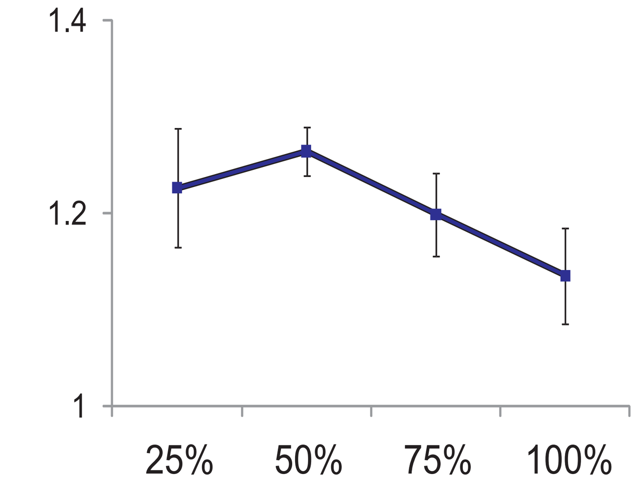


In trial number constant task, resistance to extinction was significantly different among different reward probabilities. (N = 12)

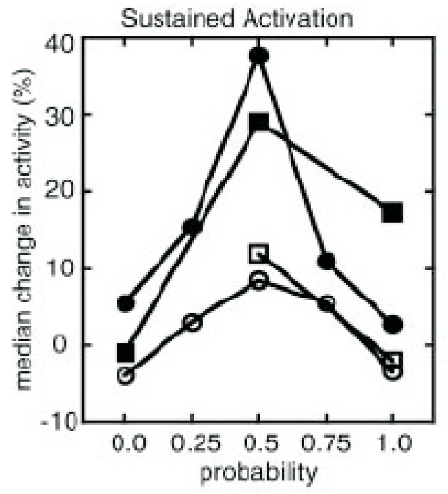


Reconstructed from Lewis and Duncun (1958) [1].

Probability dependent resistance to extinction is not cognitive, but emotional

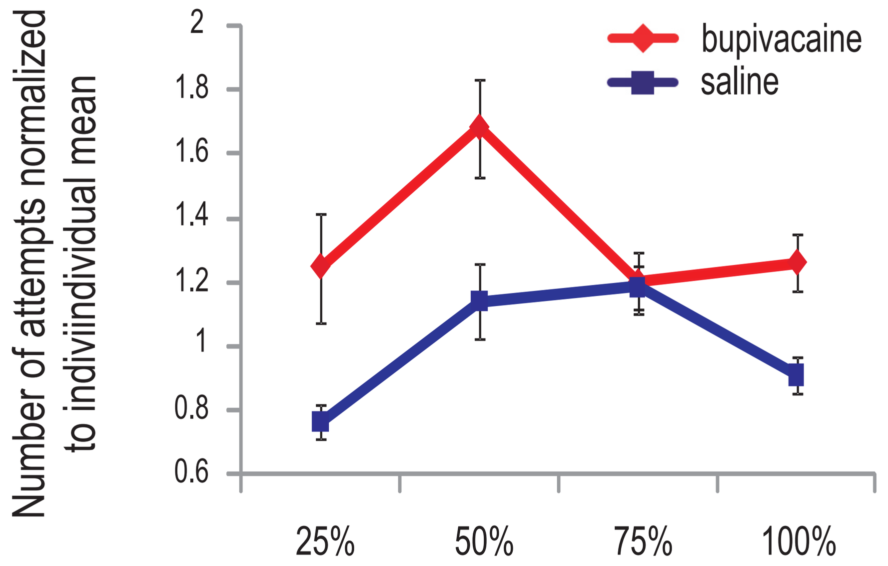


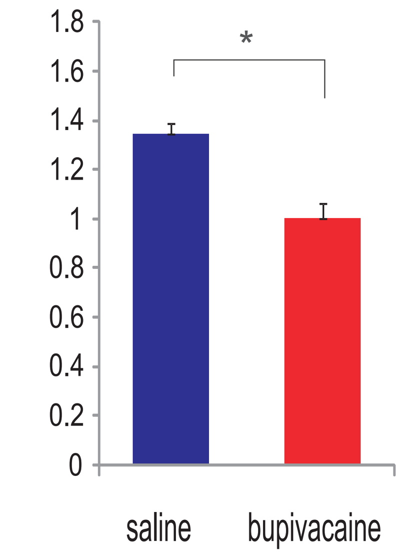
No significant difference among different probabilities found in pellet number task . (N = 9)



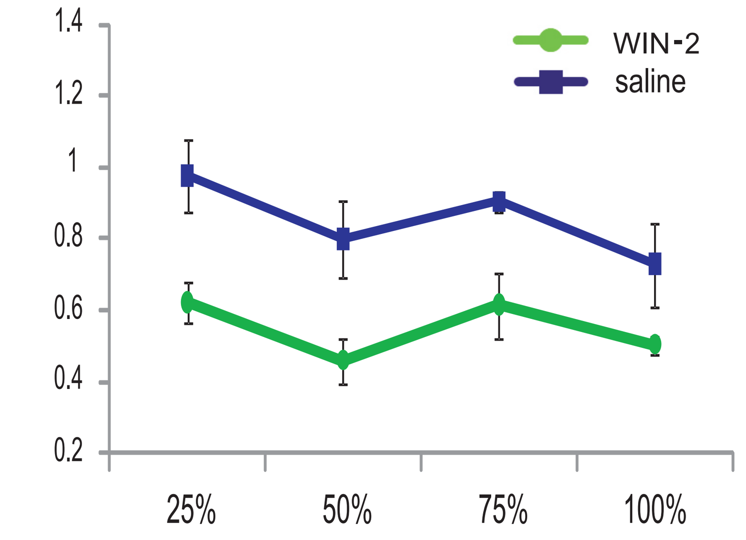
Adopted from Fiollio et al. (2003) [4]

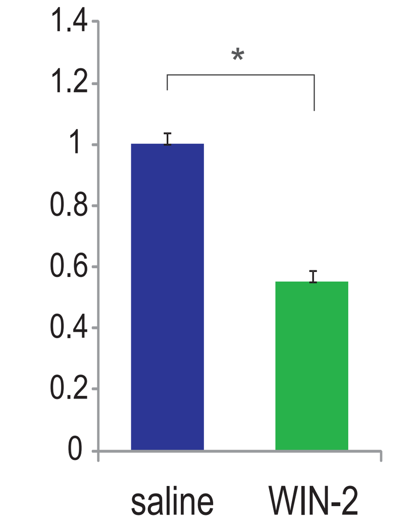
Dopamine neuron activation decreased resistance to extinction but preserved the effect of probability





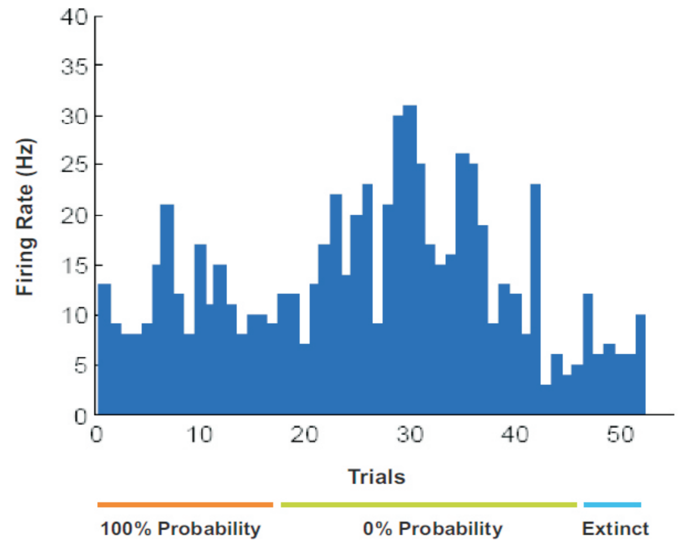
Bupivacaine significantly increased the general level of resistence to extinction (t-test; p < 0.05). In both experiment and control group, extinction resistence didn't meaningfully vary with different reward probabilities. (N = 5)





WIN-2 significantly decreased the general level of resistence to extinction (t-test; p < 0.05). In both experiment and control group, extinction resistence wasn't meaningfully different with different reward probabilities. (N = 2)

Dopamine neuron whose activity reflect the level of saliency was found.



CONCLUSIONS

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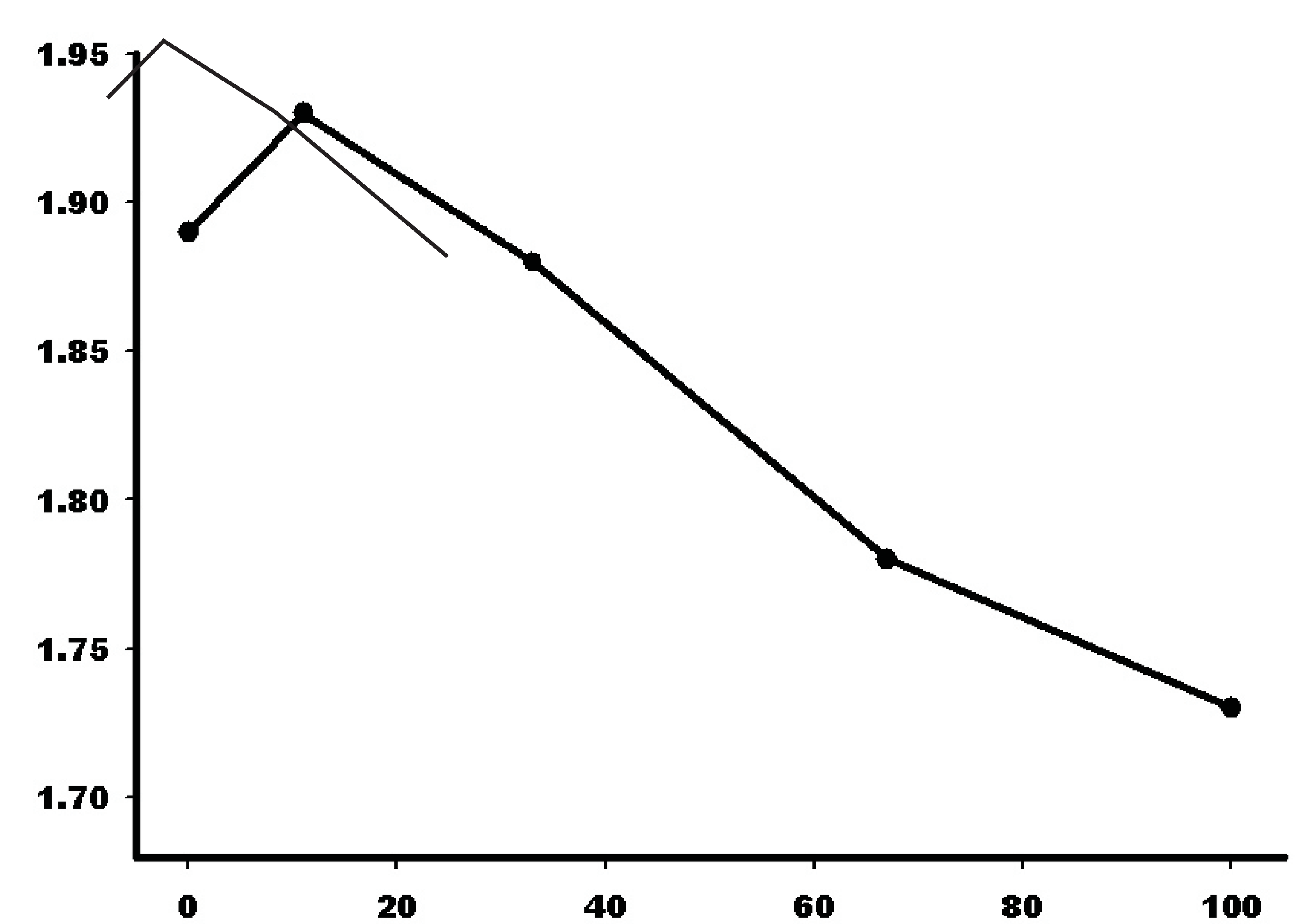
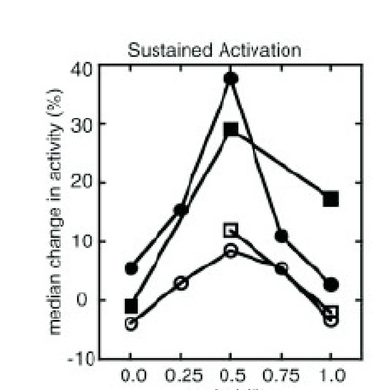
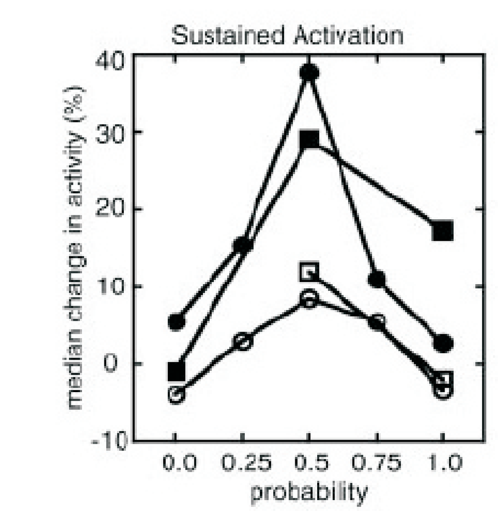

1.95
1.90
1.85
1.80
1.75
1.70
0
20
40
60
80
100


Sustained Activation
median change in activity (%)
probability


Sustained Activation
40
30
20
10
0
-10
median change in activity (%)
0.0
0.25
0.5
0.75
1.0
probability