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

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INTRODUCTION

- Extinction depends on the probability of getting the reward [1].
- A potential neural substrate that could account for this phenomenon is the ventral tegmental area (VTA) in the midbrain. Previous studies have shown that dopamine neurons in the VTA are involved in coding the values of rewards delivered with different probabilities, the expectation of rewards associated with a cue. VTA is also involved in reward related motivation [2,3].
- We hypothesize that VTA plays a role in probability-dependent resistance to extinction.

METHODS

Behavioral experiment

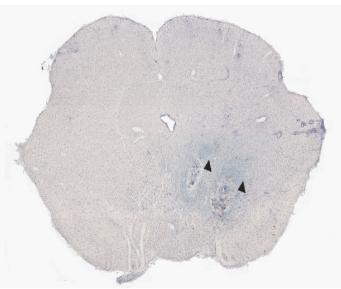
	Acquisitio	on session		Extinction
	Trial # constant	Pellet # constant	No time gap	session
25%	20 (5)	80 (20)		Until the rat makes no attempt for 5
50%	20 (10)	40 (20)		
75%	20 (15)	27 (20)		
100%	20 (20)	20 (20)		consecutive trials

Inactivation / activation of the VTA

Day	Saline (trial # constant)			Bupivacaine / WIN-2 (trial # constant)	
	Acquisition	Extinction		Acquisition	Extinction
1	100%	Until the rat	1 hour	50%	Until the rat
2	75%	makes no		25%	makes no
3	50%	attempt for 5 consecutive trials		100%	attempt for 5
4	25%			75%	consecutive trials

Bupivacaine (2.5%, 2µL), WIN-55212-2 mesylate (3.7%, 2µL) or saline (2µL) were injected bilaterally in the VTA just before the acquisition phase of each experiment.





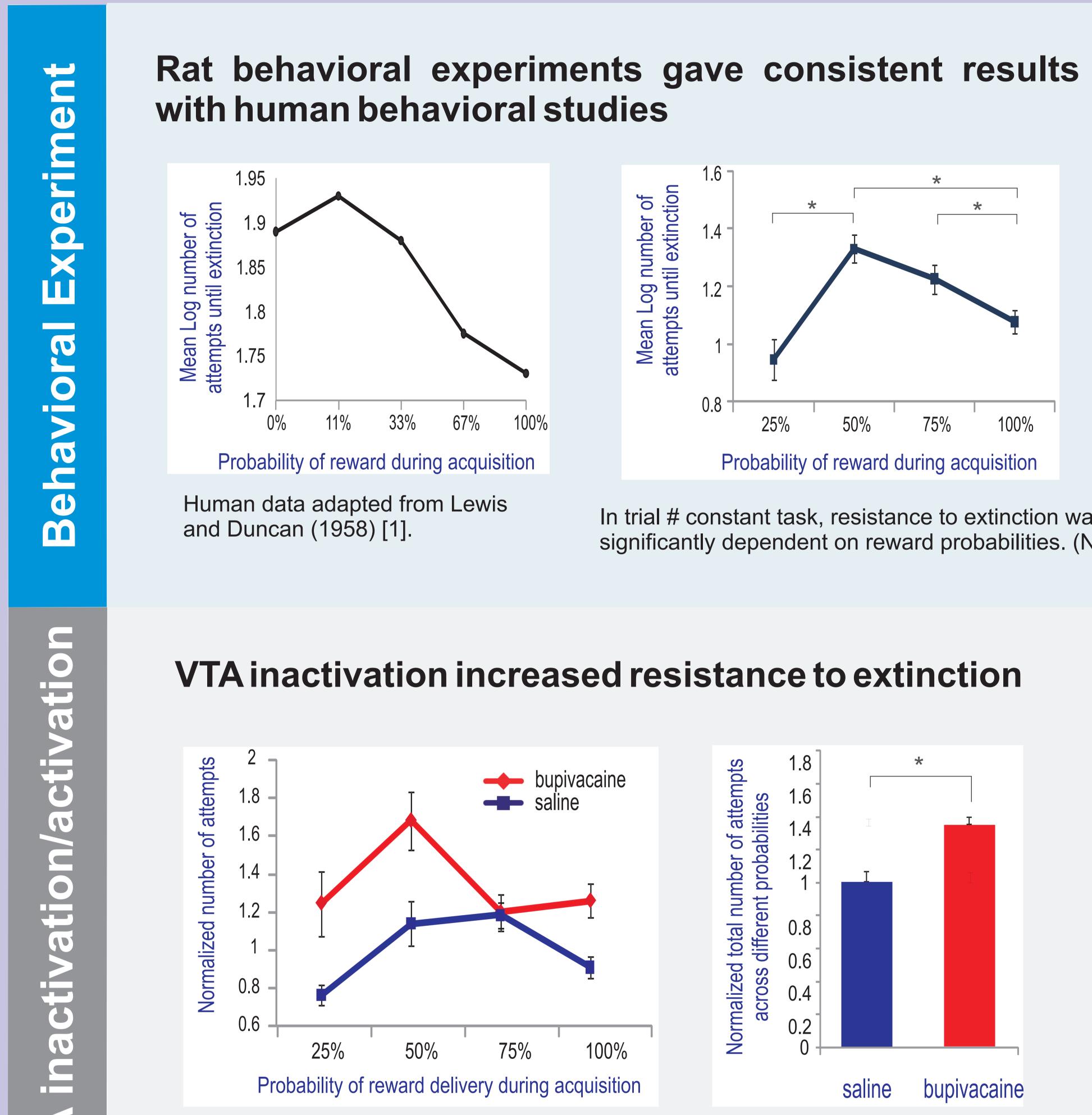
High density electrophysiology

Acquisition (trial # constant)	No	Extinction
25%	time	
50%	gap	No reward
75%		INUTEWAIU
100%		



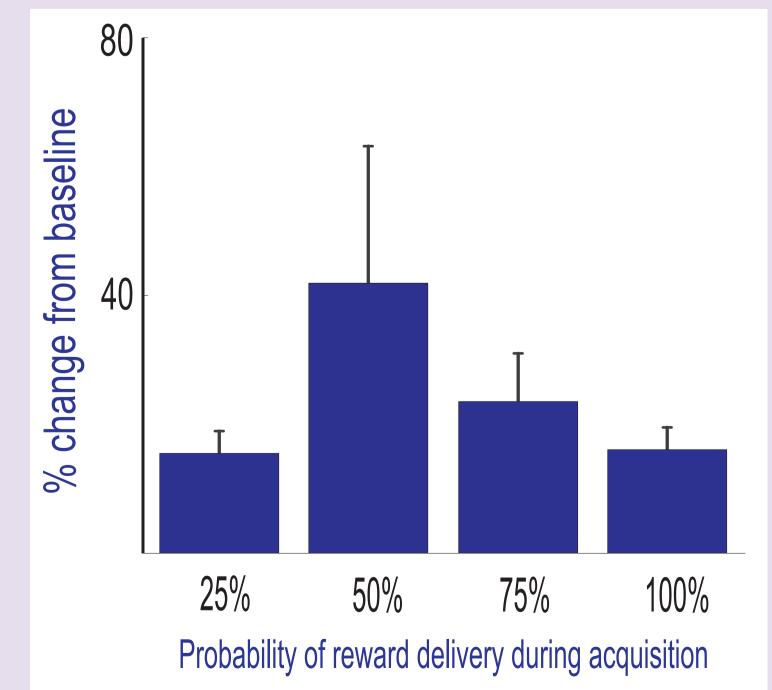
Each rat was implated with a hyperdrive consisting of 12 independently movable tetrodes. We recorded neuronal activity in the VTA in awake and freely moving animals.

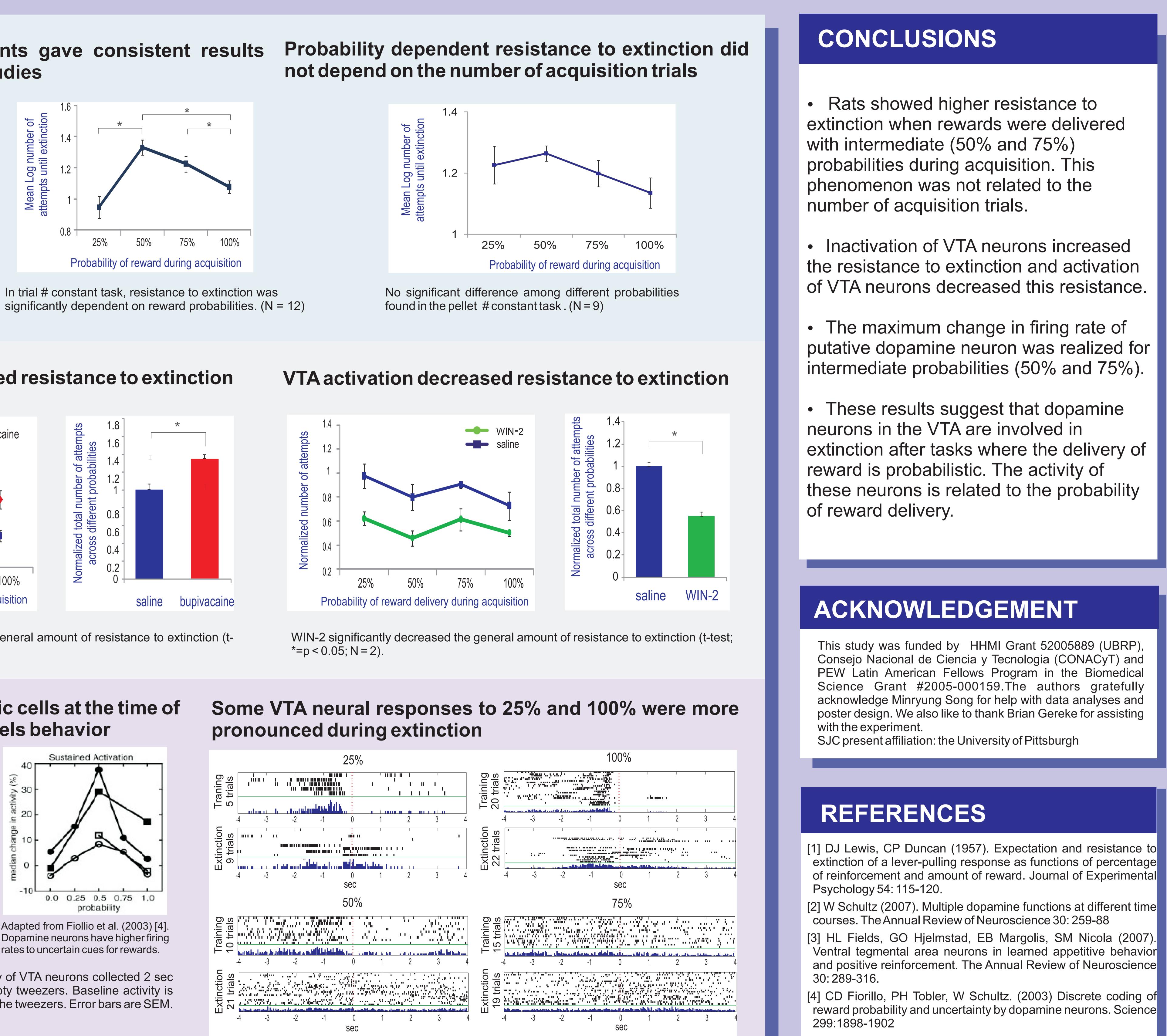
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Bupivacaine significantly increased the general amount of resistance to extinction (ttest; *=p < 0.05; N = 5).

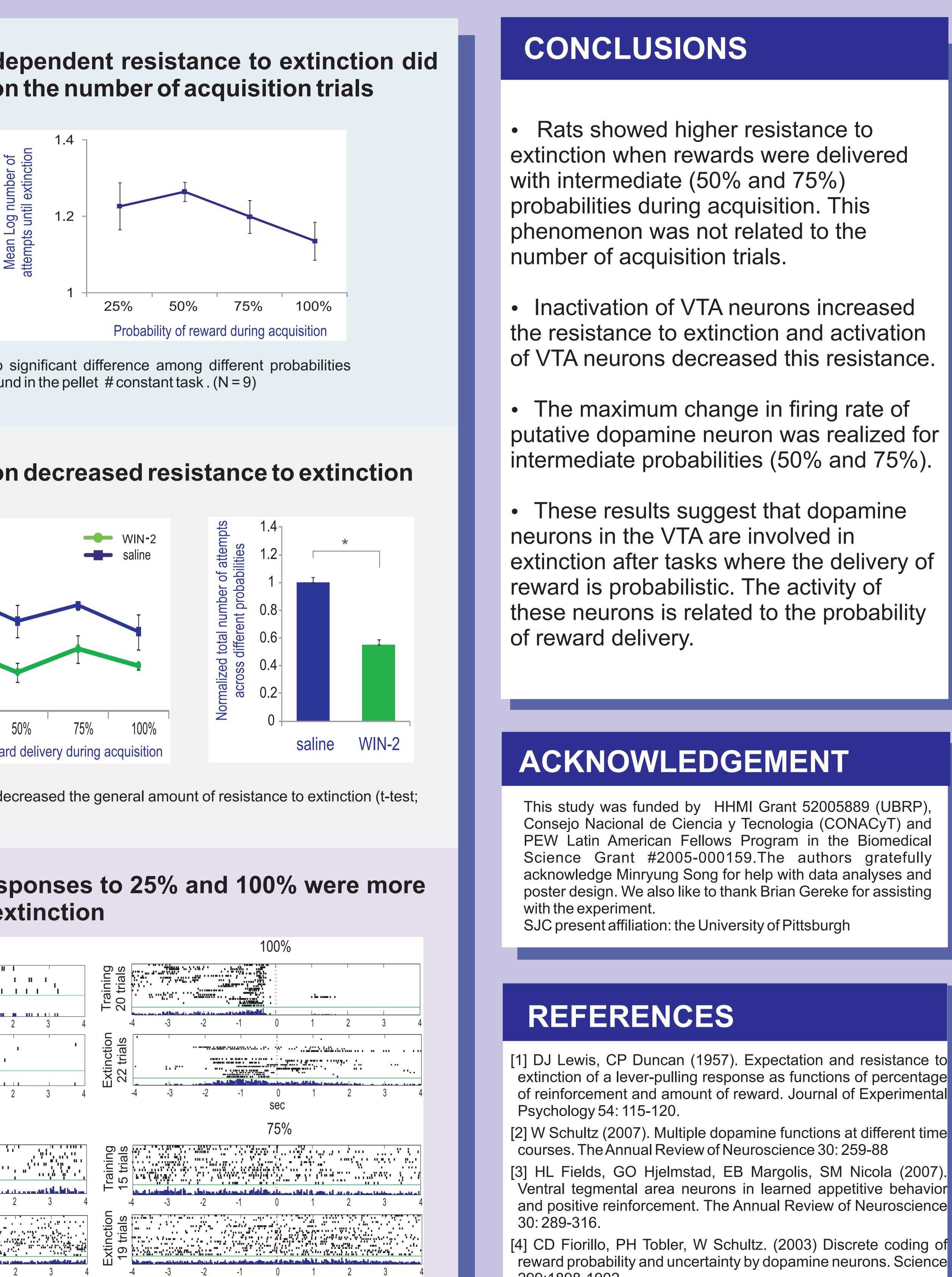
The level of non-GABAergic cells at the time of reward presentation parallels behavior pronounced during extinction

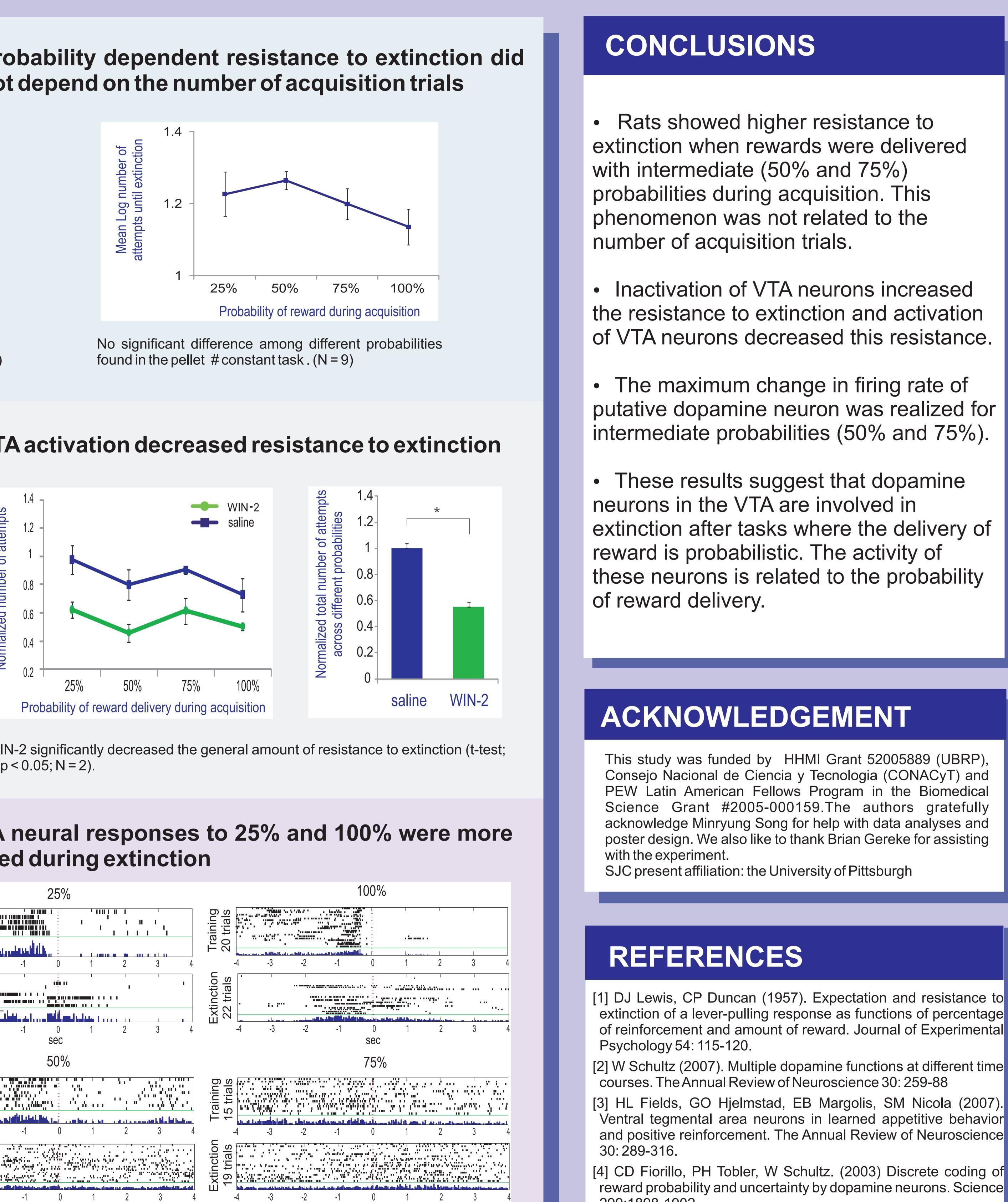




Dopamine neurons have higher firing rates to uncertain cues for rewards.

Change in firing rate during extinction. Activity of VTA neurons collected 2 sec before the animal made contact with the empty tweezers. Baseline activity is computed 2 - 4 sec before the presentation of the tweezers. Error bars are SEM. (N=32)





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