

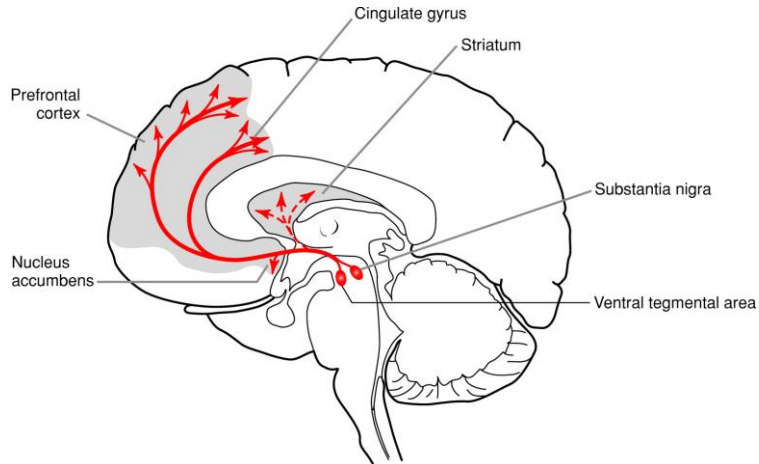
The Neural Bases of Habits and Obsessions

TIAGO V. MAIA

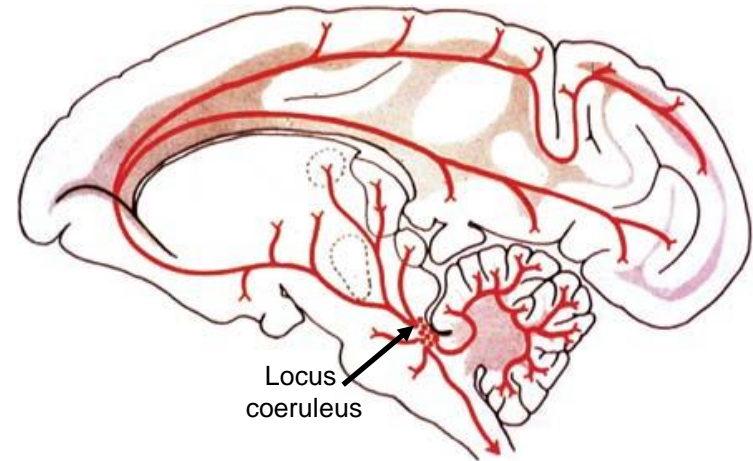
Institute for Molecular Medicine
School of Medicine
University of Lisbon

Department of Psychiatry
Columbia University

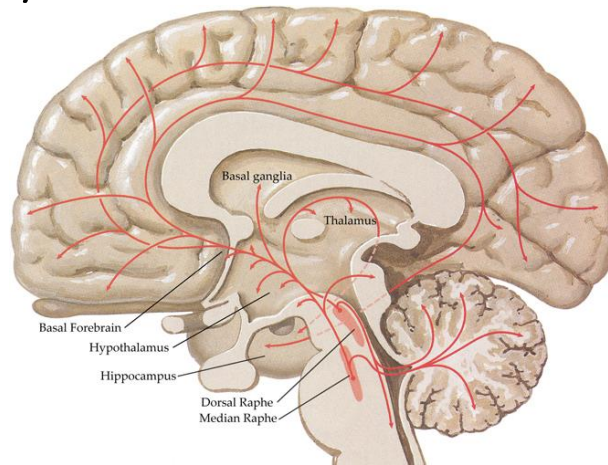
Neuromodulatory Systems



Dopaminergic Pathways



Noradrenergic Pathways

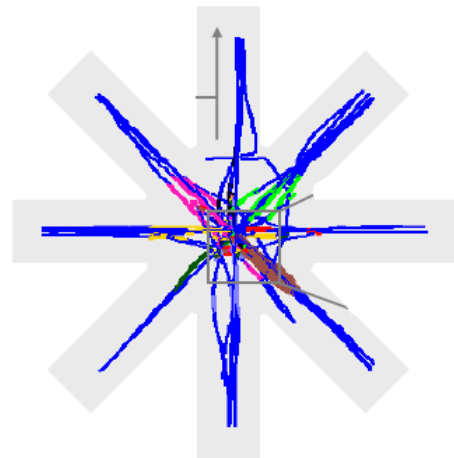
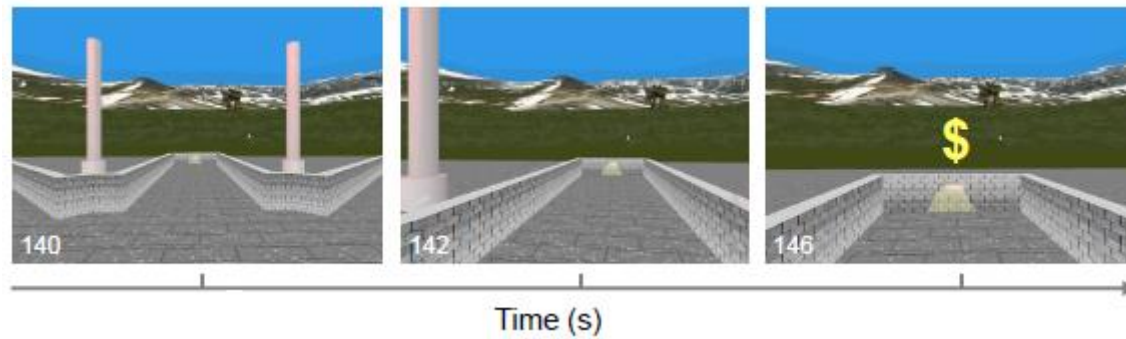


Serotonergic Pathways

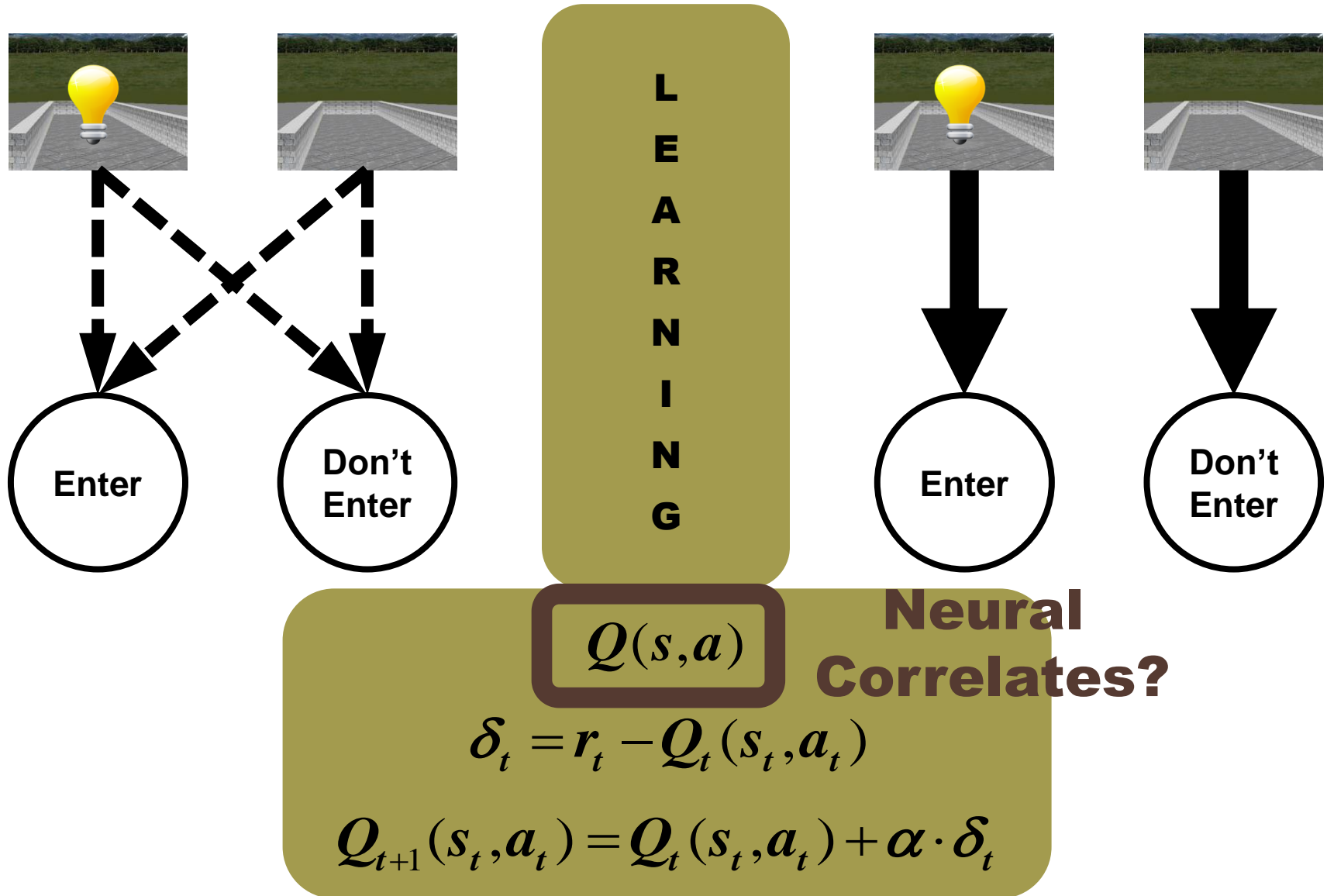
Habit Learning in Healthy Humans

(with Guillermo Horga, Bradley Peterson, and others)

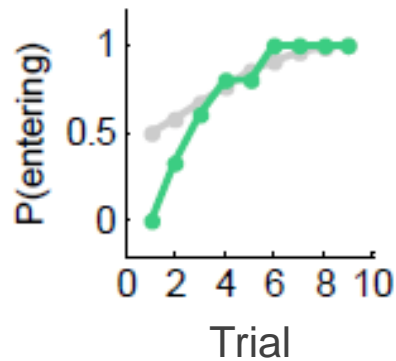
Virtual-Reality Maze



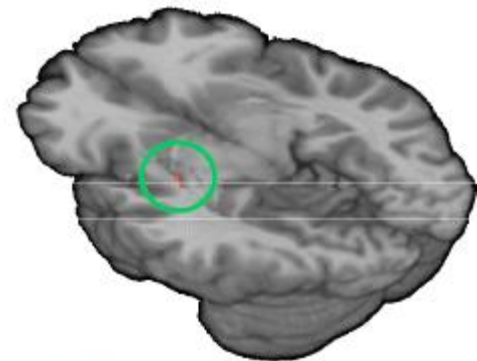
Learning Stimulus-Response Associations



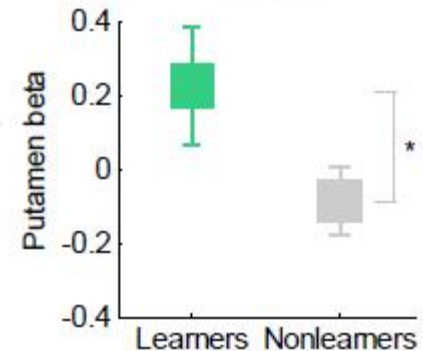
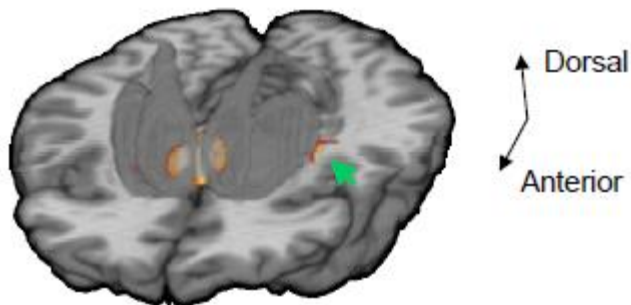
Example model fit



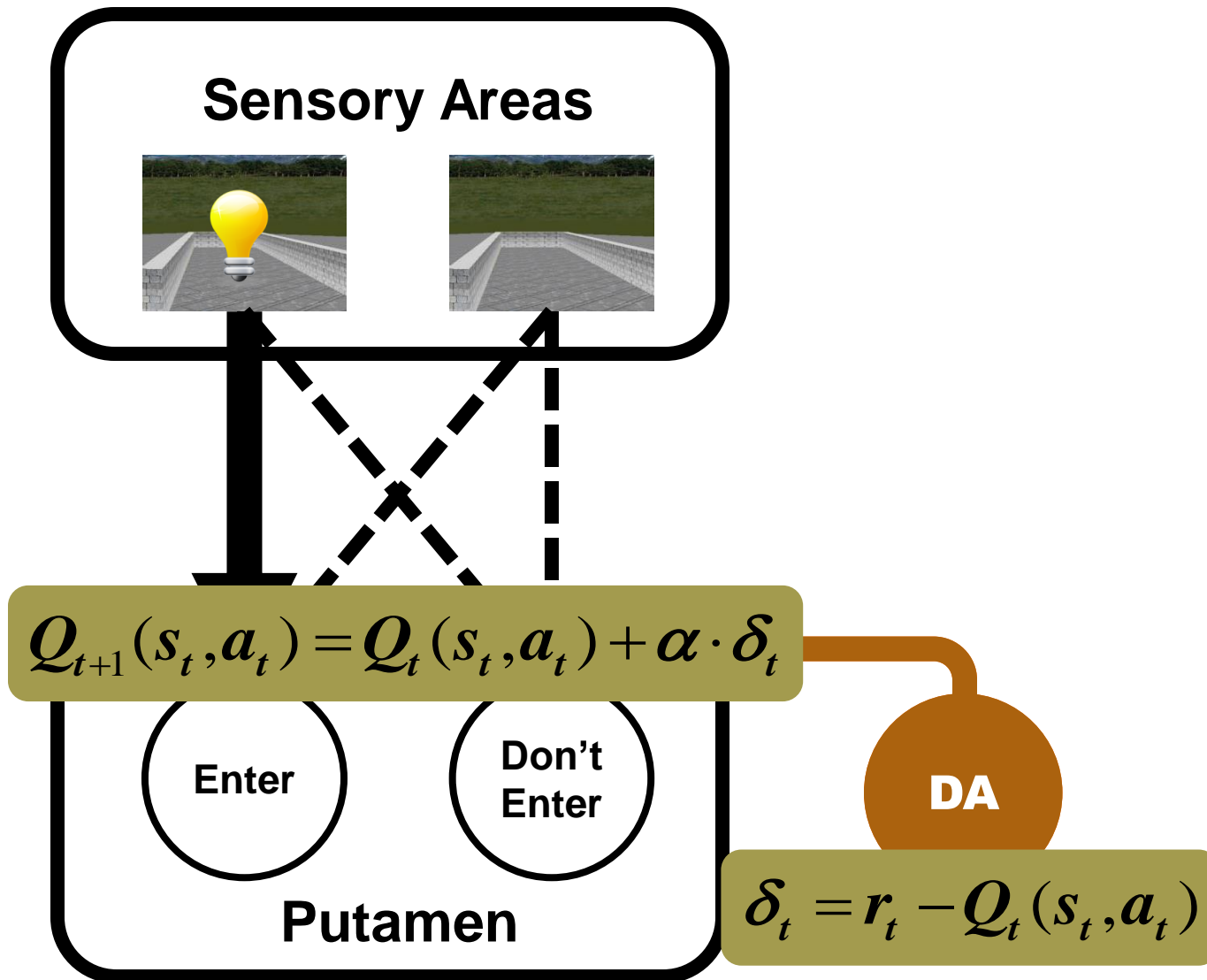
Putamen activity distinguishes learners from non-learners



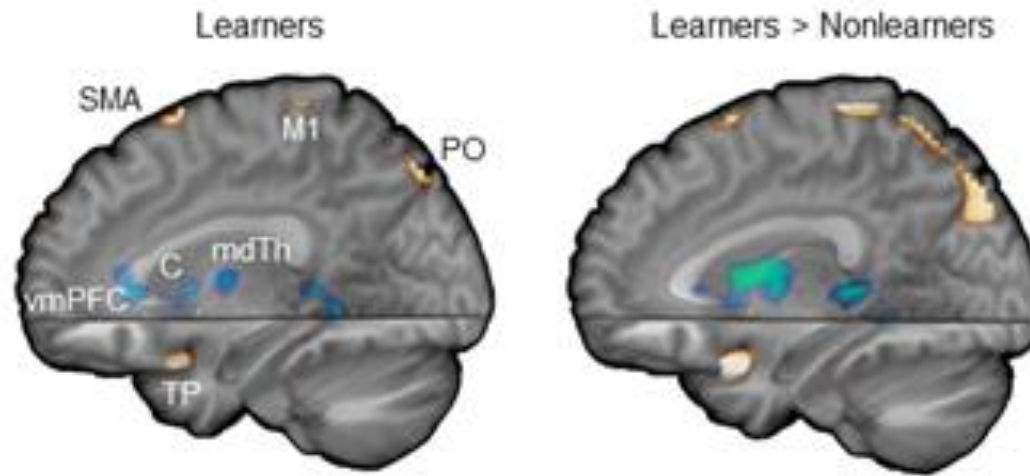
Areas whose activity correlates with the strength of the habit [$Q(s,a)$]



Learning Depends on DA-Modulated Plasticity



Changes in Putamen Connectivity with Learning



Q x posterolateral putamen PPI

Strengthening of connections between putamen and sensory and motor areas

Weakening of connectivity between limbic areas and putamen

The Neural Basis of Habit Learning: Summary

- Habit learning in humans involves the putamen
Consistent with animal studies
- Changes in connectivity during habit learning confirm predictions from reinforcement-learning models about changes in synaptic efficacy

Serotonin in Obsessive-Compulsive Disorder

(with Maria Cano-Colino)

Obsessive-Compulsive Disorder

Obsessions: recurrent, persistent, and intrusive ego-dystonic thoughts, impulses, or images

Compulsions: repetitive behaviors or mental acts that are executed with the goal of preventing or reducing distress

Serotonin in OCD

Pharmacological treatment of OCD:

- SSRIs
- Clomipramine

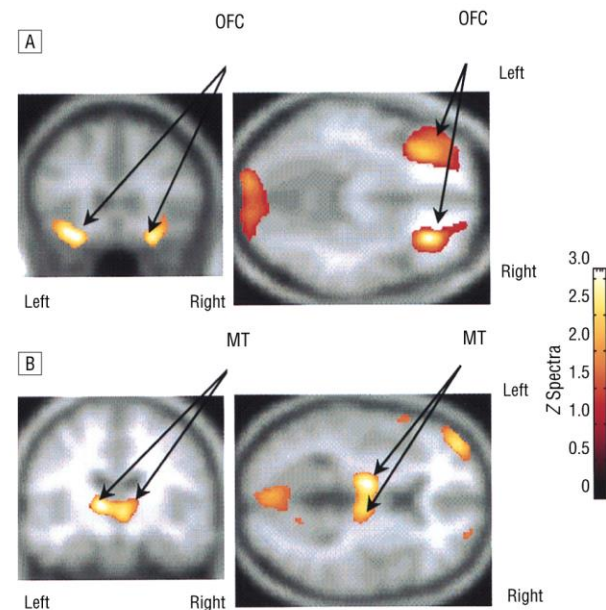
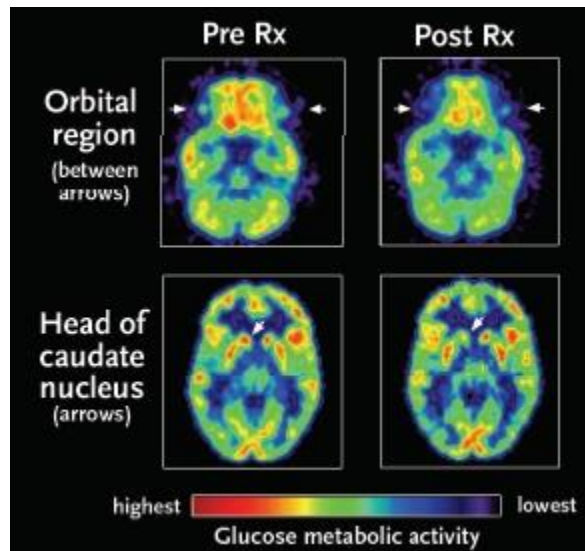
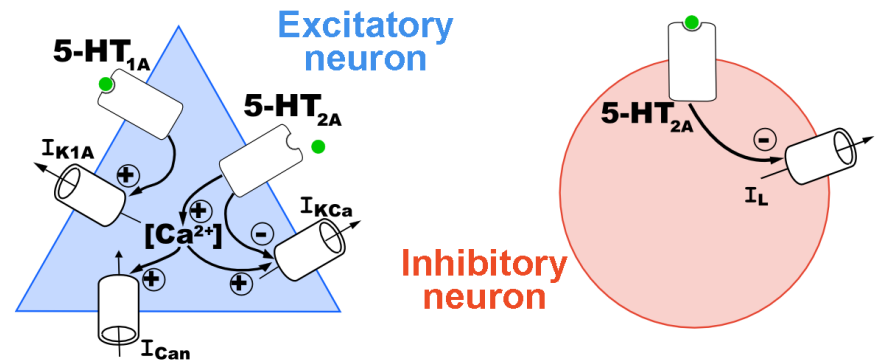
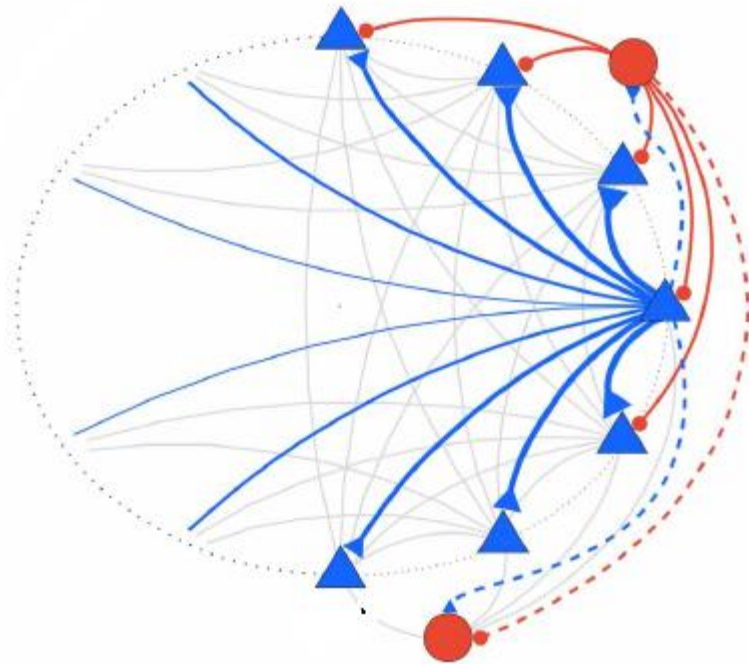


Figure from Saxena et al. (2002)

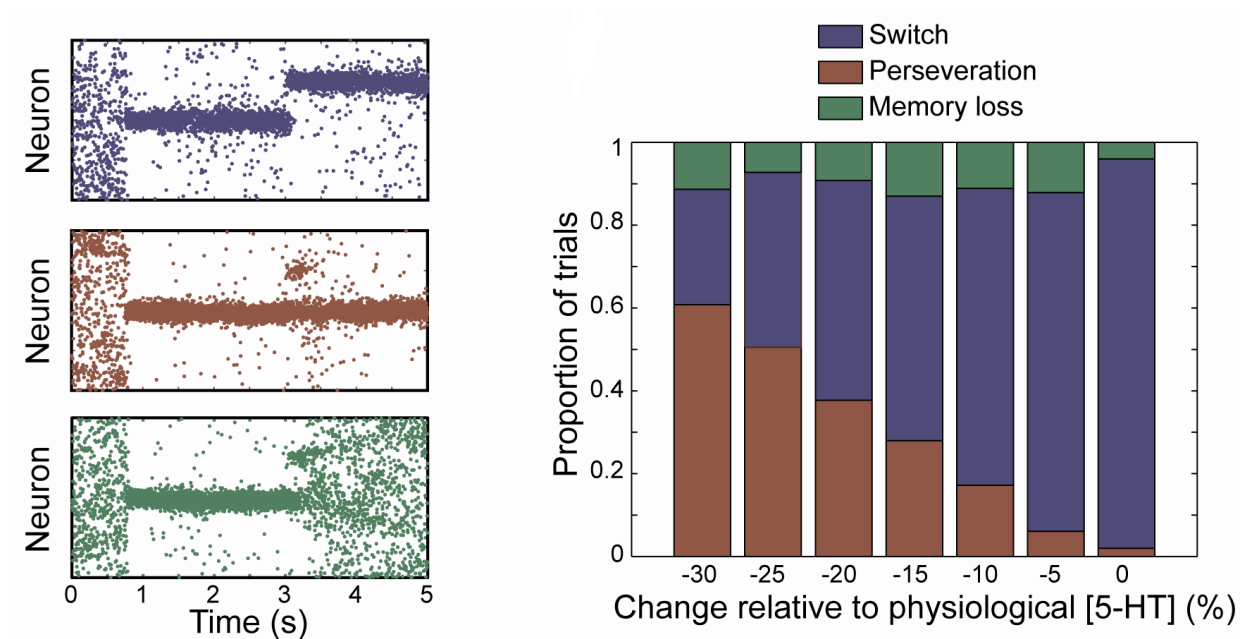
Computational Model



Biophysically detailed model

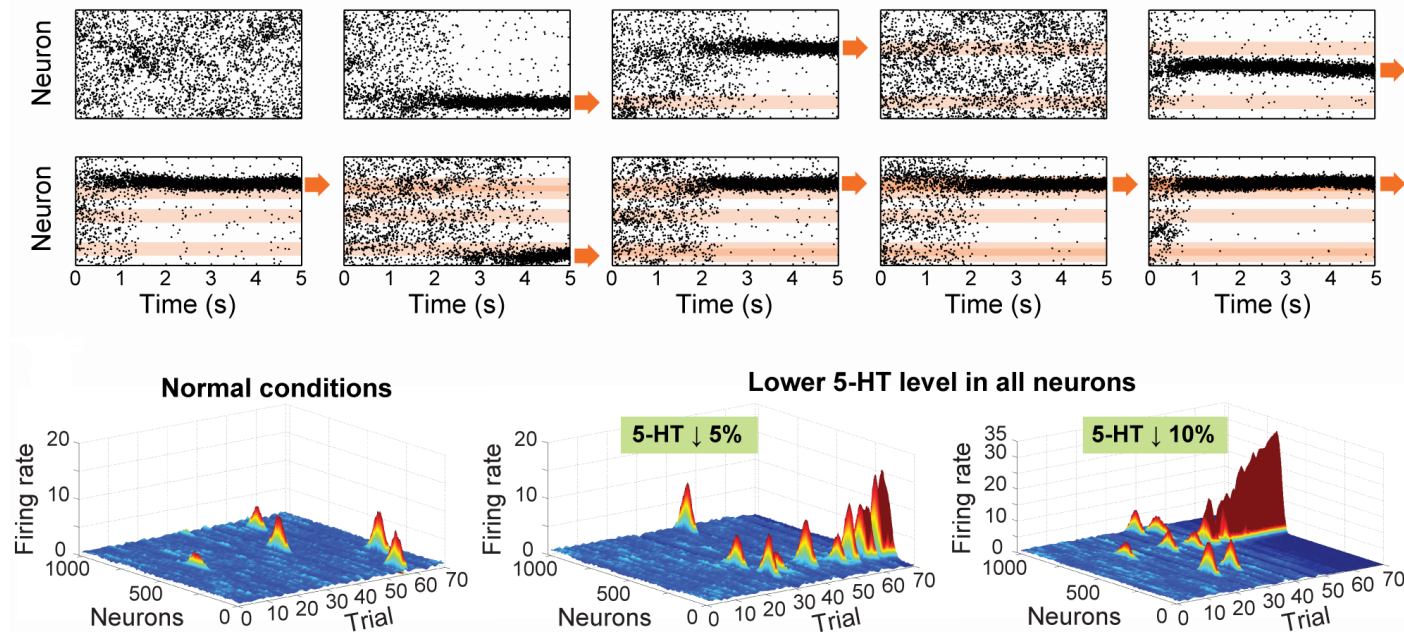
Manipulate (tonic) levels of serotonin

Low Serotonin Increases Perseverative Neuronal Activity

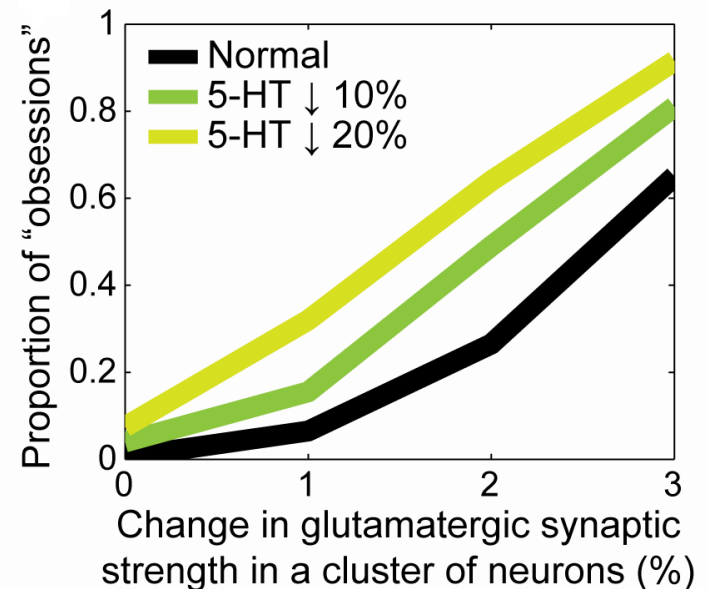
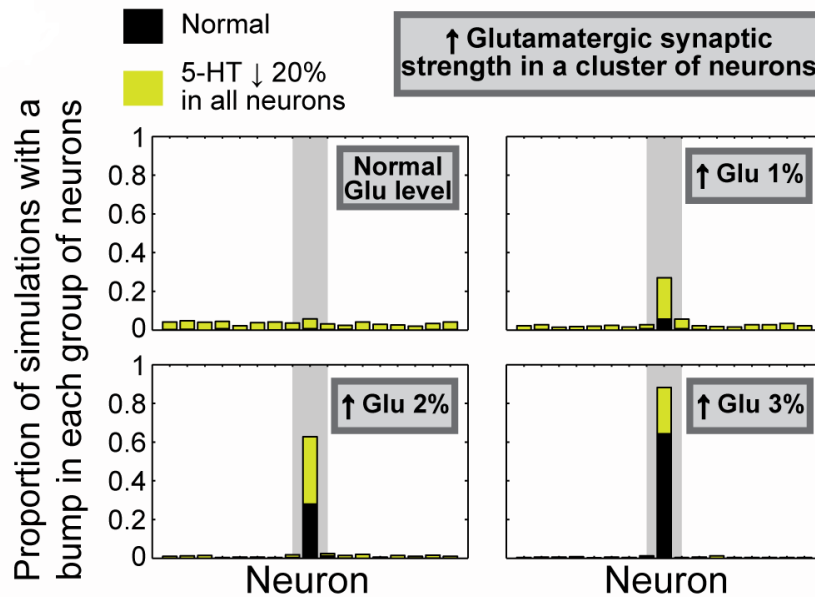


Substantial evidence linking low serotonin to perseverative behavior (e.g., in reversal learning)

Low Serotonin Increases the Tendency to Develop Obsessions

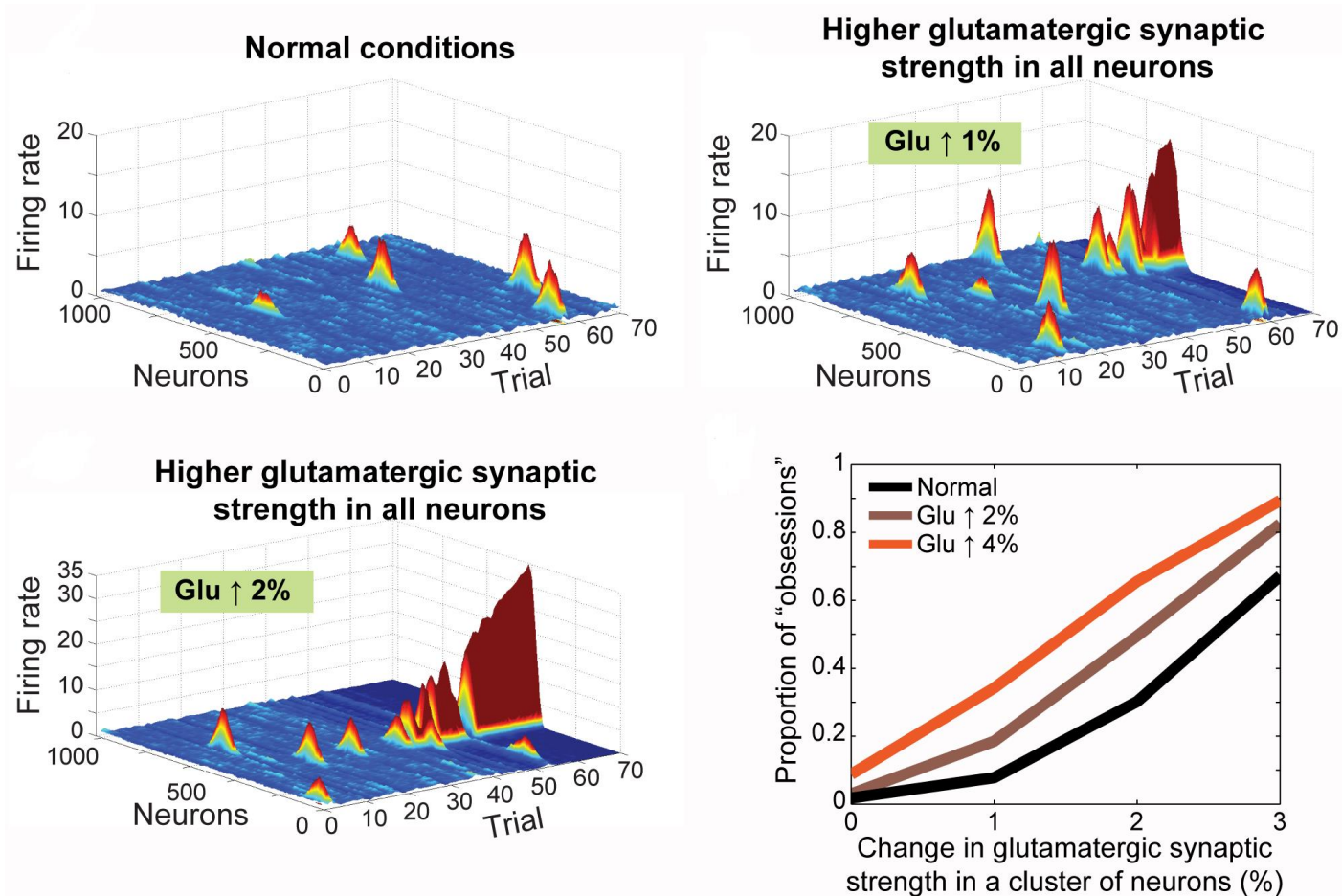


Low Serotonin Increases the Tendency to Fall into Existing Obsessions

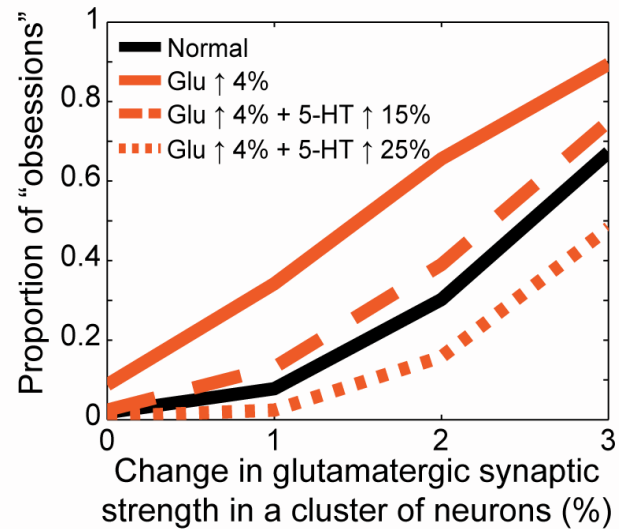
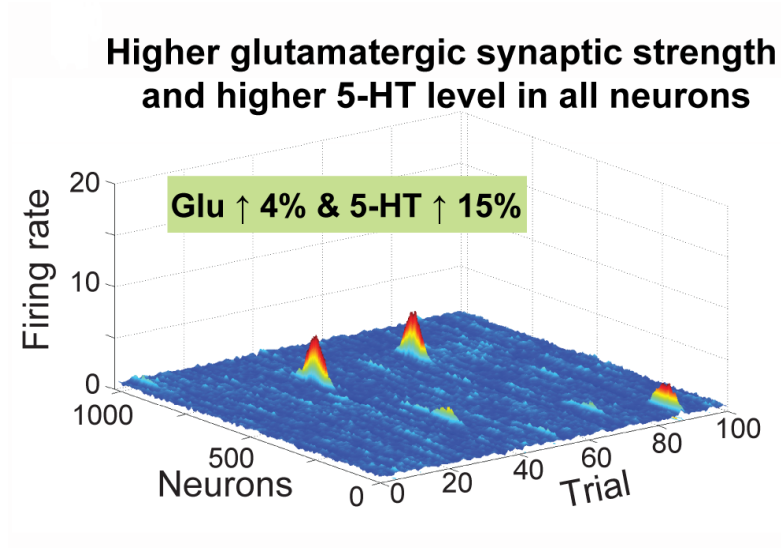


High Glutamate Increases the Tendency to Develop Obsessions and Fall into Existing Obsessions

Substantial interest in a role of glutamate in OCD



Increasing Serotonin Reverses the Tendency to Develop Obsessions and Fall into Existing Obsessions Due to High Glutamate

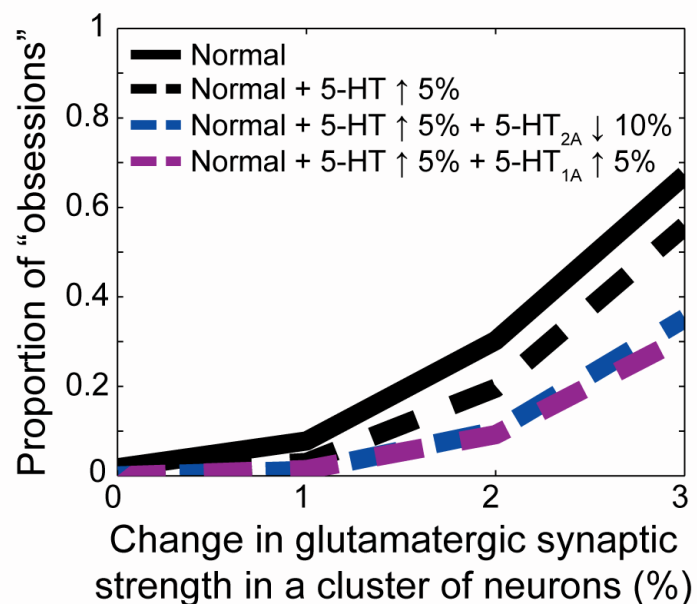


Increasing serotonin beneficial even if the underlying deficit is glutamatergic

→ *Implications for reverse inference going from treatment effects to pathogenesis (relevant for many areas of psychiatry)*

Pharmacological Augmentation

- SSRIs often augmented with antipsychotics (e.g., risperidone)
 - 5HT_{2A} blockade but several other effects
 - 5HT_{2A} important for therapeutic effect?
- Role for 5HT_{1A}?



5HT_{1A}: pre- vs. post-synaptic effects

Serotonin and OCD: Summary

- Both low serotonin and high glutamate increase the tendency to develop obsessions and to fall into existing obsessions
- Increasing serotonin reverses these tendencies (even when they are caused by high glutamate)
- 5HT_{2A} antagonists, and possibly 5HT_{1A} agonists, may augment the therapeutic efficacy of SSRIs
 - But current 5HT_{1A} agonists may be of limited use because of presynaptic effects
- Mechanistic insights

Overall Conclusions

The synergistic use of computational modeling, brain imaging, and neuropsychological testing is a powerful approach to the neural substrates of neuropsychiatric disorders.

Acknowledgments

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- [Guillermo Horga](#)
- [Bradley Peterson](#) (now at the Univ. Southern California)
- Rachel Marsh
- Andrew Gerber
- Zhishun Wang

University of Lisbon

- [Maria Cano-Colino](#) (now at the Champalimaud Neuroscience Program)