



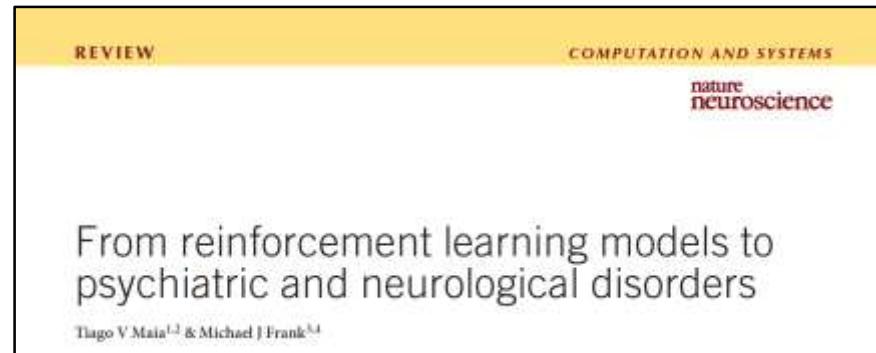
Brain Imaging and Computational Models in the Study of Psychiatric Disorders

Tiago V. Maia

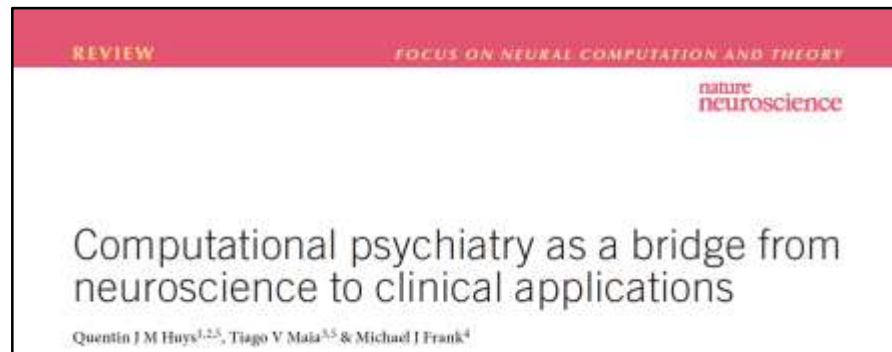
Faculty of Medicine
Institute for Molecular Medicine
Mind-Brain College
University of Lisbon

Computational Psychiatry

Understanding mechanisms



Moving towards clinical applications

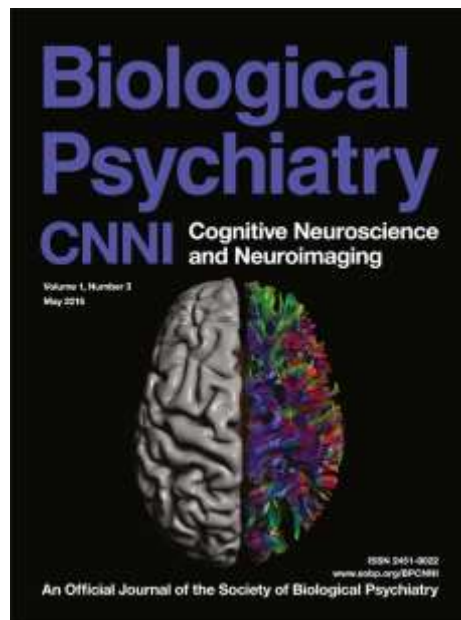


Computational Psychiatry: Special Issues

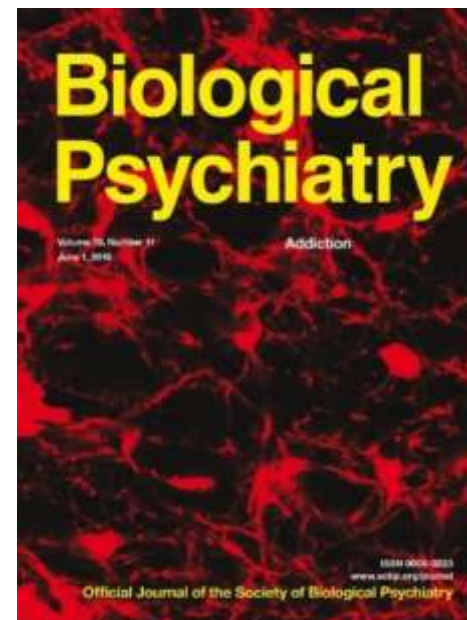
2015



2016



2017



Martin Paulus



Quentin Huys

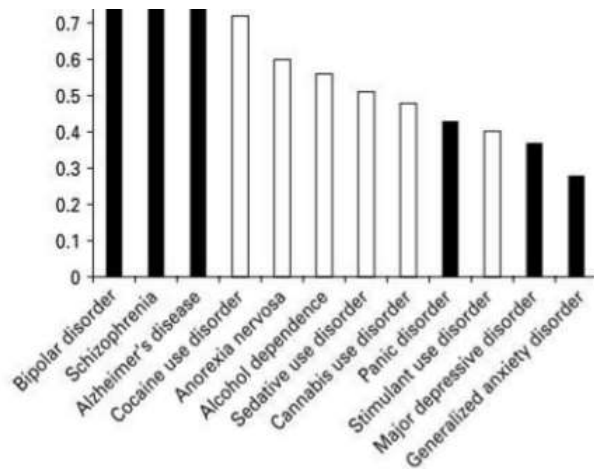


Quentin Huys



Michael Frank

Heritability of Psychiatric Disorders



Bienvenu et al. Psychiatric 'diseases' versus behavioral disorders and degree of genetic influence. Psychological Medicine 2011;41:33-40.

Heritability of Other Disorders



Repetitive Thoughts and Behaviors

Habits

Automatic responses independent of goals

Tourette Syndrome

Tics: Repetitive motor actions

Obsessive-Compulsive Disorder

Obsessions: Recurrent, persistent, and intrusive thoughts

Compulsions: Repetitive behaviors or mental acts

Habit Learning in Healthy Humans



Guillermo Horga



Rachel Marsh



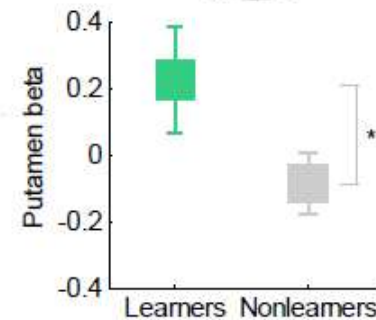
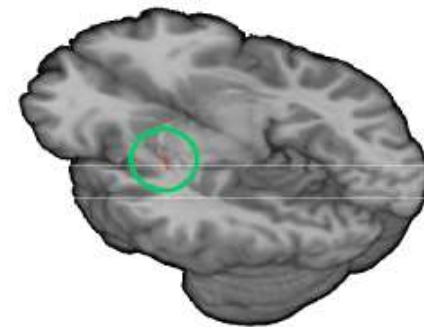
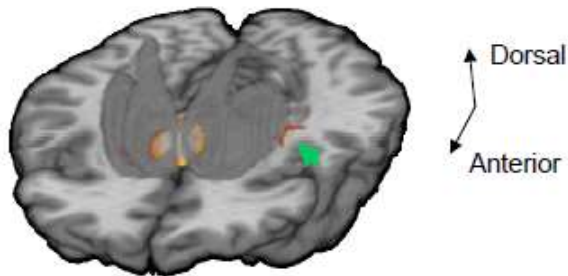
Bradley Peterson

Habit Learning Involves the Putamen

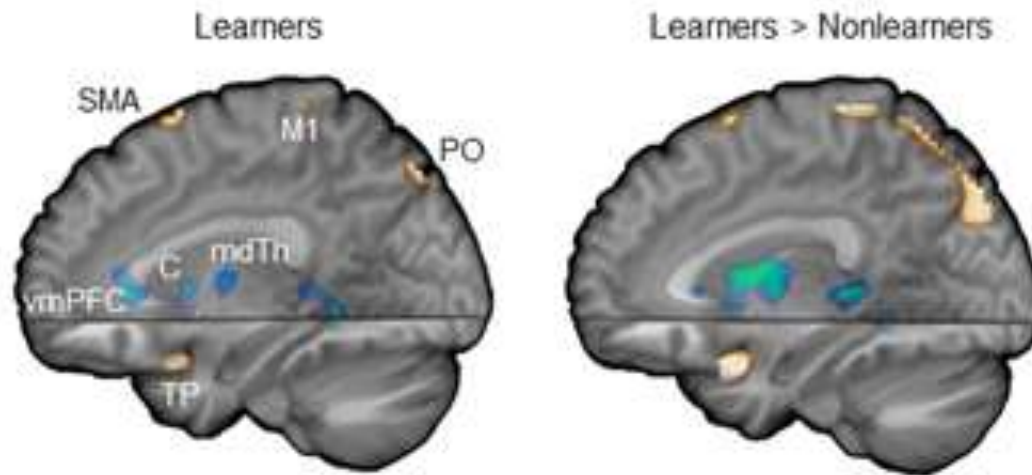
Habits correspond to stimulus-response (S-R) associations

Putamen activity distinguishes learners from non-learners

Neural correlates of habits
(S-R associations)



Habits Learning Depends on Changes in Connectivity Between Sensory and Motor Areas and the Putamen



Tourette Syndrome



Zhishun Wang



Rachel Marsh



Bradley Peterson

Motor Loop Through the Basal Ganglia

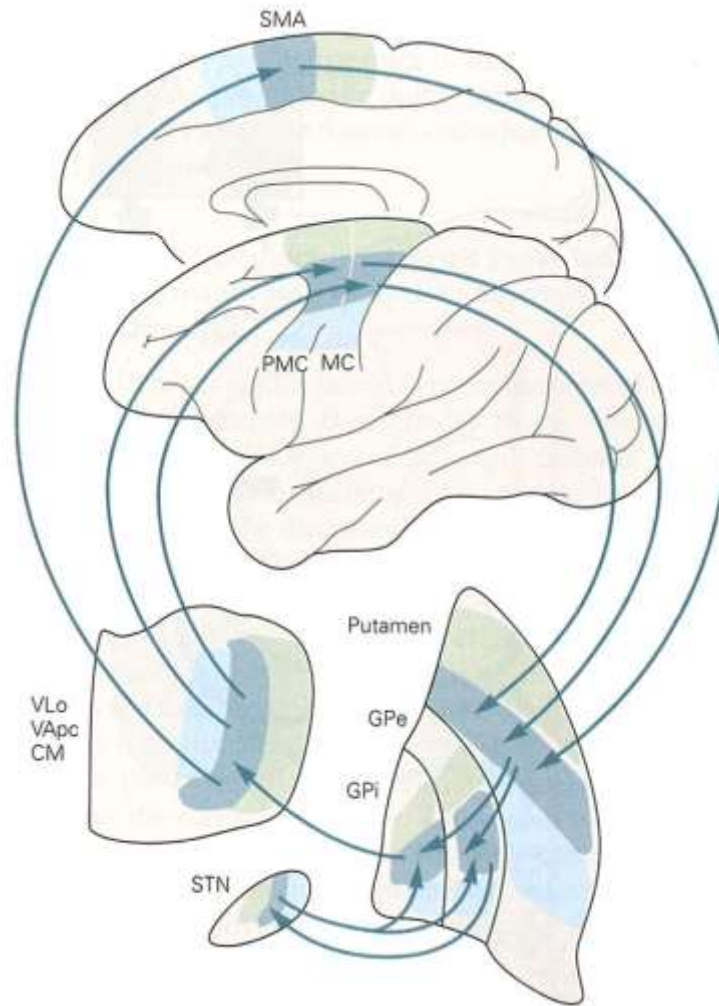
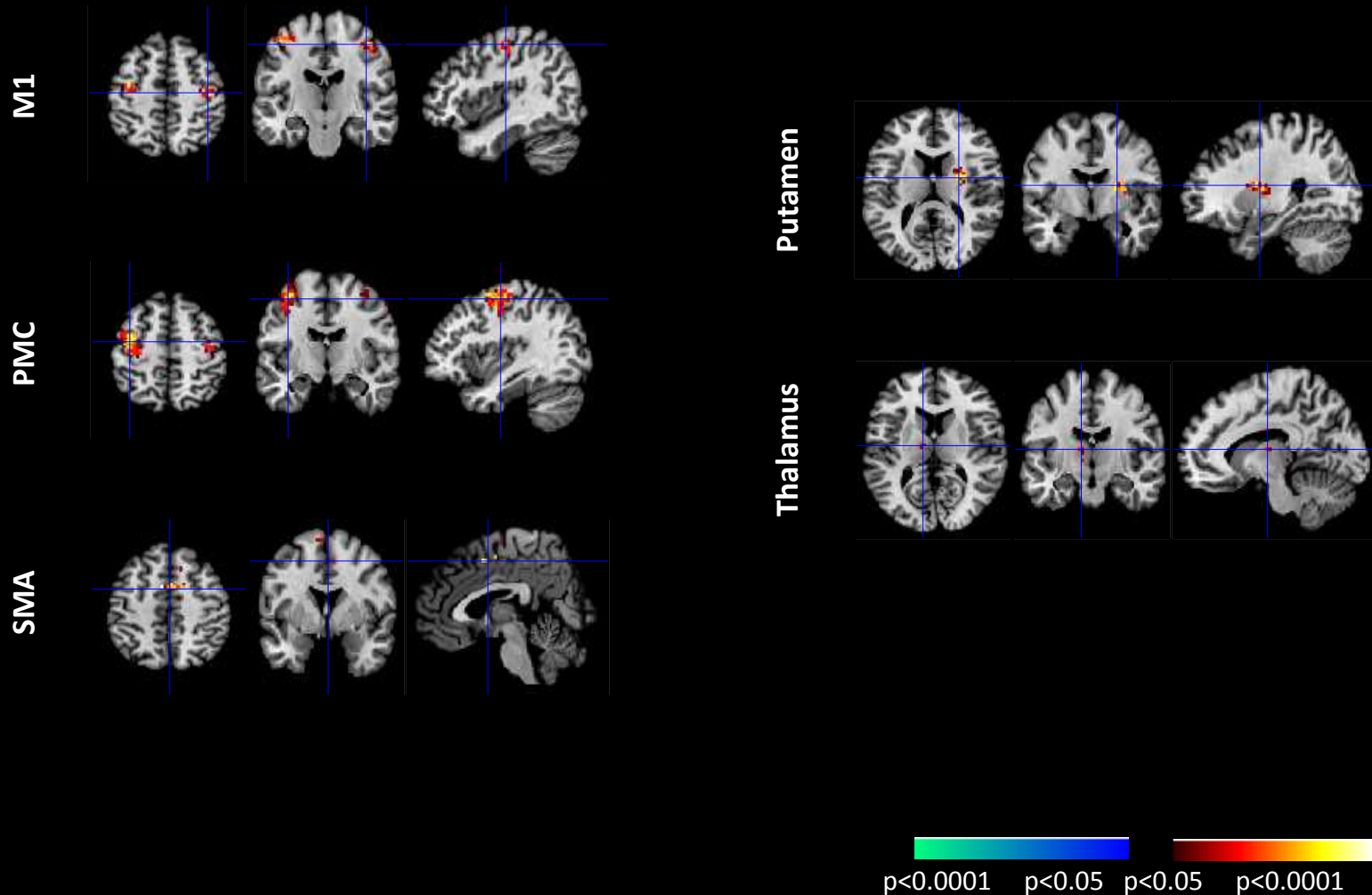
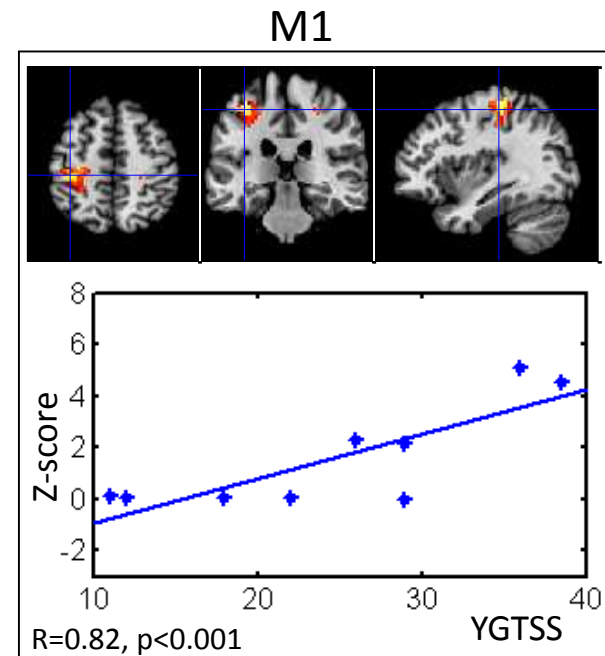
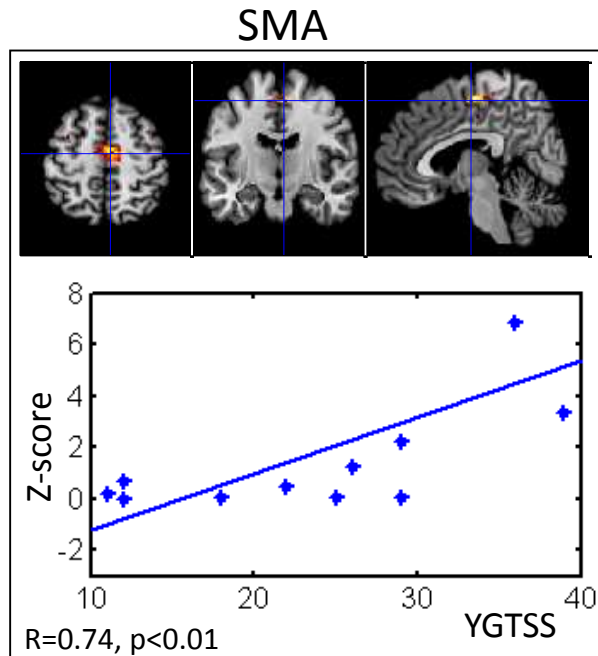


Figure from Kandel et al. (2000)

Hyperactivity in the Motor Loop in Tourette's



Correlations with Symptom Severity



Tics and Habits: Summary

The same circuit that is involved in habit learning in healthy humans seems to underlie tics

Tics may therefore result from a motor habit-learning circuit gone awry

Serotonin in Obsessive-Compulsive Disorder



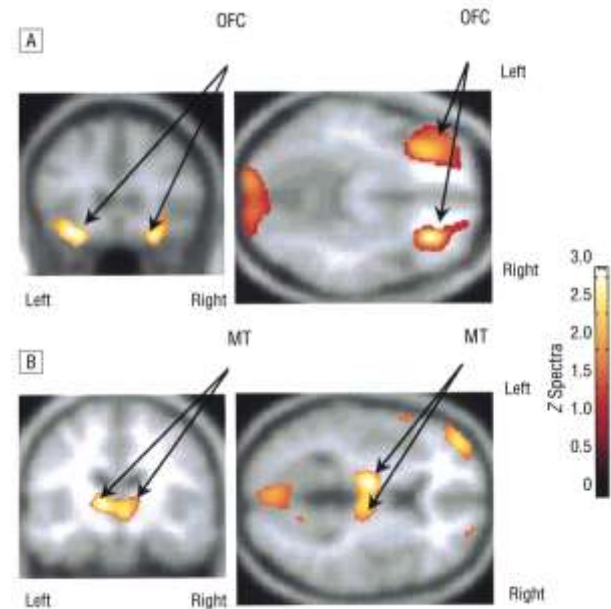
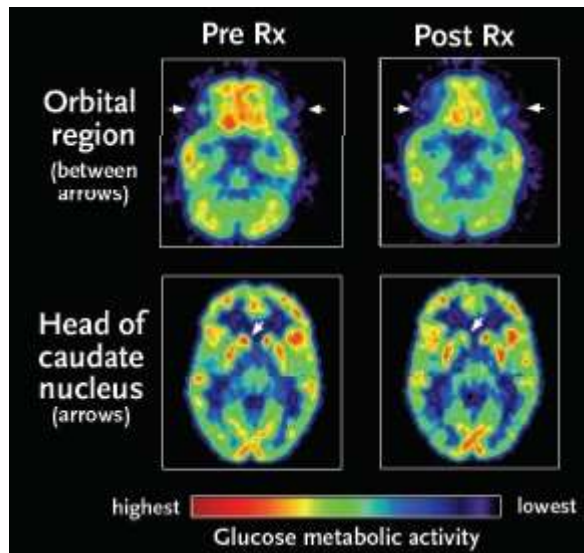
Maria Cano-Colino

Serotonin in OCD

Pharmacological treatment of OCD:

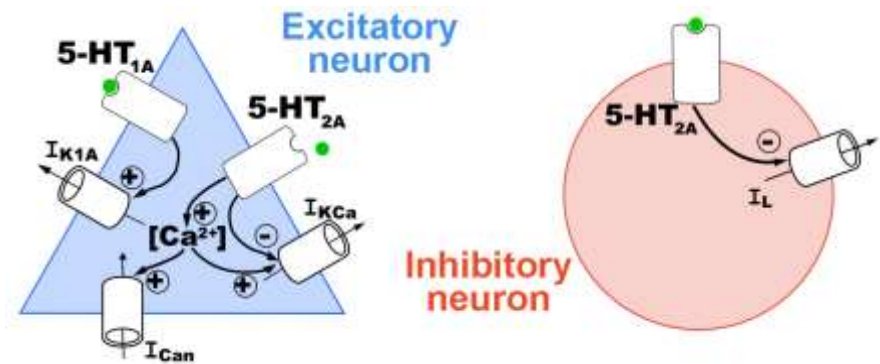
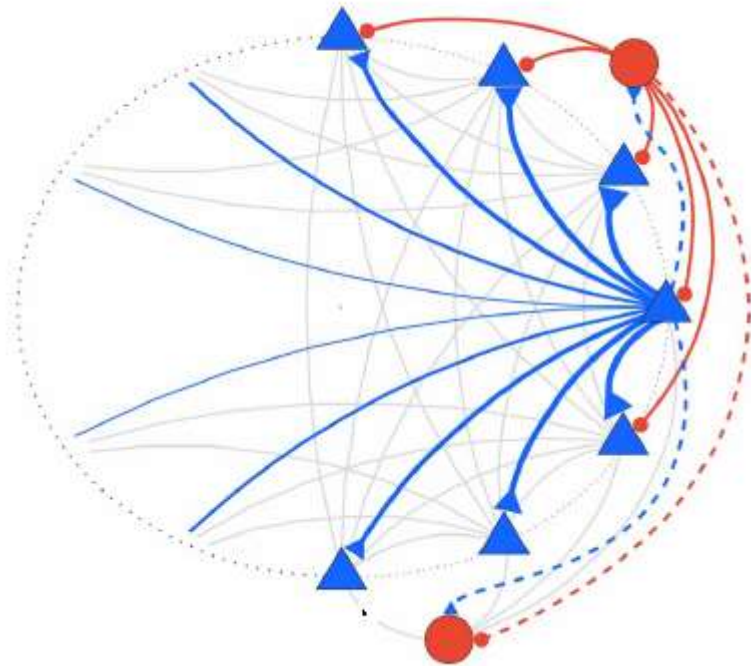
SSRIs

Clomipramine



Saxena et al. (2002)

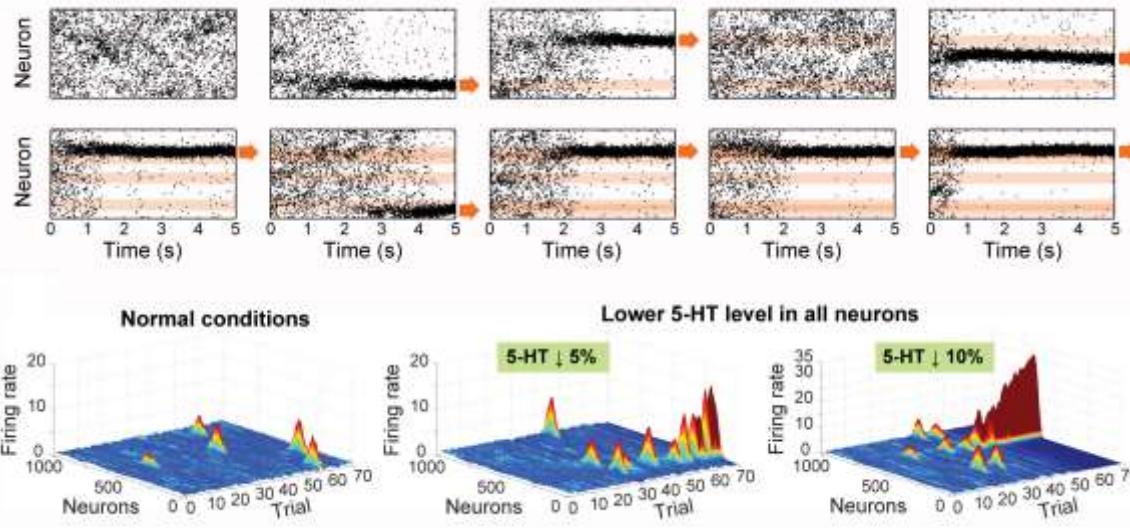
Computational Model



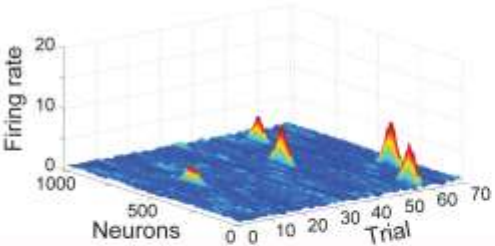
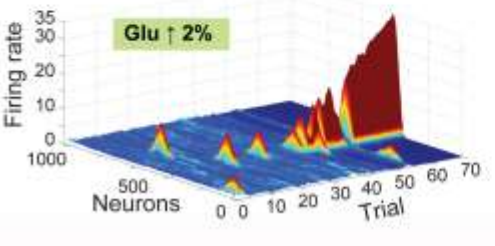
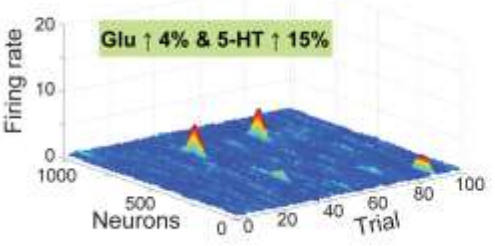
Biophysically detailed model

Manipulate (tonic) levels of serotonin

Low Serotonin Increases Tendency to Develop Obsessions



Interplay between Glutamate and Serotonin

<p>Normal conditions</p>	<p>Normal conditions</p> 
<p>High glutamate increases the tendency to develop obsessions</p>	<p>Higher glutamatergic synaptic strength in all neurons</p> <p>Glu ↑ 2%</p> 
<p>Increasing serotonin reverses the disturbances caused by high glutamate</p>	<p>Higher glutamatergic synaptic strength and higher 5-HT level in all neurons</p> <p>Glu ↑ 4% & 5-HT ↑ 15%</p> 

Reverse Inference in Psychiatry

Increasing serotonin is beneficial even if the underlying deficit is glutamatergic

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

Conclusions

The synergistic use of computational modeling, brain imaging, and other empirical techniques is a powerful approach to understand the neural substrates of neuropsychiatric disorders.

Participate in Research!

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Tourette Syndrome

Obsessive-Compulsive Disorder

Attention-Deficit/Hyperactivity Disorder

Healthy Controls

Children and Adults

Collaborators

IMM/FMUL/ULisboa

Postdoctoral Fellows

Lena Ernst

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

Ph.D. Students

Ana Portêlo

Andreia Leitão

Ângelo Dias

Catarina Farinha

Vasco Conceição

Gabriela Ribeiro (with
Albino Maia)

Columbia University

[Guillermo Horga](#), Assistant Professor

[Zhishun Wang](#), Research Scientist

[Rachel Marsh](#), Associate Professor

Univ. Southern California

[Bradley Peterson](#), Professor & Director of
Institute for the Developing Mind

Brown University

[Michael Frank](#), Professor

Laureate Institute for Brain Res.

[Martin Paulus](#), Director

ETH Zurich

Klaas Stephan, Professor & Director of
Translational Neuromodeling Unit

[Quentin Huys](#), Senior Research Fellow

Frederike Petzschner, Postdoctoral Fellow