Computational Psychiatry:

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Computational Psychiatry:

- Existing psychiatric diagnostic system and treatments for mental or psychiatric disorder lacks biological foundation [1].
- Complexity of brain presents challenges in developing hypothesis to lead the research in psychiatry.

[1] Wang, Xiao-Jing, and John H. Krystal. "Computational psychiatry." *Neuron* 84.3 (2014): 638-654.

Computational Psychiatry:

Computational Psychiatry aims to [2]:

-> model the computations that brain performs to find solutions to problems.

-> understand how the ‘abnormal’ thoughts and behaviors, (considered as psychiatric disorders) relate to normal function and neural processes.

-> provide tools to identify the causes of particular symptoms by establishing mathematical relationship between symptoms, environments and neurobiology.

[2] Adams RA, Huys QJ, Roiser JP. Computational Psychiatry: towards a mathematically informed understanding of mental illness. J Neurol Neurosurg Psychiatry. 2015 Jul 8:jnnp-2015.

Computational Psychiatry:

- It encompasses two approaches [3]:
  - Data-driven: Data analysis method from Machine Learning (ML): Diagnostic classification, treatment selection, relationship between symptoms.
  - Theory-driven: Mathematically specify relations between variables.

[3] Huys QJ, Maia TV, Frank MJ. Computational psychiatry as a bridge from neuroscience to clinical applications. Nature neuroscience. 2016 Mar;19(3):404.

Theory-driven approach:

Models can be classified in many different ways: [3]

- Synthetic / Biophysically detailed model
- Algorithmic model
- Optimal model

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[3] Huys QJ, Maia TV, Frank MJ. Computational psychiatry as a bridge from neuroscience to clinical applications. Nature neuroscience. 2016 Mar;19(3):404.

Synthetic / Biophysically detailed model:

- Helps to link biological abnormalities in psychiatric disorder to neurodynamical and behavioral consequences [3].
- One such model has been described in [4].
- Objective of the model was to:

-> Study the effects of disinhibition associated with schizophrenia in a cortical working memory model.

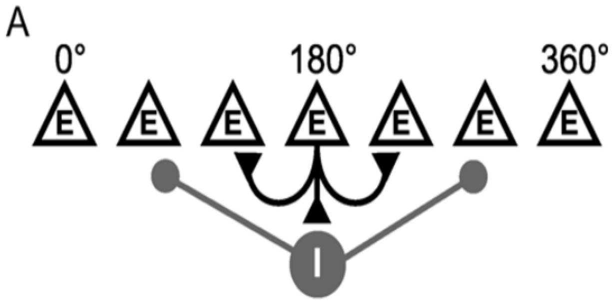
-> How stable the Working memory trace is, when perturbed by an additional distracting input.

[4] Murray, John D., et al. "Linking microcircuit dysfunction to cognitive impairment: effects of disinhibition associated with schizophrenia in a cortical working memory model." *Cerebral cortex* 24.4 (2012): 859-872.

Synthetic / Biophysically detailed model:

The model included:

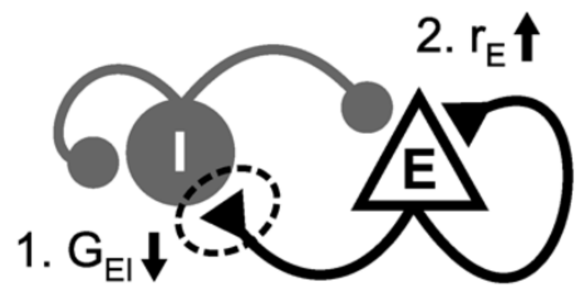
- Recurrently connected pyramidal neurons (Excitatory)
- GABAergic interneurons (Inhibitory)
- N_E = 2048 pyramidal cells
- N_I = 512 inhibitory interneurons



[4] Murray, John D., et al. "Linking microcircuit dysfunction to cognitive impairment: effects of disinhibition associated with schizophrenia in a cortical working memory model." *Cerebral cortex* 24.4 (2012): 859-872.

Synthetic / Biophysically detailed model:

- Disinhibition is implemented through a reduction of NMDA conductance on interneurons.
- This weakens the recruitment of feedback inhibition i.e. inhibitory interneurons are less strongly recruited by pyramidal-cell activity,
- More pyramidal cells can be activated by recurrent collaterals.



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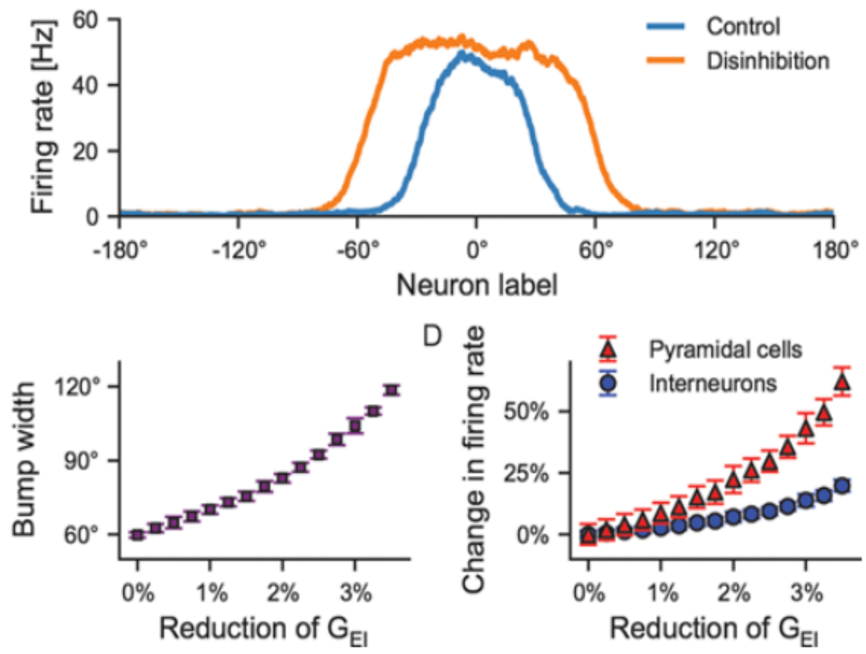
Synthetic / Biophysically detailed model:

- With increasing reduction of conductance, bump width and firing rate of excitatory neurons increase.



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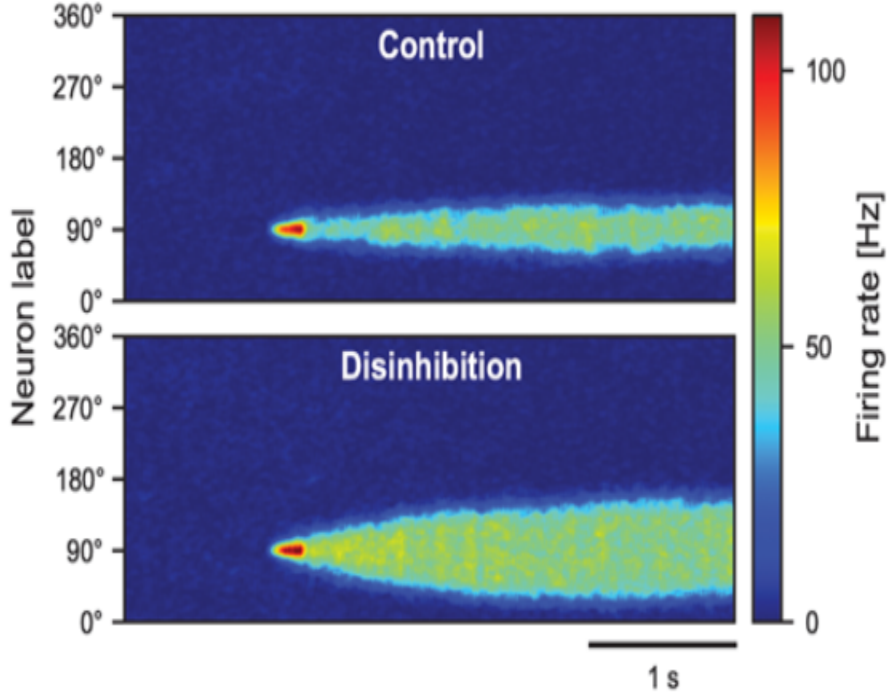
[4] Murray, John D., et al. "Linking microcircuit dysfunction to cognitive impairment: effects of disinhibition associated with schizophrenia in a cortical working memory model." *Cerebral cortex* 24.4 (2012): 859-872.

Synthetic / Biophysically detailed model:

- Broadening of the bump width in disinhibition case during persistent activity in working memory.



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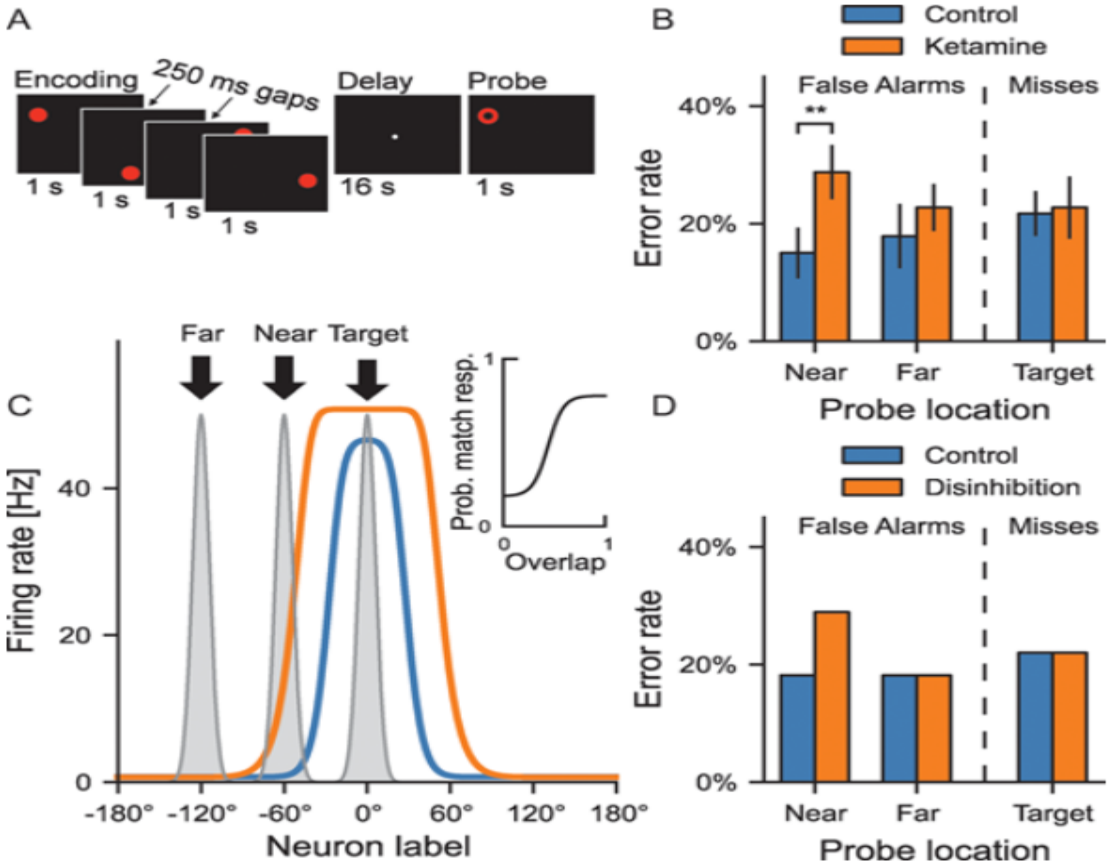
[4] Murray, John D., et al. "Linking microcircuit dysfunction to cognitive impairment: effects of disinhibition associated with schizophrenia in a cortical working memory model." *Cerebral cortex* 24.4 (2012): 859-872.

Synthetic / Biophysically detailed model:

Error:

Misses:
Nonmatch response to a probe at a target location.

False alarms:
Match response to a probe at a nontarget location.



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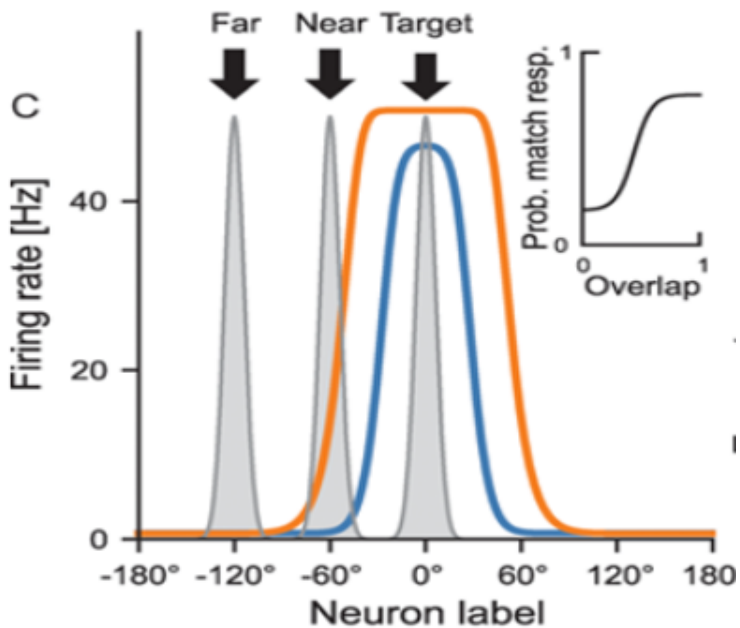
Synthetic / Biophysically detailed model:

- Disinhibition broadening overlaps more with the near probe location cases, hence results in increasing error rate.



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Algorithmic model:

- Reinforcement Learning model
- Applied extensively to deal with issues like emotional decision-making, motivation, affect etc. [3].
- One such model has been described in [5]:

  Negative symptoms are a core feature of schizophrenia and the objective of the model was to establish relationship between reinforcement learning abnormality with negative symptoms.

[5] Gold, James M., et al. "Negative symptoms and the failure to represent the expected reward value of actions: behavioral and computational modeling evidence." *Archives of general psychiatry* 69.2 (2012): 129-138.

Algorithmic model:

It was found that [5]:

Patients in the high-negative symptom group

-> demonstrated impaired learning from rewards but intact loss-avoidance learning

-> failed to distinguish rewarding stimuli from loss-avoiding stimuli in the test phase.

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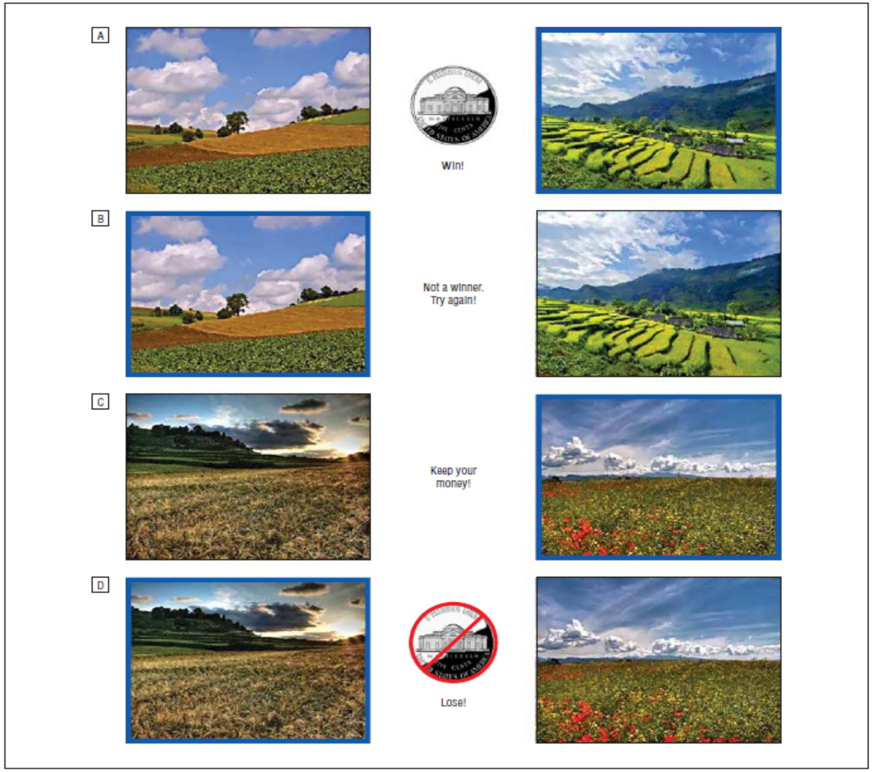
[5] Gold, James M., et al. "Negative symptoms and the failure to represent the expected reward value of actions: behavioral and computational modeling evidence." *Archives of general psychiatry* 69.2 (2012): 129-138.

Algorithmic model:

- First two pair corresponds to reward earning and last two pair relates to loss avoidance.



[5] Gold, James M., et al. "Negative symptoms and the failure to represent the expected reward value of actions: behavioral and computational modeling evidence." *Archives of general psychiatry* 69.2 (2012): 129-138.

Algorithmic model:

- Patients with high negative symptoms tend to learn from loss-avoidance instead of reward earning.

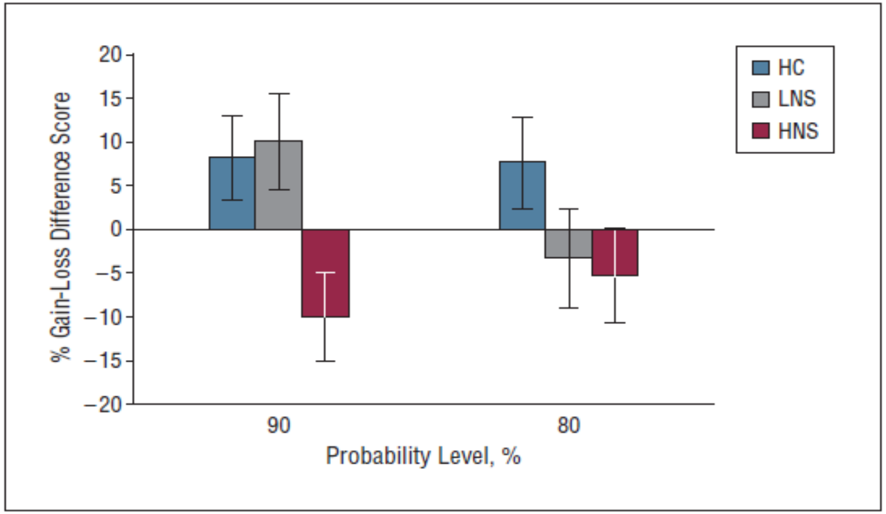


Figure 3. Performance on the gain and loss-avoidance difference score among patients and healthy control (HC) subjects. The difference score was calculated using block 4 performance. Scores above zero indicate better learning from gain than from loss avoidance, while scores below zero indicate better learning from loss avoidance than from gain. HNS indicates high-negative symptom; LNS, low-negative symptom.

[5] Gold, James M., et al. "Negative symptoms and the failure to represent the expected reward value of actions: behavioral and computational modeling evidence." *Archives of general psychiatry* 69.2 (2012): 129-138.

Bayesian model:

- It is used to better understand the nature of the problems and their solutions [3].

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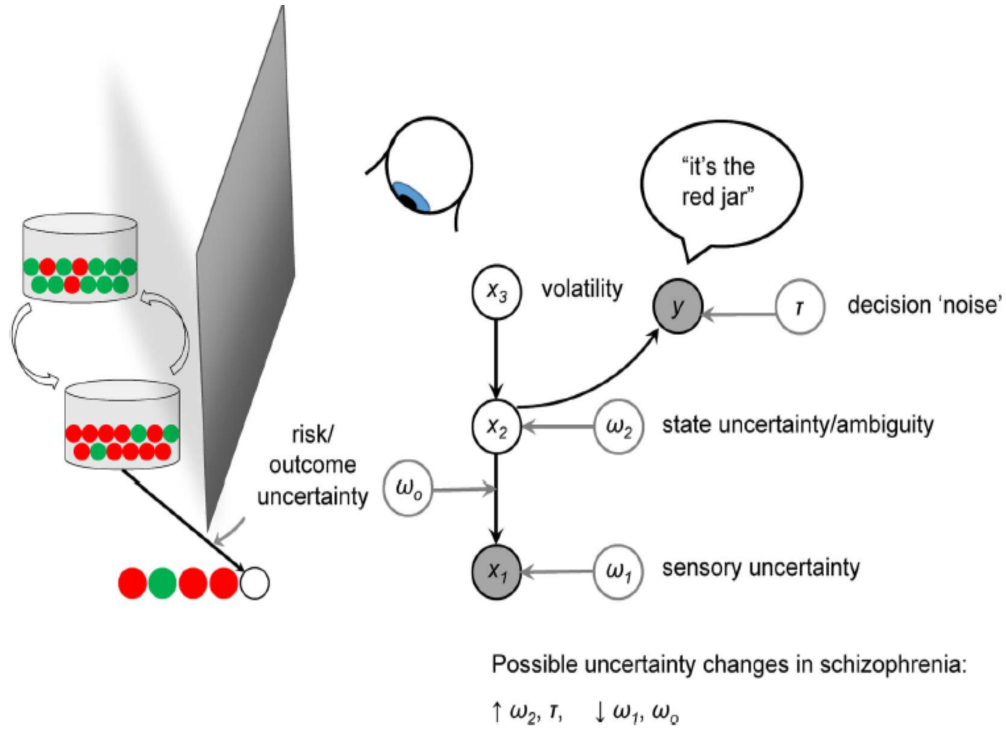
Generative model of decision making:



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Generative model of decision making:

- x1-> input;

  w1-> associated uncertainty

- x2-> identity of the jar;

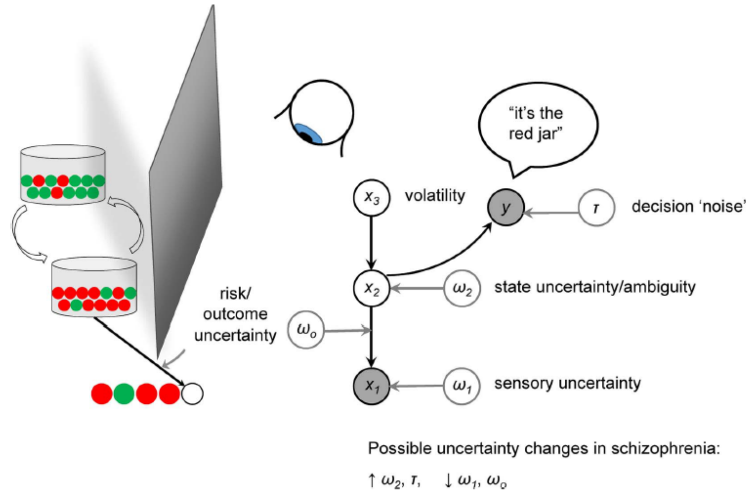
  w2-> associated uncertainty;

  wo-> uncertainty about next outcome

- x3-> belief that jar can be swapped

- y-> decision;

  tau-> Uncertainty/noise in decision



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[2] Adams RA, Huys QJ, Roiser JP. Computational Psychiatry: towards a mathematically informed understanding of mental illness. J Neurol Neurosurg Psychiatry. 2015 Jul 8:jnnp-2015.

To conclude,

Computational psychiatry helps understand mental disorder by allowing fitting computational model to behavioral data.

[5] Gold, James M., et al. "Negative symptoms and the failure to represent the expected reward value of actions: behavioral and computational modeling evidence." *Archives of general psychiatry* 69.2 (2012): 129-138.

Thank You….