

Mathematical Modeling of the Neuronal Processes in Sugar Addiction

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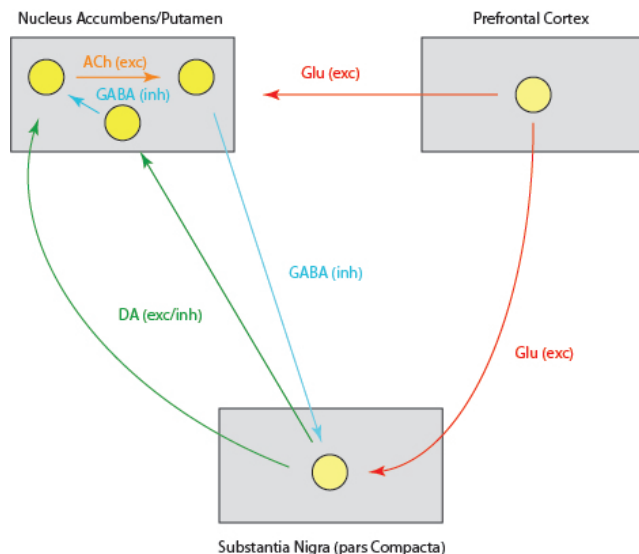
It has already been demonstrated that the body responds to enhanced intake of sugar and is conducive to a natural form of addiction. There are substantial neurochemical changes in the brain (especially dopamine and acetylcholine systems) similar to other addictive drugs. A mathematical model comprised by a system of delayed leaky integrate-and-fire equations is established to simulate the effects of sugar on a reward-circuitry. Simulations with NEURON suggest in agreement with the neurobiological hypotheses a hyperactivity of neural systems due to binge sugar intake.

Physiological Hypotheses

- Neurochemical similarities between drug self-administration and intermittent sugar intake. [1,2]
- **Dopamine Hypothesis:** Daily intermittent sugar intake repeatedly release dopamine in the accumbens [1,2].
- **Acetylcholine Hypothesis:** Accumbens acetylcholine release is delayed during sugar binges and eliminated during sham feeding [2].
- In withdrawal, there is an imbalance between acetylcholine and dopamine. Both systems respond in opposite directions.[1]

Mathematical model

- A system of delayed leaky integrate-and-fire equations for neural activities coupled with neurochemical dynamics;
- **Electrophysiological:** Generation of synaptic potentials depending on the dynamics of neurotransmitters;
- **Sugar Addiction:** It was modeled by including a delay term in the acetylcholine dynamics in the accumbens.



A schematic representation of the neurobiological systems involved in sugar addiction.

$$\frac{du_i(t)}{dt} = I_i^{-1}(R_i I_i(t) - u_i(t) + \sum_{j=1}^4 \lambda^j u_j(t - \tau_j)), \quad i = 1, \dots, 4, \quad i \neq j$$

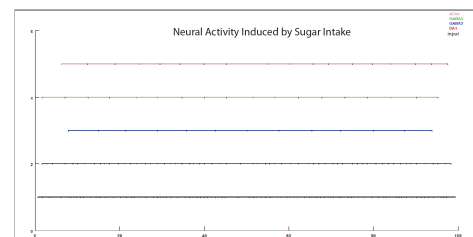
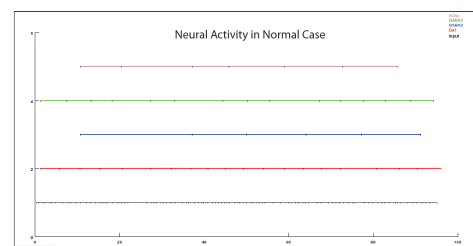
Simulation

- NEURON's computational engine has been used to describe the neuronal properties in the reward circuit. [3]
- Neurons have been integrated into the simulation software as artificial cells.

Results

- Neural hyperactivity [46 66] % due to abnormal sugar intake;
- Insignificant alterations in GABAergic-interneurons activity ;

Substance	Neural activity in normal case (spiking frequency)	Neural activity in sugar addiction (spiking frequency)	Difference (in %)
ACh	7	38	61.1
GABA-Interneurons	17	18	5.6
GABA-Projection Neurons	7	13	46.1
DA	21	62	66.1



- **Qualitative agreement with dopamine hypothesis:** The increase in the dopamine release due to intermittent daily sugar intake has been demonstrated;
- The systems quantitative behavior shows strong sensitivity related to the choice of ACh-delays;

Outlook

- Improving the model by extending it with additional substances and brain regions;
- Including the temporal effects of sugar synthesis;
- Understanding the neurobiological effects of sugar addiction on neural activities ...

Publication

1. B.G. Hoebel, N.M. Avena, P. Rada, (2007) Accumbens dopamine-acetylcholine balance in approach and avoidance. *Curr. Opin. Pharm.* 7: 617-27.
2. N.M. Avena, P. Rada, B.G. Hoebel, (2008) Evidence for sugar addiction: behavioral and neurochemical effects of intermittent, excessive sugar intake. *Neurosci. biobehav. Rev.* 32: 20-39.
3. NEURON, <http://www.neuron.yale.edu/neuron/>.