Mathematical Modeling of the Neuronal Processes in Sugar Addiction

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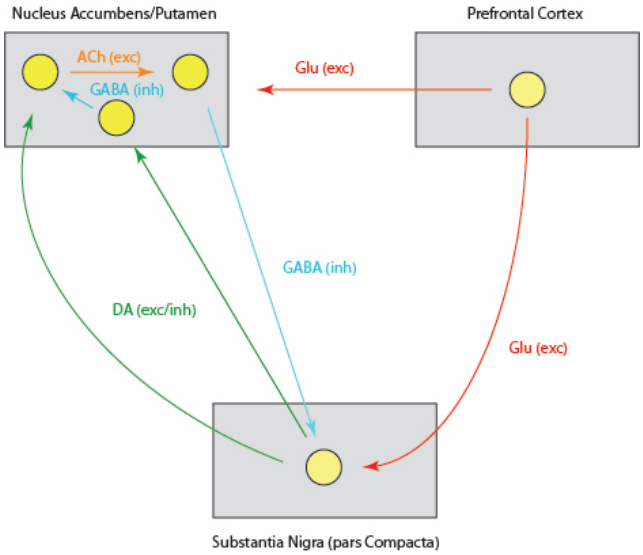
It has already been demonstrates that the body responds to enhanced intake of sugar and is conducive to a natural form of addiction. There are substantial neurochemical changes in the brain (especially dopamine and acetylcholine systems) similar to other addictive drugs. A mathematical model comprised by a system of delayed leaky integrate-and-fire equations is established to simulate the effects 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:**
- **Electorphysiological:** 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.

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

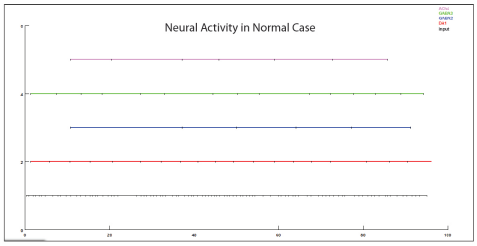
Simulation

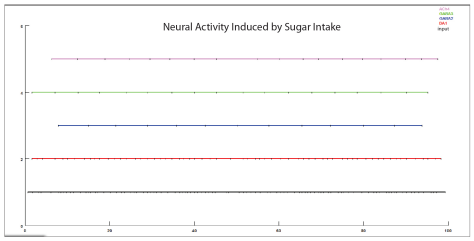
- NEURON's computational engine has been used to describe the neuronal properties in the reward circuit. [3]
- Neurons have been integrated into the simulation software as artificial cells.

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 addicition (spiking frequency)	Difference (in %)
Ach	7	18	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/.