Neurochemical Mechanisms of Perceptual Deficits in Schizophrenic Patients: A Spiking Neural Network Approach

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Background

- Schizophrenia is characterized by positive symptoms and negative symptoms as well as cognitive and perceptual deficits [1].
- Dysfunction of GABAergic neurons is hypothesized to be an important factor in the pathophysiology of schizophrenia [4].
- Decreased center-surround suppression (CSS, i.e. the mutual inhibition of a focal visual stimulus and its surrounding) has been interpreted in terms of GABAergic dysfunction [3].
- Consistently, strongly decreased CSS is reported in schizophrenic patients [2].
- **But:** Exact neural basis and perceptual consequences of a compromised GABAergic system remain unclear

Aim

In order to further elucidate the influence of distorted GABAergic neurotransmission on perception, we modeled the effects of manipulating particular aspects of GABAergic neurotransmission on center surround suppression strength.

Methods I - Neuron Model

We built a model of primary visual cortex based on anatomical and physiological data, using the neuron model from Izhikevich [5]. Each neuron model is governed by:

$$v' = 0.04v^2 + 5v + 140 - u + I, \quad \text{with} \quad I = I_{input} + I_{syn}$$

$$u' = a(bv - u).$$

$$\textbf{if} \quad v = 30mV \quad \textbf{then} \quad v \leftarrow c, u \leftarrow u + d$$

Total synaptic current:

$$I_{syn} = g_{AMPA}(v - 0) + g_{NMDA}\frac{((v + 80)/60)^2}{1 + ((v + 80)/60)^2}(v - 0)$$

$$+g_{GABA_A}(v + 70) + g_{GABA_B}(v + 90).$$

where each current is governed by:

$$g_i' = -g_i/\tau_i.$$

with $\tau_i = 5, 150, 6\,\text{ms}$ for $i =$AMPA, NMDA, and GABA$_A$, respectively.

Structure:

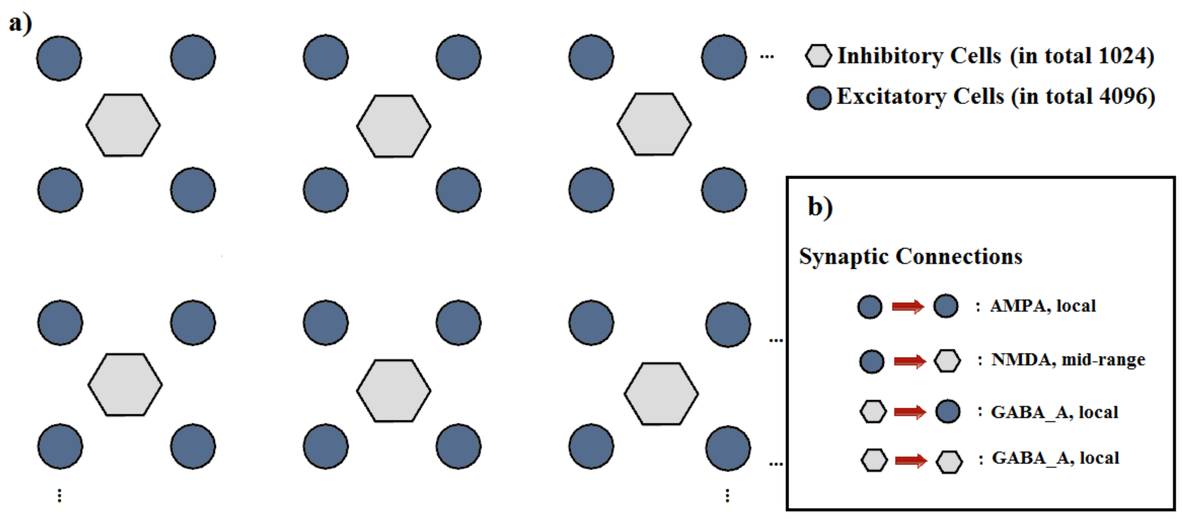

Figure 1: (a) 2D network arrangement of regular spiking excitatory cells and fast spiking inhibitory cells.(b) Synaptic connections.

Methods II - Input and Analysis

- Input based on established psychophysical CSS measurement protocols [2].
  - Center stimulation: 10×10 patch in the grid center with low intensity.
  - Surround stimulation: 20×20 patch around center with high intensity.
- We measured average spike rate of excitatory cells in the central region for two conditions:
  - Center stimulation.
  - Center+surround stimulation.
- The difference in spike rate was used as a measure of CSS.
- 'Schizophrenia' condition is modelled by prolonging GABA$_A$ synaptic decay time from 6 ms to 25 ms [6].

Results

Healthy Network:

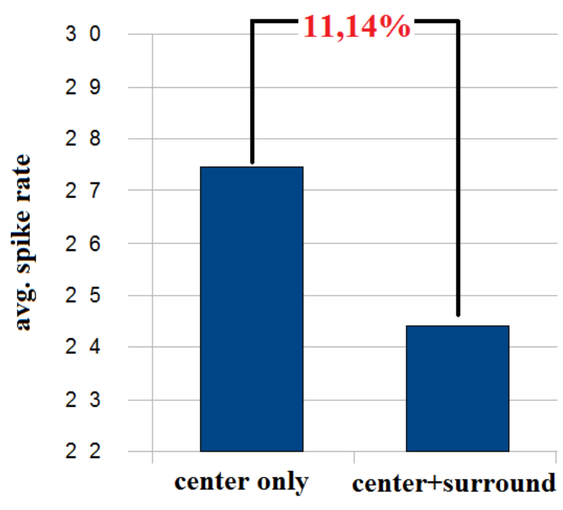

Figure 2: Comparison of spike rates in the central patch for (a) center only and (b) center+surround stimulation in the reference network. Spike rate is reduced by 11.14 % in the center+surround condition.

Schizophrenic Network:

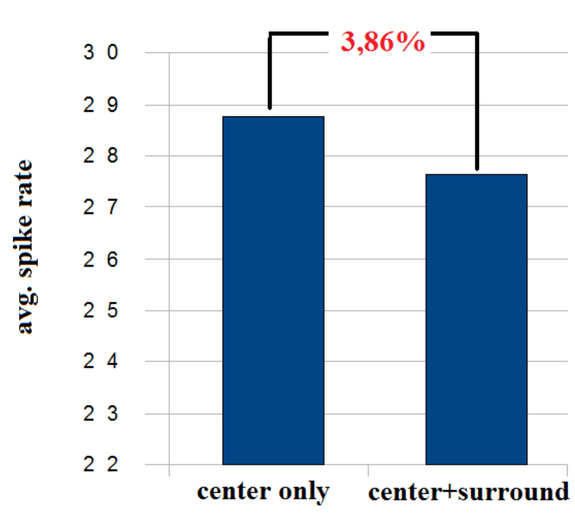

Figure 3: Comparison of spike rates in the central patch for (a) center only and (b) center+surround stimulation in the 'schizophrenia' network. Spike rate is reduced by only 3.86 % in the center+surround condition.

Discussion

- Model exhibits reduced activation due to CSS effects in the reference network.
- CSS effects are strongly reduced in the 'schizophrenia network'.
- Consistent with psychophysical studies reporting a reduction of CSS effects [2].
- Results suggest that prolonged IPSC decay times at GABAergic synapses is one factor in altered perception in schizophrenia and might even be solely sufficient to explain experimental results in patients.
- Confirms results of [6] with a different modeling approach in a different sensory modality.

Outlook

- We will test other possible factors:
  - Reduced GABAergic neuronal density.
  - Reduced synthesis and release of cortical GABA.
  - NMDA hypofunction at GABAergic interneurons.
- We will include synaptic plasticity to investigate compensatory effects.

References

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