Alterations in Parvalbumin Immunostaining in Prefrontal Cortex of Schizophrenic Brains

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Abstract

Schizophrenia is a neuropsychiatric disorder that is developmental in its origin. Previous studies have found that brains diagnosed with schizophrenia present a decrease in basilar dendrites and lower density of dendritic spines. In addition, our research of Parvalbumin positive neurons produced evidence that supports the theory of alterations in PV-positive neurons that are present in brains diagnosed with schizophrenia. There is a marked decrease in area fraction compared to those of the control brains. This decrease can attribute to the imbalance of excitation/inhibition that is vital to local circuit signaling.

Introduction

Schizophrenia is a debilitating neurological disorder that affects a variety of different brain regions. It is developmental in its nature and, like other developmental disorders of the brain, results from an imbalance between excitation and inhibition of pyramidal cells. Its symptoms include both positive outward manifestations as well as negative symptoms and cognitive deficits. There are two (2) primary types of PV (Parvalbumin) positive interneurons. The chandelier cells which connect to the axon hillock of pyramidal cells and basket cells that connect to the cell body and dendrites of pyramidal cells. Parvalbumin is a calcium-binding protein that is commonly found in chandelier and basket cells, both of which are inhibitory neurons. The main action of pyramidal cells is to undergo recurrent excitation between each other for continuous signaling. Another name for these excitatory cells are projection neurons due to their role in local and long distance signaling. Studies have shown a decrease in dendrites and dendritic spines along with reduced expression of parvalbumin in pyramidal cells, specifically in area 9 of the prefrontal cortex. Area 9 is involved in mental imagery, active memory, and higher cognitive functions of the brain. These are important factors since neurons, dendrites, and their spines are crucial in local circuit signaling of the brain.

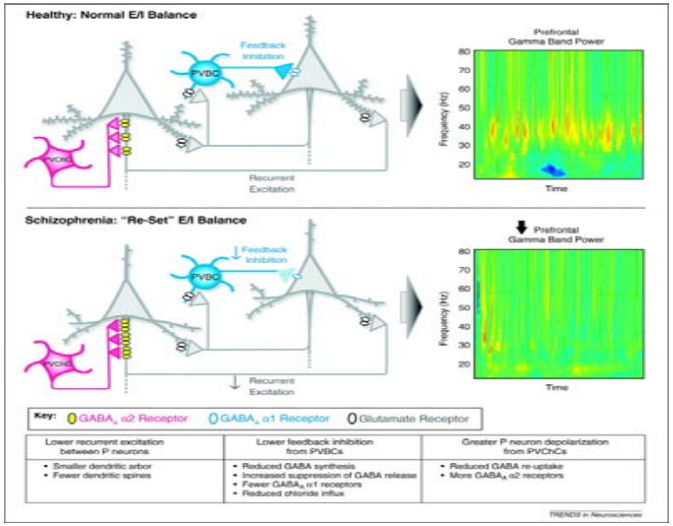
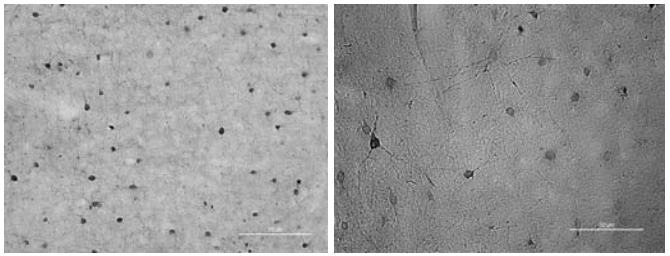


Figure 1*: Local circuits and excitation/inhibition imbalance in Human Pre-frontal cortex*

Methods and Materials

Brain tissues of individuals diagnosed with schizophrenia and control specimens from the Harvard Brain Tissue Resource Center (HBTRC) were used. These tissues were matched for age, gender, and postmortem interval (PMI). Parvalbumin immunostained neurons were examined and counted under 20x magnification. Bioquant software was used for Area Fraction Analysis, which is the ratio of the area immunopositive cells occupy compared to the total area of the viewing box. The total area of the sampling box was 325722.93µm



10x **Photomicrographs of pyramidal neurons.** **20x**

Results

Brain #	Layers II/III (µm)	Layers IV/V (µm)
3557	.03	.027
3625	.059	.067
3742	.053	.082
3875	.038	.047

Table 1*: Area Fraction Analysis*

Discussion

Reviewing the preliminary results gives evidence that coincides with the original hypothesis as well as previous studies. There is a noticeable decrease in area fraction of parvalbumin positive cells in layers II/III and IV/V of Area 9 of the Prefrontal Cortex. There is about a 28% - 49% decrease in area fraction for layers II/III and between 43% - 60% reduction for layers IV/V compared to the control. These differences have been theorized to cause alterations in local circuit signaling by shifting the balance between the excitation of pyramidal cells and the inhibitory actions of chandelier and basket cells.

References

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