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Mini Review

Schizophrenia and Decreasing in Corticolimbic Gabaergic Function

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Introduction

Glutamic Acid Decarboxylase (GAD) and Gamma Amino Butyric Acid (GABA) activities in the cortex, nucleus accumbens and thalamus would be decreased in schizophrenia. Also, there would be a reduction in presynaptic markers in some GABAergic interneurons in hippocampus and frontal cortex. Glutamic acid decarboxylase 65 KDa is expressed in axons and terminals while Glutamic acid decarboxylase 67 is expressed in dendrites and perikarya. Neurons which express GAD 67 mRNA in prefrontal cortex and other brain parts are reduced in numbers than ones expressing GAD 65 [1].

Calcium binding proteins like Parvalbumin (PV), Calbindin and Calretin expressions are done by GABAergic interneurons and modulated by afferent synaptic activity. Calbindin is found in double bouquet cells while calretin is found in bipolar neurons and double bouquet cells. PV is found in basket and chandelier cells in the cortex and pyramidal neurons send input to that also. Cartridges and pyramidal cells are the centre for their synaptic contacts and pyramidal cell firing is influenced by them, results in cortical excitatory output coordination. PV expression reduction is found in the prefrontal cortex of the patients with schizophrenia [2]. The amount of neurons with PV mRNA in prefrontal cortex in schizophrenia is intact while the amount of mRNA per neuron is decreased [3]. Calretin mRNA expression would not be altered in schizophrenia while mRNA encoding for GABA-A receptors, GAT1, GABA membrane transporters, GAD 67, Somatostatin and PV is decreased in primary visual and motor, anterior cingulate and primary motor cortex. GAT1 expression reduction in hippocampus and prefrontal cortex is seen in schizophrenia. Also, cartridges of GABAergic terminal boutons density reduction are seen in schizophrenia [4,5].

GAT1 and GAD67 reductions would cause different results, GAT1 reduction causes GABAergic neurotransmission enhancement while GAD67 reduction causes GABAergic neurotransmission reduction [6,7]. Increasing in GABA-A receptors can be found in intermediate layers of the cortex located in pyramidal neurons. GABA-A receptor subunits including Alpha 5 and Alpha 1 are increased in prefrontal cortex [8,9].

The overall results of these findings suggest that corticolimbic GABAergic function would be decreased in schizophrenia [10].

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