



Confluence Elements in the Psychopathology and Neurobiology of Schizophrenia

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Abstract:

In the light of recent development of neurosciences, multiple studies aim to establish brain dysfunctions linked to psychiatric disorders. Schizophrenia is a severe long-term mental illness and recent research identified neurobiological changes with psychopathological effects.

The dopamine hypothesis has been one of the most enduring theories dominating the etiopathogenesis of schizophrenia. This theory is supported by the efficacy and potency of many antipsychotic drugs acting on dopamine and on another neurotransmitter with effects on dopamine, the serotonin. The dopamine theory postulates a mesolimbic dopaminergic hyperactivity linked to positive symptoms and a prefrontal cortex dopaminergic hypoactivity causing negative and cognitive symptoms in schizophrenia. Multiple theories implicating dysfunctions of glutamate and GABA prefrontal neurons integrate the above-mentioned dopamine abnormalities.

Schizophrenia is also conceptualized as a disconnection syndrome, therefore a lack of coordination between different cortical regions is argued, with emphasis on cortico-thalamic circuits. The thalamo-cortical dysconnectivity implies decreased connections between thalamus and dorsolateral prefrontal cortex.

In order to control perceptive and cognitive processes, the GABA prefrontal neurons are synchronized in the γ frequency band (30-80 Hz). In schizophrenia, there is a disturbed synchronicity in γ band and an increased activity in θ band, consistent with a hyper polarization with reduced control function of the prefrontal cortex. Also, chronic stress is associated with an inappropriate immune activation. Stress may increase pro-inflammatory cytokine. The activated immune system in turn activates the enzyme indoleamine 2,3-dioxygenase (IDO) of the tryptophan/kynurenine metabolism which influences the serotonergic and glutamatergic neurotransmission.

Epigenetic mechanisms may stem for the environmental contributions to schizophrenia, too. DNA methylation or histone acetylation could imply an active or inactive transcription in the case of some well-known enzymes intervening in the pathophysiology of schizophrenia like BDNF, COMT, GAD1 or RELN gene.

According to the "theory of self" in schizophrenia the structures implicated in "sense of self" elaboration are ventral medial, dorsal medial prefrontal cortex, anterior and posterior cingulate cortex, superior temporal sulcus, inferior parietal cortex.

Keywords

Schizophrenia, Dopamine Hypothesis, GABA Neurons, Immune Activation, Epigenetic Mechanisms