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Biomolecular Aspects of Schizophrenia

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Abstract

Schizophrenia is a common psychiatric disorder, which is characterized by severe distortion of reality; disturbances in thoughts, feelings and behavior; according to DSM V is a disorder form deviations fundamentals and characteristics of thought and perception, and by the innapropriate or blunted affect. The influence of genetics is believed to have a role in psychiatric disorders, especially if the disorder has occurred in young adults or adolescents. The pathophysiology of schizophrenia is closely related to disorders of the biomolecular aspects of the central nervous system. Dopamine activity in the striatal area and prefrontal cortex is a mechanism believed to be the cause of the emergence of positive and negative symptoms in schizophrenia. Meanwhile, neuronal cell apoptosis and increased oxidants, especially in the basal ganglia and prefrontal cortex areas cause worsening of negative symptoms experienced by schizophrenic patients.

Keywords: biomolecular, schizophrenia

Introduction

Schizophrenia is a common psychiatric disorder, which is characterized by severe distortion of reality; disturbances in thoughts, feelings and behavior; according to DSM V is a disorder form deviations fundamentals and characteristics of thought and perception, and by the innapropriate or blunted affect. Schizophrenia is a psychiatric disorder that occurs in about 1% of the world's population. Differences in sex ratios vary depending on sample and study population. Age at first suffered differ between men and women, which is in late 20s - early in

women and teens and mid-20s in men. The influence of genetics is believed to have a role in psychiatric disorders, especially if the disorder has occurred in young adults or adolescents.

Clinical symptoms of schizophrenia consist of positive symptoms (delusions, hallucinations, agitation, language and communication distortion, organized speech, and catatonic behavior), negative symptoms (blunted affect, bad rapport, passivity, apathetic, alogia, anhedonia, *avolition* , difficulty in abstract thinking , reduced spontaneity), cognitive symptoms (difficulties in setting goals, focusing / focusing attention, processing information, determining priorities, solving problems), affective symptoms (depressed mood or anxiety, feelings of guilt, tension, irritability), and aggressive symptoms (overhostility , *self-injury*, impulsivity). [1]

Pathophysiology of Schizophrenia

It is believed that schizophrenia occurred in many ways. Dopamine 2 receptors are believed to play a role in the pathophysiology of schizophrenia. Positive symptoms result from excessive dopamine activity in the striatal area and mesolimbic area. While negative symptoms are associated with a decrease in dopamine activity in the prefrontal cortex. The use of antipsychotics plays a role in the action of dopamine 2 receptors because it can block dopamine receptors, so that the symptoms of schizophrenia can be reduced.[1,2]

Apoptosis is thought to play a role in the occurrence of schizophrenia. Apoptosis is a programmed cell death that occurs when the cell has irreparable damage. The formation of oxidants or reactive oxygen species can cause cells to experience oxidative stress, then activate the caspase which will later cause cell apoptosis[3]. In addition, neuronal cell death is thought to be caused by an excitotoxicity process caused by excessive stimulation of the glutamate receptor NMDA subtype. Excessive glutamate neurotransmitters will cause overexitation of NMDA receptors. Then there will be excessive influx of Ca^{2+} ions and cause stress on the endoplasmic reticulum. This is what activates the caspase and lysis cells, resulting in cell death. [4]

Dopamine also has a connection with the occurrence of neuronal cell death. Dopamine metabolism causes the formation of oxidants in the central nervous system. Dopamine (DA) has a dihydroquinone structure and in physiological conditions non-enzymatically oxidized by oxygen molecules and produces hydrogen peroxide (H_2O_2) and *corresponding o-quinone* . [3,4] Non-

enzymatic oxidation of catecholamines and PUFAs, in combination with antioxidant deficiencies in the brain, lead to increased lipid peroxidation, which will affect membrane fluidity, integrity and permeability.[5]

Oxidative stress in schizophrenia

Oxidative stress is a condition that occurs due to an imbalance between toxic reactive oxygen species (ROS) and antioxidants. Each network has a difference in succeptibility to oxidative stress. The brain is a network that is relatively susceptible to oxidative damage because of its low antioxidant level, high levels of polyunsaturated fatty acids (PUFA), high mineral content and high oxygen demand (oxygen binding function) [1,3,5]. In addition, easily oxidized neurotransmitters such as dopamine (DA), epinephrine and norepinephrine, are also present in the brain. The metabolism of neurotransmitters requires large amounts of hydrogen peroxide and neuronal mitochondria produce superoxide radicals (O^2).[5] Furthermore, the presence of toxic amino acids can lead to cell proteolysis. From all brain regions, basal ganglia is an area that has a greater risk of free radical damage due to the highest iron content. [6,7]

Increased oxidative stress is thought to be relevant and related to the pathophysiology of schizophrenia, but the majority of outcomes in schizophrenic patients are very different. Several lipoperoxidation metabolites including *malondialdehyde* (MDA) and 4hydroxynonenal (4-HNE), are thought to be the most specific and sensitive measurements of lipid autooksidation. The potential toxicity of free radicals can be resisted by a number of cytoprotective and antioxidant enzymes which reduce the amount of tissue damage. The function of the protective mechanism works through a cascade involving various antioxidant enzymes such as superoxide dismutase (SOD) and glutathione peroxidase (GPX) [5-8].

Most measurements of oxidative stress in schizophrenic patients are carried out through peripheral body tissue. There is little information about oxidative processes that occur in cerebrospinal fluid and the brain. This may be due to peripheral oxidative damage that may originate from various other tissues in the body and hence, peripheral indications cannot show clearly the conditions or processes of oxidative stress that occur in the brain. [9]

Red blood cells are often used to evaluate oxidative stress in patients with schizophrenia. Some diseases related to abnormalities of red blood cells can describe abnormalities in neurons, which have so far been difficult to examine in vivo. [10] Because of its accessibility, red blood cells are commonly used as a "window" for the central nervous system. Even so, there are still many shortcomings that cannot be revealed through the examination of red blood cells (Berger 2006). Furthermore, changes in phospholipid metabolism have been demonstrated through post-mortem brain examination in schizophrenic patients. *Magnetic resonance spectroscopy* provides an invivo evaluation of phospholipid metabolism in the brain. Using this noninvasive technique Williamson *et al* . have demonstrated abnormalities of brain phospholipid membranes in schizophrenia, but they cannot prove that these abnormalities are specific to schizophrenia. [10-11]

GSH, GpX and gluthatione reductase levels were significantly lower in the brains of schizophrenic patients compared to controls, which correlated with peripheral measurements [12-14]. In addition, there are studies of proton magnetic resonance which report a non-significant reduction, or even an increase in GSH concentration in the brain [14].

There are studies that state peripheral nitric oxide (NO) metabolites can be used as markers of CNS changes related to NO. Total serum nitrate increases in the *demyelinating disease* group, forexample multiple sclerosis, *inflammatory neurological disease* and AIDS patients. [15]

Based on heterogeneous empirical evidence, there are no studies that clearly state peripheral biomarkers as markers of central oxidative status. Therefore, it can be concluded, the results of studies on CNS (cerebrospinal fluid, postmortem or experimental animals) show a slight correlative tendency in biomarker studies in erythrocytes, plasma or polymorphonuclear. [16]

Conclusion

Schizophrenia is a disorder form deviations fundamentals and characteristics of thought and perception, and by the innappropriate or blunted affect. The pathophysiology of schizophrenia is closely related to disorders of the biomolecular aspects of the central nervous system. Dopamine activity in the striatal area and prefrontal cortex is a mechanism believed to be the cause of the

emergence of positive and negative symptoms in schizophrenia. In addition, neuronal cell apoptosis and increased oxidants, especially in the basal ganglia and prefrontal cortex areas cause worsening of negative symptoms experienced by schizophrenic patients.

GSH, GpX and gluthatione reductase levels were significantly lower in the brains of schizophrenic patients compared to controls, which correlated with peripheral measurements. Increased lipoperoxidation of metabolites including malondialdehyde (MDA) and 4hydroxynonenal (4-HNE) in schizophrenic patients is needed to be further examined and approved as one of the causes of worsening clinical symptoms in schizophrenia.

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