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Stem Cell Transplant a New Alternative in the Treatment of Schizophrenia

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Niche

Review

Abstract

Until recently, it was thought that there is no neuronal regeneration and neuron loss is irreversible, but today the existence of neural regeneration and neural plasticity have been documented. The effectiveness of stem cell treatment in numerous degenerative diseases, as well as some neurodegenerative diseases, has created hopes toward the use of stem cell treatment in schizophrenia, which is a disease that progresses with neuronal degeneration and loss of neurons, and is characterized with worsening clinical outcomes and impairment.

Key words: Schizophrenia, neurodegeneration, stem cell therapy

Schizophrenia is a chronic, debilitating neuropsychiatric disorder that affects approximately 1% of the world population. The symptoms of schizophrenia have been grouped under three subcategories: positive symptoms, negative symptoms and cognitive symptoms. Auditory and visual hallucinations, delusions, disorganized speaking and behaviors and formal thought disorders are defined as positive symptoms; shortening of affect intervals, poor speech and lack of interest, enthusiasm and motivation are defined as negative symptoms; deficits in attention, memory, abstract thinking and daily functioning are defined as cognitive symptoms (1).

The etiology and pathophysiology of schizophrenia have not been understood yet. Twin studies have shown that 73-90% of schizophrenia cases are hereditary (2) and family studies have shown that cognitive deficits can be present in the family members of schizophrenia patients, who do not suffer from schizophrenia (3). More than 30 genes have been reported to have polygenetic inheritance (4, 5), but none of them have been found to be specific to schizophrenia (6-8). In some studies, it has been claimed that complications at birth (9) or prenatal exposure to a viral infection (10) could cause schizophrenia.

Initially, controlling positive and negative symptoms was the major goal of schizophrenia treatment, but in recent years, cognitive symptoms have become an important target for the pharmacotherapy of schizophrenia (11). Increased dopaminergic activity has been mentioned in studies with typical antipsychotics that antagonize dopamine 2 (D2) receptors (12). The appearance of schizophrenia-like psychotic episodes with amphetamine, phencyclidine, ketamine, which are agents that increase the release of dopamine in the brain; and the discoveries of the associations between over stimulation of D2 receptors with positive symptoms and reduced function of D1 receptors with negative symptoms in imaging studies, support the view that dopamine has a role in the pathophysiology of schizophrenia (13). However, D2 receptor antagonists have no effect on negative symptoms of cognitive deficits.

Increase in the positive and negative symptoms of schizophrenia have been shown after using N-methyl-D-aspartate receptor antagonists (14). This finding seems to support the hypoglutamatergic hypothesis in schiozephrenia etiology. In studies conducted with ketamine on voluntary, healthy subjects, it has been shown that ketamine could also cause cognitive deficits (15-17).

It has been published that there are morphological changes in the brains of schizophrenia patients. Decreases in the volume and metabolic speed of the prefrontal cortex, defects in neuronal placement, decreases in synaptic proteins and dendritic branches have been reported and these findings can be associated with the cortical network (18, 19). Gamma Aminobutyric Acid (GABA) levels with neuronal damage are explained by the compensatory increase of GABA

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receptors and neurotoxicity stemming from reduced GABA stimulation (14).

A progressive loss of grey matter in early episodes of schizophrenia has been shown in some studies, and this loss has been explained by neural apoptosis. Apoptosis is programmed cell death regulated by pro and anti-apoptotic proteins. However, as in some Alzheimer's disease cases, it could also be the result of non-fatal terminal neuritic and synaptic elimination. Most recent studies have reported changes in apoptotic regulating proteins and DNA sequencing in the cortical regions of schizophrenia patients (20).

Neural stem cell studies in adult mammals have shown that neural stem cells situated in supraventricular and subgranular zones generate new neuronal or glial cells in the hippocampus (21, 22), and while some neuronal cells generate neurons, others create neuronal plasticity, memory structuring or stress response (23).

In bone marrow transplant studies with rats, it has been reported that, in the presence of microglia and astrocytes stemming from the bone marrow, bone marrow associated cells could differentiate into neurons (24, 25). The existence of neuronal cells in the cerebral cortex and hippocampus has been documented in patients undergoing bone marrow transplant (26).

In events such as cerebral infarction, ithas been proposed that the central nervous system stem cells contribute to recovery but have a limited effect due to being low in numbers, so for treatment purposes, these stem cells should be administered externally (27). In experimental spinal injury studies, it has been shown that regeneration can be possible through stem cell treatment (28).

The existence of neuronal regeneration and the fact that stem cell treatment can be effective in neurodegenerative diseases create hopes for the future use of stem cell treatment in schizophrenia, which progresses with cell degeneration. There is a need for experimental and clinical studies in this field.

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