Review Article

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Epilepsy: Next Target of Stem Cell Therapy

Aprajita

Stem Cell Engineering, Barkatullah University, Bhopal (M.P), India

*Corresponding author
Aparajita, Stem Cell Engineering, Barkatullah University, Bhopal (M.P), India, E-mail: aparajitasrivastava98@gmail.com

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Abstract

Epilepsy is fourth common neurological disorder rummaging for its best treatment. Patients with epilepsy suffer through harsh psychological and behavioral changes and due to widespread superstitions; epileptic patients have to face constant discrimination and stigmatization from society. Epilepsy is an electric disturbance resulting from a disorderly discharge resulting in blackouts and fits. The present study is about how stem cell research is in forefront of medication for epilepsy.

Epilepsy isn't easy to handle as it is a spectrum condition with a wide range of alteration and resulting types of seizures that varies individually. There is some imbalance in signals of neuron formation of burst and burst terminations are major role players in seizure stimulation. Several studies mark that these burst result in neural damage.

Although, at present, different anti epileptic drugs (ADE) are available to minister seizures. But the dosages of ADE are always fluctuating in treatment tenures according to seizure and results are around 50% to 65%. These drugs target the abnormality of different chemical channels, whereas stem cells therapy aims on sending an army of neural stem cell to brain where they become neurons and head towards area in need of repair and regeneration. As for epilepsy, stem cell research is still in its infancy but it is considered that stem cells are able to integrate and repair the deep brain circuits.

Keywords: Seizures, Stem cells, Interneuron, Antiepileptic Drugs, Burst, Stimulations

Introduction

"Epilepsy is a condition characterized by repeated seizure due to a disorder of the brain cells"[1]. Some of the epilepsies are confined to a particular age but some people suffer for their life time. Seizure is a result of excess nerve cell discharges in brain and these are classified on the basis of location in brain and pathophysiology. As proposed by the "Commission on Classification and Terminology of International League Against Epilepsy" approved on 1981, Seizures are classified into partial seizures and generalized seizures [1].

Partial seizures are characterized by the abnormal electrical discharges starting in a localized area of brain whereas in generalized seizure it starts in both the hemisphere of the brain simultaneously. Most common of both are complex partial seizures and generalized absence seizures.

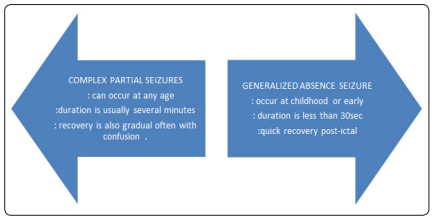


Figure 1: Comparison of factors between Complex partial seizures and generalized absence seizure, according to the data given by World Health Organization

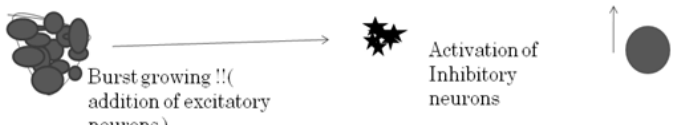
There could be a number of causes for epilepsy , for newborns , lack of oxygen during birth , brain malformations, inborn errors can be the triggering factors where as for adults genetic factors , head trauma , strokes are some of the common epilepsy causes. Low levels of blood sugar, blood calcium, blood magnesium or other electrolyte problems can also be the major causes because as known the levels of calcium, potassium plays a major role in maintaining the neuron action potential.

Mechanism

As explained by M.C Maheshwari, in a normal condition there is balance between the excitatory neurons and inhibitory neurons in CNS.

In epileptic brain these potential of group of brain cells , which are of similar nature are added and result in a burst activity and this initiation of burst activity or susceptibility of these cells may be altered by injury , disease process, chemical , genetics and others . So, as the Burst grows to a critical level there is a electric discharge which physically expresses itself as seizure [2]. On the other hand, while the burst activity is building up, the inhibitory cells of brain are also stimulated. This inhibitory influence plays a major role in seizure termination.

Development of degree of seizure activity depends on certain local characteristics of brain where such activity originates.



Individual variability is seen in epileptic cases, as the action potential depends upon calcium and potassium channels the Calcium, potassium and sodium have important roles in burst generation and propagation. In some articles it is mentioned that 1he thalamic-cortical dysfunction can be due to structural, functional or biochemical basis. These changes may cause generalized epilepsy.

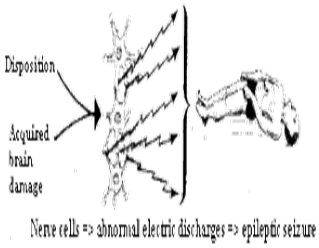


Figure 2: Concluding mechanism of epileptic seizure

Diagnosis and Current Treatment

AEDs (anti-epileptic drugs) work by controlling the electrical activity in the brain that causes seizures. They do not cure epilepsy and are not used to stop seizures while they are happening. The aim of treatment is to stop all of your seizures with the lowest dose of the fewest number of AEDs and with the least side effects. Usually treatment starts using a single AED at a low dose, which is increased slowly (called titration), until your seizures are controlled.

If your seizures are not controlled with given drug, a different AED is usually tried (by adding in the new drug and then slowly withdrawing the first one). If your seizures are not controlled with a single drug, another drug might be added, so that you take two different AEDs each day. Anti-epileptic drugs or seizure medications work well for 50- 65 % of cases as the data says, but we need more effective therapies for people who still have seizures or side effects of currently used antiepileptic drugs.

Table 1: Data from WHO manual on epilepsy 2002

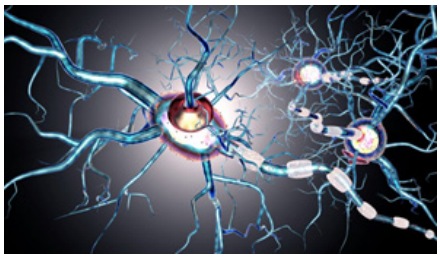
Anti Epileptic Drug	Side Effects
Phenobarbitone	Drowsiness , hyperactivity in children
Phenytoin	Drowsiness, allergy , rashes , hypertrophy
Carbamazepti	Drowsiness, ataxia skin rash
Valporate	Nausea , vomiting , diarrhoea, hair loss
Ethosuximide	Drowsiness hallucination
Clonazepam	Drowsiness, weakness ataxia secretion aggressiveness

What Stem Cell Therapy Promises?

The aim of stem cell treatment for epilepsy is to send an army of stem cells to the brain, where they become neurons and head to the areas in need of repair and regeneration. It has been demonstrated that people who suffer from chronic epilepsy often can have a reduced neuron population in the region of the brain where seizures originate. The fresh stem cells could replace neurons that are overly active in electrical production. Unusually high elevations of electrical output by neurons are another trigger for seizures. In this case, the stem cells would replace the abnormally functioning neurons. One of the major candidates for stem cell therapy for epilepsy is Neural stem cells, scientist have found an small amount of stem cells in epileptic and damaged brain.

Neural stem cells and neural progenitors (NSC/NPs)

Neural stem cells and neural progenitors (NSC/NPs) hold great promise in neuro-restorative therapy due to their remarkable capacity for self-renewal, plasticity, and ability to integrate into host brain circuitry. Some of the major types of NSC/NPs and how they have been studied with regard to synaptic integration into host brain circuits. It also reviews how these transplanted cells develop and interact with host brain cells in animal models of epilepsy. And also the research on how skin cells can be reprogrammed as brain cells is in its way to lab.



Dr. Scott's Findings

There are two main ways in which stem cell therapy can be used in epilepsy. Experiments exploring the use of stem cells in epilepsy have been pioneered by Dr. Scott Baraban at University of California, San Francisco (UCSF).

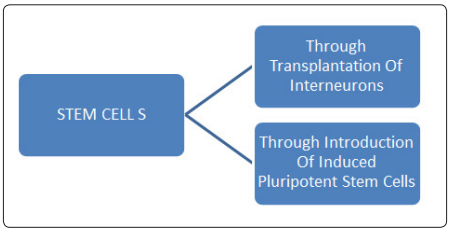


Figure 3: Two methods suggested by Dr. Scott.

Transplantation of Interneurons

A similar approach has been tested with stem cells. Specific groups of inhibitory neurons (also called interneurons) are formed from a specific area of the brain (called the medial ganglionic eminences). When scientists took these neurons and transplanted them into the brains of animals that had been treated to have seizures, they found that these cells were able to work and increase inhibition [3]. This reduced seizures. These results are promising, but more work needs to be done before they can be tested in people with epilepsy.

Induced Pluripotent Stem Cells (iPSC)

Some epilepsies are caused because of a genetic mutation or change in neurons. For example, Dravet syndrome is a devastating form of childhood epilepsy caused by a mutation in a specific sodium channel. Scientists have found a way to take the adult stem cell from people with Dravet syndrome and program them to become any

type of cell in the body. These new cell types are called pluripotent stem cells. These new cells can be made into neurons. In a research laboratory, these neurons can be used to study the effects of specific drugs and give scientists a better understanding of Dravet syndrome. iPSC can also be used by reprogramming them into neural progenitor cells.

Conclusion

For epilepsy, stem cell research is still in its infancy and has been carried out in experimental animals. Although, stem cell therapy has candidates for treating several focal seizures .With discovery of stem cells in epileptic brain, it may be considered that in future stem cell may integrate and repair the deep brain circuits and remove the neurons those are functioning improperly [4-6].

References

1. PA Dekker MD (2002) "Epilepsy: A Manual for Medical and Clinical In Africa", Revised Edition, World Health Organization, WHO, Geneva, Switzerland.
2. M.C Maheshwari (1989) "All You Want To Know About Epilepsy" by, Popular Science Series, ISBN 81-237-0554-9, National Book Trust of India.
3. Parisa Goodarzi, Hamid Reza Aghayan, Masoud Soleimani, Abbas Norouzi-Javidan, Fereshteh Mohamadi-Jahani, et al. (2014) "Stem Cell Therapy For Treatment Of Epilepsy ". Acta Medica Iranica 52: 651-655.
4. Steve, Dennis A. Steindler (2013) "Stem Cells as a Potential Therapy for Epilepsy" by, Expérimental Neurology 244: 59-66.
5. "Types Of Seizures" https://www.cdc.gov/epilepsy/about/types-of-seizures.html
6. https://www.ncbi.nlm.nih.gov/books/NBK2510/.

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