Review Article

Neuroanatomical Changes in Brain Structures Related to Cognition in Epilepsy: An Update

K. Saniya, B. G. Patil[1], Madhavrao D. Chavan[2], K. G. Prakash, Kumar Sai Sailesh[3], R. Archana[4], Minu Johny[3]

Departments of Anatomy and [2]Pharmacology, Azeezia Institute of Medical Sciences, Kollam, [3]Department of Physiology, Little Flower Institute of Medical Sciences and Research, Angamaly, Kerala, [1]Department of Anatomy, Shri B. M. Patil Medical College, Bijapur, Karnataka, [4]Department of Anatomy, Saveetha Medical College, Saveetha University, Chennai, Tamil Nadu, India

Abstract

Understanding the microanatomical changes in brain structures is necessary for developing innovative therapeutic approaches to prevent/delay the cognitive impairment in epilepsy. We review here the microanatomical changes in the brain structures related to cognition in epilepsy. Here, we have presented the changes in major brain structures related to cognition, which helps the clinicians understand epilepsy more clearly and also helps researchers develop new treatment procedures.

Keywords: Brain structures, cognition, epilepsy, Neuro-Anatomical changes

Introduction

Epilepsy (also called "Seizures") is characterized by uncontrolled excessive activity of either part or all of the central nervous system. Although epilepsy is not a specific disease, it is considered as a group of syndromes as a result of chronic neurological disorders.[1] Epilepsy can be classified into three major types: grand mal epilepsy, petit mal epilepsy, and focal epilepsy.[2] Global prevalence of epilepsy is approximately 0.5% affecting predominantly early childhood and late adulthood resulting in psychological and social consequences.[3] The causes and treatment protocols vary widely.[4] In India, over 10 million patients suffer from epilepsy, which equates to a prevalence rate of 1%.[5] Impairment of cognition is a common condition in epilepsy, and the features include mental slowness and memory and attention deficits in adults.[6] Learning disabilities, poor academic outcome, behavioral problems, and language stagnation or deterioration are additional features observed in children.[6] Underlying cause of cognition impairment may be lesion in particular brain area consequence to seizures or epileptic dysfunction,[7] with age-associated increase in the vulnerability.[8] However, seizures in children have reported to cause long-term adverse effects.[9] Further, the extent of brain damage also depends on number, duration, and severity of seizures.[10] Understanding the microanatomical changes in brain structures may lead to innovative therapeutic approaches to prevent/delay the cognitive impairment in epilepsy. Hence, we aimed to review the microanatomical changes in the brain structures related to cognition in epilepsy.

Access this article online

Quick Response Code:

Website: www.jnsbm.org

DOI: 10.4103/0976-9668.210016

Materials and Methods

A detailed literature review was performed between February 2016 and August 2016, through MEDLINE, Google, PubMed, Scopus, British Medical Journal, Medline, Eric, Frontiers, and other online journals using the terms "epilepsy," "micro-anatomical changes," "basal ganglia," "cerebellum," "brain volume," "thalamus," "hypothalamus," "limbic system," "locus coeruleus," and "cerebral cortex." Article selection was based on their relevance to the present topic.

Changes in Hippocampus in Epilepsy

Hippocampus plays a crucial role in cognition and it is involved in minute-to-minute cognitive processing.[11] Hippocampus and associated areas were reported to be affected critically

Address for correspondence: K. Saniya, Department of Anatomy, Azeezia Institute of Medical Sciences, Meeyyannoor, Kollam, Kerala, India. E-mail: saniyaudma@gmail.com

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How to cite this article: Saniya K, Patil BG, Chavan MD, Prakash KG, Sailesh KS, Archana R, *et al*. Neuroanatomical changes in brain structures related to cognition in epilepsy: An update. J Nat Sc Biol Med 2017;8:139-43.

in epilepsy, especially temporal lobe epilepsy, which is more common in adults.[12] It was reported that recurrent seizures might cause hippocampus damage throughout the lifetime of the patient.[13] Structural (histological) and functional changes occur in hippocampus in epilepsy. Histological changes include selective and extensive hippocampal neuronal loss in CA1 and CA3 regions and around the end folium where the cells of CA2 region are spared.[14-18] In other types of epilepsy, neuronal loss can be observed in all hippocampal areas. Apart from neuronal loss and gliosis, granule cell dispersion in dentate gyrus is also observed in epilepsy.[19] Atrophied hippocampus is reported to be responsible for seizures, and surgical removal of hippocampus is reported to improve the condition.[20,21]

Changes in Basal Ganglia in Epilepsy

The role of basal ganglia in cognitive functions is well established.[22] Earlier studies hypothesized that basal ganglia functions as a part of a modulatory control system over seizures rather than a propagation pathway.[23] Although no specific epileptic electroencephalography changes were observed in basal ganglia, involvement of basal ganglia in distribution of epileptic activity was reported.[24] Dopamine is reported to involve in the control of seizures related to the type of epilepsy.[25] Sufficiently, sustained seizures cause damage of substantia nigra pars reticulate (SNR) and globus pallidus.[26] Interestingly, epilepsy has been reported to have inverse relationship with Parkinson's disease as incidence of seizures is less in patients with Parkinson's disease.[27,28] Seizures may lead to progressive microanatomical changes in putamen of both hemispheres.[29] As the SNR plays a major role in the modulation of seizures, the seizures may be treated with high-frequency stimulation of SNR.[30-32]

Changes in Piriform Cortex in Epilepsy

Cortical, subcortical neuronal networks play a key role in generation, maintenance, and spread of epileptic activity. The piriform cortex (PC) and amygdala generate seizures in response to chemical and electrical stimulation and as an amplifier of epileptic activity when seizures are generated elsewhere. Structural abnormalities were observed in PC in frontal lobe epilepsy.[33]

MR imaging reported that the PC amygdala is extensively damaged in chronic temporal lobe epilepsy patients, particularly in those with hippocampal atrophy.[34] Changes in the PC are responsible for complex partial seizures, i.e., the most common type of seizures in human epilepsy.[35-38]

Changes in Gray Matter in Epilepsy

It was reported that gray matter volume was associated with cognitive functions.[39] Decreased gray matter was observed in epileptic patients.[40-44] Most important area where gray matter abnormalities occurs is hippocampus. Other areas include thalamus, parietal lobe, and cingulate gyrus. Changes have also been described in the parahippocampal gyrus, middle temporal gyrus, superior temporal gyrus, inferior temporal gyrus, fusiform gyrus, temporal pole, entorhinal cortex, amygdala, and perirhinal cortex.[45-48] It was reported that abnormalities of gray matter are essential to produce reductions in episodic memory recall.[6] Most commonly seen cognitive dysfunctions due to gray matter abnormalities in children are decline in verbal intelligence quotient, freedom from distractibility, and executive function and mental slowness, memory impairment and attention deficits in commonly observed among adults.[49-51]

Changes in Glial Cells in Epilepsy

Defects in the glial cells, especially astrocytes, may cause epilepsy as they play an important role in regulation of transmission and extracellular ions.[52,53] Indeed, alterations in distinct astrocyte membrane channels, receptors, and transporters have all been associated with the epileptic state.[54]

Changes in Hypothalamus in Epilepsy

The relationships between the hypothalamic mass and the different types of seizures remain unknown.[55] Sex steroid hormone axis abnormalities occur more commonly in people with epilepsy. Release of sex steroid hormones is controlled by the hypothalamic–pituitary–gonadal axis; the medications used to treat epilepsy can have direct effects on regulation of these hormonal systems. The changes in the hormone may lead to hypogonadism and sexual dysfunction and are linked to polycystic ovary syndrome, decrease in fertility and childbirth rate, premature menopause, and thyroid disorders. It may also cause hormonal contraceptive interaction. Endogenous hormones can influence seizure severity and frequency, resulting in catamenial patterns of epilepsy.[56,57] Women who are taking antiepileptic drugs have increased risk of maternal and fetal complication; hence, good planning and effective caring is necessary during and after the pregnancy.[58] Epilepsy and sleep have reciprocal relationships, lack of sleep may lead to seizures, and seizures adversely affect the sleep pattern. Treating sleep disorders, which are potentially caused by or contributed to by autism, may impact favorably on seizure control and on daytime behavior.[59] In nearly one-third of patients, the occurrence of seizures was during the sleep state. This is caused by an intimate relationship between the physiological state of sleep and the pathological process underlying epileptic seizures. Hence, control of seizure can improve sleep. Seizures, antiepileptic drugs, and vagus nerve stimulation all influence sleep quality, daytime alertness, and neurocognitive function.[60] Cold and shiver and piloerection are rare ictal signs in focal epilepsies and are often associated with an epileptic seizure focus within the temporal lobe. Hypothalamic lesions can impact thermoregulation; hence, temperature dysregulation is commonly observed during epileptic condition.[61]

Changes in Thalamus in Epilepsy

Anterior thalamus influences memory processing and spatial navigation through its interactions with hippocampus and

cortex.[60] Other studies reported that intralaminar thalamic nucleus, the parafascicular thalamus, also contributes to behavioral flexibility, whereas the mediodorsal thalamic nucleus plays a key role in acquiring goal-directed behavior.[61] Thalamic lesions in patients with seizure disorders are wider and are associated with atrophy of limbic system.[62] Prolonged partial status epilepticus may lead to thalamic diffusion-weighted imaging hyperintense lesions, and thalamus is likely to participate in the evolution and propagation of partial seizures.[63] Further, it was observed that selective reductions in gamma-aminobutyric acid receptor subunits in thalamus may play a role in pathophysiology of absence epilepsy.[64]

Changes in Cerebellum in Epilepsy

Role of cerebellum in cognition and behavior is well documented.[65] Cerebellar atrophy was reported in patients with epilepsy.[66] Although peri-ictal changes in cerebellar perfusion was observed in epilepsy, its contribution to cerebellar atrophy was minimum.[67] Cerebellar stimulation especially in anterior lobe and thalamic region is reported to be effective in patients with seizures.[68,69]

Changes in Olfactory Cortex in Epilepsy

Primary olfactory cortex (piriform cortex) is central to olfactory identification and is an epileptogenic structure.[70] Epilepsy appears to cause a generalized decrease in olfactory functioning although increased sensitivity may occur in some epileptic patients at some time in the pre-ictal period. Other sensory modalities are also affected by the epileptic process which, in some cases, involve limbic-related temporal lobe structures. Many of the olfactory deficits previously attributed to temporal lobe resection actually exist preoperatively. Confusions in taste and unpleasant auras are associated with hyperresponsiveness of neurons, which may explain why most epilepsy-related olfactory auras are described as bad. Interesting parallels exist between the effects of the neuroendocrine system on seizure activity and olfactory function.[71]

Changes in Amygdala in Epilepsy

Following stimulation of amygdale, a full spectrum of experiential symptoms is observed in patients with temporal lobe epilepsy. Selective amygdalotomy has proved to be an effective treatment for temporal lobe epilepsy. Lateral amygdala is a nucleus of the amygdala that projects to the temporal neocortex and hippocampus. Rodent studies have shown that spontaneous discharges occur in the lateral amygdala of epileptics. In two patients, interictal spikes, spike-wave, and polyspike complexes were observed intraoperatively in the amygdala; however, evidence of its origin from the amygdale is lacking.[72] Recent research in humans have indicated that amygdala lesions may impair selective domains of affect and cognition, which are related to the appraisal of emotional and social significance of sensory events. Damage to the amygdala may cause a wide range of deficits in the appraisal of emotional and social significance of sensory events although these deficits are often variable and still poorly understood.[73]

Conclusion

We have presented the gross changes in major brain structures related to cognition deficits associated with epilepsy, which we hope will help the clinicians and biomedical researcher to further understand the epilepsy.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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