Surgical Management of Epilepsy: Emerging Paradigms

Surg Capt KI Mathai*, Lt Col SK Sengupta⁺

MJAFI 2010; 66 : 61-62

Key Words : Epileptogenesis; Chloride-cation cotransporters; Amygdalohippocampectomy; Implantable devices

Introduction

Epilepsy affects between 0.5 and 0.9 % of the world population. Despite newer antiepileptic drugs, around 30% of epileptics remain medically refractory. Contemporary understanding on the aetiopathogenesis of seizures is yet to translate to clinical paradigms. 70% of medically refractory epileptics become seizure free with surgery. Some cases remain refractory. Newer modalities of seizure control are therefore necessary.

Emerging paradigms: Seizures and Epilepsy

Neuronal hyper-excitable states, due to membrane pump disorders cause seizures. Epileptogenesis involves aberrant synaptogenesis, loss of inhibitory interneurons and the hyper excitability of individual neurons. The Central Nervous System (CNS) milieu are dynamic with synaptive realignment and neurogenesis [1].

Depolymerisation of actin allows plasticity, long term potentiation and epileptogenesis [2]. Calcium influx facilitates the depolymerisation of F-actin and new spine formation. Some compounds like FK 506 block this.

In the adult CNS, Gamma Amino Butyric Acid (GABA) ergic signalling is inhibitory. In the developing CNS and Peripheral Nervous System (PNS), GABA ergic signalling is excitatory. The polarity of GABA signalling is determined by the intracellular chloride concentration, which is determined by cation – chloride cotransporters [3]. The $\text{Na}^+\text{-K}^+\text{-2Cl}^-$ cotransporter (NKCC) mediates chloride influx while KCC2 and KCC3 extrude chloride. If the neuronal Cl^- increases, GABA becomes depolarizing. This occurs in neonatal seizures. Excitatory GABA ergic neurotransmission contributes to neurogenesis. Activation of NKCC1 is an important mechanism of cerebral edema. Blockage of NKCC1 by bumetamide reduces neuronal and glial swelling.

Brain derived neurotrophic factor (BDNF) shifts neurons to the immature phenotype. Neuro-peptide Y

(NPY) is an endogenous peptide anticonvulsant which inhibits pre-synaptic glutamate. Transfer of a gene, expressing endogenous NPY reduces seizures and arrests epileptogenesis [4]. NPY1 receptors mediate excitatory effects in the hippocampus. NPY2 receptors are mediation of the anti convulsant.

Surgical Treatment of Epilepsy

The surgical procedures for epilepsy are conventionally grouped into resective and disconnective procedures.

Resections

Temporal lobe epilepsy (TLE), occurs in a setting of perinatal or early insult to the medial temporal structures. TLE commonly demonstrates pharmacoresistance. On coronal magnetic resonance (MR) images there is a loss of hippocampal volume and T2 weighted hyper-density. Medial temporal lobe sclerosis (MTS) shows selective hippocampal neuronal loss on histopathopathology. The treatment of TLE is amygdalo-hippocampectomy. The amygdala and hippocampus are excised en bloc. Ninety percent seizure free results are expected [5].

Disconnective procedures

Disconnective procedures include hemispherotomy, multilobar disconnection, hypothalamic hamartoma disconnection and corpus callosotomy. Disconnection prevents seizures from getting generalized. In multiple subpial resections, a lattice work of subpial incisions which prevent the lateral spread of an electrical epileptic discharge is made.

Patients of intractable seizures with congenital hemiplegia, hemimegalencephaly syndromes, Sturge-Weber syndrome, hemiconvulsion - hemiplegia epilepsy and Rasmussen encephalitis may be considered for hemispherotomy.

Hypothalamic hamartomas often manifest as Gelastic

*Senior Advisor (Neurosurgery), INHS Asvini, Colaba, Mumbai. ⁺Resident (Neurosurgery), Command Hospital (SC), Pune-40.

seizures or behavioural disorders. The hamartoma can be disconnected by open surgery and by the endoscopic route.

Deep Brain Stimulation for Seizure Control

Focal brain stimulation of the cerebellum, hypothalamus and various parts of the thalamus have been used to suppress seizure activity. Similar in principle to implanted defibrillators in cardiology, they detect the abnormal electrical rhythms and trigger an aborting impulse. The patient himself, on perceiving an aura can manually trigger the aborting stimulus.

The anterior nucleus of the thalamus was used as a stimulation target in the stimulation of the anterior nucleus of the thalamus in epilepsy (SANTE) trial [7]. Implantation of devices that effuse antiepileptic drugs locally, focal cooling and transcranial magnetic stimulation have all been tried.

The vagus nerve stimulator (VNS) is a device that has received FDA approval for epilepsy control. The VNS is attached to the left vagus and can abort seizures on periodic stimulation by manual triggering.

Stem Cells in Epilepsy

Transplantation of inhibitory neurons is a potentially useful method for seizure control [8]. Restoring inhibitory mechanisms of the dentate gyrus by embryonal cell transplantation has shown efficacy in the rat model [9].

Conclusion

The strides made in the understanding of epilepsy and epileptogenesis have not yet translated into changes in practice norms. Pharmacological intervention to regulate neosynaptogenesis, better drugs to stabilize neuronal membranes and transfection with endogenous anticonvulsive peptide inducing genes are amongst

newer approaches that offer fresh promise. Surgery is a useful option in many cases. The implantation of seizure detection and termination devices is evolving.

It is hoped that the emerging paradigms will soon impact epilepsy management.

Conflicts of Interest

None identified

References

1. Wong M. Modulation of dendritic spines in epilepsy: Cellular mechanisms and functional implications. *Epilepsy Behav* 2005; 7: 567-77.
2. Ouyang Y, Wang M, Capani F. A transient decrease in F-actin may be necessary for translocation of proteins into dendrite spines. *Eur J Neurosci* 2005; 22: 2995-3005.
3. Gamba G. Molecular physiology and pathophysiology of electro neural cation chloride co-transporters. *Physiol Rev* 2006; 85: 423-93.
4. Francesco Noe, Allan- Hermann Pod, Annamario Vezzani. Neuro Peptide Y Gene therapy decreases chronic spontaneous seizures in a rat model of temporal lobe epilepsy. *Brain* 2008; 131: 1510-5.
5. Salanova V, Markland O, Worth R. Temporal lobe epilepsy surgery: Outcome, complications and late mortality rate in 215 patients. *Epilepsia* 2002; 43:170-4.
6. Guarato PP, Di Gennaro G, Mascia A, Gramaldo LG, Meldolesi GN, Picardi A. Temporal lobe epilepsy surgery : different surgical strategies after a non invasive diagnostic protocol. *J Neurol Neurosurg Psychiatry* 2005; 76: 815-24.
7. Graves NM, Fisher RS. Neurostimulation in epilepsy, including a pilot study of anterior thalamic nucleus stimulation. *Clin Neurosurg* 2005; 52: 127-34.
8. Richardson RM, Fillmore HL, Holloway KL, Braddus WC. Progress in cerebral transplantation of expanded neuronal stem cells. *J Neurosurg* 2004; 100: 659-71.
9. Alvarez-Dolado M, Colcagnotto ME, Kaskar M, et al. Cortical inhibition modified by embryonic neural precursors grafted into the post natal brain. *J Neuro Sci* 2006; 26: 7380-9.