

re-conceptualization of epilepsy as a distributed or network abnormality includes the potential to treat at sites other than the ictal onset zone, as the anterior nucleus of the thalamus stimulation trial demonstrated. Better understanding of the network abnormality is arising from resting-state imaging studies. Resting-state imaging is the identification of regions of brain activity are not elicited by functional tasks. These regions were first identified through analyses of the rest-state across a variety of task-related imaging studies, such as language and motor mapping. Although an actual rest-state actually does not exist for the brain, resting-state imaging provides insights into the background functional connectivity across regions, as can be identified with several analysis approaches, including region-of-interest (seed) based connectivity, independent component analyses, and graph theory metrics. Connectivity has now been identified as abnormal in several brain disorders. For temporal lobe epilepsy, resting-state imaging has identified differences between left and right temporal lobe epilepsy and abnormalities of increased connectivity to some regions and decreased connectivity to others. Each finding clarifies the underlying abnormality of epilepsy.

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#### How do network and neurotransmitters interact in epileptogenesis?



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It is difficult to understand when the process of epileptogenesis is complete and which mechanisms develop with time-course that produces clinically detectable epileptiform activity. Changes in network characteristics and functional connectivity are shown to be associated with epileptogenesis. Excessive neuronal synchronization is also the hallmark of epileptic discharges. Several mechanisms have been implicated in the initiation of epileptic synchronization. Hyper-synchronous synaptic transmission can spread epileptiform activity from a single neuron to different regions of the brain by recruiting local area neurons as well as distant neurons. These neurotransmitter-mediated activities will convert a normal neuronal network to an epileptogenic network. The widely accepted principle that is applied to the process of epileptogenesis is disruption of mechanisms that normally create a balance between excitation and inhibition. Any alteration in the glutamatergic and GABAergic synaptic transmission can create a micro-environment of epileptic activity which can propagate to other cortical regions. Measurement of excitatory and inhibitory postsynaptic currents, using patch-clamp technique, in slice preparations of resected brain specimens assist in investigating modulation of neurotransmission. The comparison of GABA and glutamate-mediated synaptic transmission in specimens obtained from two different regions will throw light on the magnitude of change in epileptic activity. Understanding the propagation and maintenance of the functional connectivity and network configurations through neurotransmitter mediated abnormal

synaptic activity in complex brain regions in epilepsy may open avenues for novel surgical interventions as well as for the accurate localization of the epileptic focus, thus resulting in a better surgical outcome.

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#### Endogenous activity of NMDA receptors contributes to the enhanced glutamatergic tone and hyperexcitability in resected brain samples obtained for patients with mesial temporal lobe epilepsy



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Altered excitatory synaptic transmission is one of the primary causes of seizure generation in patients with mesial temporal lobe epilepsy (MTLE). The present study is designed to delineate the contribution of glutamatergic tone under resting conditions to the hyper excitability in patients with MTLE. Resected hippocampal tissues were obtained from patients with MTLE. In these samples spontaneous excitatory postsynaptic currents (EPSCs), sensitive to NMDA receptor antagonist APV (50  $\mu$ M) and AMPA receptor antagonist CNQX (10  $\mu$ M) were recorded from pyramidal neurons at  $-70$  mV. We observed that frequency of EPSCs were 28.2% higher in slices obtained from patients with MTLE compared to that in case of non-epileptic controls. We also examined spontaneous fast current transients (CTs) recorded from these pyramidal neurons under cell-attached configuration. The frequency of CTs increased in the absence of extracellular  $Mg^{2+}$  in brain slice preparations and was completely blocked by APV. We found that the frequency of CTs in pyramidal neurons were higher in case of MTLE samples compared to nonepileptic controls. This study suggests that enhanced endogenous activity of NMDA receptor contributes to excitability in pyramidal neurons of slice preparations obtained from patients with MTLE.

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#### Ictal MEG yield in patients with drug refractory epilepsy undergoing magnetoencephalography



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**Background:** It is not uncommon for a person with epilepsy (PWE) who is referred for a magnetoencephalography to have a seizure during the procedure. The aim of this study was to