Neural epileptic activity

Neural epileptic activity refers to abnormal, excessive, or hypersynchronous neuronal activity in the brain, often associated with epilepsy. It is characterized by sudden and transient disturbances in brain function, which can result in seizures.

1. Underlying Mechanisms

Hyperexcitability: Neurons exhibit an increased tendency to fire action potentials due to imbalances in excitatory (glutamate) and inhibitory (GABA) neurotransmission. Hypersynchrony: Groups of neurons fire together in an abnormal, synchronized manner, leading to the electrical bursts observed in epilepsy. Ion Channel Dysfunction: Mutations or dysfunctions in sodium, potassium, calcium, or chloride channels can lead to abnormal neuronal firing. Neuroinflammation: Inflammatory processes may contribute to hyperexcitability and seizure susceptibility. Neuroplasticity: Chronic epilepsy can result in structural and functional changes in neuronal circuits, such as sprouting of axons or loss of inhibitory neurons. 2. Patterns of Activity Interictal Activity: Abnormal discharges occurring between seizures, often seen as spikes or sharp waves on electroencephalography (EEG). Ictal Activity: The activity observed during a seizure, typically characterized by rhythmic, repetitive discharges. Postictal Activity: The state following a seizure, often involving suppressed neural activity and cognitive impairment. 3. Localization and Spread Focal Epileptic Activity: Confined to a specific region of the brain (e.g., temporal lobe in temporal lobe epilepsy). Generalized Epileptic Activity: Involves widespread brain regions, often resulting in tonic-clonic or absence seizures. Propagation: Seizure activity may start in a focal area and spread to other parts of the brain (secondary generalization). 4. Clinical Implications Neural epileptic activity is the hallmark of epilepsy, a neurological disorder affecting millions worldwide. Seizures caused by this activity can range from mild (e.g., brief lapses in awareness) to severe (e.g., convulsions and loss of consciousness). Continuous or recurrent seizures, as seen in status epilepticus, are medical emergencies requiring immediate intervention. 5. Diagnostic Tools EEG: Used to detect abnormal electrical discharges associated with epileptic activity. Imaging (MRI, CT): Identifies structural abnormalities such as tumors, cortical dysplasia, or hippocampal sclerosis. Functional Imaging (PET, SPECT): Helps localize areas of hypermetabolism or hypometabolism related to seizure foci. 6. Therapeutic Approaches Pharmacological: Antiepileptic drugs (AEDs) aim to suppress neural epileptic activity by enhancing inhibition (e.g., benzodiazepines, barbiturates) or reducing excitation (e.g., sodium channel blockers). Surgical: Removal of epileptogenic zones in refractory cases. Neuromodulation: Techniques like vagus nerve stimulation (VNS) or responsive neurostimulation (RNS) help modulate epileptic activity. Dietary: Ketogenic and modified Atkins diets can reduce seizure frequency in some patients.

Identification

To date, the identification of objective biomarkers of neural epileptic activity (EA) remains challenging. We therefore investigated whether neuronal complexity could serve as an interictal electroencephalographic measure of EA, independent of interictal epileptiform discharges (IEDs). By tapering anti-seizure medication (ASM) during video-EEG (electroencephalography) monitoring (VEM), we studied whether changes in neuronal complexity could reliably indicate the increase in EA and identify patients with epilepsy.

Methods: The study included 27 patients with unilateral mesial temporal lobe epilepsy (TLE) and 24 control patients with non-epileptic episodes (NEEs) only, each undergoing ASM reduction during VEM. Thirteen additional patients undergoing intracranial recordings during VEM were included to study the relation of surface EEG complexity to intracranial IED. Neuronal complexity was quantified using sample entropy. Delta power served as a control parameter. Receiver-operating characteristic (ROC) analysis was used to evaluate diagnostic performance.

Results: As ASM was reduced, patients with epilepsy showed a significant decrease in neuronal complexity over consecutive days ($p = .0008$). In contrast, patients with NEE showed no significant change in neuronal complexity ($p = .78$). Delta power in contrast increased and did not differ significantly between patients with TLE and patients with NEE ($p = 1$). ROC analysis demonstrated that neuronal complexity effectively distinguished between patients with epilepsy and patients with NEE (area under the curve [AUC] = .76), whereas delta power performed at chance level (AUC = .5). Analysis of simultaneously recorded surface and intracranial EEG showed that hippocampal IEDs are followed by an increase in surface EEG delta power ($p = 1.8 \times 10\text{-}18$) without any significant change in complexity ($p = .39$).

Significance: An increase in EA caused by ASM reduction resulted in a loss of neuronal complexity in surface EEG recordings of patients with epilepsy, independent of IEDs. These findings suggest that neuronal complexity could serve as a potential biomarker to differentiate between epilepsy patients and those with NEEs only. This holds promise for improving the clinical evaluation of EA in epilepsy, addressing the limitations of seizure frequency and IED identification [1)].

1)

Kienitz R, Strüber M, Merkel N, Süß A, Spyrantis A, Strzelczyk A, Rosenow F. Neuronal complexity tracks changes of epileptic activity and identifies epilepsy patients independent of interictal epileptiform discharges. Epilepsia. 2024 Dec 12. doi: 10.1111/epi.18218. Epub ahead of print. PMID: 39666315.