WEBVTT

00:00.250 --> 00:07.000
Nerve cells or neurons constantly work to maintain an electrical charge on their surface by pumping ions out of the cell,

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creating a polarized state, meaning there's a different charge on the outside versus the inside of the cell.

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Neuron impulses, called action potentials, take place when an electrical impulse causes voltage-activated sodium or calcium channels to open, depolarizing the membrane.

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These voltage-gated ion channels are critical to the propagation of action potentials, and therefore are an important target for the development of therapeutics that modulate overactive signaling in the brain.

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The wave of depolarization travels down the axon to its terminus where it triggers the release of neurotransmitters which enable neurons to communicate with one another.

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Dysfunction in voltage-gated channels can cause serious malfunction leading to hyperexcitability in these nerve channels responsible for several forms of epilepsy, movement disorders, and pain syndromes.

01:00.750 --> 01:10.000
Epileptic encephalopathy with continuous spike and wave during sleep, which can be referred to as EE-CSWS or just CSWS,

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is a rare pediatric epilepsy that impacts less than 2% of the children living with epilepsy worldwide.

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While the underlying causes of this condition are often unknown, in some instances the disorder is caused by structural brain abnormalities, brain injury,

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or genetic mutations that make certain neurons more excitable.

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CSWS causes continuous seizures detectable on an EEG,

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typically during sleep, and may also present as clinical seizures.

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These seizures interfere with processes critical to learning and memory.

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As a result, patients experience cognitive stagnation and regression associated with the onset of an abnormal EEG pattern.

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The typical age of onset for CSWS seizures is between two and four years.

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While seizures often resolve around puberty, the neurocognitive regression can remain.

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Diagnosis is achieved by recognizing the unique EEG pattern

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for electrical status epilepticus in sleep, or ESES, and

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observing cognitive stagnation and regression in the patient.

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Scientists hypothesize that the unique pattern of CSWS is due to the interplay between inhibitory and excitatory neurons in the thalamocortical oscillatory circuit,

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a network of neurons that provide communication pathways between specific regions of the brain, which are important for sleep.

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T-type calcium channels play a key role in this circuit and the generation of spike-wave activity during sleep

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by allowing for low-threshold depolarization of neurons.

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Currently, there are no approved therapies for CSWS.

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Neurocrine is working to develop a precision medicine approach to potentially treat CSWS with NBI-827104, an investigational, orally active, potent, brain-penetrating T-type calcium channel blocker.

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By blocking overactive T-type calcium channels, specifically Cav3.1, Cav3.2, and Cav3.3,

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NBI-827104 has the potential to reduce the excitability of brain cells and the potentiated spike-wave discharges that are the hallmark of CSWS.

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Neurocrine Biosciences is currently conducting a Phase 2 study of NBI-827104 in children living with CSWS.