

# **AUTOIMMUNE ENCEPHALITIS**

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# DEFINITION OF AUTOIMMUNE ENCEPHALITIS

- ✘ Encephalitis refers to an acute inflammation of the brain
- ✘ Autoimmune encephalitis is a type of encephalitis resulting from an attack of the brain by the body's immune system

# TYPES OF AUTOIMMUNE ENCEPHALITIS

- ✘ Autoimmune Encephalitis may be triggered by infection in which case the term "**Post-infectious Encephalitis**" is used. ADEM( *Acute Disseminated Encephalomyelitis* ) is a Post-infectious Encephalitis. The illness usually follows in the wake of a mild viral infection (such as those that cause rashes in childhood) or immunizations.
- ✘ There are other types of **Autoimmune Encephalitis** resulting from an attack of the brain by the body's immune system. Some of these types of autoimmune encephalitis are identified by finding a specific antibody in blood

# TYPES OF AUTOIMMUNE ENCEPHALITIS

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## × Post Infectious Encephalitis

- + *Acute Disseminated Encephalomyelitis (ADEM)*

## × Other Autoimmune

- + *Hashimoto's Encephalitis*

- + *NMDA Encephalitis*

- + *Limbic Encephalitis*

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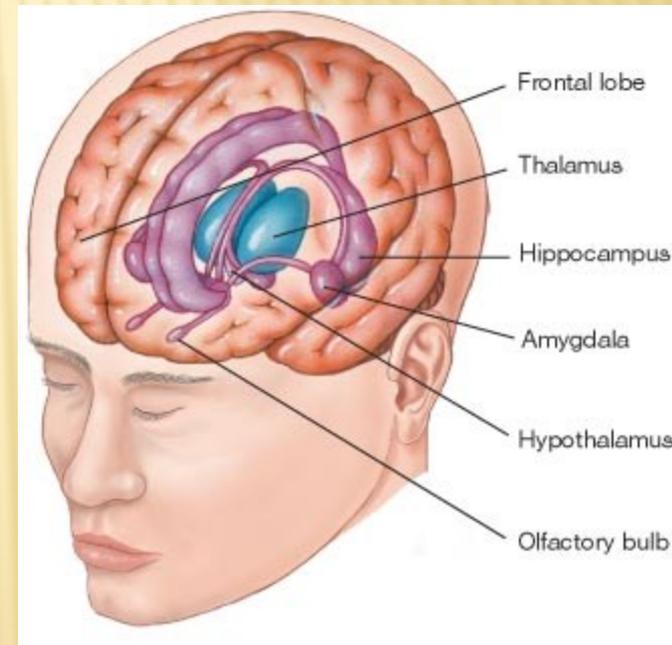
- + *Hashimoto's Encephalitis*

- + *NMDA Encephalitis*

- + *Limbic Encephalitis*

# WHAT IS LIMBIC ENCEPHALITIS?

- ✘ The main regions of the limbic area of the brain include – hippocampus, thalamus, hypothalamus, and amygdala
- ✘ The limbic area of the brain controls functions such as memory, learning, and emotions such as sexual desire, love, anger, sadness and jealousy
- ✘ The term ‘limbic encephalitis’ is used when the limbic system is inflamed (swollen) or not functioning properly



# SYMPTOMS OF LIMBIC ENCEPHALITIS

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- ✘ Memory loss
- ✘ Seizures
- ✘ Confusion
- ✘ Disturbances of sleep
- ✘ Psychological disturbances such as altered personality or behavior

# CAUSES OF LIMBIC ENCEPHALITIS

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2 main categories

- × **Infectious Encephalitis**

- × **Autoimmune Encephalitis**

Of which there are broadly 2 forms

- + *Paraneoplastic Limbic Encephalitis (PLE)*

- + *Non-Paraneoplastic Limbic Encephalitis (NPLE)*

# INFECTIOUS LIMBIC ENCEPHALITIS

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- ✘ Any infection of the brain can potentially cause an inflammation of the limbic area of the brain
- ✘ Some of the viruses particularly target the limbic system, such as the **herpes simplex virus (HSV)**
- ✘ It is sometimes also called 'Herpes Simplex Encephalitis'

# AUTOIMMUNE LIMBIC ENCEPHALITIS

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## ✘ Paraneoplastic Encephalitis (PLE)

*(Paraneoplastic refers to disease or syndrome caused by or resulting from the presence of cancer in the body but not the physical presence of cancerous tissue in the part or organ affected)*

- + Patients with cancer develop antibodies in their attempt to attack growth. When these antibodies start to react with the limbic area of the brain, it is called 'Paraneoplastic Limbic Encephalitis'
- + It is not known why the immune system starts to react with the limbic area
- + Most individuals with PLE turn out to have a **cancer of the lung, thymus gland, breast or the testis**
- + PLE can be diagnosed by testing for a group of paraneoplastic autoantibodies in the blood (we will discuss this later in detail)

# AUTOIMMUNE LIMBIC ENCEPHALITIS

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## ✘ Non-Paraneoplastic Encephalitis (NPLE)

- + Patients have symptoms similar to PLE but do not have any marker of the paraneoplastic antibodies in blood nor have any tumor
- + Caused by specific antibodies in the patients' blood that target the limbic system
  - ✘ Voltage-Gated Potassium channel (VGKC) complex antibody
  - ✘ AMPAR and GABABR antibodies
  - ✘ NMDAR antibodies

# VOLTAGE-GATED POTASSIUM CHANNEL (VGKC) COMPLEX ANTIBODY

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- ✘ VGKC antibody attacks proteins that are tightly linked within the potassium channels in the brain
- ✘ The majority of these antibodies target **Lgi1 (leucine-rich glioma inactivated 1)**
- ✘ Lgi1 is a protein that is important in controlling the electrical activity in the brain

# **LGI-1 ANTIBODY ASSOCIATED ENCEPHALITIS**

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- ✘ Symptoms and brain scan can look very similar to infectious encephalitis
- ✘ A normal CSF and a low blood salt (sodium) can assist doctors to differentiate the two conditions and prompt a test for Potassium channel complex/Lgi-1 antibody
- ✘ Potassium channel complex/Lgi-1 antibody has also been found in patients with a particular type of seizure before the onset of full-blown limbic encephalitis

# VOLTAGE-GATED POTASSIUM CHANNEL (VGKC) COMPLEX ANTIBODY

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- ✘ Antibodies against other protein in the voltage-gated potassium channel/LGi1 complex, such as **Caspr2 (contactin-associated protein 2)** and **contactin-2**, have been shown to also cause autoimmune limbic encephalitis; but this is less common.

# VGKC – DUMMY REPORT

Test Description	Observed Value	Biological Reference Interval
VGKC-Voltage gated potassium Channel Abs serum,IF	<b>NEGATIVE</b>	Negative Sample dilution - 1:10

*VGKCs are a family of voltage-gated potassium channels & are membrane proteins - Leucine-rich glioma inactivated protein 1(LGI1) & Contactin-associated protein 2 (CASPR2), responsible for controlling the cell membrane potential. Serum VGKC Ab have been detected in peripheral nervous system disease specifically associated with the clinical spectrum of acquired neuromyotonia (NMT) and cramp-fasciculation syndrome (CFS), and disorders of the central nervous system, including Morvan syndrome, epilepsy and limbic encephalitis (LE).Most cases (>80%) are not associated with paraneoplastic syndrome, however it has been observed with tumours like thymoma (around 20%) and small cell lung cancer (<5%).*

# AMPA AND GABABR ANTIBODIES

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- ✘ AMPA is a trans-membrane receptor for glutamate that mediates fast synaptic transmission in CNS
- ✘ GABA-B receptors are trans-membrane receptors for gamma-aminobutyric acid (GABA) that are linked to potassium channels
- ✘ AMPA and GABAB, are now known to be less common causes Autoimmune Limbic Encephalitis. The majority of these patients have an underlying tumour
- ✘ These patients often respond to treatment relatively well

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# NMDAR ENCEPHALITIS

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- ✘ NMDA receptor (N-methyl D-aspartate) is a protein in brain that helps control the electrical activity of the nerves
- ✘ This Encephalitis affects many more brain regions than purely the limbic system, and therefore it is not classified as a Limbic Encephalitis

# NMDAR ENCEPHALITIS- SIGNS AND SYMPTOMS

The signs and symptoms seen in patients with NMDAR antibody are distinctive

- ✘ Mainly affects **young people**; 30% of cases under 18 years of age
- ✘ **Women** are more affected than men
- ✘ At the onset most distinctive features are prominent psychiatric symptoms, seizure, confusion and memory loss. 10 to 20 days later, patients develop a movement disorder, variations in blood pressure, heart rate and temperature and may become less conscious
- ✘ The above distinctive features prompt clinicians to look for NMDAR antibody

# NMDAR ANTIBODY ENCEPHALITIS AND TUMOR ASSOCIATIONS

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- ✘ Once a patient has been diagnosed with NMDAR Ab, underlying tumor should be looked for
- ✘ While very few males have tumours detected (typically <5%), recent reports suggest that between 20 and 57% of females may have an underlying tumor
- ✘ The most common tumor found in women is called an ovarian teratoma and is a non-cancerous tumor but is thought to stimulate the production of NMDA receptor antibody.

# TREATMENT OF NMDAR AB ENCEPHALITIS

- ✘ Immune therapies and removal of tumor, if present
- ✘ As patients improve, there is a reduction in the amount of NMDAR Ab in the blood
- ✘ However, recovery is usually slow and many patients spend a few months in hospital, including time on the intensive care unit. Those who return to work typically only do so after a year or two