AUTOIMMUNE ENCEPHALITIS (AE)

What is Autoimmune Encephalitis (AE)?

- Autoimmune encephalitis is a disease occurring when antibodies produced by the body's own immune system attack receptors in the brain.
- Receptors are proteins that control electrical impulses in the brain.
- The functions of receptors are critical for judgement, perception of reality, human interaction, the formation and retrieval of memory, and the control of unconscious activities (such as breathing, swallowing, etc).

What are the symptoms of Autoimmune encephalitis?

The symptoms of AE are as follows:

- Memory deficits, including loss of short-term memory.
- Sleep disorders
- Flu-like symptoms
- Speech dysfunction
- Cognitive and behavioral disturbances – confused thinking, hallucinations, delusional thinking, disinhibited behaviors.
- Seizures
- Movement disorders
- Loss of consciousness
- Autonomic dysfunction – erratic breathing, heartbeat, and blood pressure; loss of bladder control and bowel movements.
- Vision and/or hearing may also be impaired.

What causes encephalitis?

- Common viruses: HSV, mumps, Epstein-Barr virus, HIV, cytomegalovirus
- Childhood viruses: chicken pox (very rare), measles, rubella, Arboviruses

Which are the important Diagnostic Tests for AE?

1. **NMDA** (N-methyl-D-Aspartate) Receptor Antibody, IgG,
2. **AMPA** (α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid) Receptor Antibody,
3. **GAD65** (Glutamic Acid decarboxylase **65**-kilodalton isoform) antibody.
4. **GABA** (Gamma-AminoButyric Acid)
5. **Anti-GluR-2 Antibody,** Serum
6. **VGKC** (Voltage-Gated Potassium Channel), Antibody, Serum
7. **CASPR2** (Contactin Associated Protein 2), Serum

NMDA (N-methyl-D-Aspartate) Receptor Antibody, IgG:

- It is a glutamate receptor and ion channel protein found in nerve cells or patients with autoimmune limbic encephalitis and may occur with or without associated tumor.
- The NMDA receptor is one of three types of ionotropic glutamate receptors.
- Decreasing antibody levels may be associated with therapeutic response.
- It Confirm diagnosis of anti-NMDAR encephalitis
- May be used in monitoring treatment response in individuals who are antibody positive

AMPA (α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid) Receptor Antibody:

- It is a compound that is a specific agonist for the **AMPA** receptor, where it mimics the effects of the neurotransmitter glutamate.
- AMPA receptors are responsible for the bulk of fast excitatory synaptic transmission throughout the CNS
- Its modulation is the ultimate mechanism that underlies much of the plasticity of excitatory transmission that is expressed in the brain.
- Increasing the post-synaptic response to a stimulus is achieved either through increasing the number of AMPA receptors at the post-synaptic surface or by increasing the single channel conductance of the receptors expressed.

GAD65 (Glutamic Acid decarboxylase 65-kilodalton isoform) antibody:

- It is a biomarker of autoimmune central nervous system (CNS) disorders and, more commonly, non-neurological autoimmune diseases.

GABA (Gamma-Amino Butyric Acid):

- GABA is an inhibitory neurotransmitter, which means that it weakens or slows down signals. Because of its inhibitory function,
- GABA plays an important role in anxiety.

- When nerve signals fire too quickly and carry anxiety-inducing signals, GABA acts to slow the signals down, reducing overwhelming feelings of anxiety.

Anti GluR (Glutamate receptors) antibody test:

- Glutamate receptors are the predominant excitatory neurotransmitter receptors in the mammalian brain and are activated in a variety of normal neurophysiologic processes.
- These receptors are heteromeric protein complexes with multiple subunits, each possessing transmembrane regions, and all arranged to form a ligand-gated ion channel.

VGKC (Voltage-Gated Potassium Channel), Antibody, Serum:

- Voltage-Gated Potassium Channel (VGKC) antibodies are associated with neuromuscular weakness as found in neuromyotonia (also known as Issacs syndrome) and Morvan syndrome.
- VGKC antibodies are also associated with paraneoplastic neurological syndromes and limbic encephalitis.

CASPR2 (Contactin Associated Protein 2) Antibody, Serum:

- It is a subunit of the potassium channel complex (VGKC) and is included in the group of extracellular antigens.
- Anti-CASPR2 antibodies are found in patients with the acute or subacute onset of symptoms of limbic encephalitis, peripheral nerve hyperexcitability, and neuromyotonia.

Clinical clues in the recognition of particular types of Autoimmune Encephalitis:

S.No.	Clinical Finding	Detail About Disease	Associated Autoantibody Disorders
1	**Psychosis**	Psychosis is a condition that affects the way your brain processes information. It causes you to lose touch with reality. You might see, hear, or believe things that are not real.	NMDAR, AMPAR, GABA
2	**Dystonia, chorea**	Dystonia is a movement disorder in which a person's muscles contract uncontrollably. The contraction causes the affected body part to twist involuntarily, resulting in repetitive movements or abnormal postures. Dystonia can affect one muscle, a muscle group, or the entire body.	NMDAR

3	**Chorea**	Chorea is an abnormal involuntary movement derived from the Greek word “dance”. It is characterized by brief, abrupt, irregular, unpredictable, non-stereotyped movements. In milder cases, chorea may appear purposeful. The patient often appears fidgety and clumsy.	NMDAR
4	**Hyperekplexia**	Hyperekplexia is a rare hereditary, neurological disorder that may affect infants as new-borns (neonatal) or prior to birth (in utero). It may also affect children and adults. Individuals with this disorder have an excessive startle reaction (eye blinking or body spasms) to sudden unexpected noise, movement, or touch.	GlyR
5	**Status epilepticus**	Status epilepticus (SE) is a single seizure lasting more than five minutes or two or more seizures within a five-minute period without the person returning to normal between them.	GABA
6	**New onset type 1 diabetes**	A chronic condition in which the pancreas produces little or no insulin. It typically appears in adolescence. Symptoms include increased thirst, frequent urination, hunger, fatigue, and blurred vision.	GAD65
7	**Fasciobrachial Dystonic Seizures**	Fasciobrachial Dystonic Seizure (FBDS) is a rare form of epilepsy characterized by frequent brief seizures, which primarily affect the arm and face. It has been described as the pathognomonic semiology for autoimmune limbic encephalitis (ALE) [1].	LGI1
8	**Neuromyotonia, muscle spasms, fasciculations**	Neuromyotonia (NMT) is a form of peripheral nerve hyperexcitability that causes spontaneous muscular activity resulting from repetitive motor unit action potentials of peripheral origin. NMT along with Morvan's syndrome are the most severe types in the Peripheral Nerve Hyperexciteability spectrum.	Caspr2
9	**Stiff-person syndrome and/or exaggerated startle**	Stiff-person syndrome (SPS) is a rare neurological disorder with features of an autoimmune disease. SPS is characterized by fluctuating muscle rigidity in the trunk and limbs and a heightened sensitivity to stimuli such as noise, touch, and emotional distress, which can set off muscle spasms	GAD65, GlyR
10	**Cerebellitis**	Cerebellitis is an inflammatory syndrome characterized by acute onset of cerebellar signs/symptoms (such as ataxia, nystagmus or dysmetria) often accompanied by fever, nausea, headache, altered mental status and	GAD65

		brain magnetic resonance imaging (MRI) abnormalities of the cerebellum	

Test Details:

S. No.	Test Name	Test Code	MRP	Technique	Specimen	TAT / Reported on
1.	Autoimmune Encephalitis Panel (NMDA, AMPA-Glu R1 & R2, GABA B receptor, VGKC (LGI1, CASPR2)	RP10109	21000	IFA (Immunofluorescence Assay)	2 ml. (1 ml. Min.) Serum from 1 SST (Gel tube). Separate serum in a vial & freeze.	5th working day by 7:00 p.m.
2.	NMDA (N-METHYL D ASPARATE)	RIM10366	9000		3 ml. Serum from 1 SST (Gel tube). Separate serum in a vial & freeze.	4th Working Day by 7:00 p.m.
3.	NMDA Receptor Antibody (NR1), CSF	RIM10431			3ml CSF in sterile container	
4.	VGKC (Voltage gated potassium channel)	RIM10365	9500		3 ml. Serum from 1 SST (Gel tube). Separate serum in a vial & freeze.	
5.	GAD -65 IgG Antibody Glutamic Acid Decarboxylase Antibody	RIM10214	8470	EIA (Enzyme Immunoassay)	2 ml. (1 ml. Minimum) Serum from 1 SST (Gel Barrier Tube).	5th working day by 7:00 p.m.