Anti-NMDR receptor encephalitis

Anti-NMDAR Encephalitis

What is anti-NMDA Receptor Encephalitis?

Anti-NMDA receptor encephalitis is a neurologic disease first identified by Dr. Josep Dalmau and colleagues at the University of Pennsylvania in 2007. It is an autoimmune disease, where the body creates antibodies against the NMDA receptors in the brain. These antibodies disrupt normal brain signaling and cause brain swelling, or encephalitis. It can affect both men and women, however is more common among women. It primarily affects the young, including children and young adults. Some patients also have a tumor associated with this disease; the most common type is an ovarian teratoma in women. The name of this disease describes an immune attack on the NMDA receptors and can be explained as follows:

- ***Anti-*** Autoimmune Response
- ***NMDA Receptor-*** against NMDA receptors in the brain
- ***Encephalitis-*** causing swelling and disruption in brain signaling

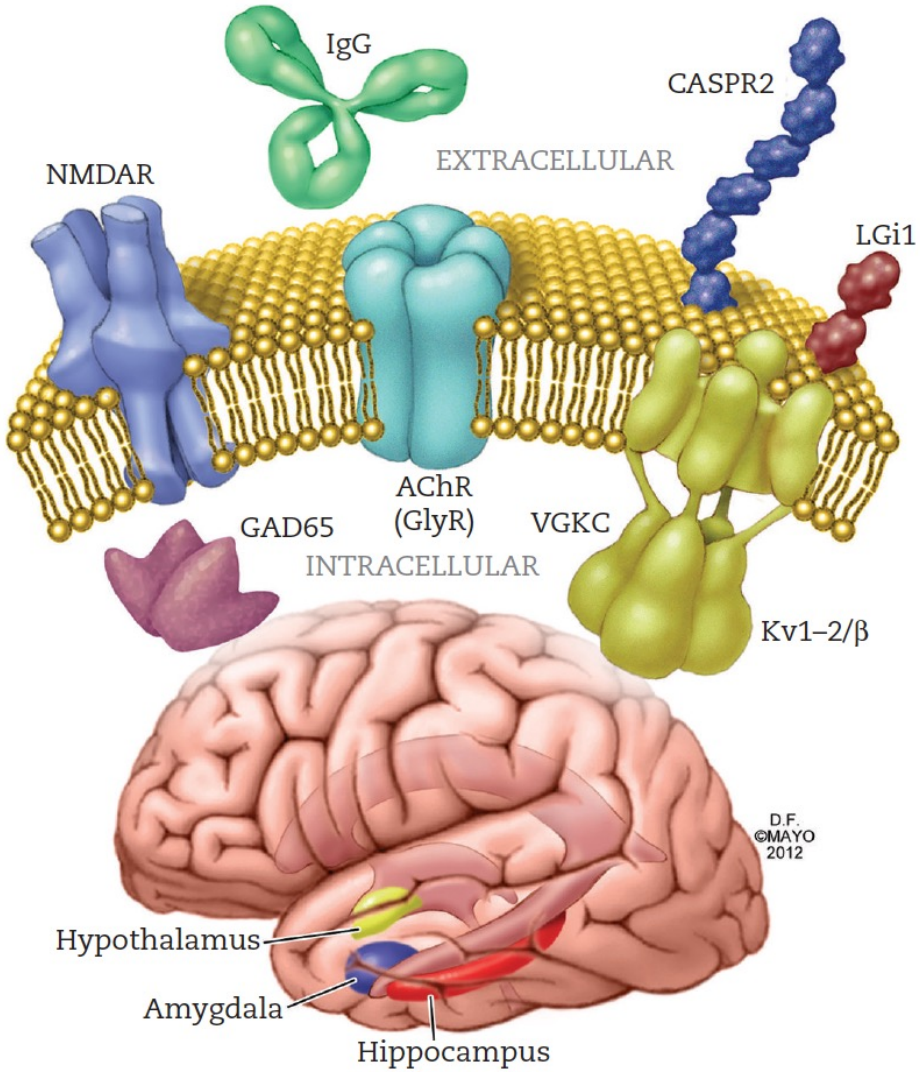


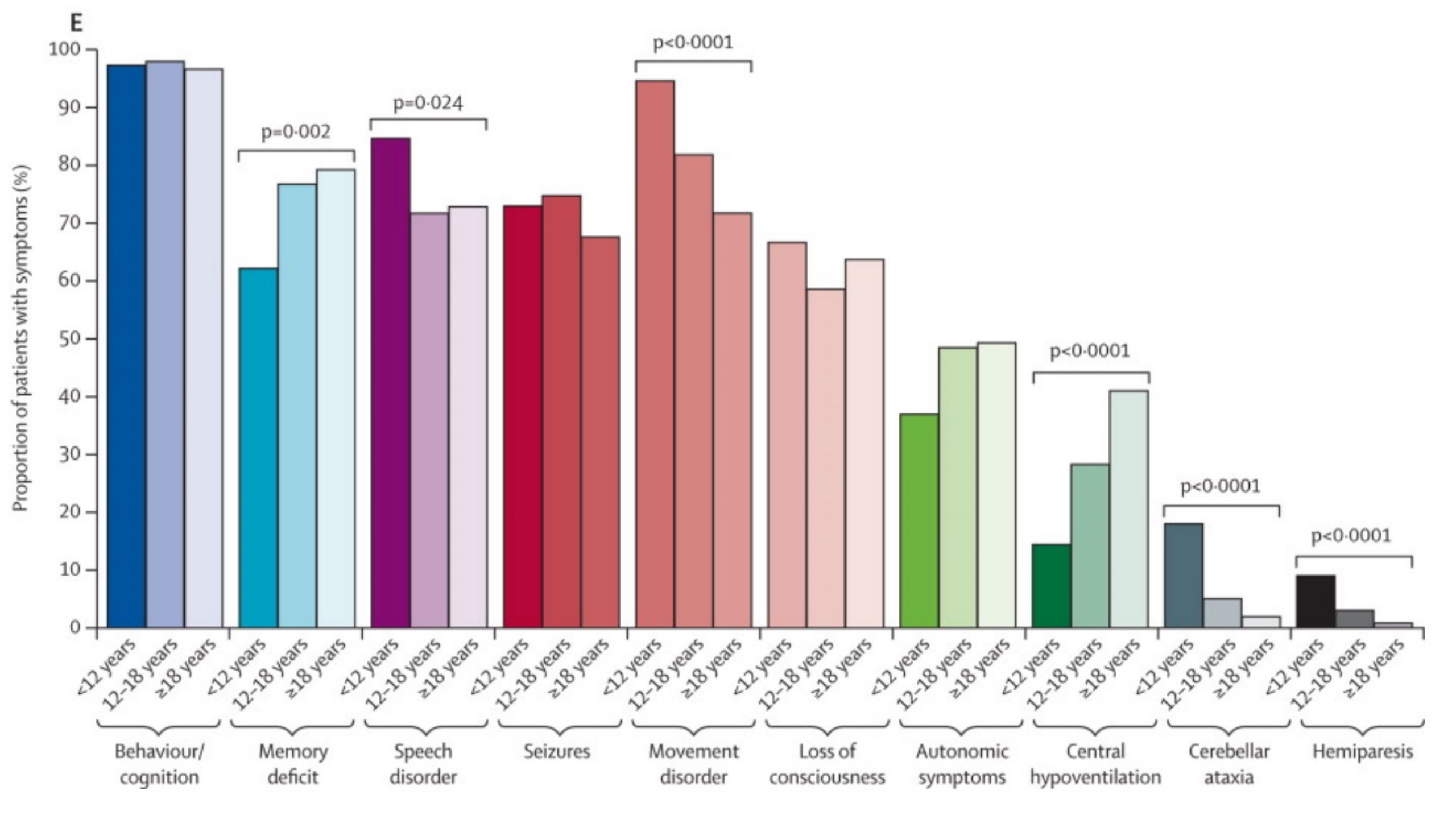
FIGURE 35.1: Main antigens causing autoimmune encephalitis.

From Wijdicks. Handling Difficult Situations. Core Principles of Acute Neurology: Oxford University Press, 2014.

Signs & Symptoms

Anti-NMDA receptor encephalitis causes a wide range of symptoms varying in severity. Patients typically start with less severe symptoms, and then rapidly progress to a condition requiring hospitalization. The list below includes the most common symptoms. Most patients with this disease exhibit nearly all of these symptoms; it is extremely uncommon for patients to have only one or two.

- Behavior (paranoia, hallucinations, aggression, etc.)
- Cognition
- Memory Deficit
- Speech Disorder
- Loss of Consciousness
- Movement Disorder (rhythmic motions with arms or legs, abnormal movements with the face or mouth)
- Seizures
- Autonomic Dysfunction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Proportion of patients with symptoms (%)
100
90
80
70
60
50
40
30
20
10
0
p=0·002
p=0·024
p<0·0001
p<0·0001
p<0·0001
p<0·0001
<12 years
12–18 years
≥18 years
Behaviour/ cognition
Memory deficit
Speech disorder
Seizures
Movement disorder
Loss of consciousness
Autonomic symptoms
Central hypoventilation
Cerebellar ataxia
Hemiparesis

Diagnostic criteria for definite autoimmune limbic encephalitis

All four of the following criteria must be met:*

1. Subacute onset (rapid progression of <3 months) of working memory deficits (short-term memory loss), seizures, or psychiatric symptoms suggesting involvement of the limbic system
2. Bilateral brain abnormalities on T2-weighted fluid-attenuated inversion recovery MRI highly restricted to the medial temporal lobes¶
3. At least one of the following:
   - CSF pleocytosis (>5 white blood cells per mm^3)
   - EEG with epileptic or slow-wave activity involving the temporal lobes
4. Reasonable exclusion of alternative causes

CSF: cerebrospinal fluid; EEG: electroencephalogram; MRI: magnetic resonance imaging.

* If one of the first three criteria is not met, a diagnosis of definite limbic encephalitis can be made only with the detection of antibodies against cell-surface, synaptic, or onconeural proteins.

¶ 18-flueorodeoxyglucose positron emission tomography (FDG-PET) can be used to fulfil this criterion and may be more sensitive than MRI for detecting medial temporal lobe abnormalities.

Treatment

Treatment of anti-NMDA receptor encephalitis can vary according to patient, but typically includes a combination of the following:

First Line Treatment:

- Tumor removal (if tumor is present)
- Steroids
- Plasma Exchange (plasmapheresis)
- Intravenous immunoglulin (IVIG)

- the most common type of tumor is an ovarian teratoma in women

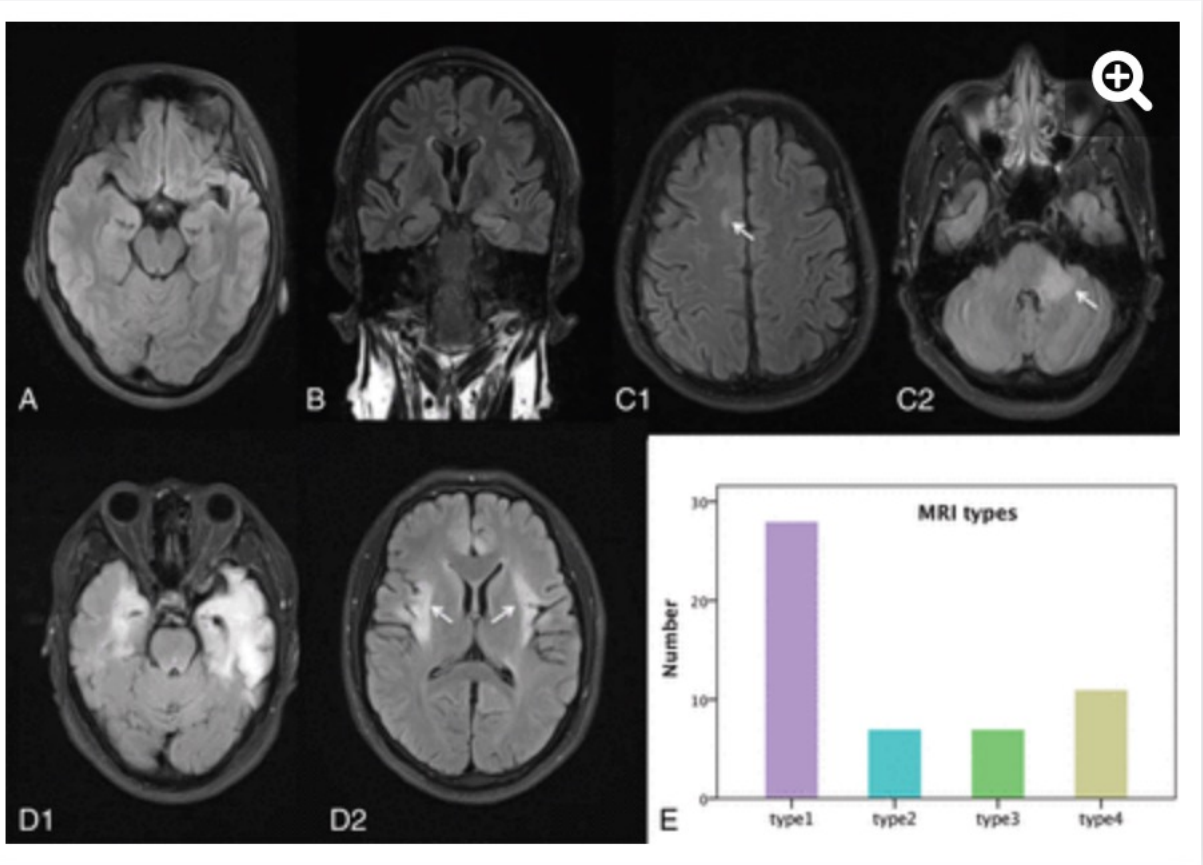
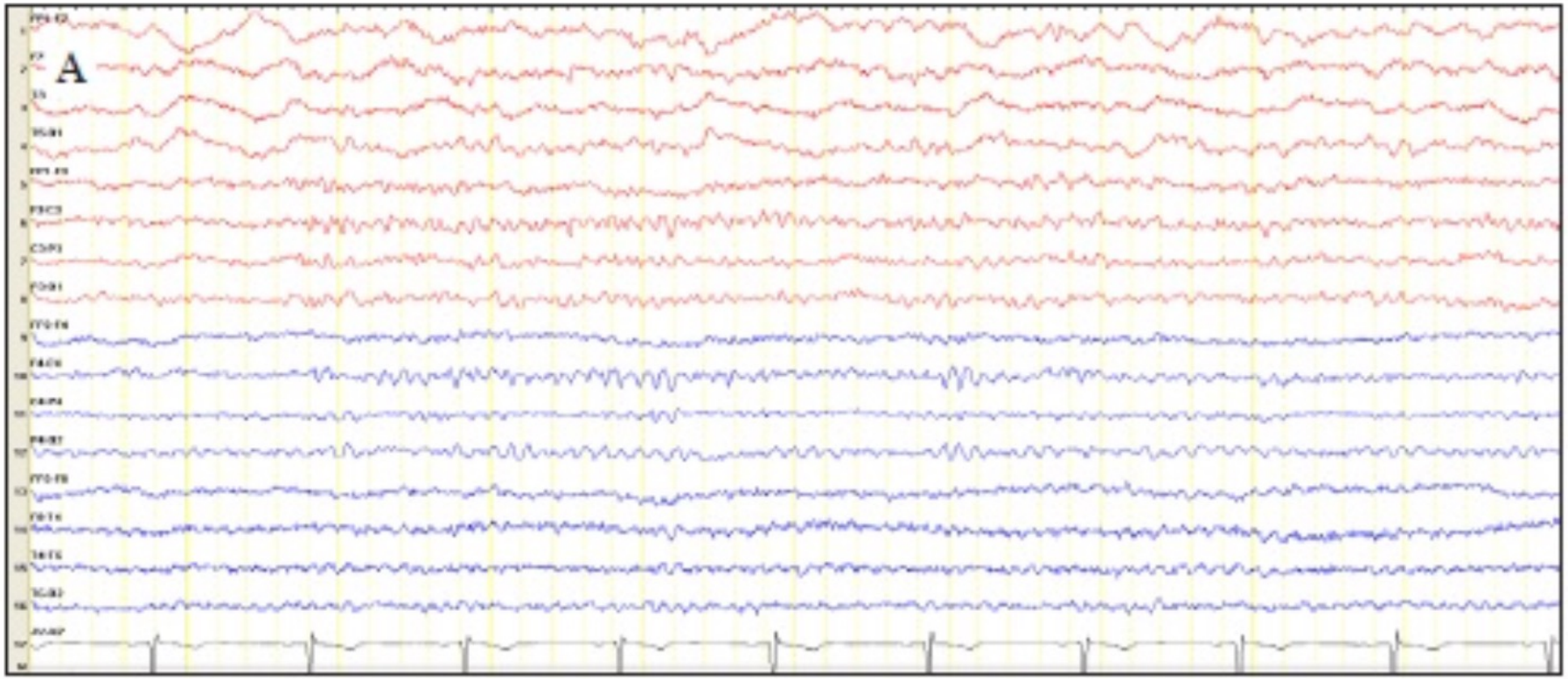
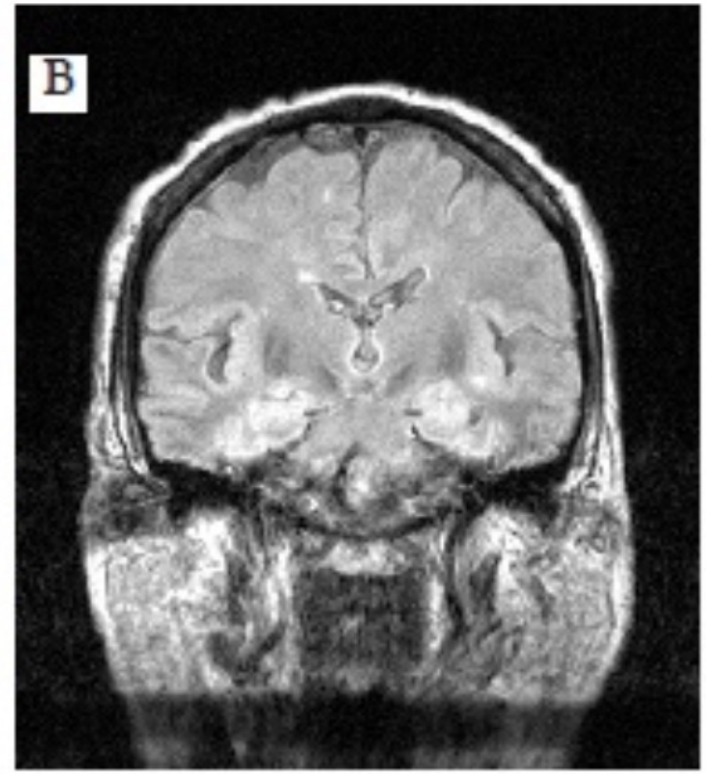


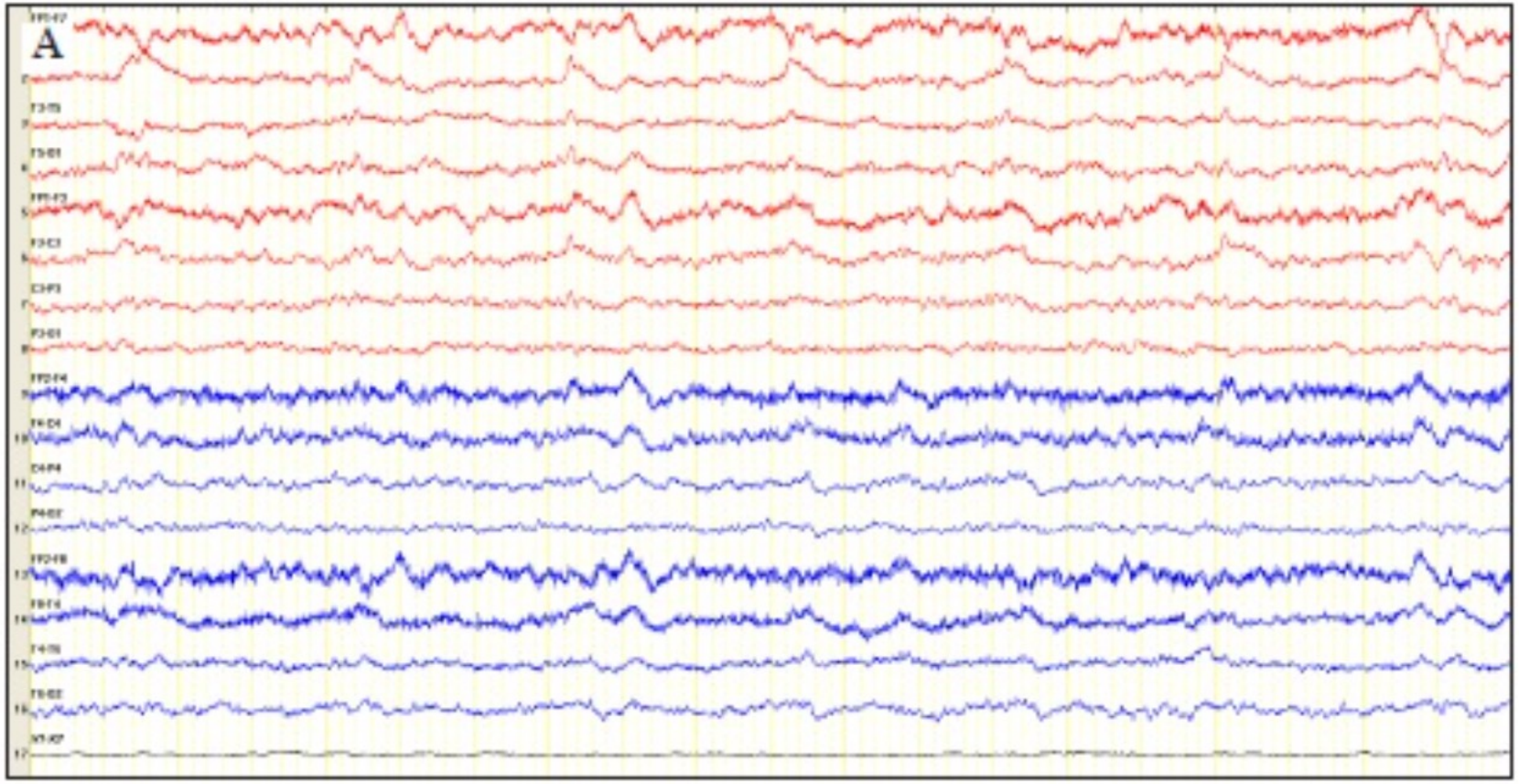
Fig 1.

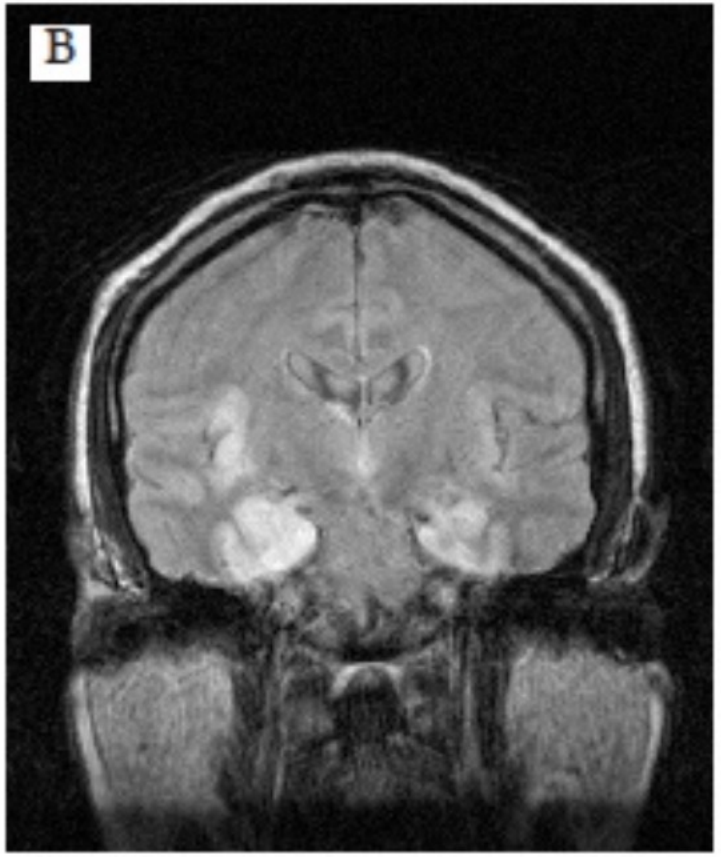
Four types of brain MR imaging appearances in patients with anti-NMDA receptor encephalitis, and the histogram o the 4 types of brain MR imaging appearance. Axial (*A*, *C*, and *D*) and coronal FLAIR images (*B*) come from 4 patients (*C1* and *C2* from same patient, *D1* and *D2* from same patient). *A*, Type 1, a 23-year-old male patient with anti-NMDA receptor encephalitis, with normal brain MR imaging findings. *B*, Type 2, a 29-year-old female patient. Lesions are in the left hippocampus with bilateral mild volume loss in the hippocampus. *C*, Type 3, a 28-year-old male patient. Lesions are in the right frontal lobe (*white arrow*) and middle cerebellar peduncle (*white arrow*) and brain stem. *D*,





Patient 1. Male, 56 years. A) EEG, longitudinal bipolar mountage: continuous slow activity in the left temporal region. B) MRI-FLAIR, coronal image: bilateral increased signal over the insula, hippocampus and temporal basal cortex.





Screenshot Male, 51 years. A) EEG, longitudinal mountage: PLEDs occuring every 3 sec in the left temporal region. B) MRI-FLAIR, coronal image: hyperintense signal over medial temporal regions, parahippocampal cortex, hippocampus and insula, with right sided predominance.

- Periodic lateralized epileptiform discharges (PLED)

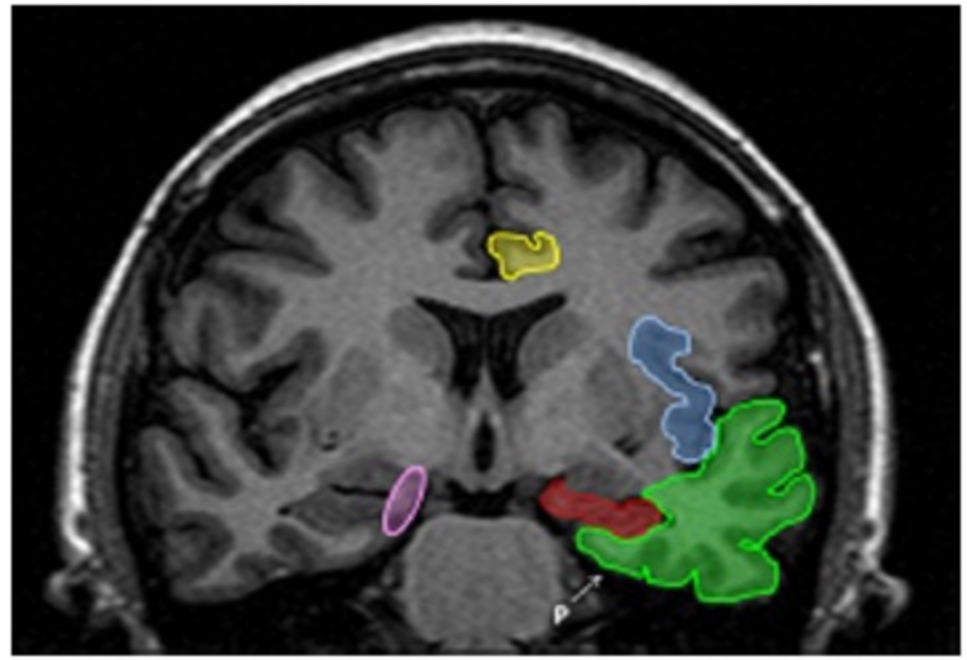


Figure 1. T1 weighted – IR (inversion recovery) coronal MRI. The structures most commonly involved of the limbic system in herpes encephalitis are identified (Yellow: cingulate gyrus; red: hippocampus; green: temporal lobe neocortex; blue: insula, pink: uncus; P: parahippocampal gyrus).

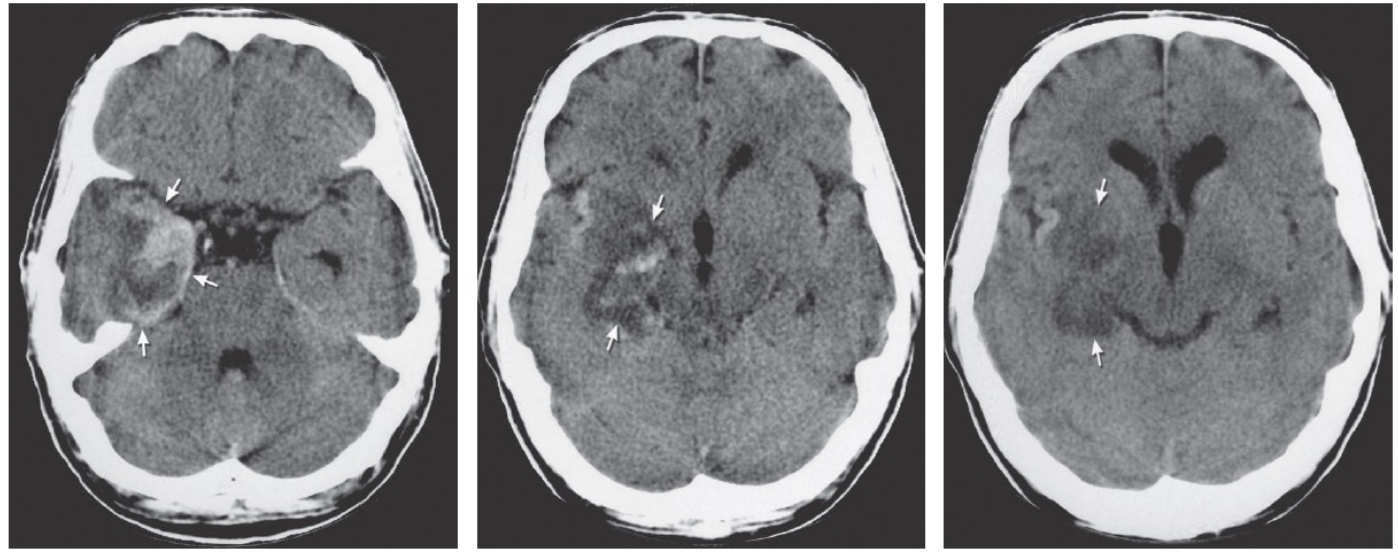


FIGURE 35.2: Herpes simplex encephalitis. Computed tomographic scans showing unilateral swollen, hypodense, and partly hemorrhagic temporal lobe lesion from herpes simplex encephalitis (*arrows*).

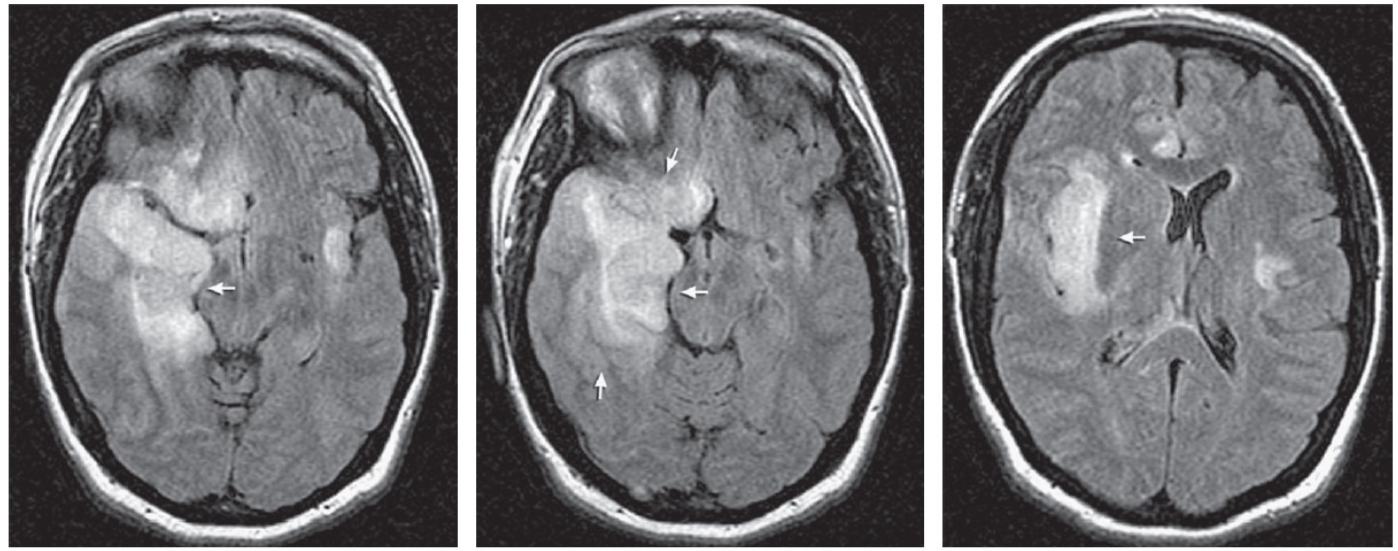


FIGURE 35.3: Herpes simplex encephalitis. Magnetic resonance images with typical hyperintensities in temporal, frontal lobe, and insular regions (*arrows*).