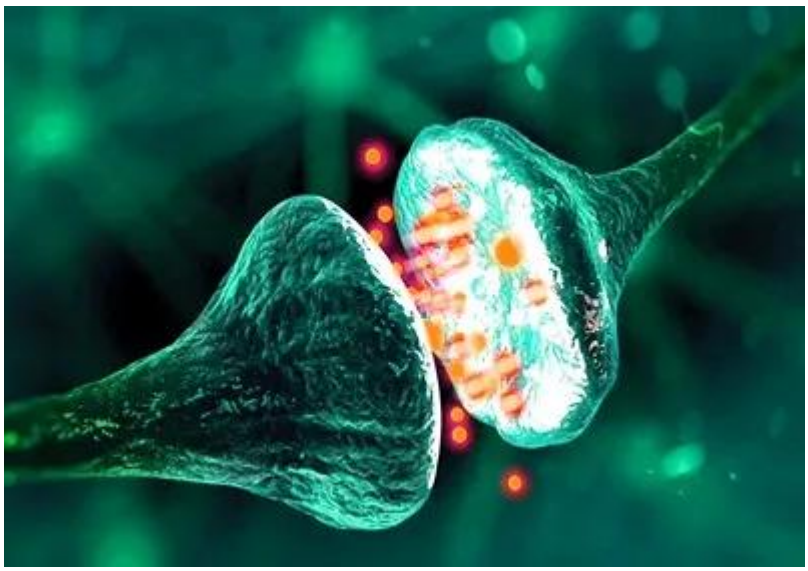
The synapses are the fundamental information-processing units in neuronal circuits. They form the basis for all brain functions by controlling the excitation-to-inhibition balance. Various cellular and molecular mechanisms underlying synapse formations have been identified. Gamma-aminobutyric acid (GABA) is an amino acid that acts as the primary inhibitory neurotransmitter for the central nervous system (CNS). GABA receptors are the main inhibitory receptors in the CNS, and they respond when GABA is released into the post-synaptic nerve terminal. In this case report, the authors from Switzerland and the United Kingdom presented a patient who developed autoimmune anti-GABAA receptor encephalitis after double autologous hematopoietic stem-cell transplantation for multiple myeloma.

GABA receptors are subdivided into GABAA and GABAB. GABA-A receptor (GABAAR) is a ligand-gated ion channel that mediates fast inhibitory synaptic transmission in the CNS. At the synapse, most GABAARs contain 2 α subunits, 2 β subunits, and 1 γ subunit, which are arranged as γ-β-α-β-α. The pharmacologic or genetic alteration of this receptor causes seizures. It has been reported that human autoantibodies to the α1 and β3 subunits are associated with seizures and *status epilepticus* in the context of autoimmune encephalitis.

The γ2 subunit is a target of autoantibodies. It is unclear whether the clinical features associated with antibodies against the γ2 subunit differ from those associated with antibodies against the α1 and β3 subunits. As the spectrum of symptoms has not been fully defined, it is important to recognize encephalitis associated with autoantibodies against GABAA receptors. The seizures may be refractory to antiepileptic drugs unless the autoimmune response is treated.
https://www.neurology.org/doi/10.1212/WNL.0000000000003713



The case of anti-GABAA receptor encephalitis

The 57-year-old male patient developed several neurological symptoms, including rapid progressive gait instability, memory deficits, hypomania, and recurrent complex tic-like involuntary outbursts of vocalization. He underwent double autologous hematopoietic stem-

cell transplantation for multiple myeloma 15 and 18 months before the symptom onset.

The cerebrospinal fluid (CSF) examination showed 19 mononuclear cells/µL. Brain magnetic resonance imaging (MRI) findings demonstrated progressive multifocal cortico-subcortical T2/FLAIR-hyperintensities, whereas fluorodeoxyglucose–positron emission tomography (PET)/computed tomography (CT) findings showed a high metabolic activity.

Histopathological analysis of a biopsied lesion demonstrated sparse inflammatory changes in cortico-subcortical areas.

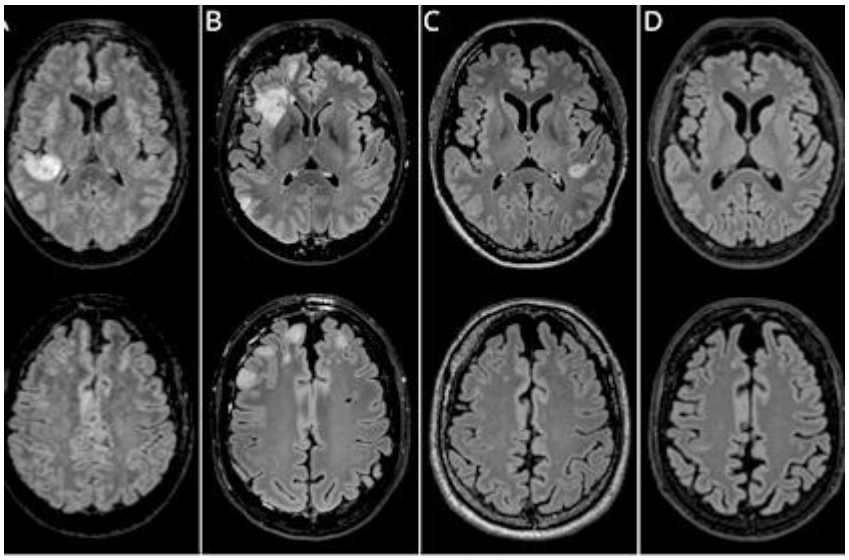


Illustration from original article of Togni CL al, Neurology 2024. Axial MRI (A) on admission (day 0) with multiple, asymmetric, cortical/subcortical FLAIR lesions without contrast enhancement; (B) on day 20 with progression of lesions; (C) on day 33 with incomplete regression; and (D) on day 159 with complete remission of all lesions.

Within the next two weeks, the patient developed continuous rhythmic myoclonic jerks in the left hand (“myoclonia continua”), initially with, and later without epileptic activity on electroencephalography.

Differential diagnoses, such as intracerebral viral, malignant, demyelinating, or other autoimmune diseases were excluded and the patient was diagnosed with autoimmune encephalitis associated with autoantibodies against GABAA receptors, presumably triggered by aberrant posttransplant immune reconstitution.

The patient was treated with corticosteroids, a plasma exchange, and rituximab. Within several months, he almost fully recovered.

Conclusion

The authors concluded that it is important to recognize encephalitis associated with autoantibodies against GABAA receptors because seizures may be refractory to antiepileptic drugs unless the autoimmune response is treated.

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Journal Reference

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