

PSYCHIATRIC MANIFESTATIONS OF AUTOIMMUNE ENCEPHALITIS

Autoimmune encephalitis is a disorder in which antibodies accidentally created by the immune system attack parts of the brain. This can lead to inflammation and nerve damage.

WHY WE DID THIS WORK

Psychiatric problems are common in autoimmune encephalitis and can imitate mental health conditions, for example psychotic illnesses like schizophrenia. It is important to separate patients with AE from those with mental illness as treatments are very different.

There are different subtypes of AE. Some cases are due to the presence of detectable auto antibodies (a protein targeting the person's own nerve endings) which is known as 'sero positive' AE. In 'sero negative' AE, there is no detectable antibody when using currently available techniques for detection.

Within the 'sero positive' group are different AE categories depending on the type of antibody. We discuss this further in the next section.

ANTI-NMDAR ENCEPHALITIS

- The most common type of AE and typically occurs in young women. Psychiatric problems are the presenting feature in most patients and many are seen first by a psychiatrist. Symptoms start abruptly and progress rapidly over days to weeks.
- Common features include psychosis (disruption of person's thoughts and perceptions that can make it difficult for them to understand what is real versus what is not real). They can present with hallucinations (seeing or hearing things that are not there) and paranoia (false beliefs; for example believing that people are out there to get you, or having unfounded mistrust of others), agitation, and elevated mood. Occasionally, anti NMDAR encephalitis patients can present with catatonia (complete lack of movement or lack of communication). Almost 90% of patients develop other related neurologic features (including seizures, abnormal movements and speech, and drowsiness) within a month. However, some may have only psychiatric problems without neurologic signs.

ANTI-LGI1 ENCEPHALITIS

- The second most common AE and typically affects older males. Seizures are usually the first symptom and often occur before patients develop psychiatric and/or memory problems. These seizures can be very brief, i.e. seconds long, and subtle (face and arm twitching known as "faciobrachial dystonic seizures"), but can be very frequent (up to 100s of times per day).
- Memory difficulties develop slowly over months and may be accompanied by disinhibition (actions or words that might seem inappropriate or rude or inconsiderate).
- They can also present with compulsive behaviors (performing an action persistently repetitively), including excessive eating, cleaning and hoarding.
- Psychotic symptoms such as hallucinations and paranoia can occur but are less common, and usually are not an early or major feature.

ANTI-CASPR ENCEPHALITIS

- Involves confusion, memory difficulties and 'slow' thinking which may be associated with depressed mood. Memory problems can slowly worsen over 12 months or longer in a proportion of patients. These individuals may appear like they have dementia.
- Psychotic symptoms such as hallucinations, delusions and paranoia can occur as inflammation of the brain worsens, and usually develop with other neurologic symptoms including seizures, unsteadiness and abnormal jerking and twitching movements.

ANTI-AMPA ENCEPHALITIS

- Typically presents with short-term memory problems, confusion and behavioural changes which get worse over weeks to months.
- Psychotic symptoms are variable (20-90% of patients) and may be associated with manic (abnormally elevated or extreme in mood, emotions, energy or activity levels)

Red Flags for Autoimmune Encephalitis in Psychiatric Presentations

- Preceding physical symptoms such as fever, headache, stomach upset and dizziness
- Seizures
- Neurologic symptoms such as abnormal movements, speech difficulties, clumsiness, weakness and changes in sensation
- "Catatonic" features such as abnormal posturing, repeating another person's speech (echolalia), lack of movement or erratic movements
- Memory problems
- Psychotic symptoms that start rapidly and/or worsen quickly

Table 1 - Red Flags for psychiatric presentation

ANTI-GABA-A ENCEPHALITIS

- Most commonly presents with seizures.
- Memory loss and confusion develop slowly over weeks to months and are associated with personality and behavioural changes in approximately half of patients.
- Features of psychosis with hallucinations and paranoia are uncommon but can occur later in severe cases.

ANTI-GABA-B ENCEPHALITIS

- Commonly presents with seizures.
- Memory difficulties, confusion and abnormal behaviour develop with or after seizures start.
- Patients often become depressed and/or anxious at a later stage, usually 1 to 2 years after other symptoms have started.
- Memory difficulties are slow to improve and may remain even after treatment.
- Psychosis is not a feature.

References

Hannah Ford, Sarah Griffith, Nicola Warren, Adrew Swayne, Stefan Blum, Helmut Butzkueven, Terence J. O'Brien, Dennis Velakoulis, Jayashri Kulkarni, Mastura Monif. Psychiatric manifestations of autoimmune encephalitis. *Autoimmunity Reviews*. 2022; Volume 21, Issue 9, 103145,

AUTOIMMUNE ENCEPHALITIS CAN PRESENT WITH A VARIETY OF PSYCHIATRIC SYMPTOMS AND CAN SOMETIMES MIMIC PRIMARY PSYCHIATRIC DIAGNOSIS. HENCE UNDERSTANDING THE OVERLAP BETWEEN AE AND PSYCHIATRY IS IMPORTANT TO DELINEATE THE PRIMARY DRIVING CONDITION AND MANAGE THE PATIENT APPROPRIATELY.

ANTI-DPPX ENCEPHALITIS

- Preceded by diarrhoea and weight loss for several months, followed by mild, slowly worsening memory and cognitive difficulties associated with depression and anxiety.
- Months or even years later patients develop psychotic features including hallucinations, delusions and aggression with neurologic symptoms such as seizures, limb shaking and jerking.

ANTI-MGLUR5 ENCEPHALITIS

- A rare type of AE with three major features – psychosis, memory problems and drowsiness.
- Patients experience headaches, fevers, weight loss and nausea followed by rapid onset of memory problems, slowed thinking and severe psychiatric symptoms including hallucinations, depression, anxiety and major mood swings.
- Many different neurologic symptoms can occur, including seizures, abnormal movements and difficulty using the eyes and face.

ANTI-NEUREXIN-3A ENCEPHALITIS

- The disorder develops quickly over several days with headaches, fevers and nausea, followed by confusion and agitation.
- Patients then experience severe neurologic symptoms of drowsiness, abnormal movements, seizures and breathing problems.

DIAGNOSIS AND TREATMENT

- Features (“red flags”) that may indicate AE as a cause of psychiatric presentation are shown in table 1.
- Diagnosis of AE is challenging, and is confirmed by identifying the antibody in the blood or fluid from around the brain and spinal cord (cerebrospinal fluid), however these tests are not always available and may take a long time to return. Other test results that indicate AE may be the cause of psychiatric symptoms include high white cells or inflammation in cerebrospinal fluid, abnormal brain imaging on MRI and abnormal brain electrical activity on EEG (electroencephalogram; refer to our previous summary on EEG in AE diagnosis here: <https://autoimmune-encephalitis.org/wp-content/uploads/2022/07/PLS-Using-Electroencephalogram-for-quicker-diagnosis.pdf>)
- Early treatment of AE can lead to partial or full recovery.

WHAT DO THE FINDINGS MEAN?

- Each subtype of AE presents with different psychiatric features. Our research can help clinicians identify patients with psychiatric symptoms due to AE rather than a mental illness.
- Early consideration of AE as a differential for psychiatric presentations is important as patients respond well to appropriate treatment (immunotherapy), particularly if given early.
- Further studies are needed to continue describing the syndromes associated with each subtype. Fast and accurate testing for the diagnosis of AE is an important area for future research.



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References

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