Neuropsychiatric Systemic Lupus Erythematosus (NPSLE)

Connective tissue diseases and related disorders are chronic inflammatory diseases characterized by abnormalities and, in some cases, even complete failure of immune responses as the underlying pathology. Nearly all connective tissue diseases and related disorders can be complicated by various neuropsychiatric syndromes. Systemic lupus erythematosus (SLE) is a typical connective tissue disease that can cause neurological and psychiatric syndromes. Neuropsychiatric syndromes can result when SLE affects the central or peripheral nervous system. Neuropsychiatric systemic lupus erythematosus, or NPSLE, refers to the neurological and psychiatric manifestations of systemic lupus erythematosus.

Signs & Symptoms

The diagnosis of NPSLE is one of the most difficult challenges in medicine, because it can involve so many different patterns of symptoms, some of which may be mistaken for signs of infectious disease or stroke. The American College of Rheumatology identifies 19 neuropsychiatric syndromes associated with systemic lupus erythematosus:

Central nervous system

1. Aseptic meningitis
2. Cerebrovascular disease
3. Demyelinating syndrome
4. Headache (including migraine and benign intracranial hypertension)
5. Movement disorder (chorea)
6. Myelopathy
7. Seizure disorders
8. Acute confusional state
9. Anxiety disorder
10. Cognitive dysfunction
11. Mood disorder
12. Psychosis

Peripheral nervous system

14. Acute inflammatory demyelinating polyradiculoneuropathy (Guillain-Barré syndrome)
15. Autonomic disorder
16. Mononeuropathy, single/multiplex
17. Myasthenia gravis
18. Neuropathy, cranial
19. Plexopathy
20. Polyneuropathy

Each of the 19 syndromes listed above are also stand-alone diagnoses, which can occur with or without lupus. The most common lupus-related nervous system symptoms of SLE include **seizures**, **severe depression**, and and **stroke**.

Causes

The development of NPSLE depends on genetic, environmental, and hormonal factors. Despite decades of research, our understanding of how SLE causes these neuropsychiatric syndromes is not very clear. In many cases, it may be due to autoantibodies (antibodies that are against our own body). These antibodies, under certain conditions, are able to reach the brain and cause inflammation. In other cases, the problems are due to the release of proteins that cause inflammation within the brain. Strokes can occur in patients that have antiphospholipid antibodies in their blood. These antibodies are known to increase risk for blood clots which are usually the cause of stroke. ***Figure 1***, illustrates the possible pathogenesis for NPSLE.

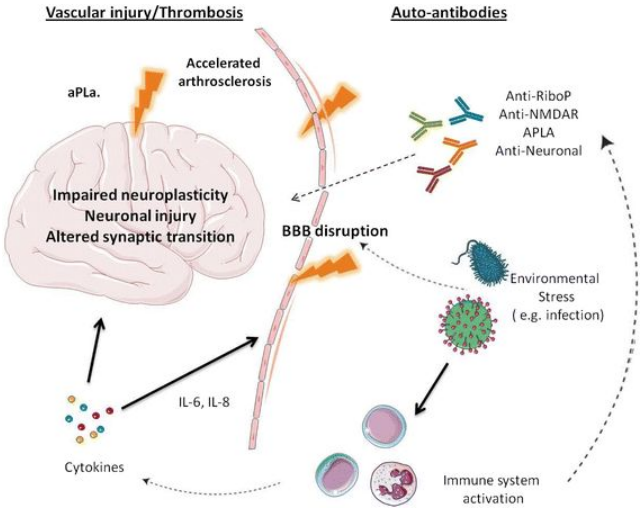

Figure 1 *- Proposed pathogenesis of NPSLE. Auto-antibodies enter the brain causing neuronal damage, including impaired neuroplasticity and synaptic transition. In order to reach the brain, the blood–brain barrier (BBB) must be transiently breached by external (e.g. infection) or internal (e.g. metabolic derangement, cytokines) triggers. Vascular injury can be antibody mediated by anti-phospholipid (aPL) antibodies or via accelerated classical atherosclerosis.*

Testing & Diagnosis

For diagnosis of NPSLE, it must be determined whether neuropsychiatric symptoms are indeed caused by SLE, whether they constitute a separate condition, or whether they are an adverse effect of SLE treatment. In addition, onset of neuropsychiatric symptoms may happen prior to the diagnosis of lupus.

Tests which aid in diagnosis include:

- Imaging studies
    - MRI - see ***Figure 2***
    - Functional MRI
    - PET scan
    - Diffusion tensor imaging - see ***Figure 3***
- Electrophysiological studies (e.g. EEG - see ***Figure 4***)
- Psychiatric evaluation
- Autoantibody tests

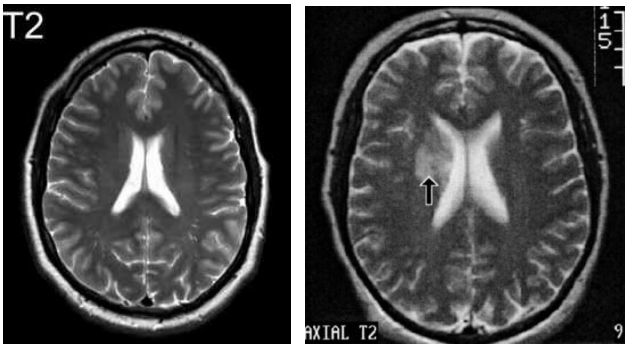

Figure 2 - *MRI of a normal brain (left) vs. a patient with longstanding SLE (right). The image on the right shows an area of ischemia (an inadequate blood supply) in the right periventricular white matter.*

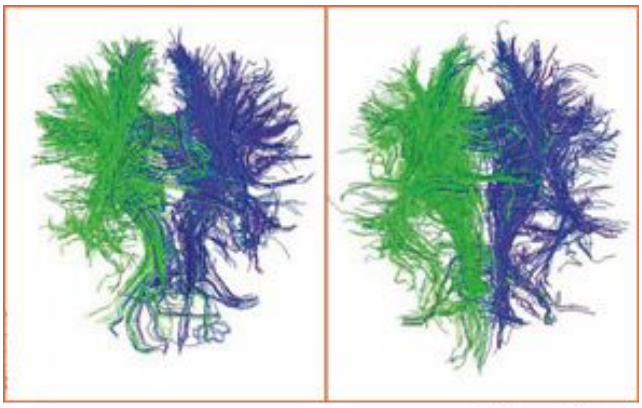

Figure 3 *- DTI showing white track connections in a normal brain (left) and a patient with SLE (right). In the patient with SLE, the quantity of tracks is less than that in a normal person.*

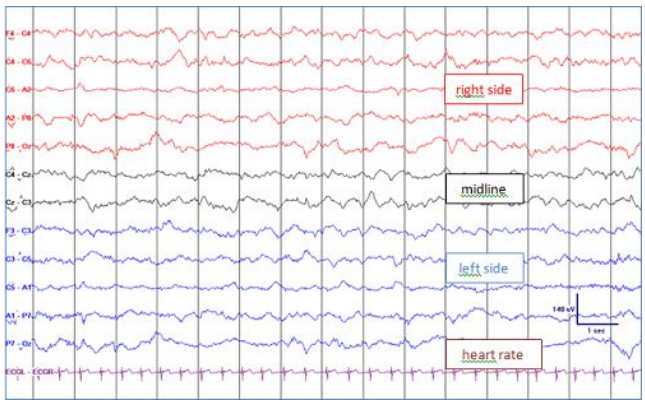

Figure 4a *- A normal EEG trace of someone that is awake. The activity of right side of the brain is represented by red lines (channels) and the left side is represented by blue lines. The heart rate is registered at the same time and demonstrated in the last trace (in violet).*

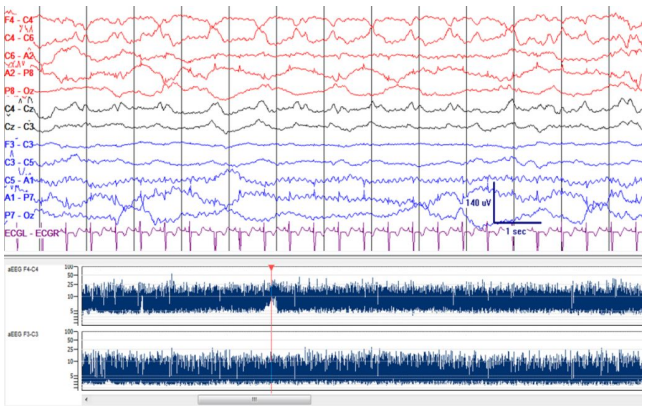

Figure 4b *- Multichannel EEG showing the rhythmic activity of a seizure (first two red channels). Below this, the time-compressed, amplitude integrated EEG is projected; the time cursor in red indicates the position of the chosen time segment. In the upper aEEG trace you can see a change of the lower band limit with the seizure.*

Treatment

Management of NPSLE is similar to the management of neuropsychiatric disease in patients without lupus. The treatment of NPSLE depends on the underlying syndrome and its cause. When the problem is due to very active lupus (flaring), the disease is treated with steroids and immunosuppressive drugs (such as cyclophosphamide, mycophenolate mofetil, azathioprine etc). In strokes that are due to blood clots, blood thinners are used, when there is no contraindication. Seizures due to lupus are also treated with anti-seizure medications.