

## Clinical Implications of Neuropsychiatric Lupus (NPSLE)

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Systemic lupus erythematosus (SLE) is the prototype multisystem autoimmune disease. Onset is primarily in women of childbearing age, with a 3:1 female to male ratio. The hallmark of SLE is the presence of autoantibodies, specifically antinuclear antibody and anti-dsDNA, anti-Smith (Sm), and antiphospholipids. Many other non-specific antibodies are also identified in patients with SLE.

The most common clinical features of SLE are mucocutaneous (malar rash, discoid lupus, alopecia, mucosal ulcers), non-erosive arthritis, and renal disease. Although less common, neuropsychiatric manifestations remain the most puzzling for understanding their pathophysiology, particularly for global manifestations such as psychosis, acute delusional symptoms and organic brain syndrome. These usually occur early in the course of SLE in the setting of other clinical features of active lupus, however they may present without other evidence of active lupus and without abnormal findings in CSF or brain MRI. Seizures and cognitive dysfunction may be explained in some cases by vascular abnormalities (CVA, atherosclerosis, hypertensive crisis), infection, or metabolic disturbances, although these manifestations of NPSLE may result from inflammatory responses to numerous brain-reactive autoantibodies. Unfortunately the presence of these autoantibodies in the peripheral circulation correlates poorly with actual NP manifestations, and availability of CSF is often limited.

Recent studies in Professor Henri Tiedge's laboratory have led to the identification of serum antibodies to brain cytoplasmic RNA in several of our SLE patients with a history of seizures during episodes of active lupus but not in SLE controls without CNS disease or in patients with other medical conditions.