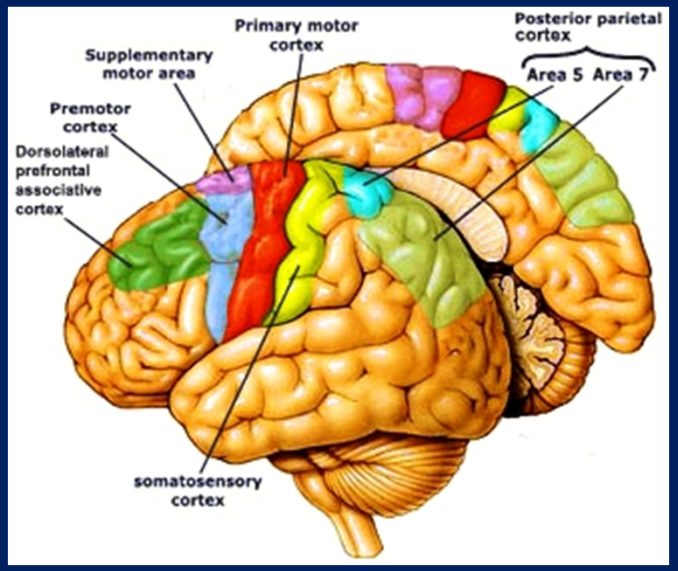
Clinical Problems / CNS Disease in Systemic Autoimmunity



Physicians in Uskadar 1
Istanbul, Turkey
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Pathophysiology:

- Autoantibody mediated vascular or direct neuronal injury
- CNS production of inflammatory mediators
- Accelerated atherosclerosis

ACR Criteria for the Classification of SLE

Central Nervous System – Brain & Spinal Cord

Cognitive dysfunction
Headache
Mood disorder
Anxiety
Psychosis
Acute Confusion-Delirium
Demyelinating syndrome
Seizures
Aseptic meningitis
Movement disorder (chorea)

Cerebrovascular disease

Myelopathy

Peripheral Nervous System

Cranial neuropathy
Polyradiculopathy
Plexopathy
Autonomic disorder
Mononeuropathy

Polyneuropathy

Myasthenia gravis

Diagnostic and therapeutic challenge:

- Work-up is unclear
- Therapy is empiric
- Prognosis after the NP event is difficult to determine

EULAR diagnostic recommendations:

- New symptoms and signs of CNS dysfunction need to be evaluated as if the dx of SLE does not exist
  - Structural –
  - Metabolic
  - Endocrine
  - Infectious
  - Iatrogenic – drugs
- Evaluation
  - LP, CSF
  - Imaging MRI (Flair, GAD, mag resonance arteriog-MRA)
  - Neuropsych; EEG

EULAR treatment recommendations:

- If non-SLE-related causes are excluded then **glucocorticoids and immunosuppressive** (in for example ACS, aseptic meningitis, myelitis, cranial and peripheral neuropathies and psychosis)
- **Antiplatelet/anticoagulation** therapy for those with antiphospholipid antibodies, particularly in thrombotic CVD- also useful for primary prevention
- Treat complications and aggravating factors
  - infection,
  - hypertension
  - metabolic
- Treat neurological disease
  - Anticonvulsants for acute seizures but not for prevention
  - Antidepressants for depression
  - Antipsychotics for thought disorder

Novel applications like B-Cell Depletion require controlled experiment

- Saito K, et al. Lupus 12: 798, 2003 Rituximab (375mg/m^2) anti-CD20 useful in life threatening refractory SLE with kidney and brain involvement – success
- Faria RM, Isenberg DA, Rheumatology 44: 561, 2005. See also letter Lupus 19: 1256, 2010. Second to use anti-CD20 – two episodes B cells depleted and recovery after third treatment died with sepsis
- Tokunaga M, et al. Ann Rheum Dis 66:470,2007. 10 patients with refractory NP-SLE B cells depleted associated with recovery; no relapse in 5 > 1 year.

Primum non nocere

- Progressive multifocal leukoencephalopathy (PML) – reactive JC (polyoma) virus is described with the use of natalizumab, rituximab, and efalizumab. Natalizumab is associated with 1:1000 incidence of PML after 18 months of therapy, while the mean interval between the most recent use of rituximab and the diagnosis of PML is 5.5 months