Cerebral volumetry in patients with systemic lupus erythematosus presenting neuropsychiatric manifestations

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Background: Systemic lupus erythematosus (SLE) involves the most extensive clinical and serologic diversity among the autoimmune diseases. Nervous system involvement occurs in up to 70% of SLE patients at some time during the course of the illness. The heterogeneity of clinical presentations makes a definitive diagnosis of neuropsychiatric SLE very difficult, since no gold standard marker has been available for such investigation, and the diagnosis has primarily been based on the clinical picture. Cerebral atrophy has been described to occur in systemic lupus erythematosus (SLE) with elevated frequency, especially in SLE patients with neuropsychiatric manifestations (NPSLE).

Objectives: This study was aimed at evaluating the brain volume of SLE patients presenting or not neuropsychiatric manifestations, in the absence of focal vascular lesions, using magnetic resonance imaging (MRI). In addition, we investigated the association of MRI findings with the active NPSLE manifestations, corticosteroids diary dose, disease activity, degree of accumulated damage by the SLE, and presence of autoantibodies.

Methods: A total of 58 patients with SLE (35 active NPSLE and 23 non-NPSLE) and 61 healthy controls were studied. Complete clinical and laboratory evaluations were performed in all patients. MRI scans were obtained through a standardized protocol. The clinical association was performed by a group composed of rheumatologist, neurologist, and psychiatrist who analyzed the clinical manifestations of NPSLE patients and the MRI findings. Anti-dsDNA, anti-Sm, anti-cardiolipin, and anti-β2 glycoprotein I antibodies were detected by enzyme-linked immunosorbent assay (ELISA). Disease activity was assessed by the SLE Disease Activity Index (SLEDAI), and the degree of accumulated damage by the disease was assessed by the SLICC/ACR (Systemic Lupus International Collaborating Clinics Damage Index approved by the American College of Rheumatology).

Results: The white matter volume and cerebral parenchyma volume were reduced in NPSLE patients (p<0.001). Reduced white matter volume was associated with higher prevalence of antiphospholipid antibodies (77%, p<0.005), diurnal dose of corticosteroid (p<0.05), accumulated damage (p<0.0001) in comparison with non-NPSLE patients, and healthy controls. The subgroup of NPSLE patients with seizures and/or cerebrovascular disease have greater loss of brain volume when compared with the subgroup of NPSLE patients without seizures and/or cerebrovascular disease (p<0.001). Abnormalities MRI were detected in higher frequency not only in NPSLE patients (82.8%), but also in non-NPSLE patients (43.4%). However, when the clinical neuropsychiatric manifestations were compared with the MRI findings it was observed a perfect match only in 37.1% of the NPSLE patients.

Conclusion: The impairment in the neuropsychiatric SLE is associated with loss of white matter, and reduction of brain volume. These findings are also associated with the presence of antiphospholipid antibodies, use of corticosteroids, and chronic cumulative damage. These associations were more significant in seizures and/or cerebrovascular disease subgroup. For the diagnosis of NPSLE, MRI showed a good sensitivity, but a low specificity indicating that other procedures must be used to confirm this diagnosis.

References


Structural and metabolic abnormalities in bipolar I vs II disorder from combined voxel-based morphometry MRI and (18)F-fluorodeoxyglucose PET brain imaging

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Objectives: Bipolar I disorders (BD I) has poorer cognitive function and worsening treatment outcome than bipolar II disorders (BD II). However, the clinical manifestations of these two disorders are often mixed. More recently, the prevalence of BD II has been increased and become a popular illness. To differentiate these two disorders, not from clinical observation only, is very important. Using multiple neuroimaging modalities, few studies reported before, may help to delineate subtypes of bipolar disorders. We aimed to investigate the structural and metabolic differences in the brain between remitted BD I and BD II, using voxel-based morphometry (VBM) and 18F-FDG (fluorodeoxyglucose) positron emission tomography (PET).

Methods: Thirty-five remitted outpatients (BDIIBDII = 17/18) received VBM study, while twenty-four patients among them (BDIIBDII = 12/12) received another PET study. Remitted was defined as both 17-item Hamilton Depression Rating Scales kept lower than 7 and Young Mania Rating scales (YMRS) scores lower than 9 for at least 2 weeks after treatment. Well-matched healthy controls (n=28) without major medical and mental disorders were also recruited. T1-weighted magnetic resonance (MR) images were acquired by a 1.5 T GE scanner and PET images by a 64-slice PET/CT GE scanner. MR images were processed by a VBM procedure for statistical inference (p<0.001) of the inter-group differences. MRI-coregistered PET data were analyzed on a volume-of-interest basis delineated by using Automated Anatomical Labeling template, and p<0.05 was deemed as statistical significance.

Results: Demographic and illness variables including age (40.8±12 vs. 41.7±13), gender (more female than males, ratio around 5/3), age at onset (30±10.7 vs. 32.9±12.6) and duration of illness (9.8±10.5 vs. 10.2±8.5) as well as episodes of mania (3±2.3 vs. 2.6±2.5) and depression (3.8±2.7 vs. 4.1±2.9), between BD I and BD II were comparable except M/D ratio (0.9±0.6 vs. 0.65±0.4) (p<0.05) in both imaging studies. Compared to BD II and normal subjects, BD I patients presented decreased gray matter volume in right thalamus, right inferior frontal gyrus and
left insula. BDII patients exhibited smaller right middle cingulum versus normal subjects, yet BD I was not. PET analyses showed significantly lower metabolism in BD I, including right thalamus, left superior frontal gyrus and right middle cingulum, as compared to BD II. BD I also showed a widespread hypometabolism versus HC, including left insula, left anterior cingulum and bilateral superior, middle and inferior frontal gyrus.

**Conclusions:** Pathophysiology and neurocircuitry underlying subtypes of BD may be quite different and only account for more cognitive deficits and poorer outcome in BD I disorder. Smaller gray matter volume and lower metabolic activity of the right thalamus were identified in BD I compared with BD II. Furthermore, decreased gray matter volume was not always atrophic changes with decreased metabolism. These results suggest a possible role of using neuroimaging studies to identify a biomarker in differentiating subtypes of BD, providing treatment direction and predicting clinical outcome and improving quality of life.

**References**

