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 by a 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 SLE and, presence of autoantibodies.

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), diary dose of corticosteroid (p < 0.03), 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.

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 (18)F-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 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 (30.1±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 may 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.

P1.e.031 Effect of EMDR treatment in PTSD patients: clinical and biological outcomes are stable in 1-year follow-up

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Some studies suggest that pharmacotherapy can promote increase in hippocampal volume [1,2] in Post-Traumatic Stress Disorder (PTSD) subjects. Other studies suggest that also psychological treatment, for instance Eye Movement Desensitization and Reprocessing (EMDR) can be effective in the treatment of PTSD and that the clinical effects of EMDR can be maintained at a 35-month follow-up [3].

Purpose of the study: Aim of the present study is to evaluate the long-term effects of EMDR treatment on brain structure and on PTSD symptoms, in drug-naive patients with PTSD.

Methods used: The study was articulated in three phases. During Phase I, ten patients with PTSD were examined with Magnetic Resonance Imaging (MRI) in order to evaluate the volumes of total brain, grey matter and both hippocampi. PTSD diagnosis was assessed with the Structured Clinical Interview for DSM-IV Patient Version (SCID-P) and the severity of PTSD symptoms was established by means of Clinician Administered Post-Traumatic Stress Disorder Scale (CAPS). The EMDR treatment followed standard guidelines defined by Shapiro and was given in a 90-minute session. After six months of EMDR treatment, all PTSD patients were re-evaluated with MRI and CAPS (Phase 2). Finally, one year after the end of the therapy, five patients underwent a new evaluation with MRI and CAPS (Phase 3).

Results: Statistical analysis of the data was carried out, and a p less than 0.05 was chosen to indicate statistical significance. Volumetric data were analyzed with repeated measures Analysis of Variance. Group means and SD of hippocampal volumes for each Phase are as follows: for Phase 1 [left (mean 2876.23 [SD 309.41]), right (mean 3144.59 [SD 388.39])]; for Phase 2 [left (mean 3145.70 [SD 371.33]), right (mean 3408.72 [SD 448.95])]; and for Phase 3 [left (mean 3192.18 [SD 420.57]), right (mean 3515.24 [SD 517.54])]. The ANOVA showed a significant difference in hippocampal volumes among the three Phases [F(2,8) = 11.63, p = 0.048] and between hippocampal side (left vs. right) [F(1,4) = 9.87, p = 0.027]. However, no interaction between side and Phases was found (p = 0.774). In addition, no differences were found on total brain volume and grey matter among the three Phases. Detailed analyses were carried out with a paired sample t-test. Detailed statistical analyses showed that patients treated with EMDR showed a non significant increase on left hippocampus between Phase 1 and Phase 3 [t = -2.32, df = 4, p = 0.081] and a significant increase in right hippocampus between Phase 1 and Phase 3 [t = -3.52, df = 4, p = 0.024]. EMDR treatment led to a significant reduction in PTSD symptoms, as evaluated with CAPS total score (Phase 1, 72.00 [SD 20.03]; Phase 3, 13.40 [SD 13.31] [t = 7.38, df = 4, p = 0.002]).

Conclusions: The results indicate that EMDR treatment appears to be associated with both an increase of hippocampal volume and an improvement of PTSD symptoms, and that the effects of EMDR have a long-term nature. These promising results suggest considering the potential long-term effects of psychotherapy on both the neurobiology and the clinic of PTSD.

References

P1.e.032 Gray matter volume reduction in right middle temporal gyrus and orbitofrontal cortex in panic disorder – a voxel-based morphometry MRI study

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Introduction: In regard to current neurobiological theories, the temporal and frontal lobe play a pivotal role in etiology of panic disorder (PD). In an earlier performed quantitative volumetric MRI study we have found a volume reduction of temporal lobes and right frontal lobe in patients with panic disorder [1]. Amygdala-hippocampus complexes were normal. In the present study we reanalyzed the same sample with a more advanced approach (voxel-based morphometry). The aim of this study was to assess the exact localization of the above mentioned abnormalities.

Methods: Seventeen inpatients with PD and a group of healthy control subjects (HC) matched for age and gender were enrolled in the study. A voxel-based morphometric approach as implemented in SPM5 was used. Voxel-by-voxel one-way ANOVA was performed with modulated gray matter (GM) images to test for differences between controls and patients with panic disorder in regional GM volume. Only voxels with absolute GM values above 0.20 entered the analysis. A predefined mask image was applied, which consisted of frontal and temporal lobe as well as amygdala-hippocampus complex to test our a-priori hypothesis and to confer