Perfusion Weighted MR in NPSLE

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Introduction

Systemic lupus erythematosus (SLE) is an autoimmune disease caused by antibodies acting against cellular components and DNA fragments of the patient. Up to 70 percent of SLE patients develop neuropsychiatric (NP) symptoms and are classified as NPSLE patients. It is still unknown whether these NP symptoms are directly initiated by neuronal damage caused by antibodies or are secondary to (global or focal) ischemia. It has been suggested that in SLE patients, ischemia could be caused by endothelial damage by anti-endothelial antibodies and increased circulating inflammatory mediators.(1;2) Another possible cause of vascular problems in SLE could be that antiphospholipid antibodies are leading to hypercoagulability by binding to anti-thrombotic substances in the blood.(3) The few SPECT and perfusion weighted MRI studies hat have been performed in NPSLE patients have shown patchy hypoperfusion abnormalities. (4;5) One recent SPECT study suggested that regional perfusion abnormalities in the thalamus correspond with neuropsychiatric symptoms.(6) However, in non of these studies cerebral blood flow (CBF), mean transit time (MTT) or cerebral blood volume (CBV) values were compared. Also, the influence of disease activity on these perfusion abnormalities has not been studied. The aim of the present study was to determine the CBF, MTT and CBV of white matter, gray matter and the thalamus in active and inactive NPSLE patients to determine whether these parameters indeed reflect changes which are seen in global or focal ischemia.

Materials and Methods

We applied bolus-tracking perfusion MR in 16 NPSLE patients with active disease (mean age 39.2 y sd 13.9 y, 12/4 f, mean disease duration 8.1 y sd 7.4 y), 27 with inactive disease (mean age 36.7 y sd 11.8 y, 23 m/3 f; mean disease duration 10.3y sd 9.1y) and 11 control subjects (mean age 50.9 y, sd 11.8 y, 6m/5f). Controls were recruited from subjects who underwent MRI because of routine follow-up of small acoustic nerve tumors. Control subjects did not have any further abnormalities on MRI. Bolus-tracking perfusion MR parameters were: 9 slices of 6 mm thickness, FOV 250 mm, scan matrix 89x55, segmented EPI (5 shots), TR 400 ms, TE 30 ms, flip angle 90 degrees, 25 ml of Gd-DTPA was injected at 5 ml/sec and this injection of contrast agent was followed by a saline chaser of 15 ml at 5 ml/s. Scans were processed on an off-line workstation using circular SVD (7). The arterial input function (AIF) was manually determined in the medial cerebral artery, after which CBF, MTT and CBV maps were reconstructed. Anatomical scans were manually segmented, resulting in ROIs of the gray and the white matter as well as the thalamus on both sides. These ROIs were co-registered to the CBF, the MTT and CBV maps and the mean pixel intensity was determined for each ROI. Since only the shape and not the amplitude of the AIF could be measured, the CBF and CBV were normalized for each patient with respect to the CBF of white matter (set at 24 ml/100ml/min). (8) One-way ANOVA and post-hoc Bonferroni analysis was used to test for significant differences among control subjects, active and inactive NPSLE patients.

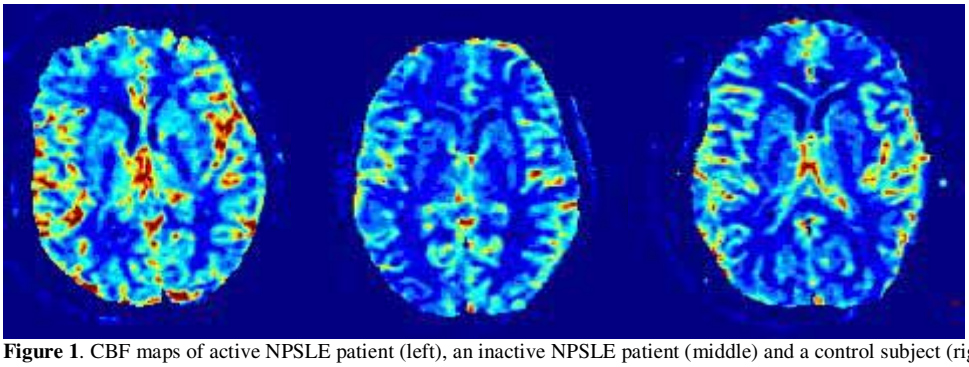

Figure 1. CBF maps of active NPSLE patient (left), an inactive NPSLE patient (middle) and a control subject (right).

Results

There was no significant difference in CBF in gray matter or in the thalamus between all three groups. The CBF of gray matter in inactive patients was 50.2 ml/100ml/min, (sd 6.7 ml/100ml/min) in active patients 50.4 ml/100ml/min (sd 6.0 ml/100ml/min) and in controls 47.0 ml/100ml/min (sd 3.7 ml/100ml/min). The CBF of the thalamus in inactive patients was 62.4 ml/100ml/min (sd10.6 ml/100ml/min) , in active patients 61.2 ml/100ml/min (sd 11.3 ml/100ml/min) and in controls 56.3 ml/100ml/min (sd 9.2 ml/100ml/min). Typical examples of CBF maps in all three groups are shown in figure 1. The previously reported patchy areas of hypoperfusion could not visually be replicated in our study. Inactive NPSLE patients demonstrated lower MTT values in the thalamus (5.6s) compared to control subjects (6.1s, $p<0.05$) and to active NPSLE patients (6.0s, $p<0.05$). In the gray and white matter no significant differences were found. There were no differences in CBV in the gray or white matter nor the thalamus between all three groups.

Discussion

In patients with global or focal cerebral ischemia the MTT is typically prolonged, whereas the CBF (hypoperfusion) is reduced, sometimes accompanied by increased CBV (vasodilatation). By comparing NPSLE patients with control subjects none of these typical ischemia perfusion abnormalities were observed. Therefore, our findings do not indicate widespread ischemia in acute NPSLE patients. Effects of medication as well compensatory mechanisms to longstanding disease processes possibly explain the reduction of the MTT in the thalamus of inactive patients. A limitation of the current study is the use of a scan protocol that has a relatively low temporal resolution and some inherent sensitivity to T1-effects. However, these aspects would influence both patient and control groups and will therefore not change the inter-group comparisons. In conclusion, our findings do not suggest that widespread ischemia is involved in the etiology of NP symptoms of active SLE patients. The origin of the changes in patients with longstanding inactive disease needs to be studied further.

References

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