A MOLECULAR NETWORK FOR FATIGUE IN PRIMARY SJÖGREN’S SYNDROME


Objectives: The underlying mechanisms for fatigue are not completely understood, but may influence fatigue through complex networks (IL-1b-related signaling are essential, we wish to investigate how molecules that influence IL-1β activity may influence fatigue through complex networks (IL-1β, IL-1Ra, IL-1RII, IL-6, and S100B). We also hypothesised that the neuropeptide hypocretin-1 (Hcrt1), a regulator of sleep and wakefulness, could be an element in a network for fatigue.

Methods: In cerebrospinal fluid (CSF) from 49 patients with pSS, Hcrt1 was measured by RIA and the other proteins by ELISA. Fatigue was rated using the fatigue visual analogue scale (IVAS), and results analysed by univariate-, multiple regression, and principal component analysis (PCA).

Results: It was possible to measure IL-1β due to low concentrations in CSF. In simple univariate regression analysis with fatigue as a dependent variable a significant association was observed for depression (R²=0.20, p<0.01), and pain (R²=0.23, p<0.01) and the biochemical variable IL-1Ra (R²=0.19, p<0.01). With multiple regression with IVAS as dependent variable a model was obtained with depression, pain, and IL-1Ra as significant contributors (R²=0.37; p<0.001). In multiple regression with fVAS as dependent variable a model was obtained with depression, pain, and IL-1Ra as significant contributors (R²=0.37; p<0.001). In depression, pain, and IL-1Ra as significant contributors (R²=0.37; p<0.001). In multiple regression with fVAS as dependent variable a model was obtained with depression, pain, and IL-1Ra as significant contributors (R²=0.37; p<0.001).

Conclusions: The S1P1 pathway is involved in the regulation of EPC differentiation by type I IFNs. Defects in S1P1 signalling pathway in lupus EPCs may contribute to the development of endothelial dysfunction in SLE.

References:

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classification of the disease by pathological conditions. However, the association with MFG-E8 expression and clinical features of SLE patients is not fully understood.

**Objectives:** To clarify the clinical significance of MFG-E8 in SLE, we analysed the correlation between the expression level of MFG-E8 in circulating phagocytic leukocytes and clinical parameters of the patients.

**Methods:** We selected patients with no history of NP symptoms and 6 HCs were recruited (all female). All subjects underwent NP testing and DCE-MRI on a 3.0 tesla magnet (Siemens Healthineers, GERMANY). MRI sequences were acquired according to standard protocols; permeability imaging used DCE technique with axial 3D-SPGR T1-WI sequences and 80 cine phases using TR=25 ms, TE=3.8 ms, FOV=24 mm, and matrix size of 128x256. Magnevist Gadolinium contrast (Bayer Healthcare, GERMANY) was dosed IV at 0.1 mmol/kg, at 5cc/sec following a 5 s delay. Post-processing of images into BBBB parameters of K-trans (mL/100 gm/min) and VE (mL/100 gm) was performed using Olea Sphere 2.2, 2.3.

**Results:** A total of 108 cases were enrolled, consisting of 36 active (mean age: 44.2±18.6, female: 80.6%, nephritis: 69.7%), 38 inactive SLE and 24 HC cases. The absolute number and the proportion of MFG-E8-positive-monocytes to total monocytes were significantly higher in the active SLE group (p<0.01), whereas serum MFG-E8 level showed no significant difference among the group. Notably, the proportion of MFG-E8-positive-monocytes to total monocytes was observed in the patients with cutaneous or musculoskeletal involvement or leukocytopenia. In addition, the proportion of MFG-E8-positive-monocytes to total monocytes significantly decreased from the baseline in active SLE patients after 6 months treatment and increased concordantly with disease activity in 6 refractory cases.

**Conclusions:** Our study indicate that the proportion of MFG-E8-positive monocytes to total monocyte in peripheral blood was positively associated with disease activity of SLE and may be a novel mechanistic biomarker to determine the disease activity.

**REFERENCES:**

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**DEMONSTRATES HIPPOCAMPUS PERMEABILITY IN SLE**

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**Background:** Cross-reactive, anti-dsDNA/N-methyl d-aspartate receptor antibodies (DNRAb) have been implicated in the pathogenesis of cognitive impairment in SLE. The mouse model demonstrates selective effects of DNRAb on hippocampal neurons following blood brain barrier (BBB) breach. We previously identified abnormal hippocampal glucose hypermetabolism in SLE patients that correlated with serum DNRAb titers and poor performance on neuropsychological (NP) testing. However, little is known about how antibodies access brain in humans.

**Objectives:** BBB permeability (BBBP) in SLE and healthy control (HC) subjects was evaluated with DCE-MRI. We hypothesised that brain areas with abnormal hypermetabolism in SLE subjects would also demonstrate altered BBBP.

**Methods:** 6 SLE subjects with no history of NP symptoms and 6 HCs were recruited (all female). All subjects underwent NP testing and DCE-MRI on a 3.0 tesla magnet (Siemens Healthineers, GERMANY). MRI sequences were acquired according to standard protocols; permeability imaging used DCE technique with axial 3D-SPGR T1-WI sequences and 80 cine phases using TR=25 ms, TE=3.8 ms, FOV=24 mm, and matrix size of 128x256. Magnevist Gadolinium contrast (Bayer Healthcare, GERMANY) was dosed IV at 0.1 mmol/kg, at 5cc/sec following a 5 s delay. Post-processing of images into BBBB parameters of K-trans (mL/100 gm/min) and VE (mL/100 gm) was performed using Olea Sphere 2.2, 2.3.

**Results:** BBB permeability was standardised with the arterial input function centred in the cavernous ICA segment for all subjects. Analyses: Regions-of-interest (ROI) from previously identified hypermetabolic regions (hippocampus, orbitofrontal cortex, posterior putamen/globus pallidus/thalamus) were selected. Mirror ROIs were placed in bilateral MRI cerebral hemispheres for sampling at same brain levels. Regional DCE curves were generated to compare permeability phases. T-tests were used to evaluate demographic and NP testing differences.

**Conclusions:** Our study indicate that the proportion of MFG-E8-positive monocytes to total monocyte in peripheral blood was positively associated with disease activity of SLE and may be a novel mechanistic biomarker to determine the disease activity.

**REFERENCES:**

**Disclosure of Interest:** None declared