

**CLINICAL ASSOCIATIONS OF COGNITIVE DYSFUNCTION IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)**

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**Background:** Cognitive symptoms are commonly reported by SLE patients, but the prevalence and clinical associations of cognitive dysfunction (CD) is poorly understood.

**Objectives:** To examine the relationship between SLE disease parameters and CD.

**Methods:** Patients with SLE were consecutively recruited from 2018-2020. Cognitive assessment was performed using the one-hour conventional neuropsychiatric test battery recommended by the American College of Rheumatology for SLE. Three binary definitions of CD and seven cognitive test z-scores were included in analysis. Clinical parameters included disease activity (SLEDAI-2K) and damage (SDI). Multivariate regression analysis was performed to determine associations with cognitive endpoints using variables with p < 0.1 on univariate testing; likelihood ratio tests were used to select for inclusion from collinear pairs. A subgroup univariate analysis was performed to look for associations with interferon gene signature (IGS) and metabolic indices.

**Results:** 91 SLE patients and 48 age, sex, and premorbid IQ matched controls were recruited. The median (range) age was 45 (21-64) and median disease duration 13 years (0.2-39). 60% were Caucasian and the rest predominantly Asian, and all had good English proficiency. Prevalence of CD varied based on definition used; 16% had ≥2 cognitive domains ≥1.5 SD below the healthy control mean, whereas 48% were considered impaired if this threshold was reduced to ≥2 SD below. Age and premorbid IQ were significantly associated with multiple cognitive endpoints, and SDI was associated with four endpoints including the most severe definition of CD. Increased parity and past strokes correlated with poorer cognition in two endpoints. In contrast, clinical variables such as SLEDAI, antiphospholipid antibodies and past seizures only correlated with one endpoint each. There were no associations with other antibodies or any medications including glucocorticoids. Subgroup analysis showed univariate associations of CD with increased waist circumference, hypertriglyceridemia and low IGS.

**Conclusion:** Clinical associations of CD in SLE vary according to the cognitive domain or impairment definition used. SDI was the disease-related factor most associated with CD. Studies of CD in SLE should use standardised methods to determine CD.

**REFERENCES:**


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**POSO732**

**IDENTIFICATION OF AUTOPHAGY-RELATED PHENOTYPES IN PRIMARY SJÖGREN’S SYNDROME**

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**Background:** Primary Sjogren’s syndrome (pSS) is a chronic systemic autoimmune disease characterized by disorders of effector T cell subpopulations such as Th1, Th2, Th17, regulatory T cells, and follicular helper T cells. 1 Autophagy is an evolutionarily conserved self-digestion process that plays an important role in T cell-mediated immune response. 2 The relationship between autophagy and T cell subsets was unclear in pSS up till now.

**Objectives:** To landscape the autophagy-related multiple gene expression signature in pSS classification and discover the influence of autophagy in T cell subsets.

**Methods:** Gene expression profiles of pSS samples (GSE67795, GSE51092, GSE154926) were acquired from GEO database. A set of significant G-ATGs were intersected from the global gene of patients and 232 autophagy genes (ATGs) which were obtained from the Human Autophagy Database (HADb, http://www.autophagy.lu/). In training dataset (GSE67795, including 155 patients and 29 healthy controls), non-negative matrix factorization was used to divided patients by G-ATGs expression microarray data. An autophagy score model divided patients into the high-autophagy score and low groups by ssGSEA scores of gene according to normalized G-ATGs training data. Further, new classifications were validated by both peripheral blood samples (GSE10592, 90 patients) and salivary gland tissue (GSE154926, 43 participants).

**Results:** Two distinct subtypes were identified and validated by 206 selected significant G-ATGs in training datasets (figure 1A,B) and validation datasets according to the autophagy score (figure 1D,E,F). Combined with clinical information of salivary gland dataset, it was found that most patients with early pSS were grouped in the high autophagy, while advanced patients were grouped in the low (figure 1G). Patients in high-autophagy group had higher levels of Treg cells and Th2 cells but lower concentrations of Th17 and Th1 in peripheral blood (figure 1C, P <0.05). Similar results were also observed in salivary gland tissue (figure 1H, P<0.05).

**Conclusion:** Patients with different autophagy status differs from each other. Autophagy is closely correlated with lymphocyte subpopulations in patients with pSS. This work may help inform therapeutic decision-making for the treatment of pSS.

**Table 1. Multivariate Analysis of Clinical Predictors of Cognitive Dysfunction in SLE**

<table>
<thead>
<tr>
<th>Cognitive Dysfunction Definitions</th>
<th>Individual Cognitive Domains (Tests)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2 domains</td>
</tr>
<tr>
<td>Odds ratio (logistic regression)</td>
<td>Coefficient (linear regression)</td>
</tr>
<tr>
<td>Age</td>
<td>1.04*</td>
</tr>
<tr>
<td>Premorbid IQ</td>
<td>0.89**</td>
</tr>
<tr>
<td>SLEDAI</td>
<td>0.88</td>
</tr>
<tr>
<td>Time-adjusted mean SLEDAI</td>
<td></td>
</tr>
<tr>
<td>PQA</td>
<td>0.78</td>
</tr>
<tr>
<td>SDI</td>
<td></td>
</tr>
<tr>
<td>Past stroke or TIA</td>
<td>7.84</td>
</tr>
<tr>
<td>Past seizures Methotrexate</td>
<td></td>
</tr>
<tr>
<td>Ant Ro</td>
<td>0.22</td>
</tr>
<tr>
<td>Anti-cardiolipin</td>
<td>0.38</td>
</tr>
<tr>
<td>Any APLS abs</td>
<td>0.037**</td>
</tr>
<tr>
<td>Parity</td>
<td>2.21**</td>
</tr>
<tr>
<td>Substance use</td>
<td>2.58</td>
</tr>
</tbody>
</table>

1Impairment defined by number of cognitive domains either 1.5 or 2 SD below healthy control group mean*p value <0.05 *p value <0.005**Abbreviations: SLEDAI - SLE Disease Activity Index, PQA - Physician global assessment, SDI - SLE International Collaborating Clinics Damage Index, TIA - Transient Ischaemic Attack, abs - Antibodies, APLS - Antiphospholipid Syndrome, ROCF - Rey-Ostreich Complex Figure Test, CVLT - California Verbal Learning Test, COWAT - Controlled Oral Word Association Test, LNS and Coding - Letter Number Sequencing & Coding subsets of Wechsler Adult Intelligence Scale IV, TMT - Trail Making Test.
Disclosure of Interests:
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Arealife physical activity in SLE patients: associations with fatigue and quality of sleep
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Background: Fatigue is among the top complaints of patients with systemic lupus erythematous (SLE), but only in part associated with SLE disease activity. Physical activity can help to reduce fatigue and should therefore be recommended to SLE patients. Vice versa, fatigue may arguably lead to reduced physical activity.

Objectives: To investigate the extent of physical activity and the perception of fatigue and sleep quality in patients with SLE.

Methods: Starting in February 2019, SLE patients were invited to participate in a cross-sectional survey study of fatigue and physical exercise during their routine outpatient clinic visits. Participants filled out a ten-page paper questionnaire focused on physical activity. To evaluate fatigue, we primarily used a 10 cm visual analogue scale (0=100 mm, with 100 meaning most fatigued), but also the FACIT fatigue score (range 0-52). Sleep quality was estimated using grades from 1 (excellent) to 6 (extremely poor).

Results: 93 SLE patients took part in the study. All patients fulfilled the European League Against Rheumatism/ American College of Rheumatology (EULAR/ACR) 2019 classification criteria for SLE. 91% of the patients were female. Their mean (SD) age was 45.5 (14.3) years and their mean disease duration 12.1 (9.4) years. The mean BMI was 25.2 (5.6). Of all patients, 27% were working in essentially sedentary jobs and 26 (40%) were in positions where they were mildly physically active in part. The mean fatigue VAS was 31 (24) mm for patients with partly active jobs and 27 (30) mm for those in sedentary jobs. Sleep was graded 2.9 (0.9) by those with active and 3.1 (1.3) by those with sedentary jobs.

Conclusion: A majority of SLE patients in remission or low to moderate disease activity regularly practiced sports, and those doing so reported lesser fatigue and better sleep quality. The absolute values on the fatigue VAS were in a moderate range that made fatigue as the main cause of not performing sports rather unlikely for most patients.

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POSO734 Extrapolation of long-term outcomes in systemic lupus erythematosus: replicating a Hopkins Lupus Cohort Analysis with the Systemic Lupus International Collaborating Clinics (SLICC) Inception Cohort

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Background: A disease model of systemic lupus erythematous (SLE) that predicts short-term outcomes (disease activity and prednisone use) and links them to long-term outcomes (accrual of organ damage and mortality) was previously developed in a single center SLE cohort (Johns Hopkins [JH]) to support health economic analyses (Watson 2015), which has not been comprehensively replicated in other cohorts or contexts.

Objectives: As part of an effort to develop and refine this existing disease model, the aim of this study was to replicate the previously estimated network of risk equations for short- and long-term outcomes in the SLICC Inception Cohort, an international cohort of patients (33 centers, 11 countries).

Methods: As part of an effort to develop and refine this existing disease model, the aim of this study was to replicate the previously estimated network of risk equations for short- and long-term outcomes in the SLICC Inception Cohort, an international cohort of patients (33 centers, 11 countries).

Methods: The SLICC Inception Cohort enrolled patients fulfilling ACR Classification Criteria for SLE within 15 months of diagnosis from 1999-2011 with annual follow-up time to April 2020. The network of risk equations included two linear random effects models to predict (1) change in annual average Systemic Lupus Disease Activity Index (SLEDAI) score based on patient characteristics and the presence of renal, hematological, and immunological involvement in the prior year and (2) average annual prednisone dose based on SLEDAI score in the same year. These equations were then linked to parametric survival models that predicted annual incidence to the occurrence of organ damage (system-specific based on the ACR/SLICC Damage Index) and mortality. We assessed model performance between the SLICC Cohort and the original analysis from the JH Cohort.

Results: In comparison to the JH cohort (N=1354), the SLICC cohort (N=1697) had a smaller fraction of patients of African descent (39% vs 17%) and shorter