

Purpose Longitudinal studies specifically addressed to describe the development of systemic autoimmune diseases in anti-phospholipid (aPL) positive healthy subjects are not available. Thus, we longitudinally followed a single-center aPL carriers cohort to evaluate the rate of disease evolution, focusing on anti-phospholipid syndrome (APS) and Systemic Lupus Erythematosus (SLE).

Methods Healthy subjects positive for aPL in at least two consecutive determinations were enrolled. Medical history was recorded and laboratory evaluation was performed [aCL and anti- β 2GPI IgG/IgM, lupus anticoagulant (LA), antinuclear antibody (ANA), C3/C4 levels, genetic thrombophilia screening]. All subjects were evaluated every six months to register the occurrence of clinical and laboratory features suggestive of APS or SLE.

Results Ninety-five subjects (M/F 20/75, median age at first determination 46 years, IQR 19) were enrolled; aCL were identified in 75 carriers (78.9%), β 2GPI in 60 (62.5%) and LA in 45 (47.3%). We prospectively followed our cohort for a median period of 72 months (IQR 84). In detail, eight aPL carriers (8.4%) were lost to follow up. At the last visit, 6 (6.3%) subjects became persistently negative after a median interval of 21 months (IQR 43.5); all of them were female with aCL positivity at low titer in 83.3% of cases. During a total follow-up of 7692 person-months, we found an absolute risk for systemic autoimmune diseases development equal to 0.9%. In detail, four patients (4.2%) developed a thrombotic event and were classified as affected by APS. Notably, all of these subjects shared a laboratory phenotype, characterized by LA and ANA positivity. Interestingly, this phenotype was observed only in two out of the remaining persistently positive carriers (2.7%, $p = 0.0001$). Furthermore, three patients could be classified as affected by SLE according to the 2019 ACR/EULAR classification criteria. All these patients were then treated by HCQ 5 mg/Kg/daily.

Conclusions In the present study, we evaluated the progression from asymptomatic aPL positivity condition to clinically manifested autoimmune disease. The tight and prolonged monitoring of our cohort allowed to observe the evolution to APS or SLE in almost 7% of cases. To the best of our knowledge, this is the first longitudinal cohort study specifically addressing the transition to systemic autoimmune diseases in aPL positive healthy individuals. Of note, it should be considered not only the expected APS development, but also the progression to SLE.

S13.2 ANTI-PHOSPHATIDYLSERINE/PROTHROMBIN ANTIBODIES AND THROMBOSIS ASSOCIATE POSITIVELY WITH HHLA-DRB1 *13 AND NEGATIVELY WITH HLA-DRB1*03 IN SLE

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Purpose Emerging evidence demonstrate that anti-phosphatidylserine/prothrombin complex antibodies (anti-PS/PT) associate with thrombotic events. Genetic predisposition, including HLA-DRB1 alleles, is known to contribute to the occurrence of conventional antiphospholipid antibodies (aPL, anti-

beta2glycoprotein-I (beta2GPI) and anti-cardiolipin (CL)). We investigated associations between anti-PS/PT and HLA-DRB1* alleles and thrombosis in SLE. Conventional aPL were included for comparison.

Methods We included 341 consecutive SLE patients, with information on general cardiovascular risk factors, including blood lipids, lupus anticoagulant and thrombotic events. Anti-PS/PT, anti-beta2GPI and anti-CL of IgA/G/M isotypes and lupus anticoagulant were quantified.

Results Anti-PS/PT antibodies associated positively with HLA-DRB1*13 (OR 2.7, $P = 0.002$), whereas anti-beta2GPI and anti-CL antibodies associated primarily with HLA-DRB1*04 (OR 2.5, $P = 0.0005$). These associations remained after adjustment for age, gender and other HLA-DRB1* alleles. HLA-DRB1*13, but not DRB1*04, remained as an independent risk factor for thrombosis and APS, after adjustment for aPL and cardiovascular risk factors. The association between DRB1*13 and thrombosis was mediated by anti-PS/PT positivity. HLA-DRB1*03, on the other hand, associated negatively with thrombotic events as well as all aPL using both uni- and multi-variate analyses. HLA-DRB1*03 had thrombo-protective effect in aPL positive patients. Additionally, HLA-DRB1*03 was associated with a favorable lipid profile regarding high-density lipoprotein and triglycerides.

Conclusions HLA-DRB1*13 confers risk for both anti-PS/PT and thrombotic events in lupus. The association between HLA-DRB1*13 and thrombosis is largely, but not totally, mediated through anti-PS/PT. HLA-DRB1*03 was negatively associated with aPL and positively with favorable lipid levels. Thus, HLA-DRB1*03 seems to identify a subgroup of SLE patients with reduced vascular risk.

Friday 07 October 2022 from 09:50 to 11:20

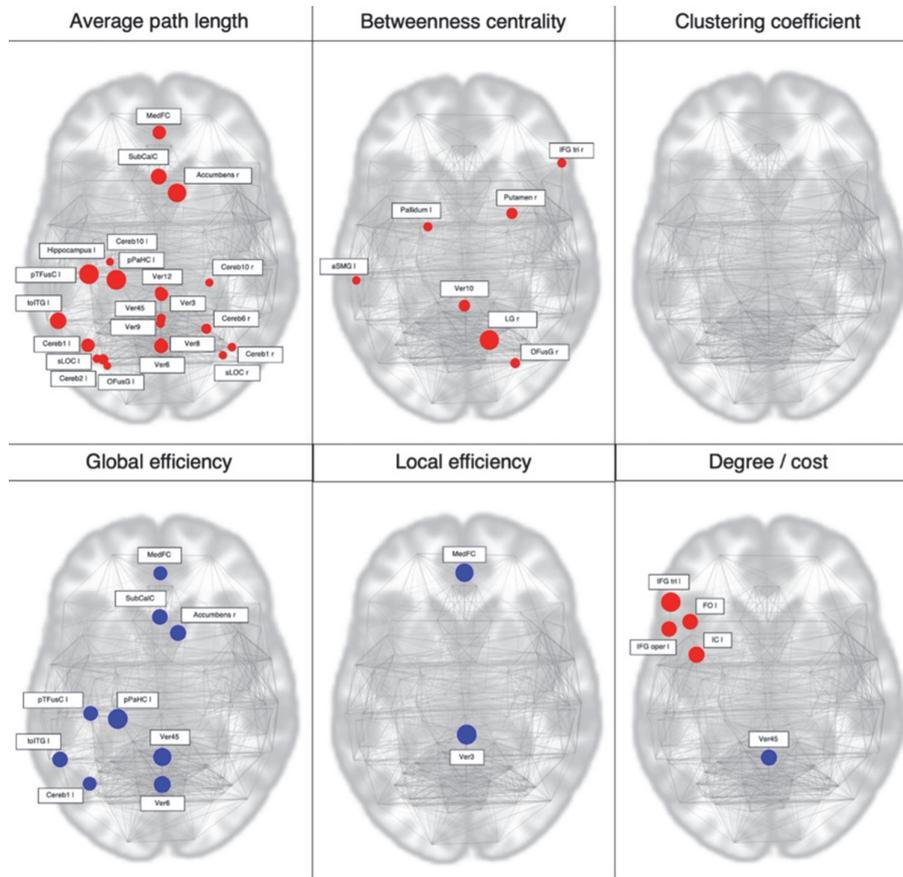
S14 NPSLE and associated symptoms with patients

S14.1 THE EFFECT OF ANTI-RIBOSOMAL-P AND ANTI-DWEYS ANTIBODIES ON DEPRESSION AND BEHAVIORAL COGNITIVE PROCESSES IN SYSTEMIC LUPUS ERYTHEMATOSUS : AN INTEGRATED CLINICAL AND FUNCTIONAL MRI STUDY

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Purpose Cognitive dysfunction (CD) and mood disorders (MD) are among the most frequent neuropsychiatric (NP) events in Systemic Lupus Erythematosus (SLE), but their pathogenesis has not been fully clarified yet. A potential role of antineuronal antibodies in NP-SLE patients is currently being investigated. The primary aim of the study was to explore the effects of anti-ribosomal-P (anti-Rib-P) and anti-DWEYS antibodies on CDs and MDs and their relationship with



Abstract S14.1 Figure 1 Results of rs-fc MR Analysis 1 (effects of Anti-rib-P titer) on cerebral networks. The regions with decreased or increased properties are shown in blue and red nodes, respectively ($p < 0.01$). The node size represents the significance of the between-group differences in the nodal degree

functional Magnetic Resonance Imaging (MRI) brain connectivity in patients affected by SLE.

Methods A cross-sectional study was conducted between April 2019 and February 2020, including consecutive adult patients who fulfilled the ACR/EULAR 2019 SLE criteria.

Demographics, serological, ongoing medications, SLEDAI and SLICC/Damage Index (SDI) were recorded. Serum level quantification for anti-Rib-P and anti-DWEYS antibodies were performed using an ELISA. A battery of neuropsychological testing exploring cognitive domains, depression and quality of life was interpreted by a neuropsychologist. A resting-state functional connectivity (rs-fc) MRI analysis was performed within 2 weeks since the neuropsychological status assessments. Two region of interest to region of interest (ROI-to-ROI) analyses with the graph theory was performed.

Results Thirty-three SLE patients (9% male) were enrolled, mean age 43.5 (+14) years, and median disease duration of 10.4 years (IQR 2.9–25.4). The daily median prednisone (PDN) dose was 6.4 mg (3.8–13.5). Anti-Rib-P were positive (range 0–255 U/ml) in 6 patients (18.2%) and anti-DWEYS (range 0–1.8 OD) in 14 (42.4%).

Nineteen out of 33 patients (57.6%) showed at least a cognitive test alteration. The most frequent cognitive deficits were memory disturbances, found in 6.1–27.3% of the population evaluated, according to the cognitive test used, followed by alterations in executive functions (12.1–21.9%), psychomotor speed (18.2%) and attention (3–12.1%), but no significant association with antibodies was found. Depression was found

in 14 (42.4%) patients using the Center for Epidemiologic Studies Depression Scale (CES-D) as a screening instrument. In multiple regression backward models, after correction for age, disease duration, SLEDAI and SDI, the CES-D showed an independent association with anti-Rib-P titer ($\beta = 0.32$ per U/ml; $p = 0.049$) and PDN daily dose ($\beta = 0.38$ per mg/day; $p = 0.023$). The rs-fc MRI analysis revealed a statistically significant association between the titer of anti-Rib-P and many altered properties of the brain ROIs (Figure 1), but no effects of PDN daily dose on specific cerebral networks.

Conclusions Anti-Rib-P antibodies and PDN daily dose are associated with depressive symptoms. Anti-Rib-P antibodies are also associated with changes in brain network properties in SLE patients, which add knowledge to their pathogenetic effect.

S14.2 FAVORABLE OUTCOME OF PATIENTS WITH INFLAMMATORY NEUROPSYCHIATRIC LUPUS TREATED WITH IMMUNOSUPPRESSION

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Purpose Neuropsychiatric manifestations in patients with systemic lupus erythematosus (SLE) can have many underlying