100 – Brain injury in SLE

101 INCREASED BLOOD BRAIN BARRIER PERMEABILITY ASSOCIATES WITH INCREASED HIPPOCAMPAL GLUCOSE METABOLISM IN SLE

Meggan Mackay*, An Vo, Chris Tang, Bruce Volpe, Betty Diamond, David Eidelberg. *The Feinstein Institutes for Medical Research, Manhasset, NY, USA*

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Background Mechanisms for SLE-mediated cognitive impairment (SLE-CI) include autoantibodies and inflammatory molecules normally excluded from the brain by an intact blood brain barrier (BBB). However, the BBB permeability may be altered in response to molecular signals from the periphery and activated microglia in the brain. We have hypothesized that in SLE-CI the hippocampus is targeted by autoantibodies leading to microglia activation and neuron dysfunction. Dynamic Contrast Enhanced (DCE) MRI was used in SLE subjects concurrently assessed with FDG-PET brain imaging to determine regional BBB permeability and association with metabolism.

Methods Data from 10 SLE and 6 healthy control (HC) subjects enrolled in a larger observational study were analyzed. Important exclusion criteria for SLE included any history of neuropsychiatric disease, current psychiatric medication use, active disease, and steroid dose > 10 mg. Statistical Parametric Mapping (SPM) analysis was used to perform voxel-wise comparison of different imaging data from the same cohort. Parametric maps created from DCE-MRI data were registered to MNI templates used in SPM analysis, allowing comparison between maps in the MNI space. Voxel-wise comparison of DCE-MRI permeability parameters, V_e , K_{ep} and K_{trans} , was conducted on data from all subjects and compared to voxel-wise assessments of glucose metabolism from FDG-PET imaging. Clusters were identified by voxel-wise analysis of the parametric maps for K_{ep} and V_e data. SPM contrasts were thresholded at $p < 0.05$ within a hippocampal hypothesis-testing volume. Student t-test was used to compare permeability parameters between SLE and HC.

Results Abnormal increases in K_{ep} (red) and V_e (green) were found in the SLE group hippocampus (figure 1); they overlapped with the area of increased hippocampal metabolism (yellow) reported previously.¹ Hippocampal increases in V_e were smaller in both extent and magnitude compared to K_{ep} (color scales). K_{trans} , V_e and K_{ep} are all highly related such that $K_{trans} = K_{ep} \times V_e$. The voxelwise contrast for K_{trans} was similar to K_{ep} , and corresponding values were highly correlated ($r = 0.92$, $p < 0.0001$) in the overlap region. To simplify visualization, only K_{ep} and V_e contrasts are displayed in figure 1A. Scatterplots of permeability parameters measured in

Abstract 101 Figure 1 Abnormal hippocampal BBB parameters in relation to elevations in regional glucose metabolism in SLE

the hippocampal overlap region for the SLE and HC subjects (figure 1B).

Conclusions SPM analysis of DCE-MRI and FDG-PET data demonstrates abnormal increased hippocampal BBB permeability and glucose metabolism in SLE subjects with inactive disease and no history of neuropsychiatric disease. These data support the hypothesis that BBB permeability is altered in SLE, allowing access of inflammatory mediators to the brain.

102 POTENTIAL BIOMARKERS OF COGNITIVE IMPAIRMENT IN THE CONTEXT OF CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS

^{1,2}Santiago Arciniegas, ^{3,4}Sarah I Mossad, ⁴Tala El Tal, ⁴Lawrence Ng, ⁴Paris Moaf, ⁵Helen M Branson, ⁶Adrienne Davis, ⁴Linda Hiraki, ⁴Deborah Levy, ^{3,4}Ashley Danguedan, ^{1,4}Andrea M Knight*. ¹Department of Neurosciences and Mental Health, Hospital for Sick Children, Canada; ²Institute of Biomedical Engineering, University of Toronto, Canada; ³Department of Psychology, Hospital for Sick Children, Canada; ⁴Department of Rheumatology, Hospital for Sick Children, Canada; ⁵Department of Diagnostic Imaging, Hospital for Sick Children, University of Toronto, Canada; ⁶Division of Emergency Medicine, Hospital for Sick Children, Canada

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Background Cognitive complaints are common in children with childhood-onset systemic lupus erythematosus (cSLE), but neuropsychiatric lupus (NPSLE) remains challenging to diagnose and treat. To increase understanding of contributing mechanisms, we examined the association between cognitive function, disease measures and structural neuroimaging metrics.

Methods We examined a cross-sectional sample of 24 patients with cSLE (ages 12-17) meeting ACR or SLICC classification criteria. Patients completed standardized neurocognitive tests quantifying domains of attention and inhibition (CPT-3, Conners' Continuous Performance Test 3rd ed), working memory (WISC-V, Wechsler Intelligence Scale for Children 5th ed), and cognitive flexibility (D-KEFS, Delis-Kaplan Executive Function System). Cognitive impairment was defined as a score of 1.5 standard deviations below the mean in any domain. T1-weighted brain magnetic resonance images (MRI) were obtained using a 3T scanner. Advanced structural MRI analysis was used to extract volume, cortical thickness, and surface area metrics for brain segments. Demographic and disease measures were extracted from medical records. We used Partial Least-Squares Regression (PLS2), to examine the association between cognitive function (continuous outcome) and its potential predictors, comprised of structural brain metrics as well as disease and demographic measures. PLS2 analysis enables description of interactions between multivariate and potentially collinear data with a relatively small sample size. Each predictor's relevance criteria (i.e., stability and significance) were based on the bootstrapped sample distribution of its variable importance in projection (VIP) value, which measures the relative weight of a predictor across all outcome variables.

Results The mean age of the sample was 15.4 years (standard deviation 1.7), 20/24 (83%) were female, and 16/24 (67%) were on non-White race/ethnicity. The median disease duration was 1.8 years (interquartile range 1.0, 3.1). Cognitive impairment was present in 10/24 (42%) of patients; only one subject had a diagnosis of NPSLE. In PLS2 analysis (figure 1), 52 predictors were found to be relevant in the estimation of cognitive function (CI = 95%, VIP > 1.18). Of these, 50 were