1633 Linear- versus conformational-protein directed autoantibodies in neuropsychiatric systemic lupus erythematosis

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Systemic Lupus Erythematosis (SLE) is a multi-system autoimmune disease. Putative biomarkers for neuropsychiatric SLE (NPSLE) include antibodies against the DWEYS peptide, a sequence present on the extracellular portion of NR2A/B receptors. We tested for binding of antibodies to conformational state neuronal proteins, including the NMDA receptor to understand potential pathogenicity of these antibodies. Paired serum and CSF from 35 patients SLE/NPSLE were studied. No binding was observed to natively expressed NMDARs or live hippocampal neurons. A DWEYS-reactive ELISA showed by comparison to healthy controls, SLE patients (p=0.0001) and disease-controls (predominantly MS (n=36, (p=0.016)) but not antibody-controls (aquaporin-4- (n=11), LGI1- (n=13) and NMDAR- (n=10) antibody diseases, p=0.375) showed greater binding, suggesting this assay is not selective for NPSLE/SLE. Binding was unaffected by a scrambled or charge altered DWEYS peptide. However, the same samples also showed similar binding to the plate without the DWEYS peptide. Uncoated versus coated plate ELISA data showed Spearman's correlations>0.79 across all cohorts. NPSLE does not associate with antibodies to NR1 or NR2A/B homomers/heteromers or cultured hippocampal neurons in their native, conformational state. The DWEYS assay is not a reliable way to test for NPSLE, and literature discrepancies may result from the propensity of SLE patients to bind ELISA plates. We would not recommend further use or exploration of the DWEYS assay in SLE.