accumulation of longer polynucleosomal DNA fragments in circulating microparticles, and to autoantibody responses to microparticle-associated DNA and protein antigens.

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902 REGULATORY RNAS IN NEUROPSYCHIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

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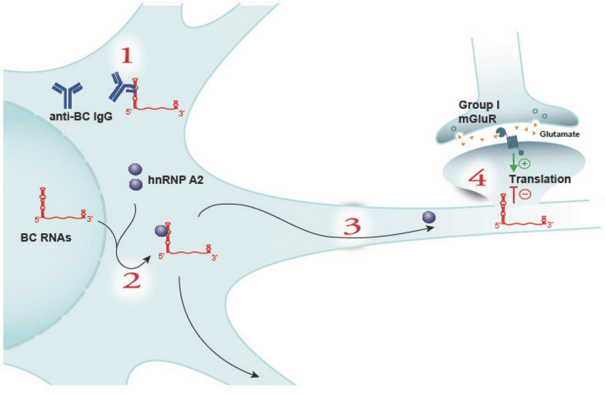
Background Brain-specific Cytoplasmic (BC) RNAs operate as translational regulators at neuronal synapses. BC RNAs are delivered to synapto-dendritic sites of function by transport factors heterogeneous nuclear ribonucleoprotein A2 (hnRNP A2) and Purα. Dysregulation of BC RNA control has been associated with epilepsy and cognitive impairment. We hypothesized that structural motifs in BC RNAs can become targets of autoimmune reactivity in neuropsychiatric SLE.

Methods Sera were collected from patients with SLE, rheumatoid arthritis (RA), multiple sclerosis (MS), and from healthy subjects (HS).[1] RNA-protein interactions were examined by electrophoretic mobility shift assays (EMSAs). Microinjection RNA transport analysis was performed with sympathetic neurons in primary culture. Sera or purified antibodies were injected i.v. into wild-type (WT) mice, in conjunction with i.p. injection of lipopolysaccharide to permeabilize the blood-brain barrier.[2]

Results Autoantibodies against BC RNAs (anti-BC abs) were detected in a subset of SLE patient sera. Strength of SLE anti-BC autoimmune reactivities and occurrence of neuropsychiatric manifestations, in particular seizures, correlated strongly (Spearman's $r_s = 0.89$, $P < 0.0001$). Anti-BC abs were not detected in sera from RA or MS patients or in sera from HS. In human BC200 RNA, a noncanonical dendritic targeting element (DTE) is responsible for binding of transport factors hnRNP A2 and Purα and for specifying delivery to synapto-dendritic domains. The same DTE is complexed by SLE anti-BC abs with high affinity and essentially irreversibly, in interactions that cause displacement of transport factors and inhibition of synapto-dendritic transport.



Abstract 902 Figure 1 SLE anti-BC abs: molecular – cellular mode of action. SLE anti-BC abs target transport-specifying DTEs in BC RNAs (here represented by rodent BC1 RNA; Scene 1). They prevent binding of hnRNP A2 (and Purα, not shown) to such DTEs (which occurs normally in the absence of SLE anti-BC abs; Scene 2). Dendritic delivery of BC RNAs (Scene 3) is thus compromised by SLE anti-BC abs. Lack of BC RNAs at the synapse results in aberrant local translational control ((due to unbalanced metabotropic glutamate receptor stimulation of synaptic translation; Scene 4), causing network hyperexcitability and consequential phenotypic alterations. From ref. [1].

Lack of BC RNAs in neurons, either cell-wide or locally at the synapse, causes seizure susceptibility and cognitive impairment.[3-5] We posited that introduction of SLE anti-BC IgGs into the brains of naïve WT mice, which causes BC RNA dendritic transport inhibition and thus depletion at the synapse, would result in analogous phenotypes. Indeed upon auditory stimulation, such mice succumbed to severe generalized tonic-clonic seizures (seizure rate 100%, mortality 100%). Mice injected with non-SLE IgGs (RA, MS, HS) never seized. Significantly, when SLE anti-BC IgGs were coinjected with human BC200 RNA, seizures did not materialize (Fisher's Exact Test, $P < 0.0001$).

Conclusions Our data show that SLE anti-BC IgGs, isolated from sera of lupus patients with a history of seizures, cause severe seizures in animals. Seizures are completely prevented if SLE anti-BC IgGs are complexed with BC200 RNA. We propose that this approach may lend to the development of therapeutic interventions using BC200 decoys.

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1000 – Patient-reported outcomes

1001 LONGITUDINAL CHANGES IN TYPE 2 SLE ACTIVITY

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Background The Type 1 & 2 SLE Model categorizes signs and symptoms as Type 1 (arthritis, nephritis, and rash) and Type 2 (fatigue, brain fog, and widespread pain). It is currently unknown whether Type 2 SLE symptoms vary over time. In this study, we measured longitudinal changes in Type

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2 SLE activity as measured by the Polysymptomatic Distress (PSD) Scale.

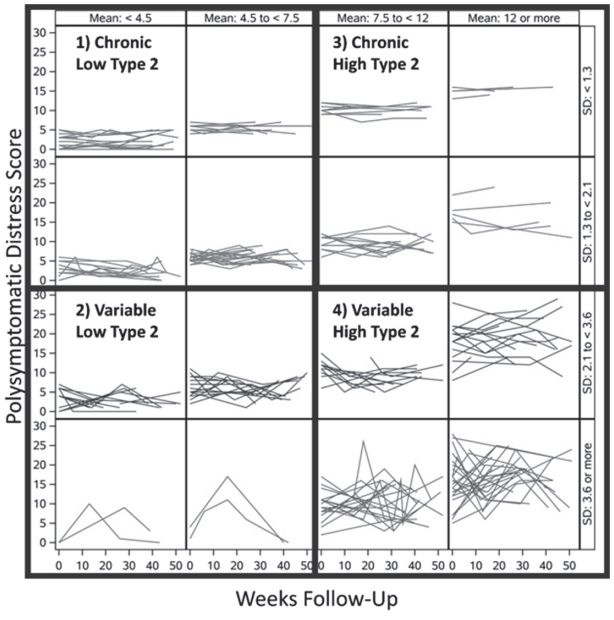
Methods Lupus patients meeting ACR or SLICC criteria in a university lupus registry completed the PSD. SLEDAI scores were also recorded. Patients with ≥2 clinical visits over a 52-week period were included. Groups were selected based on mean, indicating severity of symptoms, and the standard deviation, indicating variability of symptoms, of PSD scores across visits. Differences across groups were assessed with chi-square and ANOVA tests.

Results The study included 204 patients. Four Type 2 SLE activity groups were identified (figure 1): chronic low (n=71; 35%), variable low (n=31, 15%), chronic high (n=31, 15%), and variable high (n=71, 35%).

Patients in the chronic low and variable low Type 2 groups had similar demographics, with two-thirds being Black and 54 and 68%, respectively, having a history of nephritis. The chronic low Type 2 group had stable minimal Type 2 SLE, with an average PSD score of 3.7 that ranged from 2.8 to 4.7. Similarly, these patients had minimal Type 1 SLE activity, with average clinical SLEDAI scores of 0.7. The variable low Type 2 group had higher PSD scores (average: 4.5), ranging from 1.8 to 7.7, as well as higher SLEDAI scores than the chronic low Type 2 group, with ~25% having a SLEDAI ≥8.

Patients in the chronic high and variable high Type 2 groups also had similar demographics with half being Black and two-thirds having no history of nephritis. Additionally, both groups had average SLEDAI scores of 4. Patients in the chronic high Type 2 group had stable high PSD scores ranging on average from 10.3 to 12.7. Patients in the variable high Type 2 group had average scores of 14.1 with a larger range: 10 to 18.5.

Conclusion These findings indicate that patients with lupus differ in their Type 2 SLE activity. One-third of patients had constant high Type 2 activity, and about half had fluctuating Type 2 symptoms. Future studies will determine if this fluctuation is due to inflammation or non-inflammatory etiologies such as perceived stress, extent of social support, PTSD, illness perception, or resilience factors.



Abstract 1001 Figure 1 Change in Polysymptomatic Distress Scores over time in four Type 2 SLE trajectory groups

1002 THE MITIGATING EFFECTS OF SELF-EFFICACY ON PAIN INTERFERENCE DIFFER BY DEPRESSION IN BLACK WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background Pain is a pervasive and distressful symptom in patients with SLE, particularly among high-risk individuals. Self-efficacy can mitigate the negative impact of pain on daily activities. However, depressed patients face challenges to control pain. We examined whether self-efficacy affects pain interference in Black women with SLE and whether depression alter those relationships.

Methods Baseline PROMIS measures of Pain interference, Self-efficacy to manage symptoms (SEMS), Self-efficacy to manage medications and treatments (SEMMT), and Depression were transversally collected among Black women with SLE who participated in the Women Empowered to Live with Lupus (WELL) Study. We examined the relationship between Pain interference and self-efficacy (SEMS and SEMMT), and the interaction of depression with self-efficacy, after adjusting for confounders.

Results Of 699 participants, 143 (21%) were 18-34, 329 (47%) 35-54, and 227 (33%) ≥55 years old; 262 (38%) attained ≤high school, 226 (32%) some college, and 211 (30%) ≥bachelor's degree. Pain interference declined by 2.8 points per 5-point increase in SEMS (slope=−0.556, p-value<0.001) and by 1.4 points per 5-point increase in SEMMT (slope=−0.282, p-value<0.001). The table depicts the adjusted slopes and adjusted means of Pain interference on SEMS and SEMMT by depression severity. Depression showed a statistically significant interaction with SEMS (R^2=0.41, p-value for the interaction=0.05). Pain interference was inversely and significantly associated with SEMS in patients without depression (adjusted slope=−0.196, p-value<0.001); however, the association was not statistically significant in those with mild depression (adjusted slope=0.035, p-value=0.7), nor those with moderate/severe depression (adjusted slope=−0.080, p-value=0.3). No significant mean difference (p-value=0.11) was observed among patients without depression (adjusted mean=56.9), mild depression (adjusted mean=58.2), and moderate/severe depression (adjusted mean=58.9). Although depression did not show an overall statistically significant interaction effect with SEMMT (R^2=0.40, p-value for interaction=0.06), we did observe a statistically significant mean difference (p-value=0.003) among patients without depression (adjusted mean=56.2), mild depression (adjusted mean=58.0), and moderate/severe depression (adjusted mean=59.2).

Conclusion Self-efficacy (to manage symptoms and to manage medications and treatments) was inversely related to pain interference in Black women with SLE. However, depression altered those relationships, particularly decreasing the potential benefits of self-efficacy to manage symptoms of pain interference. Depression is a highly prevalent and often underdiagnosed comorbidity in patients with SLE; consequently, untreated depression may limit the potential benefits of self-management interventions that rely on self-efficacy to achieve better pain control in this population. Programs designed to build self-efficacy should consider these findings to determine how to maximize intervention effectiveness.

Trial Registration Number NCT02988661

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