Spatial-Relational Learning and Memory Deficits Associated with NMDAR Autoantibodies in Systemic Lupus Erythematosus

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Abstract

Individuals with Systemic Lupus Erythematosus (SLE) have been reported to experience inflammation that may target any organ within the body, including the central and peripheral nervous systems. Additionally, these individuals often demonstrate psychological dysfunctions including emotional and cognitive deficits; however, the research is inconsistent as to the nature and cause of these dysfunctions. While there are multiple factors that may increase risk for variability in cognitive function, such as population differences, SES factors, mood disorders (depression and anxiety), medication effects, and disease activity, these factors do not reliably predict the severity and extent of cognitive deficits. A growing body of animal research has associated autoantibodies (Abs) in SLE with cognitive impairment. A specific Ab that targets *N*-methyl-*D*-aspartate receptors (NMDAR) and neuronal DNA, referred to as DNRAb, has been associated with hippocampal damage and spatial memory deficits in mice. The goal of this project is to examine the relationship between the DNRAb and cognitive deficits specific to spatial and relational memory within a human SLE population. Two cohorts of healthy controls (HCs) and SLE patients were recruited. Cohort A included 33 HCs and 39 SLE participants (23 DNRAb -, 11 DNRAb +, 5 unknown Ab status). Cohort B included 11 HCs and 21 SLE participants (11 DNRAb-, 10 DNRAb+). All participants completed measures of emotional functioning and neuropsychological measures of visuospatial learning and memory, processing speed, and executive function. Cognitive testing of spatial memory and relational learning was evaluated by two laboratory developed computerized tasks. Antibody status was determined after participants were recruited in the study. After controlling for age, education, and performance on a cognitive switching task, the performances across the HCs and SLE (DNRAb+ or DNRAb-) groups were comparable. For group differences that did emerge, the differences were more likely due to age, education, and TMT-B performance rather than to SLE disease or Ab status. Although the findings specific to group status were not significant, this work provides a foundation for future research to analyze how SLE and Ab status could influence cognitive functioning. Future studies can continue to examine subtle cognitive deficits in SLE, consider the possibility of other brain areas to compensate for cognitive deficits in SLE, and provide additional breakthroughs to guide interventions for SLE patients.