The Role of Autoantibodies and B Cells in Traumatic Brain Injury

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Cognitive impairment after traumatic brain injury (TBI) correlates with immune cell infiltration and neuroinflammation. Myelin basic protein (MBP) is an integral component of myelin and contains the immunodominant peptide E83-P99, which has been the focus of several studies from rodent models to clinical trials in multiple sclerosis and stroke. These studies have focused on the T cell response to this peptide, but none have investigated the B cell response to this epitope after TBI. Immunomodulatory therapies that alter antibody responses to MBP epitopes will guide future therapeutic strategies to preclude secondary neurodegeneration after TBI. We hypothesize that activation of MBP-specific B Cells will accelerate neurodegeneration after TBI, while systematic immunosuppression will improve outcomes. To pursue this hypothesis, mice are immunized with an immunostimulatory liposomal formulation either containing or lacking MBP(E83-P99) and/or monophosphoryl lipid A (MPLA) adjuvant. Systemic B Cell suppression is accomplished by injecting anti-CD20+ IgG in a separate group. Antibody titers toward the peptide and full-length protein are quantified by ELISA and compared before and after controlled cortical impact, used as a TBI model. Neurodegeneration and immunological infiltration are quantified through NeuN, B220+, immunoglobulin and Iba-1 immunohistochemistry 7 days post injury. Cognitive changes are scored through a novel object recognition (NOR) test. Neurological changes are then compared to antibody levels toward MBP(E83-P99) and contrasted to the control and immunosuppressed groups. No correlations were associated with cognitive deficit or immunological infiltration between treatment groups. An ongoing study utilizes the same MBP/MPLA liposome formulation, but will investigate the chronic effects of TBI 42 days post injury. Together, these data will provide guidance toward novel therapeutics for TBI-induced secondary neurodegeneration.