Anti-NMDA receptor antibodies and CNS Lupus

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Cognitive impairment, one of the most prevalent (40-90%) and most debilitating symptoms in neuropsychiatric lupus (NPSLE), is a result of poorly defined pathological processes in the brain of lupus patients. Most of the pathological processes leading to characteristic of lupus multiple organ damage, are mediated by autoantibodies and autoantibodies containing complexes. In our mouse model of NPSLE a subset of such autoantibodies, anti-dsDNA antibodies cross-reactive with NMDA receptor (DNRAbs) mediate acute neuronal damage and subsequent long-term alteration in neuronal arborization and synaptic density, leading to spatial memory impairment. Of interest, DNRAbs are associated with spatial memory impairment in lupus patients. We demonstrated a critical role of activated microglia and C1q in this pathology, as the pathology does not occur in C1Q-/- mice, or in mice depleted of microglia. More importantly, we showed in the mouse model, that captopril and perindopril, both centrally acting angiotensin converting enzyme (ACE) inhibitors, can suppress microglia activation and preserve neuronal integrity and function, including cognitive performance.

ACE inhibitors are widely used to control hypertension and are usually well tolerated. This opens the opportunity to consider the use ACE inhibitors in clinical trials to improve cognitive impairment in NPSLE patients.

Current studies are undertaken to learn more about the mechanisms of neuronal injury and of complement and microglia involvement in these processes.

Speaker Biography

Czeslawa Kowal has completed her PhD from The Institute of Organic Chemistry of the Polish Academy of Sciences, Warsaw, Poland. She is associate professor of The Feinstein Institute for Medical Research and Zucker School of Medicine at Hofstra Northwell, USA. She has over 40 publications that have been cited over 1500 times, and her publication H-index is 16.

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