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It takes a lot of nerve to tell the immune system what to do in autoimmune arthritis

Dianne Lorton[1] and **Denise L Bellinger**[2]
[1]Kent State University, USA
[2]Loma Linda University, USA

Statement of the Problem: In 80% of patients, major life stressors precede onset of autoimmune diseases, including rheumatoid arthritis (RA) linking stress pathway activation to disease onset. We examined the contribution of high sympathetic nervous system activity to RA onset using the adjuvant-induced (AA) arthritis model in Lewis rats.

Methodology: Rats were immunized with complete Freund's adjuvant to induce AA. From day (D) 12 (disease onset) through D28, rats were treated with vehicle or 2 mg/kg/day moxonidine, an imidazoline receptor-1 agonist that acts centrally to reduce SNS tone. Disease outcome was assessed using dorsoplantar widths and X-ray analysis. Cytokines critical for inflammation and CD4+ Th cell development (interleukin (IL)-1beta, IL-10, tumor necrosis factor (TNF)-alpha, IL-6, IL-2, IL-4, IFN-gamma, and tumor growth factor (TGF)-beta) were assessed in spleen, draining lymph node (DLN) and peripheral blood mononuclear cells (PBMCs) by enzyme-linked immunoassays.

Findings: Treatment with moxonidine dramatically prevented hind foot inflammation and joint destruction in AA compared with vehicle treatment. In DLN cells, moxonidine treatment had no effect on cytokine production. In contrast, moxonidine treatment significantly reduced IL-1beta, IL-2, IL-4 and IFN-gamma in PBMCs. Drug treatment decreased splenocyte production of TGF-beta and IFN-gamma by ~50% and ~30, respectively.

Conclusion & Significance: Lowering SNS tone effectively reduced clinical signs of disease and altered production of cytokines involved in inflammation and shifting the balance between auto-reactive CD4+Th cells and T regulatory cells in directions expected to limit disease activity. This research implicates high nerve firing rates as a contributor to the pathogenesis of autoimmune arthritis. A better understanding of the role of the SNS in autoimmunity is a necessary step in devising rational preventative and better therapeutic interventions.

Recent Publications

1. Lorton D, Bellinger D L (2015) Molecular mechanisms underlying β-adrenergic receptor-mediated cross-talk between sympathetic neurons and immune cells. Int J Mol Sci. 16:5635-65.
2. Lorton D, Bellinger D L (2015) Sympathetic nervous system regulation of Th cells in autoimmunity: Beyond Th1 and Th2 cell balance. Clin Cell Immunol 6:5.
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4. Bellinger D L, Lorton D (2014) Autonomic regulation of cellular immune function. Auton Neurosci. 182:15-41.
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Biography

Dianne Lorton has completed her PhD in Neurosciences from Indiana State University in affiliation with Indiana University School of Medicine. She has completed her Post-doctoral training in Pharmacology from Duke University and in Neuroimmunology from the University of Rochester. She is currently an Assistant Professor at Kent State University in the College of Arts and Sciences. She has published over 70 papers (manuscripts, reviews, and book chapters) on neuroimmunology focusing on sympathetic nervous system regulation of immunity.

ddifran7@kent.edu

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