

CLINICAL-ELECTROPHYSIOLOGIC-PATHOLOGIC CORRELATIONS IN SEVERE MURINE EXPERIMENTAL AUTOIMMUNE NEURITIS

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ABSTRACT

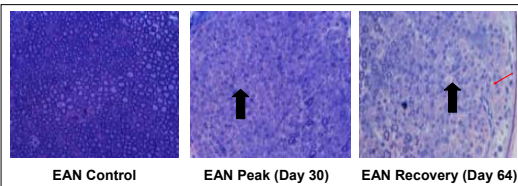
Severe murine experimental autoimmune neuritis (sm-EAN) is a reliable animal model of Guillain-Barré Syndrome. There is insufficient data characterizing the inflammatory infiltrates in this model or correlating neuromuscular severity with electrophysiological parameters.

Sm-EAN was induced in 8-12 week old female SJL/J mice as previously published. Disease onset occurred at 9-13 days, with maximal severity between 26-32 days post-induction (p.i.). There was residual mild weakness >2 months p.i.

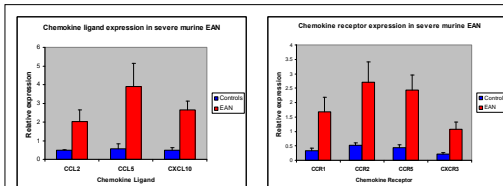
Severe multifocal or diffuse demyelination with some mild axonal loss was observed at peak severity, associated with mononuclear cell infiltrates (F4/80+ macrophages, CD3+ and CD4+ T-lymphocytes and CD19+ B-cells). There was increased expression of CCL2-CCR2, CCL5-CCR1, CCR5 and CXCL10-CXCR3 at peak severity. Residual infiltrates and rudimentary 'onion bulb' formation were seen during the recovery phase.

Serial electrophysiological studies of the dorsal caudal tail nerve and bilateral sciatic nerves showed statistically significant reductions in mean compound motor action potential (CMAP) amplitudes and conduction velocity and increases in mean CMAP durations compared to controls. Regression analyses demonstrated correlations ($r^2=0.78-0.99$) between neuromuscular severity and the above parameters, with stronger correlations seen with the dorsal caudal tail motor nerve responses.

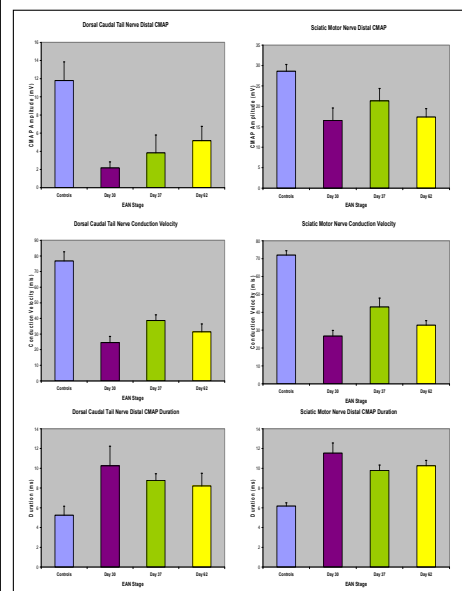
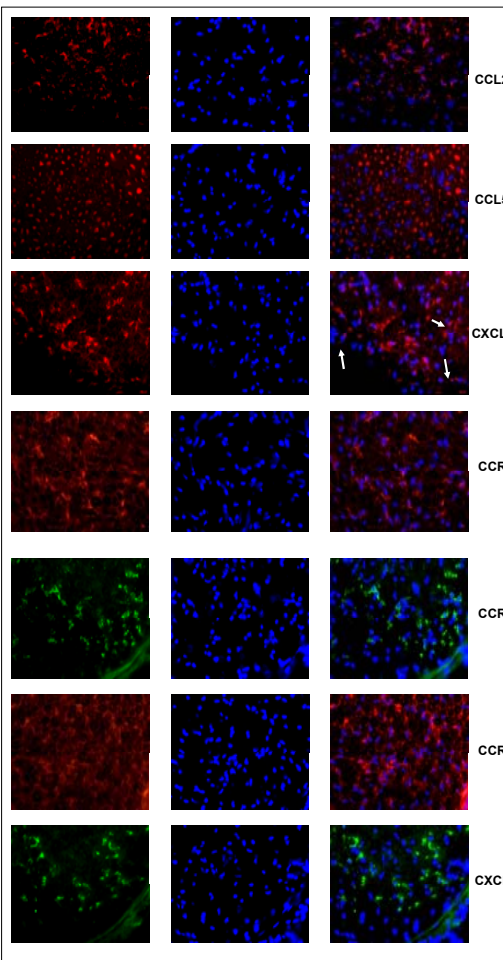
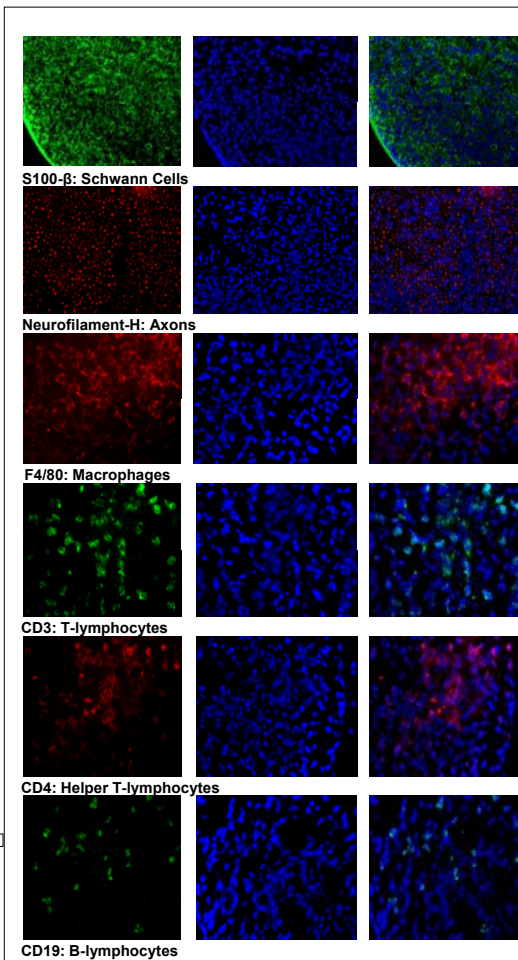
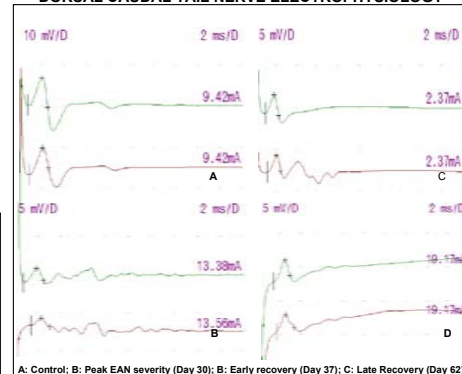
HISTOPATHOLOGICAL FEATURES OF SM-EAN



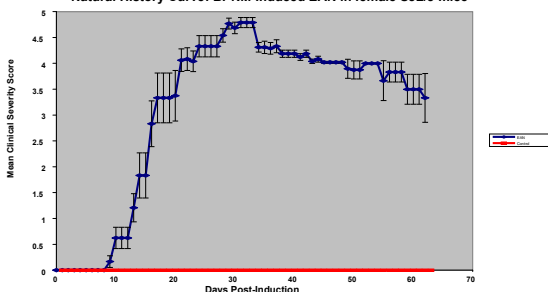
CHEMOKINE LIGAND/RECEPTOR EXPRESSION IN SM-EAN



DORSAL CAUDAL TAIL NERVE ELECTROPHYSIOLOGY



Natural History Curve: BPNM-Induced EAN in female SJL/J mice



Bovine Peripheral Nerve Myelin-induced severe murine experimental autoimmune neuritis is a reliable animal model with correlating neuromuscular, electrophysiological and pathologic features that closely resemble Guillain-Barré Syndrome. Specific pro-inflammatory chemokine ligand/receptor pairs are expressed in pathologically involved sciatic nerves suggesting that targeted blockade of chemokine signaling may provide a novel avenue for treating peripheral nerve inflammation.