Arthritis Rheumatol. 2014 Apr 9. doi: 10.1002/art.38662. [Epub ahead of print]

Evidence of abnormal epidermal nerve fiber density in fibromyalgia: Clinical and immunologic implications.

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Abstract

Objective.

A subset of fibromyalgia (FM) patients exhibits a large fiber, demyelinating peripheral polyneuropathy, akin to that seen in chronic inflammatory demyelinating polyneuropathy (CIDP). It has been suggested that this demyelinating process is likely to be immune mediated. Since it is known that similar, large fiber neuropathic lesions may be associated with a cutaneous small fiber neuropathy (SFN), we sought to determine the prevalence of SFN, as measured by epidermal nerve fiber density (ENFD), in a series of FM patients and clinically healthy controls.

Methods.

Forty-one consecutive FM and 47 control subjects underwent a 3 mm punch skin biopsy at the proximal thigh and distal leg near the ankle for ENFD analysis. FM subjects with clinical evidence of a disorder known to be associated with SFN were excluded. FM subjects also underwent clinical study for stocking distribution hypesthesia by pinwheel and vibratory testing, and serologic investigation of a series of cytokine, CIC, and complement measurements.

Results.

All FM subjects had evidence of stocking distribution hypesthesia. The mean ENFD for FM subjects was lower than for controls at both the calf (5.8 ± 2.8 SD vs. 7.4 ± 1.9 SD; $P < 0.0002$) and thigh (9.3 ± 3.2 SD vs. 11.3 ± 2.0 SD; $P < 0.0007$). There was an inverse correlation between calf ENFD and age, at the time of skin biopsy, in FM subjects ($r = - 0.29$; $P = 0.03$), but not in controls. ANCOVA showed that this relationship could not be explained by aging alone, however. Serologic evaluation showed an inverse correlation between calf ENFD in FM subjects and the T-cell/macrophage activation marker, IL-2R ($r = - 0.28$; $P = 0.04$). Correlation analysis of thigh ENFD and serum IL-2R did not reach significance ($P = 0.08$). Analysis of calf/thigh ENFD ratios suggests that ENFD decline in FM is affected by both a diffuse, and a length dependent, process

Conclusion:

Calf and thigh ENFD in FM are significantly diminished compared to controls. Advancing age, alone, can not explain this finding. Calf ENFD correlated, though weakly, in an inverse fashion with serum IL-2R ($P = 0.04$). These findings suggest that SFN is likely to contribute to FM pain complaints; that pain in this disorder arises, in part, from a peripheral immune mediated process; and that measurement of ENFD may be a useful clinical tool in FM. © 2014 American College of Rheumatology.