

CENTRAL AND PERIPHERAL CONTRIBUTIONS TO FIBROMYALGIA PHENOTYPES: ROLE OF MIGRAINE COMORBIDITY AND SMALL FIBRE PATHOLOGY

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Background. Fibromyalgia (FM) is a heterogeneous chronic pain condition involving peripheral and central mechanisms. Migraine is a prototypical disorder of central nervous system dysregulation, while small fibre pathology (SFP) reflects peripheral nociceptive dysfunction. We investigated whether comorbid migraine and SFP identify different clinical phenotypes within the FM spectrum.

Methods. We examined 296 FM patients diagnosed according to the 2016 ACR criteria (1). Migraine was classified as episodic, high-frequency, or chronic according to IHS criteria. Clinical severity was evaluated using the Fibromyalgia Impact Questionnaire, Zung Anxiety and Depression scales, Multidimensional Assessment of Fatigue, and the Brief Pain Inventory. Skin biopsy assessed intraepidermal nerve fibre density (IENFD). A multivariate analysis of covariance (MANCOVA) tested the effects of migraine category and SFP (present/absent) on clinical variables, with age as covariate.

Results. Migraine was diagnosed in 46.6% of FM patients, including 50% with frequent or chronic forms. Reduced IENFD was observed in 64.5%. MANCOVA indicated a significant effect of migraine comorbidity ($p=0.047$) and a significant migraine × SFP interaction ($p=0.003$) on the multivariate clinical profile, whereas univariate ANOVAs were not individually significant. FM patients with chronic migraine showed higher anxiety and greater pain interference. SFP alone was associated only with higher symptom severity scores.

Conclusions. Migraine comorbidity, particularly chronic migraine, was associated with greater pain interference and higher anxiety in FM patients, whereas SFP alone did not define a distinct clinical phenotype. However, the significant migraine × SFP interaction suggests that the coexistence of central and peripheral abnormalities may contribute to the overall multidimensional symptom profile of FM. Migraine and SFP jointly influence the overall clinical expression of FM. Their coexistence delineates a mixed phenotype, supporting a model of FM as a disorder spanning central and peripheral pain mechanisms.