Identification of Differential Genetic Profiles in Severe Forms of Fibromyalgia and Chronic Fatigue Syndrome

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Background: Fibromyalgia (FM) and Chronic Fatigue Syndrome (CFS) are two illnesses that presently have a diagnosis exclusively clinical. Significant differences in the prevalence of FM and CFS (2-4% to FM and 0,2-0,5% to CFS) have been reported in almost all the works, many publications, as well as the clinical experience, put forward an important overlapping (40 - 60%) between both syndromes, what indicates a dichotomy in the data.

The definition criteria of case for FM and CFS, instead of defining the diseases by their characteristics, make special emphasis in the severity of the symptoms to perform a diagnosis. Thus, in FM it will be the widespread pain and the generalized tenderness in the methodical touch of predefined points what will lead us to the diagnosis; in the CFS we will need, as a major criterion, a physical and cognitive abnormal fatigue with an high impact of the premorbid activities of the patient. Therefore, the stratification of the symptoms makes part of the diagnosis of both diseases and it is necessary for a correct therapeutic and prognostic orientation.

The need for subtypes as been established. In this study the variation in Single Nucleotide Polymorphisms (SNPs) of different ethiopathogenic pathways, was used to take insights in the genetic profile of FM and CFS. [Polymorphisms are differences in the DNA sequences of individuals in a species.] Furthermore, we related the severity of both diseases, measured with validated self-report measures, with the variation in SNPs.

Objectives: The association study was conducted to test the hypotheses that FM and CFS are different clinical and genetic entities and that the phenotypic variation observed in both disease, is in part the result of a different genetic profile.

Methods: The ACR 90 and the Fukuda-CDC 94 diagnosis criteria were used respectively for the diagnosis of FM and CFS. A group of 403 women (186 FM / 217 CFS) and an independent validation group of 282 women (126 FM / 156 CFS) were selected. The FIQ and CDC-Symptom Inventory questionnaires were used to define severity subgroups.

A total of 107 SNPs belonging to neurotransmitters (dopamine and serotonin), Propiomelanocortin (POMC), Thioredoxin reductase, Glucocorticoid receptors, Interleukins (IL), Nitric Oxide Synthetase (NOS), Tumor Necrosis Factor (TNF), Corticotropin receptors, Catechol-O-Methyltransferase (COMT) and Tryptophan hydroxylase (TPH) genes were genotyped for each patient.

Results: We identified 15 SNPs to be able to discriminate between FM and CFS patients with a 11.5 Likelihood Ratio (LR+, 95% specificity). The analysis of further SNPs allowed differential genetic profiling between the most aggressive FM phenotype and the mild forms (12.4 LR+) and between a severe CFS phenotype and milder one (12.4 LR+).

Conclusion: **The models described in this paper are suitable for the differential diagnosis between FM and CFS, as well as to differentiate subtypes between severe and milder phenotypes of both diseases, in a female Spanish population.** These subtypes could represent different illnesses or clinical situations that, in the future, can be differentiated.