

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

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Abstract

Fibromyalgia (FMS) and Chronic Fatigue (CFS) Syndrome are two controversial diseases with overlapping symptoms, difficult to distinguish and diagnose properly^{1,2}. To date there are no biological markers for either condition and are diagnosed using separate but overlapping clinical criteria. All too often the patients concerns are dismissed as imaginary or unimportant and only recently they have started to be recognized and accepted by physicians. The severity of both diseases varies according to patient, and it affects the prognosis and the therapeutic approach with important consequences for the individual's quality of life³. Therefore it is necessary to distinguish between the subtypes. Since recent studies have started to point out the genetic background of these diseases we suggested the use of SNP analysis to investigate their different genetic profiles. Among the individuals register in the "Fibromyalgia and/or Chronic Fatigue Syndrome patients Record" (www.fundacionfatiga.org/registro_pacientes.htm) 1500 subjects diagnosed with FM, CFS or both were randomly selected and invited to participate in the study. From these, 1371 gave written consent to take part and filled in a questionnaire which included details about their diagnosis, familiar diagnosis of FM or CFS and presence of mental disorders. In addition, those patients were also asked to answer the FIQ⁴ and the CSI for CFS⁵ and to provide a blood sample for DNA extraction. Taking into account that there is a recognized gender bias in FIQ, eventually only women were included in the study. Previous treatment for psychiatric disorders was also considered an exclusion criterion. At the end of the selection process the number of recruited subjects was reduced to 403 patients (186 FM patients aged 45-54 years and 217 CFS patients aged 30-39 years). These cases were clinically diagnosed according to the 1990 American College of Rheumatology (ACR) classification for FM⁶ or the US Centres for Disease Control criteria for CFS developed by Fukuda *et al.*⁷ at the Hospital Clinic and Clinica CIMA (Barcelona, Spain). For each sample one hundred and

seven SNPs were genotyped by SNPlex™. An independent second association study with 282 women (126 FM / 156 CFS) was used to validate the results. We identified 15 SNPs 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 a milder one (12.4 LR+).

In this study we prove that genetic profiling via SNP analysis can be a very effective tool to discriminate between the more severe FM and CFS cases. In addition we claim that FM and CFS are two separate diseases with an important genetic component, and we suggest that the severe cases might be different disease subtypes with distinctive genetic profiles. However this methodology is still dependable of a preliminary reliable diagnose that fulfils all the disease inclusion and exclusion criteria.

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