Authors´ Reply

To the Director: We appreciate the interest of Dr Arboleya in our work on *COMT* gene genotypes and the severity of fibromyalgia (FM), published recently in your prestigious journal.[1] Dr Arboleya mentions the relevant scientific interest of the Val158Met genotype and others of the *COMT* gene in multiple entities and clinical situations. In fact, MEDLINE relates 423 originals that mention this gene in their title or abstract in the past 2 years (PubMed accessed 20/10/2006). Our original reveals, for the first time, the interesting relationship observed by us between the polymorphisms of a concrete functional SNP (rs4680) and the severity of FM, measured through FIQ, without this being exclusive of other observations. We emphasize the word "concrete" because the letter to the editor of our counterpart uses in its argument studies that do not include this genotype[2] next to others that do not refer to FM,[3] generating a totum revolutum that, in our opinion, confounds rather than helps. Contrary to the criteria of our colleague, we understand the fact that the mechanism of temporal summation of pain, a factor that has been implied in the pathogenesis of FM,[4] is favored by diverse *COMT* genotypes and haplotypes, among them the one correspondent with our finding,[5] does not lessen its validity, quite the opposite. The same occurs with the discrepancies in gender between the refered study and our article, because a fact that is not taken into account is that in our 110 patient sample only 7 are male, a fact that we expressly pointed out as a limitation in our study. Nor is the study of less importance because of the fact that the genotype is overtly present in persons who have substance addictions, as these are not exclusion criteria for the case definition of FM. Today, a sick person can be addicted to tobacco, alcohol, etc and suffer FM. In this case, the author includes references that analze haplotypes and not SNP´s, making it difficult to establish a parallel. The suggestion that our work may have a methodologic bias for selecting as a control group completely healthy persons and that, due to the frequency of symptoms such as pain and abnormal fatigue in the general population leads to the assumption that maybe we should have included persons with some pain and some fatigue, seems to us a more philosophical than real, because it is reasonable to think that the arbitrariness of the stratification of what is considered "normal" in pain and fatigue can induce a much larger bias and make reproducibility difficult than if obtained using rigorously selected controls, not by us but by the National DNA Bank.

We ignore the basis of Dr Arboleya´s next claim: "Regarding the establishment of the severity of FM through FIQ, whose objective seems to be only judicial, as commented in the article". The objective of our original is not this, nor is it mentioned as this in the article. The FIQ is an amply validated questionnaire that reflects, among other parameters, the functional limitations of patients with FM.[6] A recent study abounds on the efficacy of the FIQ in the evaluation of severity of FM establishing a cut-point pattern[7] that coincides in a very precise way with the one detected by our work. The prestigious AMA guides establish limitation as: "The affectation to do everyday activities."[8] The usage of this and other expert judicial-skills testing seem to confuse even Dr Arboleya, because, by definition testing should be carried out by "an expert in the field that will use the largest degree of objectivity possible when emitting a determination,"[9] "which is not an impediment to decide when to use subjective or circumstantial data or whatever other means that are considered pertinent according to the experts knowledge and understanding."[10] The interest of the study regarding the basis and genetic participation in illness has already been discussed. The research into unique SNP´s in FM continues to motivate the interest of the investigators in our country.[11] Follow-up research by our team will delve into the complex genomic analysis of FM and chronic fatigue syndrome.[12]

Note: All of the authors of the original are aware of and approve the contents of this reply.

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