Reviewer's report

Title: Frequency of SCA8, SCA10, SCA12, SCA36, FXTAS and C9orf72 repeat expansions in SCA patients negative for the most common SCA subtypes

Version: 0 Date: 13 Aug 2017

Reviewer: Antonio Elia

Reviewer's report:

This is a genetic study of a cohort of 441 unrelated patients affected by ataxia and who all turned out to be negative in genetic tests for SCA1, SCA2, SCA3, SCA6, SCA7 and SCA17. In this cohort 6 patients were found to be affected by SCA8 ataxia, one patient was found to be affected by FXTAS and one patient was affected by ataxia associated by mutation in C9ORF72 gene.

The study is of interest, however there are some methodological issues and clinical features are poorly reported.

In details, I have these remarks and comments:

Abstract:

In the "background" the C9ORF72 gene is not reported. The authors should list here all the genes that they will test in this study.

In the "methods" the cohort should be clearly defined: is it a consecutive cohort of patients? Is it defined on clinical base or on genetic base?

In the "results" SCA8 patients are 5, but in the text and table they are 6.

In the "conclusions" I suggest to add also a comment on SCA8 and C9ORF72.

Introduction:

Among the many different genetic causes of ataxia the authors choose to test the cohort for SCA 8-10-12-26, FXTAS and C9ORF72. They should indicate more clearly the reasons of these choices.
Methods:

"The cohort is clinically heterogeneous ..." The authors should clearly indicate how the cohort was defined. Is it a consecutive series of patients affected by any form of ataxia? Is it the whole cohort of patients who were found to be not carriers for common types of SCA?

Results:

"Patients that appeared homozygous for one allele in the normal fragment range were reanalyzed… " This sentence should be put in methods.

I suggest to add more clinical features of the SCA8 patients (age at onset, symptom of presentation, clinical progression).

One female patient was found to be affected by FXTAS and 4 other female patients were found to carry an allele in the grey zone of FXTAS. I suggest to add more clinical features of these patients, are they affected also by primary ovarian insufficiency?

I suggest also to add a clinical description of phenotype of the patient with C9ORF72 mutation.

Discussion:

"The symptoms of the corresponding patients comprise various neurological symptoms (Table 1) …" I suggest to add a comparison with previously reported SCA8 patients.

In line 262 I suggest to change "Huntington disease (HD)" with "Huntington disease phenocopies".

Tables and figure:

A description/legend for figure is lacking.
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Unable to assess

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

No

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

Not relevant to this manuscript

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