Author’s response to reviews

Title: Two common nonsynonymous paraoxonase 1 (PON1) gene polymorphisms and brain astrocytoma and meningioma

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Author’s response to reviews: see over
Sirs,

Thank you for your letter and for the opportunity to resubmit the manuscript MS: 2011529362335605 entitled “Two common nonsynonymous paraoxonase 1 (PON1) polymorphisms are not related with the risk for brain astrocytoma and meningioma”.

We are thankful to reviewers and we agree with their comments. Two reviewers considered the manuscript adequate for publication as it is, but another reviewer requested minor changes. The manuscript was extensively revised and all concerns are addressed in the revised version of the manuscript. Changes are in red font in the revised version of the manuscript.

Reviewer Comments:

Reviewer #3:
Reviewers: Susan Searles Nielsen

Major compulsory revisions: None

Minor essential revisions:

1. Methods: Logistic regression is what would have been used to verify (as reported later in the Results) that adjustment for age, gender and education did not affect odds ratios. Rather, when mentioning logistic regression, there is a reference to “multiple comparison analysis.” (?)

The text was modified.

2. Discussion: That controls were quite different from cases on age is of concern not because they could have later developed a brain tumor (I agree this is minor). Rather, the concern is that genotype frequencies could be changing over time.

We do not see how genotype frequencies may change over time unless some of the genotypes analyzed would lead to alterations in longevity of patients or control subjects. This is highly unlikely. No changes were made regarding this point.
Also, the age difference is one reflection that the control group may not be fully comparable to cases. The newly added text should be reframed as a comparability issue, and also shortened (while keeping the new important note that there are no genetic differences between the Madrid and Extremadura). As much as a detailed addition is appreciated, it is better to not to detract from the other key issues (lack of the highly functional C-108T SNP and PON1 enzyme levels or activity).

The text in page 9 was modified.

3. Tables: Footnote ORs to clarify which models are shown and where.
   Done.

4. Table 2: Delete the astrocytoma ORs that are not shown for meningioma or all brain tumors combined earlier.
   Thank you. The text was corrected.

The following discretionary revisions might improve the manuscript.

1. Title: The change in title to make it more neutral is appreciated, and a more simple and completely neutral alternative would be: “Two common nonsynonymous paraoxonase 1 (PON1) gene polymorphisms and brain astrocytoma and meningioma.”
   Done.

2. Introduction: Delete the 2nd sentence of the Introduction or use a word other than “common,” because primary brain tumors are not common (except among those with some sort of brain tumor, which is probably what is meant, but could be misinterpreted).
   Done.

3. Discussion: For conciseness it would be accurate to summarize references 52 and 53 together in one sentence simply as having observed no main effects or interactions with insecticides for the Q192R and/or L55M SNPs, but suggested that the functional C-108T polymorphism and insecticide exposures may be important.
   Done.
4. Correct typos throughout (e.g. “of” instead of “or” in the 3rd sentence of the Introduction; “organophosphorus” instead of “organophoshorate,” and “attending the hospitals” rather than “attending to”)

Done

We hope that you consider the revised version of the manuscript adequate for publication in BMC Neurol.
We are looking forward to hear from you.

Yours sincerely,

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