Author's response to reviews

Title: Combinatorial Mismatch Scan (CMS) for loci associated with dementia in the Amish

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Author's response to reviews: see over
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BMC Medical Genetics Editors:

Please find an attached copy of the second revision of our manuscript “Combinatorial Mismatch Scan (CMS) for loci associated with dementia in the Amish”. We have addressed the second reviewer’s single “Discretionary” suggestion, and hope that the current version is acceptable for publication. The reviewer’s comments are shown in italics, and our responses and detailed changes (bold) are indicated below.

Referee 2:

“*My only suggestion relates to the comment in the manuscript that states ‘over 93% of our entire Amish sample can be traced to a single common set of ancestors…’ Indeed such a claim could be made about any arbitrary sample of individuals in the world. What makes the Amish homogeneous, and different than an arbitrary set of people, is how many Amish have descended from so few founders some limited number of generations ago. So, how big are the ‘entire Amish sample’ and the ‘single set of common ancestors?’ Also, how many generations separate them?*

We agree with the reviewer that this statement was too vague. For purposes of this study, 27 individuals were chosen out of a total of 460 individuals whom we ascertained thus far for our studies of dementia within the Amish. Our “entire Amish sample” refers to these 460 individuals. When examining the relatedness of these individuals, we discover that 430/460 can be traced back to a single founding couple that goes back 10 generations. We believe the revised text better illustrates this information.

In fact, through use of the Anabaptist Genealogy Database (AGDB), we find that 93% of our overall study population of 460 individuals and more specifically 25/27 (93%) of the individuals used in this study can be traced back 10 generations to a single founding couple. Moreover, 100% of individuals within our entire Amish sample (460) belong to one very large extended pedigree when allowing parent-child and marriage links to be included (Agarwala, 2003).

As requested we have also made note in the manuscript that this study had sufficient approval.

For this current study we identified 13 dementia cases and 14 cognitively normal individuals who met this requirement. This study was undertaken after Institutional Review Board review and approval.
Please contact me with any additional questions or concerns.

Sincerely,

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