Reviewer’s report

Title: Clinical and Molecular Genetic Characterization of Familial MECP2 Duplication Syndrome in a Chinese Family

Version: 1 Date: 06 Feb 2017

Reviewer: Helen Leonard

Reviewer's report:

Thank you to the authors for their revisions.

There are a few points on which I would still like clarification.

First of all in relation to my first question I didn't ask about diagnostic yield from microarrays because I was sure that information would not be available. What I asked for was an estimation of the number of microarray tests carried out each year in China. Is it possible to provide such an estimate?

With regard to the second question where in the text the following has been added "Physical and neurological evaluations were completed by a neurologist and a developmental specialist." I would like the initials of the two authors, i.e. the neurologist and the developmental specialist to be added here.

Under 4. Genetic results

Where you have written: "In total, four female carriers (II:3, II:11, III:2 and III:12) and four male patients (III:6,III:16, IV:1 and IV:2) in the pedigree proved that this duplication is inherited maternally."

Could this be replaced by

In total, four female carriers (II:3, II:11, III:2 and III:12) and four male patients (III:6, III:16, IV:1 and IV:2) in the pedigree harboured the duplication demonstrating that it was maternally inherited.
Under 5. Discussion

Instead of "Now it is recognized that the MECP2 duplication is the one of key causation pathogenicity for neurodevelopmental disorders." It would be more appropriate to say "MECP2 duplication is now recognized as one cause of neurodevelopmental disorders." Because it isn't necessarily a key cause as it is still a rare disorder and we don't yet know its birth prevalence.

Next paragraph

Instead of "The survey from 700 Caucasian patients suggested that In general, the prevalence of the MECP2 duplication syndrome in male and female patients with unexplained mental retardation is approximately 1% and 0.3%, respectively"


In the background there is a sentence "To date, we have evaluated for genomic copy number aberrations more than 700 patients who have an unexplained developmental delay." But there is no mention of any survey in the methods. I believe the authors need to change the wording of their sentence so that it accurately reflects the referenced literature.

I think that the final sentence in the discussion needs to be changed from:

"Meanwhile, although we described the clinical history for each patient, the less MECP2 case reported from China was insufficient for us to summarize their differential phenotype in Asian compared with the Caucasian patients, which also proved that collaboration between countries and regions is very urgent in order to studying the global natural history of rare disease such as MECP2 duplication [38]."

to

"Meanwhile, although we described the clinical history for each of our patients, the few MECP2 Duplication cases reported from China are insufficient to allow comparison of phenotypes between Asian and Caucasian patients. Collaboration between countries and regions is urgently needed in order to study the natural history of rare diseases such as MECP2 duplication on a global scale [38]."
Finally there is some recent literature in the journal Clinical Genetics which could enhance your discussion regarding the opportunity to go beyond small case series to develop large data collections and I think you could provide a little more focus on this.

**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.

Yes

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
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Not relevant to this manuscript

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