Reviewer #1:
Scientific Quality: Grade B (Very good)
Language Quality: Grade A (Priority publishing)
Conclusion: Minor revision
Specific Comments to Authors: Clinical analysis of three cases with mental retardation, seizures and language delay caused by new SETD1B mutations This is an interesting study. The manuscript would however, benefit from the following corrections:

1. Please italicize the names of genes.

   Reply: Thank you very much for your advice. We have made corresponding modifications in the revised manuscript.

2. Please provide the OMIM number of the malformations given in the text.

   Reply: Thank you very much for your advice. We have provided the OMIM number of the malformations in the revised manuscript.

3. Please mention the variant filtration strategy for WES.

   Reply: Thank you very much for your advice. We have supplemented the filtering strategy for WES in the revised manuscript.

4. It is not clear how many variants were filtered in the last step.

   Reply: Thank you very much for your advice. We added the information to the revised manuscript. Because the actual variants detected in each individual sample is different, the specific number of variants that will be filtered out in the last step of filtering will also change. According to the WES filtering strategy, quality control is usually applied to the amount of sequencing data. In this strategy, a single WES sample contains approximately 13.5G - 14 G of raw data, which is then filtered to produce approximately 12G - 12.5 G of clean data.

5. Fig. 2. Please translate the Chinese legends/labels of the figures.

   Reply: Thank you very much for your advice. We changed Fig. 2 accordingly.

6. Please give the allele frequencies of the detected variants as reported in public databases.

   Reply: Thank you very much for your advice. We added the description of allele frequencies of the three variants in the revised manuscript. The allele frequencies of the three variants detected were not recorded in dbSNP, 1000 Genomes and gnomAD databases.

7. The clinical symptoms of the patients should be presented in a comparative table showing all cases side by side.

   Reply: Thank you very much for your advice. We tabulated the main clinical phenotypes of the three patients according to the recommendations. For details, see Table 1.

8. It is not clear if there was parental consanguinity was present in these cases.

   Reply: Thank you very much for your advice. We have added the information to table 1 and the revised manuscript. The parental consanguinity was not present in these cases.

9. Please give the differential diagnosis of the phenotypes in the patients.

   Reply: Thank you very much for your advice. We have added the information to the revised manuscript. According to the clinical characteristics of the study subjects and the analysis of the WES test results, the disease-causing genes that can lead to similar clinical phenotypes have not mutated, thus excluding the possibility of other diseases.

10. Please give the basic demographic information of the study subjects.

    Reply: Thank you very much for your advice. We have added the population information of the research object, such as age, gender, nationality and ethnicity, to table 1 and the revised manuscript. At present, there is no report on the incidence rate of disease caused by *SETD1B* mutation.