Reviewer's report

Title: Novel SPAST deletion and reduced DPY30 expression in a Spastic Paraplegia type 4 kindred

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Reviewer: Ariana Kariminejad

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The authors report a novel deletion spanning from the 5'-UTR to intron 4 of SPAST which has led to low mRNA levels of SPAST and DPY30, a gene located upstream of SPAST and discuss possible implications.

Minor Comments

1- In the Introduction reference should be made to Novarino’s et al.’s paper "Exome Sequencing Links Corticospinal Motor Neuron Disease to Common Neurodegenerative Disorders". They identified 18 previously unknown candidates for AR-HSP.


2- The authors note miscarriage in one of the affected, and bring up the possibility of it's relation to DPY30. It would be a good idea to add the number of gravida and para for female cases in Table I.

3- In the pedigree it would be better if the phenotype could also be shown in addition to the genotype. This could be done by dividing each circle or square in two, one part showing genotype and the other half showing phenotype (affected or unaffected).

4- Please elaborate on reduced penetrance in previously reported cases with mutations in SPAST gene.

5- Please discuss the possibility that IV-25 is still too young to manifest symptoms. The mean age of onset was 46.75 in the other patients, so it is possible that IV-25 might show clinical findings in the future.

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests.