Reviewer's report

Title: Spinocerebellar ataxia type 17: Haplotype analysis in pedigrees with instability of the expanded allele and absence of symptoms in a 76 year old male carrying the mutation

Version: 1 Date: 1 April 2005

Reviewer: Samir K Brahmachari

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The manuscript "Spinocerebellar ataxia type 17: Haplotype analysis in pedigrees with instability of the expanded alleles and absence of symptoms in a 76 year old male carrying the mutation" by Zuhlke et al describes the observation of instability of TBP allele containing uninterrupted CAG repeats in two affected pedigrees. Further the authors go on to show that these two pedigrees which are genealogically distinct but come from the same geographical region share a common founder using microsatellite markers which are in significant LD with this locus. They also show that this background is distinct from a sporadic case containing an expanded allele with interruption. The work suggests that expanded alleles containing interruptions can have a different mutational history than the one with interruptions. As a case report the article is suitable. However, there are a number of points the authors should take into consideration

1. There are a number of inconsistencies with respect to the number of glutamine repeats range of normal and expanded alleles
2. There are a number of spelling mistakes and grammatical errors in sentences e.g.

Background
In patients with SCA17 ------ expanded heterozygously

The clinical impact ------ is not clarified

Results

The paragraph on phenotype and genotype is not clear and needs to be rewritten

Allele frequency

An frequency of 0.3 % as the lower range (0.3 â€“ 6.8%) for the minor haplotype needs to be rechecked â€“ it should be 3%

Discussion

The authors should also discuss other mechanisms of repeat expansion through loss of CAA interruption for example simple slippage etc. This has been suggested to occur in the case of SCA2 (Choudhry S, Mukerji M, Srivastava AK, Jain S, Brahmachari SK. CAG repeat instability at SCA2 locus: anchoring CAA interruptions and linked single nucleotide polymorphisms.Hum Mol Genet. 2001 Oct 1;10(21):2437-46)

Table 1 is redundant and can be excluded