Reviewer's report

Title: Cognition is only minimally impaired in Spinocerebellar Ataxia type 14 (SCA14): a neuropsychological case-control study of ten Norwegian subjects

Date: 4 November 2013

Reviewer: Wendy H Raskind

Reviewer's report:

My overall comment is that the paper, while containing a lot of the information we requested, is now very dense and difficult to read. I provide a few specifics, but leave the work of editing to the authors.

Title – This is NOT a “case-control” study. You can specify that you had “intrafamilial” as well as population controls.

The abstract should similarly specify intrafamilial controls or related controls and not just controls.

In the methods of the abstract it does state intrafamilial, but I do not understand what is meant by “matched.” Perhaps just delete “matched."

This also pertains to the body of the manuscript. Although you specify the number of family members, it is difficult to know who they are. I would have preferred comparison of the affected subjects to their unaffected siblings and not to their spouses. It might be good to show the pedigrees or at least to have a column in table 4 that explains who the numbered subjects are. Of course there is assortative mating with respect to intelligence and education level, but the genetic background is different if you are including spouses of the affected offspring and not just the parents. This must be made clear. Perhaps a range of ages of sibs might be helpful.

In the conclusion part of the abstract it should be mentioned that the mutation in these two families is not the same as those reported by the other groups. Perhaps there is a genotype/phenotype effect. This could also be mentioned in the Discussion. That is, cognitive impairment is not a common phenotype and may be related to specific mutations.

In the Methods section of the main body, what does “ten interfamilial unaffected controls matched for age, education and gender” mean? Average age and education in the two groups? Probably should include an age range for the two groups.

In Results, rather than “The mutation was not found in intrafamilial controls,” I’d suggest stating that intrafamilial controls were relatives who did not carry the mutation.

I’d suggest referring to Table 4 earlier (change it to Table 1). Otherwise it is very
difficult to follow all the psychologic testing results. And as mentioned, having pedigree numbers without knowing who are the parents of which sibship is not sufficient.

It the whole section, I am bothered by the use of “controls” and would prefer it to be “unaffected relatives.” Otherwise it might imply unrelated controls or population norms or whatever. At least use the unaffected relative at the beginning of each section.

In the Discussion, I do not understand the use of the word “phenocopy” in the section on bias. I don’t find that sentence helpful at all.