Reviewer’s report

Title: Analysis of the XRCC1 gene as a modifier of the cerebral response in ischemic stroke.

Version: 2 Date: 2 August 2006

Reviewer: Simon Koblar

Reviewer’s report:

General

This paper is a significant contribution to the field of genetics and stroke and should be accepted for publication. The authors have investigated a novel and important hypothesis in relation to the genetic mechanisms of cerebral response to ischaemic stroke. Their finding is clearly presented in that a polymorphism of the DNA repair gene, XRCCI, is associated with a patient’s ischaemic stroke volume. This association exists in non-lacunar stroke patients as determined by MRI and CT brain imaging. Of significant importance is that this finding is biologically plausible in ischaemic stroke even though most data is derived from oncogenesis.

However, one should remain mindful that association studies are inherently weak and the sample size is critically important. The study of a common disease, like stroke, with only 247 patients in my opinion denotes a small sample size and verification of this association with significantly larger numbers of patients is essential.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

- It is important to revise Tables 1 and 2 to make them more informative so they better reflect the text results. This would greatly strengthen the paper and allow readers to draw their own conclusions with the availability of raw data.
- Table 1 â€“ more information is required and there is suggestion of inaccuracy:
  o Do not require mean age to two decimal point accuracy.
  o Ethnicity numbers add to 133 patients â€“ where is the other patient?
  o Need raw numbers of patients with clinical characteristics â€“ not just %.
- Table 2 â€“ more information is required:
  o It is necessary to give SD alongside the mean stroke volumes.
  o Another column with the actual statistical results is strongly suggested (include p values)
  o Another row demonstrating the sub-type analysis of large vessel stroke to support the last paragraph in the results section

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

- There appears to be an error in the calculation of the â€œTâ€ allele frequency in the cases and controls as stated in the second paragraph of the results section. Please revise.
- In the References the number 14 has been omitted. Please correct.
- In the first paragraph of the results section the authors state that the infarct volumes ranged from 0.2 to 482 cm³. I would question that an infarct volume of 0.2 cm³ is indeed a lacunar infarction.

Discretionary Revisions (which the author can choose to ignore)

- In the discussion section I strongly suggest the authors discuss in more detail their small sample size and the necessity to verify their study’s primary finding.

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions
Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:

'I declare that I have no competing interests'