Reviewer’s report

Title: Nonsteroidal anti-inflammatory drug use and Alzheimer’s disease risk: the MIRAGE Study

Version: 2 Date: 23 July 2004

Reviewer: Joan Lindsay

Reviewer’s report:

General

I found the paper was well-written and clear. Little work has been done on identifying differences in response to NSAIDs by those with the APOE-4 allele and those without. It is well known that the APOE-4 allele increases risk of Alzheimer’s disease, and a majority of studies support a reduction in risk of AD in those who have taken NSAIDs, but bringing the two together has been done rarely and this study contributes to looking at this combination of risk/protective factors.

The methods are appropriate and well described. It would have been preferable to have proxy interviews of the controls as well as the cases, but the authors acknowledge the bias that this might introduce. The discussion and conclusions are well balanced and the authors do not claim the study has done more than it has.

The authors note that they did not differentiate between aspirin and other NSAIDs. If further data are collected, this would strengthen the study. It would also be interesting if there were more exposure categories, e.g. occasional use of NSAIDs, continuous use for 6 months, for 1 year, for more than 1 year. It would be a strength to be able to examine dose-response relationships in the APOE-4 group and those without APOE-4. As a discretionary revision, this latter point could be mentioned in the discussion.

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

1. None.

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

2. Abstract, Background, 2nd sentence, should read, We sought to examine. . . (‘to’ is omitted).

3. Abstract, Results: Needs rewording. It now says that an OR of 0.49; 95% CI 0.24-0.98 is not significant. (Of course it is.) It means that although this OR was significant, evaluation of the interaction between NSAID use and APOE-4 status did not reveal a significant difference (p=0.40). (According to the results section.)

Discretionary Revisions (which the author can choose to ignore)

It would be a strength to be able to examine dose-response relationships in the APOE-4 group and those without APOE-4. This point could be mentioned in the discussion.
What next?: Accept after minor essential revisions

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests: None