Reviewer’s report

Title: Biological inflammatory markers mediate the effect of preoperative pain-related behaviours on postoperative analgesics requirements

Version: 1 Date: 30 Sept 2015

Reviewer: Giovanni Cucchiaro

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It is difficult to accept the Authors' premises that a meta-analysis of the literature data will allow us to find an answer to their question "does the use of Desflurane reduce the incidence of cognitive dysfunction compared to Sevoflurane or Propofol?" given the heterogeneity of the populations studied and different methodologies used in the listed studies.

I can argue that the methodology in some of the studies used for the final analysis is far from being ideal. It is hard to believe that the cognitive function of an 18 year old is the same as that of a 78 year old individual (i.e.ref 18-19) as well as that relatively simple procedures like a mastectomy (ref 21) have the same consequence on cognitive functions as a CABG (ref 22). Moreover, the Authors should explain how a meta-analysis would provide more information given that every study thus far have failed to find a difference between the different agents used during general anesthesia.

METHODOLOGY

Studies selection:

1) Population criteria. I would present the average and standard deviation of the populations' age in Table 1. Showing the range can actually trigger comments like my previous one. The range in ref 18 is 19-76 years, however the means were 62 and 60 years respectively.

2) The Authors should provide the results of the I2 index or at least the confidence intervals of the POCD reported in the listed studies.

3) There is no mention of isoflurane in the selection criteria, however, studies including isoflurane are presented in the results section.

4) Although there is a list of criteria used to justify the final selection of studies, no quality scores seemed to be have been used to show differences between the different studies considered in the final analysis.

RESULTS
1) If the primary aim was to look for differences in cognitive functions, how could the Authors present a Table (continuation of Table 1) with a list of studies where the incidence of POCD is N/A?

2) The amount of data from each study presented by the Authors is quite limited. Much more information is needed to better understand what happened in each study considered for the meta-analysis.

3) Similarly, there should be a list of the excluded studies along with the criteria that were used to disqualify them from the final analysis.

4) What was the weight of each study? It seems that in a minority of studies a significant difference was found and in the majority no difference was found.

5) How did the authors adjust for inter-studies variability in way POCD was tested?

6) What is the effect size?

7) What is the between-studies variance?

DISCUSSION

The Authors are correct in saying that they cannot draw recommendations from their data and analysis. This is not surprising.

It is also unclear whether why they say that the data at the 6 hour mark are unclear, while the data from the previous hours are more obvious.

In conclusion, I believe that the study has significant flaws and I strongly recommended doing a literature search to verify the correct methodology when looking to conduct a meta-analysis study (J De Coster, 2004, AJ Sutton 2000)

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
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