Reviewer's report

Title: Birth weight and blood lipid levels in Spanish adolescents: Influence of selected APOE, APOC3 and PPAR-gamma-2 gene polymorphisms. The AVENA Study

Version: 1 Date: 11 September 2008

Reviewer: Marie Aline Charles

Reviewer's report:

The aim of the study was to assess whether the relationship between birth weight and serum lipids concentrations were different according to known polymorphism in candidate genes in a group of 502 Spanish adolescents.

Major revision
- An association between low birthweight and high blood pressure or glucose intolerance has been described and replicated in many epidemiologic studies. Data are more controversial for blood lipid concentrations and it has been suggested that post natal growth is a likely confounder of the association. Therefore, the introduction needs to summarize the literature on that topic and give an overview of published data in both men and women before presenting results on the modifying effect of genetic polymorphisms. The discussion needs to comment the correlations described in Table 1 (found in males only) in the context of previously published data.
- The adjustment of relationships between birthweight and later cardiometabolic factors on current BMI has been a matter of debate in the literature. Therefore, the correlations with birthweight in the whole sample and according to genetic polymorphisms should be shown before and after adjustment for current BMI.
- The discussion should include the effect size of the previously published interactions between polymorphisms in the PPARgamma2 and ApoE genes and compare it to the results of the present study. The authors claim a lack of statistical power to detect an association for the Pro12Ala polymorphism, yet the number of subjects carrying the Ala allele is similar to the number of #3/#4 carriers, suggesting that they expected a lower effect size.
- A table with the main demographic, anthropometric, biological characteristics of this sample of adolescents needs to be included. Some of the details given in the text could thus be deleted.

Minor revision
- More details should be given about the comparison of the subjects with or without blood sampling. It would not be not reassuring to know that BMI is similar between the two groups if age and gender distribution were different..
- Association between the different polymorphisms and BMI should be given for all polymorphisms, not just APOE.
- Units must be added Table 2 and 3

Discretionary development
- The Holm method was used to take into account the number of statistical tests performed. However, some of the tests are not independent: i.e. if an association is found with HDL cholesterol, then a similar association is expected with apoA concentration. Was it taken into account?

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.