Reviewer's report

Title: Influence of FTO variants on obesity, inflammation and cardiovascular disease risk biomarkers in Spanish children: a case-control multicentre study.

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Reviewer: Alberto Loche

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In the paper entitled: “Influence of FTO variants on obesity, inflammation and cardiovascular disease risk biomarkers in Spanish children: a case-control multicentre study”, Olza and colleagues analyze the previously widely studied association between FTO and obesity (and related biomarkers) in the Spanish population. The authors validate the association of rs9939609, rs9928094, rs9930333 and 9935401 with obesity and report the negative association of rs8061518.

The paper is overall well written and the study is well conceived, even though the data are largely confirmatory. There are some substantial and formal problems with the manuscript that need to be addressed.

lines 50-53: the sentence states first that an association for rs8061518 was found but after the necessary corrections, this association was no longer significant. This is a clear over-statement, that have to be corrected in the abstract.

In the abstract it is reported that all the associations were not longer significant after correction, except that for leptin, but in the results (line 210), it is reported that the snp is negatively associated with obesity after correction. This is confusing and must be clarified and corrected.

lines 53-54: this sentence is incomplete and should be expanded with the description of the haplotype.

lines 64-66: the first sentence of introduction is unrelated to the overall significance of the manuscript, should be eliminated.

lines 221-226: the authors found no association of rs8061518 after adjustment for BMI. The fact that leptin remained associated is likely due to the well known leptin increase with fat mass. The authors are encouraged to comment on that.

lines 238-240: the sentence should be corrected as follow: “A comparison between patients carrying the haplotype associated with obesity-related traits (GGCCAA) and patients carrying other haplotypes, showed strong association with weight, BMI...”. The following sentence should be reformulated in a similar way.

249-251: over-statement, already commented in the results section that after...
correction the association was no longer significant for most of the parameter.

Overall, the discussion should focus a little bit more on the clinical significance of the absence of association of FTO gene SNPs with obesity-related traits, apart from BMI. This is what is mostly reported in the literature. The role of a genetic association for leptin levels should be discussed as a clear and linear relationship with the association with BMI as a fat mass indicator.

**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.

**Declaration of competing interests:**

I declare no competing interests