Reviewer's report

Title: Meta-analysis on the effect of the N363S polymorphism of the glucocorticoid receptor gene (GRL) on human obesity

Version: 1 Date: 21 November 2005

Reviewer: Dolores Corella

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General
Marti et al have conducted an study aimed to estimate the association between the N363S polymorphism of the glucocorticoid receptor gene (GRL) and obesity. A mixed approach was employed. Data from three new case-control studies were analyzed, and in addition, to increase the statistical power, a formal meta-analysis by combining data from 12 previously published studies was carried out. They conclude that although certain genotypic effects could be population-specific, there is no compelling evidence that the N363S polymorphism is associated with either average BMI or obesity risk.

In general, the study is well designed and analyzed. However, there are some aspects that require further revision to clarify the results.

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

The major limitation of this study is the high degree of heterogeneity in the pooled studies. Such studies greatly differ in the general characteristics of the subjects as well as in the magnitude of the association. For example, if only the new data obtained from the present report were included, the OR for obesity of carriers of the 363S allele as compared with NN homozygotes was statistically significant (OR= 0.45; 95%: 0.24-0.85) and in the opposite direction obtained in the previous studies carried out by Lin et al (OR>2 and statistically significant). More information about the specific characteristics of every population is needed before pooling data. Stratification of the pooled results (Fig 1-3 and Table 3) by gender or prevalence of the variant allele could be useful to understand these contradictory findings.

The discussion of the corresponding results should be included in the new version of the manuscript.

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

A detailed legend to Figures 1-3 describing the main characteristics of the study populations is needed

What next?: Accept after minor essential revisions

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

Quality of written English: Acceptable

Statistical review: No
Declaration of competing interests:
I declare that I have no competing interests