Reviewer's report

Title: Polymorphisms in Nitric Oxide Synthase And Endothelin Genes Among Children With Obstructive Sleep Apnea

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Reviewer: Pawel Krawczyk

Reviewer's report:

Chatsuriyawong et al. showed associations between risk of obstructive sleep apnea (OSA) in children and 19 single nucleotide polymorphisms (SNPs) in nitric oxide synthase (NOS) as well as endothelin (EDN) genes. The authors included 608 children in the study and identified 128 patients with OSA. Moreover, they examined 381 SNPs in the family of NOS genes and 155 SNPs in the family of EDN genes as the candidates for OSA risk. Authors also tried to assess endothelial function using measurement of time to peak reperfusion (Tmax) and EDN1 mRNA expression. Even though the study is one of the biggest, it is not without some significant weaknesses

Major revisions:

1. There are no results in the abstract. “Result” section in the abstract included only methodological aspects of the study and should be redrafted.

2. Positive value of the article is an attempt to search of relation between large number of SNPs and risk of OSA in children. However, analysis of endothelial function is of low value due to small sample size. Tmax was calculated only for 23 patients and EDN1 mRNA expression was estimated only in 9 patients with OSA. Because of the inability to examine the relationship between endothelial function and genotypes of NOS and EDN gene families, these results may be omitted and article should be shortened.

3. Authors showed associations between single SNPs and risk of OSA (Table 2). Moreover, linkage disequilibrium (LD) analysis of the SNPs in the NOS and EDN gene families was assessed for OSA and for healthy subjects (Figures). Unfortunately, authors did not present results of step-by-step multiparameter logistic regression analysis with receiver operator characteristic for estimation of impact of different examined genotypes on risk of OSA.

4. In Table 2, authors estimated risk of OSA in patients with different genotypes and in carriers of different alleles. However, only one p-value was presented. Were statistical significances calculated for genotypes or for alleles positivity?

Minor revisions:

1. Not all abbreviations are explained in the text.
2. Genes spelling should be in italics.
3. Information on the Figures 1a and 1b are duplicated. These figures should be joined.
4. Article includes as much as 69 references. The literature should be up to date.

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

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.