Reviewer's report

Title: Randomised, double-blind, placebo-controlled clinical trial of the effects of L-ornithine on stress markers and sleep quality in healthy workers

Version: 1 Date: 7 February 2014

Reviewer: Jean-Marc TADIE

Reviewer's report:

I want to thank the Editor for giving me the opportunity to review this manuscript. In this study, Miyake and al. want to demonstrate the potential effects of L-ornithine administration on stress and sleep quality. It is a randomized, double-blind, L-ornithine vs placebo study. The authors conclude that L-ornithine supplementation relieves stress and improves sleep quality; using 3 test to study mood and fatigue, and the cortisol/DHEA-S ratio to assess biological effect (stress biomarker). In a previous study, the authors found that L-ornithine could reduce stress in an animal model (mice), and wanted to confirm their finding in the present study.

Although the question raised is really interesting, I do have some major concerns about the conclusion reached by the authors.

Major compulsory revisions
i. Method section: L-ornithine was purchased from Kyowa Hakko Bio. Does this company belong to Kirin Co Ltd? If so, this should be clarified or added as a potential conflict of interest (In previous published study using L-ornithine, the authors declared conflict of interest)

ii. Method section, statistical analysis: why did the authors decide to include 52 patients?

iii. Results section, first paragraph: even if there is no differences between two groups, the authors should add work characteristics of the study population (ie shift work...)

iv. Results section, second paragraph: how could the authors conclude that mood state improvement was induced by L-ornithine, since they did not show any dosage? In my opinion, plasma ornithine level should be added.

v. Discussion section: authors should be more cautious in their conclusion since they don’t have plasma ornithine level and only tendency in their statistical results. Furthermore, a limitation paragraph should be added.

Minor essential revisions
1. Abstract, background, first paragraph: suppress the two sentences about corbicula.

2. Background, fourth paragraph: reference 13 does not match (1973 is not so recent...
3. Methods section: why did the authors decide to administrate L-ornithine for 8 weeks? Some references or an explanation should be added.

4. Discussion section: In my opinion, limits of the three tests assessing fatigue and mood states should be discussed.

Discretionary revisions

1. Background, first paragraph: the first reference does not seem appropriate; authors should find a reference which supports the idea (ie not a review).
2. Background, second paragraph: the authors should add some references about fatigue and fatigue related stress.
3. Methods, Study population first paragraph: physically demanding work should be defined

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

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

**Declaration of competing interests:**

'I declare that I have no competing interests' JM Tadie