Reviewer's report

**Title:** Ceramides predict verbal memory performance in coronary artery disease patients undertaking exercise: a prospective cohort pilot study

**Version:** 1  **Date:** 9 July 2013

**Reviewer:** Pilar Martinez

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Saleem et al. demonstrate that higher blood baseline concentrations of long chain ceramide species C22:0 and C24:0 are significantly associated with less improvement in verbal memory performance in patients with CAD undertaking CR over 1 year. Previously it was demonstrated that very long chain ceramides are significantly associated with an increased risk of memory impairment and Alzheimer’s disease over 9 years (Mielke et al. 2012). In this manuscript, the authors extend the study of the abundance of long chain ceramides to other medical conditions and demonstrate that ceramide levels predict response to treatment. The subject matter of the paper is of interest and original.

The article needs some Minor Essential Revisions:

1) It is important to mention more prominently that ceramide species in the blood were measured

2) Saleem et al. find a correlation between long ceramide C24:0 concentrations at baseline and age. It would be important to discuss this finding more in detail, since also other groups have observed that plasma ceramide concentration decreases with age (Górska et al. 2002).

3) Since some ceramide species can be transported, it would be important to mention this in the discussion, and explain that recently ceramide transporter proteins (CERTs) have been identified in the blood and described to interact with proteins relevant to neurodegeneration in Alzheimer’s disease pathology (Mencarelli and Martinez et al. 2012) (Mencarelli et al. 2012).

**Discretionary Revisions:**

1) The authors mention that “ceramide species were measured” in the material and methods section. In the result section C22 and C24 were shown. If these are the only species that were measured then the method should specify this.

2) In the discussion it is suggested that inhibition of the synthesis of C22 and C24 ceramide species may be beneficial in CAD patients, this is indeed a very interesting idea, and this could be discussed in more detail.

**Level of interest:** An article of outstanding merit and interest in its field

**Quality of written English:** Acceptable
**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests