

Format for ANSWERING REVIEWERS

August 25, 2012



Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 12298-review.doc).

Title: Psychotherapy in anorexia nervosa: what does the absence of evidence mean? Reflections on the unexpected comparative efficacy of the Specialist Supportive Clinical Management (SSCM)

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Name of Journal: *World Journal of Translational Medicine*

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The manuscript has been improved according to the suggestions of reviewers:

A. Revision has been made according to the suggestions of the reviewer

1. The title has been modified to include the reviewer's suggestion that this information would be more informative for readers.
2. Full name of SSCM, RCT, and any other abbreviations in Abstract and in main body of the manuscript have been provided according to the suggestion of reviewers **02445294** and **00742104**.
3. A reference after the first sentence of the manuscript has been provided according to the suggestion of reviewer **02445294**.

4. We agree with reviewer **02445294** regarding the abundance of research on the topic of weather related to emotional state and well-being. However, in translational terms we prefer to maintain the focus on semi-starvation human and animal research. We agree with the reviewer that the work of Guetzkow et al is outdated, but this booklet is a direct application of the Minnesota study by Keys et al., and secondly it has never been previously mentioned in the AN literature. However, we have added a new reference (number 49), in which the influence of climate and ambient temperature in AN has been revised –Gutierrez E, Carrera O, Vazquez R, Birmingham CL: Climate might be considered as a risk factor for anorexia nervosa? A hypothesis worth another look. *Eat Behav*; 2013 Aug;14(3):278-80). Thus a sentence has been added at the end of the first paragraph on page 13: “*Notwithstanding, the role of AT and climate on the course of AN has been unduly overlooked in research*⁴⁹”.
5. Reviewer **00503486** thinks that “the paper will be much more useful if the authors can propose a new mechanism for the disease”. We agree with that observation and have published several papers mentioned in the draft (References 45, 50, 55, 56, 58, 59, and 60) where we have advanced such a mechanism which is related to the link between hyperactivity and starvation as research with the animal analogous model of Activity-based Anorexia (ABA) has shown. However, our point in this paper is to stress the faulty conceptualization of AN according to the comparative efficacy of a placebo treatment (SSCM) in contrast to genuine treatments purportedly linked to characteristics of AN. Furthermore we advance that heat treatment should be a relevant factor in AN treatment as a means of reversing hyperactivity, severe weight loss, and self-starvation as we have shown in our experimental ABA research.
6. We agree with reviewer 02445294 in that “Possibly there are more similarities between these approaches than currently expected, but just not in terms of the impact of the theoretically based interventions”. Actually this seems to be the case as no differences were reported for the RCT comparing SSCM and CBT, and we have included a new paragraph and two new references (Stiles-Shields et al., 2013,46,783-789 and Brown et al., 2013). The second reference meets the concerns of reviewer **00742104** *i.e.*, “it is well- known that for the

patient to benefit from psychotherapy they must be at a certain weight as starvation decreases capacity to concentrate and limits cognitive functions”. Accordingly, we have added the following paragraph on page 11-12:

In the same line, the authors involved in the comparison of SSCM and CBT reported that: *“there were no significant differences in patient ratings of therapeutic alliance of the two treatments. Although CBT-AN and SSCM use unique interoention strategies to achieve therapy aims, both were able to promote moderate therapeutic alliance in early treatment, increasing to strong therapeutic alliance in late treatment, to relatively the same degree”* (Ref. 36, p.787). However, this common therapeutic alliance factor across the two treatments was affected by the absence of an emphasis on weight gain owing to these treatments administered to “severe and enduring anorexia nervosa” patients²⁰. Under different circumstances, where the pressure to gain weight arouses anxiety, early therapeutic alliance seems not to be associated *“with either the likelihood of completing treatment or subsequent weight gain. In contrast, both early and later weight gain were associated with the strength of subsequent alliance. These findings indicate that it might be advisable to focus on techniques to drive weight gain rather than rely on the therapeutic alliance to bring about therapeutic change”* (Ref.37, p. 216), which highlight the golden rule in AN treatment i.e., psychotherapy only works after the starvation process has been properly managed.

B. References and typesetting were corrected and doi and PMD have been added when possible.

C. Minor English problems and language polishing has been undertaken by a professional native English translator, according to the suggestion of both reviewers (00503486 and 00742104).

Thank you again for publishing our manuscript in the *World Journal of Translational Medicine*

Sincerely yours,



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