Reviewer's report

**Title:** Behavioral symptoms in patients with Alzheimer's disease and their association with cognitive impairment.

**Version:** 2  **Date:** 21 January 2010

**Reviewer:** Edmond Teng

**Reviewer's report:**

The revised version of the manuscript by Martinez and colleagues that investigates behavioral symptoms in patients with AD addresses many of the issues raised by myself and the other reviewer about the original manuscript. However, it remains difficult to understand, primarily because there are many different variables that are included in the analyses, and the large number of complicated tables. A fair number of these measures appear to be superfluous to the main thrust of this contribution. Overall, a simplification of the analyses may further improve the manuscript.

**Major Compulsory Revisions:**

1. The authors' inclusion of the previously suggested factor analysis is appreciated. However, the factor analysis probably makes more sense if it is done across the entire subject population rather than separately in the greater BPSD and less BPSD groups—thus allowing Tables 5 and 6. Furthermore, the factor analysis is superior to and performs the same function as the multiple regression analysis summarized in Table 4, which could therefore be eliminated.

2. The inclusion of prior MMSE scores (MMSE1 and MMSE2) and their marginal relationship with current ADAS-noncog scores remains confusing. It is not clear from the manuscript when and in what context that the MMSE1 and MMSE2 scores were obtained. Since it is emphasized in the Introduction that this is a cross-sectional study and in the authors' response that the cross-sectional analyses have the greatest validity, these prior MMSE scores and the analyses associated with them can probably be eliminated.

3. In their response, the authors make clear that the purpose of including the pharmacological treatment data is to demonstrate that differences in non-cognitive symptoms that might arise from anti-dementia or behavioral drug use. It would appear that the key finding is encapsulated in the sentence: “Patients with extrapyramidal symptoms had received significantly more risperidone (15%) than patients without extrapyramidal symptoms (6%).” If so, then the statistics relevant to this comparison should be shown. Additionally, since there were otherwise no differences between the more BPSD and less BPSD groups in drug regimens (as described in the text, though without statistical attribution), the inclusion of Figures 1 and 2 seems superfluous and could be eliminated.

4. The Discussion is very long and not particularly illuminating. As presently
constructed, it would appear that the authors' primary conclusion after all of their hard work is that the current contribution is simply consistent with prior work, which is a relatively uninteresting result. Late in the Discussion, the authors start to highlight the advantages of the ADAS-Noncog as a tool for assessing BPSD. If the point of the manuscript is to extol the ADAS-Noncog, than that point should be emphasized early in the Discussion, thus providing context for why the reader should care that the current results are consistent with prior results using other instruments. Once a clear framework is established, then the rest of the Discussion might be edited down to focus on the key points that most strongly support the authors’ primary conclusions.

5. The tables are overly complicated, particularly since many of the data points do not yield significant differences. For Tables 1 and 2, the column detailing describing the overall population can probably be eliminated, leaving just the data for the groups with more or less BPSD. For both of these tables, it would be more in line with statistical conventions to report the actual statistic instead of (or in addition to) the p-value, and flagging the significant statistics. Further suggestions for Table 1:

a. Eliminate the concomitant diseases rows- their definition is vague, their frequencies do not differ between groups, and the data is not referred to at all in the text.

b. The “First Diagnosis of BPSD” row would make more sense if it were labeled “Prior Diagnosis of BPSD.”

c. As previously noted above, the MMSE1 and MMSE2 related data could be eliminated.

Minor Essential Revisions:

1. In the Introduction, the authors state that behavioral disorders in AD “can be efficiently treated with drugs,” and cite 2 articles advocating the use of anti-psychotics for this purpose. Given that recent data suggests that the anti-psychotics actually don’t work that well for BPSD, and the FDA’s black box warning against using anti-psychotics in elderly dementia patients due to safety concerns, I would strongly disagree with that statement.

2. The Introduction has been bulked up and as a result, provides a more detailed context for the manuscript. However, the first sentence of the 3rd paragraph: “Historically, the study of dementias has focused on cognitive domains” is confusing, because the rest of the paragraph appears to focus on BPSD rather than behavioral symptoms.

3. The sentence construction remains awkward at times, and there are a number of spelling errors. The manuscript would benefit from careful editing to improve the readability.

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

Declaration of competing interests:
I declare that I have no competing interests.