Author's response to reviews

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

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Author's response to reviews: see over
Dear editor and reviewer:

We strongly appreciate the effort you have undertaken in reviewing the article entitled “Behavioral symptoms in patients with Alzheimer's disease and their association with cognitive impairment”.

Please find enclosed the responses to the comments you have made. We have also added the suggestions you proposed, which will undoubtedly improve the quality of the manuscript.

**Reviewer:** Edmond Teng  
**Version:** 2  
**Date:** 21 January 2010

**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 and the multiple regression analysis summarized in Table 4, which could therefore be eliminated.
Following your suggestions, we eliminate Table 4. We agree that the factor analysis is superior to the multiple regression analysis.

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.

We emphasize that this is a cross-sectional study. And so, we eliminate the MMSE1 and MMSE2 scores and the analyses associated with them.

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.

We add the p-value (p<0.001) in the text. We also eliminate Figures 1 and 2 from the manuscript.

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.

We reduce the size of the discussion. Regarding the frequency of certain behavioral symptoms, our study coincides with other studies, but not all of our findings are consistent with previous references.
Furthermore our results indicate that non-cognitive symptoms, not necessarily increase with the severity of the disease, as other studies show.
We report the presence of a new subsyndrome (Inattentinal syndrome).
At the beginning of the discussion we emphasize the role of the ADAS-Noncog as an instrument for assessing BPSD. We have rewritten the discussion from this framework.

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 labelled “Prior Diagnosis of BPSD.”
c. As previously noted above, the MMSE1 and MMSE2 related data could be eliminated.

For Tables 1 and 2, we eliminate the column detailing the overall population, leaving just the data for the groups with more or less BPSD. For both tables we also eliminate
the column describing the p-value. We add *p<0.05 and ***p<0.001 at the bottom of the Table 2.

We eliminate the concomitant diseases rows.

We change the expression “First Diagnosis of BPSD” for “Prior Diagnosis of BPSD”.

We eliminate the MMSE1 and MMSE2 related data.

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.

We eliminate both articles that advocate the use of anti-psychotics.

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.

We eliminate the first sentence of the 3rd paragraph which is certainly confusing

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.

We try to improve the manuscript readability.

Sincerely yours

M. Fernandez on behalf of all authors.