Author's response to reviews

Title: Exploratory Analysis of Obsessive-Compulsive Dimensions in Children and Adolescents: A Prospective Follow-up Study

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Author's response to reviews: see over
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Dear Dr. Hodgkinson,

Thank you for your e-mail of October 6, 2005 and the reviews of our manuscript entitled *Exploratory Analysis of Obsessive-Compulsive Symptom Dimensions in Children and Adolescents: A Prospective Follow-up Study*, by Delorme et al. (MS: 1933898887204241).

We have taken into account the comments of the referees to prepare a revised manuscript. You will find the modifications in red in the revised text as well as a detailed answer to the referees' comments in the following pages. We hope that after the modifications we have made to our manuscript, you will now find it acceptable for publication in *BMC Psychiatry*.

Yours sincerely,

Richard Delorme, M.D.
Referee 1

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

1. Although good, the literature review would be improved with the inclusion of the following relevant articles.


The first article (Mataix-cols et al., 2005) was already included in the original version of our manuscript (reference n°7). As requested by the referee, we added the article by Leckman et al.

2. Please clarify if you used the Children’s Yale-Brown obsessive compulsive scale versus the adult version (Y-BOCS).

We used the family self-report questionnaire, designed by the Tourette Syndrome Association Genetic Consortium and based on the tic inventory and ordinal severity scales of the Yale Global Tic Severity Scale and on the symptom checklist and ordinal scales of the Y-BOCS. Thus, the evaluation of the obsessive and compulsive symptoms was based on the adult version of the Y-BOCS, not the children version. Several reasons led us to this choice. First, since one of our hypotheses was that exploratory factor analysis in our sample of children and adolescents with OCD should produce similar dimensions to those reported in adult populations, we decided to use the adult version of the Y-BOCS to increase the relevance of the comparison. Second, one of the aims of our study was to compare our results with those obtained in the only study performed to date about symptom stability in pediatric OCD (Rettew et al. 1992), which used the adult version of the YBOCS checklist. Furthermore, the family self-report questionnaire was previously used in the study conducted by Leckman et al., 2003 (Obsessive-compulsive symptom dimensions in affected sibling pairs diagnosed with Gilles de la Tourette syndrome), in which adults and children were both included. Third, the children and the adult versions of the YBOCS are both very similar: the ordinal scales of the adult and the children version are the same, and the seven major obsession categories and the six major compulsion categories are also the same. Only the miscellaneous obsessions and compulsions differ in the two versions, and are subdivided in the children version in miscellaneous, magical thinking/superstitions and excessive games categories. However, miscellaneous categories were not included in previous studies conducted in adults, and are not
included in our factor analysis. These points were added in the Methods section, under Clinical Measures (page 6, last paragraph).

3. I found the procedures to be difficult to follow as they were outlined/described in various places. This could be easily remedied by combining each into one section Procedures.

All the procedures used in our paper are described in the Methods section, under the subheadings Clinical Measures and Data Analysis. We don't think that combining them into a single section called Procedures would facilitate the understanding. But maybe we didn't understand correctly the referee's suggestion?

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Minor Essential Revisions (such as missing labels on figure, or the wrong use of a term, which the author can be trusted to correct)

1. Be consistent in your use of terms. For example, at time the text says OCD; at other times OC disorder (similar issue in referring to the Y-BOCS)

Corrections made in the abstract and in pages 3 and 5.
Referee 2

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

1. The sample size may be insufficient for factor analysis. A statistician will have to confirm this but my understanding was that at least 15 subjects per item are needed. This is a critical issue.

The factor analysis method we employed was identical to that used in papers published by Leckman et al. (1997) in The American Journal of Psychiatry and in other journals (Zhang et al. 2002, Am J Hum Genet; Alsobrook et al., 1998, Am J Med Genet). Recently a letter was published concerning the limitations of such methodology (DeGeus and Denys, 2004, Am J Psychiatry). The authors maintain that the validity of factor analyses depends more on the loading and the number of the factors obtained than on the number of patients included. It is well known that factor analysis is very sensitive to the sizes of correlation. The factor loadings that we obtained in our study were in accordance with loading suggested as valid in the article by DeGeus and Denys (2004), and the factor solution that we obtained was limited to four factors. Thus, if the factors are strong and few, a sample size of 50 may be adequate, as long as there are notably more cases than factors. Nevertheless, correlation coefficients tend to be less reliable when estimated from small samples. These points were added in the Discussion section, under Limitations (page 15, paragraph 2).

2. Another important issue is the use of the adult version of the YBOCS rather than the Children’s version. The 2 versions are similar but not identical. For example the CYBOCS includes categories about magical thinking/superstitions and excessive games that aren’t present in the adult version. It is surprising that the authors decided to use the adult version! Has the adult YBOCS been validated in paediatric populations? Having said this, the authors could turn this into their advantage since their choice (intentional or not) makes it easier to compare the results of adult and paediatric studies!!

See our answer to point 2 of referee 1, in the Major Compulsory Revisions section.

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Minor Essential Revisions (such as missing labels on figure, or the wrong use of a term, which the author can be trusted to correct)

1. Introduction, middle 1st paragraph. “Indeed the correlation between the theme of obsessions with other clinical variables is weak”. This is inaccurate. CATEGORICAL studies that used mutually exclusive subgroups of patients (e.g. checkers vs washers) were relatively uninformative but correlational studies (like the current study) have been more successful. Please reword accordingly.
As requested by the referee, we modified the sentence (page 3, paragraph 1)

2. *Intro, bottom 1st paragraph (and throughout the ms).* Rettew *et al* did NOT use symptom categories but INDIVIDUAL ITEMS of the YBOCS. Please amend.

In the study by Rettew et al., individual symptoms of 79 children and adolescents with severe OCD were recorded across an average of 7.9 years, and the symptoms were then grouped according to the categories of the Yale-Brown symptom Checklist before comparison (for more details see Method section, under Symptom and Clinical Assessment subheading, bottom paragraph, page 1051, Rettew et al., 1992, *J Am Acad Child Adolesc Psychiatry*). Thus, as we wrote in the original manuscript, Rettew et al. used categorizations according to the subheading of the YBOCS ‘to standardize the recording of symptoms’ and to assess change across time.

3. *Data analysis, page 7.* Surely the authors mean DIVIDING by the number of items in each of the 13 symptom categories, not multiplying!!! Same in 2nd paragraph.

The factor analysis method we employed was identical to that used in several papers (Leckman et al., 1997 *Am J Psychiatry*; Alsobrook et al., 1998 *Am J Med Genet*; Zhang et al. 2002 *Am J Hum Genet*; Leckman et al., 2003 *Am J Med Genet*). In all of these reports, the patients’ scores on the symptom dimensions were computed by multiplying the respective category-specific coefficients by the number of items endorsed for each of the 13 symptom categories by each participant.

4. *Page 9 & table 3.* The partial correlations ranged from 0.24 to 0.59. These were considerably weaker than those reported by Mataix-Cols et al in adults. Are the symptoms less stable in children than in adults? Or perhaps the follow-up was longer in this study? Please discuss.

The referee is right to underline that the partial correlations we obtained in our study (0.24 to 0.59) were weaker than those reported by Mataix-Cols et al. in adults (0.40 to 0.86). Three main factors might explain this discrepancy. First, it is well established that correlation coefficients tend to be less reliable when estimated from small samples. The size of our sample was limited and represented one of the major limitations of our study. Second, as suggested by the referee, the follow-up was longer in our study than in that published by Mataix-Cols et al. (four years versus two years, respectively) and could thus explain why we observed a higher variability of symptom dimensions across time. Moreover, the re-evaluation of OC symptoms three times during the two years of follow-up in the study of Mataix-cols et al. could have led to an overestimation of symptom stability induced by a rememoration bias. In our study, patients only re-fulfilled the questionnaire at the end of follow-up. Third, although our results showed that after follow-up the symptom dimensions identified remained essentially unmodified, about one third of children and adolescents in our sample showed modifications in most OC categories. By contrast, in the study of Mataix-Cols et al., about 12.6 % of patients (6 to 22 %) showed modifications in symptom
categories of the Y-BOCS after one to two years of follow-up. Thus, as underlined by the reviewer, symptoms could be less stable in children than in adults when using categorical and dimensional approaches. These issues are mentioned in the Discussion, page 13, paragraph 2.

5. Page 9. Say that the cross-dimensional correlations were in fact of NEGATIVE sign.
Modification made (page 9, paragraph 2).

Correction made (page 12, paragraph 2).

7. Page 13, 1st para. Rather than “Between comparisons”, this paragraph could more efficiently start with “Multiple regression analyses also…”
Correction made (page 13, paragraph 2).

8. Page 13, 2nd para. Again, Rettew studied individual items not categories of the YBOCS.
See the reply to point 2 in the Minor Essential Revisions section.

9. Limitations. Sample size! The authors should convince the reader that they have enough sample size to run their factor analysis.
As requested by the referee, we added more information concerning limitations due to the restricted size of our sample in the Discussion section (page 15, paragraph 3).

As requested by the referee, this paragraph (page 15, paragraph 2) was reworded, and the reference was added in the Reference section.

11. Figure 1. Why are the hoarding values negative? Did the authors use the values directly derived from the factor analysis? I.e. “save as variables” option in SPSS? Rather, they should use their own calculations, i.e. nr of items endorsed in each category divided by the nr of items in that category. If they do it this way, the values should then be positive.
As specified previously, the factor analysis method we employed was identical to that used in several published papers, and negative scores are not surprising when using this statistical method. For example, in the paper by Leckman et al. (1997), patients with no chronic tic disorder had a
negative loading for hoarding (Table 3, page 915), in contrast with patients with Tourette’s disorder who had a positive loading for hoarding.

Discretionary Revisions (which the author can choose to ignore)

1. Title. This would be clearer if they could add “symptom” between “obsessive-compulsive” and “dimensions”.

Modification made.
Referee 3

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

1. The authors carry out student's paired t-tests for comparisons of the number of categories of obsessions (1.9 +/- 2.0) but these are clearly non-normally distributed variables (since the 95% CI is negative). Given the extremely small sample size, non-parametric methods should be used instead (and will likely yield similar conclusions regarding changes over time).

As requested by the referee, we used a non-parametric method, the Wilcoxon test, to compare both groups. As expected, we obtained similar results (page 8, paragraph 2).

2. The discussion at the end of the results/symptom categories section regarding was unclear. Apparently the authors used the percent drop of the total YBOCS was used as a covariate. The authors note that they "yielded nonsignificant coefficients" and suggested that this implied the independence of overall reduction. This conclusion doesn't appear to be justified given the extremely small sample sizes. It is likely that a lack of power is the cause of the lack of significant association in this second order association.

Following the comments of the reviewer, we deleted the sentence suggesting an independence of overall reduction from the Results section (page 8, paragraph 1 and page 9, paragraph 2), and reworded the last sentence of the first paragraph in the Discussion section. Note, however, that the same results and conclusions were obtained by Mataix-Cols et al. (2002) when exploring symptom stability in a sample of adults (n=63 at two years).

3. While the authors note that they intended to carry out an exploratory factor analysis, the small sample size limits their ability to answer these questions. While the paragraph in the Discussion "Third, the loadings ..." addresses the uncertainty regarding stability of factor loadings, a more general statement of this limitation should be included (not just stating that "subgroup analysis was not done because of the need for large samples").

As requested by the referee, we added more information concerning limitations due to the restricted size of our sample in the Discussion section (page 15, paragraph 3).

4. A final caveat of the robustness of these results to non-normality of the 13 symptom categories. The authors provide no justification that these scores on the 13 measures are normally distributed, which is a hugely important assumption needed for use of factor analysis (particularly when the sample sizes are so small). This information can and should be reported in Table 1 (see note below).
As requested by the reviewer we added this information on table 2 (the referee would probably that we reported the information on table 2 not on table 1).

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**Minor Essential Revisions (such as missing labels on figure, or the wrong use of a term, which the author can be trusted to correct)**

1. *It is unclear why the df=40 for the comparison of Y-BOCS scores from baseline (22.3 +- 5.3) to follow-up (17.1 +- 5.7). Were not 42 subjects observed at both time points?*

   There was an error in the original manuscript. The df is 41 and not 40 (correction made page 6, first paragraph).

2. *Table1 might be more comprehensible if the results at baseline for the 42 subjects who were observed at follow-up were also reported. It's not clear that there is a need to report both n and % here; more useful would be including the mean score (perhaps for those reporting the symptom?).*

   As requested by the reviewer, we included in Table 1 the results at baseline for the 42 subjects who were observed at follow-up. The data summarized in the table are similar to those reported in the article by Mataix-Cols et al. (2002) exploring OC symptom dimensions in adults. Our paper was constructed to facilitate the comparison between their report and ours. This is the reason why we decided to include in this table both n and %.

3. *Figure 1 reports mean and SEM for four domains over time. This presentation would be much improved by use of parallel boxplots (since that would describe the center, spread and skew of the distribution).*

   As for Table 1, Figure 1 was designed to facilitate the comparison between the article of Mataix-Cols et al., 2002 and ours. We made a new figure using parallel boxplots as suggested by the reviewer (see below). We feel that although this figure gives more information from the statistical point of view, it is hard to interpret and renders very difficult the comparison with the data obtained in adults, which was the main aim of the figure. However, if the editor and the reviewer feel that this new version of the figure is better, we agree to replace it. If the parallel boxplots figure is chosen, the figure legend ought to be modified too.
Figure 1

Figure Legend

Figure 1. Symptom dimensions at baseline and at follow-up among 73 children and adolescents with OCD. Data represent the center, spread and skew of the distribution. ***p<0.001 (Student’s paired t-test, two-tailed, t=4.80, df=41).