Author's response to reviews

Title: Hippocampal volume in early onset depression

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PDF covering letter
RESPONSE TO REVIEWERS

Reviewer #1 – Dr. Bremner
We appreciate the reviewer’s comments regarding the manuscript. We have incorporated the comments into the manuscript. Below is a point-by-point response to the comments.

1. Pages 3, 8, 9, 11 – We have changed “reduction” to “smaller” or “decrease” as suggested.
2. Page 1 – We have changed the title (“hippocampal volume” instead of “hippocampus volume”).
3. Page 2 – We have added the mean ages of the subjects into the abstract.
4. Page 3, 8 – We have added the study by Vythilingam et al (2002).
5. Page 3 – We have clarified the statement regarding “lower resolution” in negative studies.
6. Pages 9, 10 – We have removed some of the more speculative comments regarding the correlation between duration of illness and hippocampal volume. We also stated the need for replication.
7. Page 9 – We have rephrased the sentence as suggested.
8. Page 9 – We did not state that cortisol is the culprit behind the smaller hippocampal volumes. We discuss how cortisol in pediatric depression is a complex and as of yet, unresolved question. We endeavored to discuss how the simple “increased cortisol – smaller hippocampus” concept is not so simple in pediatric depression. It is an important question for future studies.
9. Page 10 – Format error in the second to last paragraph corrected.
10. Page 10 – We were unable to find Vythilingam et al’s 1999 study; however, we added the finding by Vythilingam et al (2000) regarding anxiety in panic disorder.

Reviewer #2 – Dr Rosenberg
Again, we appreciate the comments of the reviewer regarding the manuscript. We have incorporated the comments into the manuscript. Below is a point-by-point response to the comments.

1. Page 2 – We have changed “depressed” to “MDD”. As per the previous reviewer, we added the mean (and SD) of the age.
2. Page 7 – We spelled out ANCOVA in the appropriate sections. We appreciate the reviewer pointing that out.
3. Pages 3, 9, 10 – Frodl et al (2002) was added to the background and to the discussion. The MacMillian et al, 2003 was added in our discussion of right/left differences and anxiety.
4. Page 9 – We have fleshed out the discussion related to development.
5. We appreciate the comment regarding the analysis of treatment naïve subjects. The child on methylphenidate did not meet the diagnostic criteria for ADHD at the time of the study.
6. Page 10 - Amygdala volumes were not included as we have yet to develop a measure of amygdala volume that we feel is robust enough. We did discuss this as a future direction in the discussion section of the paper.
7. We did not note any differences between familial vs. non-familial MDD patients. We agree with the reviewer that this may be due to sample size considerations.