Author's response to reviews

Title: Cortical Thickness in Youth with Major Depressive Disorder

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Version: 3
Date: 2 January 2014

Author's response to reviews:

January 2, 2014

RE: MS: 1922355904978399 Cortical Thickness in Youth with Major Depressive Disorder

To the Editor:

We have revised the manuscript in accordance with the reviewers’ suggestions and feel it is a strong paper. Below are detailed replies to each point.

Thank you for your consideration,

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RESPONSE TO REVIEWERS
Reviewer #1 (Cullen)

Major Revisions

1. We appreciate the suggestion of including the Peterson et al 2009 paper. We have added to the introduction and conclusion as indicated.

Page 3 – “Peterson et al [21] found a reduction cortical thickness across a large expanse of the lateral right cerebral hemisphere (including the DLPFC) in people at high risk for developing MDD.”

Page 7 – “Additionally, cortical thickness was greater in the MDD group in the caudal anterior cingulate cortex (ACC) – similar to an effect seen in data reported by van Eijndhoven et al. [39] and Peterson et al [21].”
Page 8 – “In people at risk for developing MDD, a thinner DLPFC was also noted [21]. The sample for that study was weighted towards adults (18% were children) and no interaction with age was detected. Cortical thickness of the DLPFC is influenced by the age of onset [50] and this may be responsible for the discrepancy noted here. Further longitudinal studies are warranted, especially in high-risk samples that develop clinical MDD.”

2. As indicated we selected the DLPFC and ACC as our a priori focus for this study. QDEC was not used. We clarified this on page 6 – “For this study we restricted our focus to middle frontal gyrus and ACC.”

3. As stated before we restricted our focus to two regions – not what was possible. We corrected the partial sentence page 6 – “In order to account for multiple comparisons, p was set at 0.01”

Minor Revisions
1. It is unclear what you are referring to. In the background (first paragraph) we are not discussing our finding of left ACC.

2. We clarified our discussion of the relation to the post-mortem work. It is the relation to age that we think connects the two. Page 8 – “Nevertheless, post-mortem investigations of neuronal and glial size and density support our results given the inverse correlation noted between thickness and age in DLPFC in MDD participants.”

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Discretionary Revisions
1. Thank you for bringing this to our attention, we neglected to mention that controls did not show any significant correlations. We have corrected that. We apologize for the oversight. Page 7 – “No significant correlations were noted in controls.”

2. We are a bit reluctant to go to far with our speculation that it is differing developmental trajectories for a few reasons. Our data is cross sectional and longitudinal studies are clearly needed. We state that on page 9 – “Further longitudinal studies are warranted, especially in high-risk samples that develop clinical MDD.”

RESPONSE TO REVIEWERS
Reviewer #2 (Smith)
Major Revisions
1. The two studies are completely separate samples collected in two different countries (Canada, USA). We have added to Page 3 – “More recently, differences in cortical thickness of the ACC have been noted in MDD [22] and in people at risk for developing MDD [21].”

2. Removal of the two subjects did not alter the results – We stated so on page 7 – “It should also be noted that removal of the two subjects with a history of
substance abuse did not change the results.”

3. We clarified this (see reviewer 1; queries 2 & 3).

4. The means are provided in the text, we added the means for the right ACC for clarity. Page 6 – “Right - controls: 2.77 ± 0.26, MDD: 2.80 ± 0.28”

5. We clarified this (see reviewer 1; query 1 – discretionary revisions).

6. The number of males and females is detailed in table 1. We agree that they are of limited power and should be considered exploratory (as stated).

7. Similar to our response the other reviewer, we are a bit reluctant to go too far with our speculation that it is differing developmental trajectories for a few reasons. Our data is cross sectional and longitudinal studies are clearly needed. We state that on page 9 – “Further longitudinal studies are warranted, especially in high-risk samples that develop clinical MDD.”

8. We updated the reference.

Minor Revisions

1. We have made the suggested change: Page 6 – “There was no age difference between the two groups (t = 1.32, df = 51, p = 0.19).”