Author's response to reviews

Title: Shape (But Not Volume) Changes in the Thalami in Parkinson Disease

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Author's response to reviews: see over
January 5, 2008

Re: MS: 313547016273307 “Shape (But Not Volume) Changes in the Thalami in Parkinson Disease”

Dear Editor,

We would like to thank the editor and the reviewers for their constructive comments, and for their time and effort for reviewing this manuscript. In the document that follows, we detail our response to the minor comments raised by the reviewers.

Reviewer #1:
Accept without revision.
No changes required.

Reviewer #2:

1. While there was no relationship with handedness, side of symptoms, side of tremor, etc was there a relationship with duration of disease? This could provide evidence for a relationship with the disease process.

We agree with the reviewer that this was important. We now include an ANOVA analysis which assesses whether or not shape changes were significantly influenced by disease duration. They did not appear to be. However, we don’t preclude such a possibility in the future when we have a greater number of subjects to examine.

2. Volumetric scanning parameters are not provided from the UBC site, but should be for consistency.

We thank the reviewer for pointing this out. We have now rectified this and included the description in the manuscript.
Reviewer #3:

1. A more detailed description of methodology used to quantify thalamic volume should be provided. In particular, how was the thalamic boundary determined?

We have expanded this in the manuscript. As we now state in the manuscript, "Although the boundaries of the thalami were determined by visual inspection, in prior work we compared feature vectors derived from thalami segmented from structural scans obtained before and after giving L-dopa medication (as part of another fMRI study) [38]. As expected, no significant differences could be detected in the two groups, suggesting that independent manual segmentation did not incur significant systematic errors."

2. Specific information regarding MRI methods applied in Vancouver should be included (as they are for the North Carolina studies).

Yes we agree. Please see reply to point #2, reviewer #2, above.

3. In the Results section, 2nd paragraph, the authors refer to a "distance measure". The meaning of this is unclear and requires further description.

We thank the reviewer for pointing this out. A formal description is given in the methods (see equation #8). As we have now state in the manuscript,

In order to provide a scalar estimate how different a given thalamus shape was, we calculated the mean of the row vectors, I (Eqn 7) separately for both the left and right thalami. A distance metric, estimating how "abnormal" a given shape was estimated by determining the Euclidean distance between the given feature vector and the mean vector. For example, the distance for right thalamus for the jth subject was estimated as:

$$Dist_{right}^j = \sqrt{\sum_{k=1}^{D} (I_{jk} - I_{mean})^2}$$

We trust that the manuscript is now suitable for publication.

Sincerely,

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