Reviewer’s report

Title: White Matter Abnormalities in Adolescents with Generalized Anxiety Disorder: a Diffusion Tensor Imaging Study

Version: 2 Date: 14 June 2013

Reviewer: Robert J Dawe

Reviewer’s report:

The premise of this study seems to be straightforward: Compare fractional anisotropy between adolescents with generalized anxiety and those without. Similar studies have been undertaken in adults, but not in adolescents, the authors claim, and this seems to be true. This reviewer would be in favor of acceptance of the manuscript for publication, but there are a couple of major questions to be answered.

Major Compulsory Revisions

1. The value of the manuscript hinges largely on the single figure, Figure 1, which shows the regions of significant or marginal FA differences between GAD subjects and normal controls. However, there are numerous problems with this figure and caption. First, it is probably too small. The regions of FA difference are visible only as white “blobs.” By increasing the figure size I would hope to see the variation in color within those blobs. This leads into the second point – I suspect the colorscales need to be rescaled. If all of the blobs are entirely white or nearly so, then the top end of the colorscale should be elevated in order to increase the dynamic range, thereby maximizing the amount of information conveyed by the figure. A third, smaller point – the axial slices should be rotated ninety degrees counterclockwise. A fourth point – the caption includes figure subparts (i.e. (a), (b), and (c)), but there are no subpart labels within the figure itself.

2. TBSS, part of the FSL package, is becoming the standard method of analyzing DTI data in studies such as this one. The authors are familiar with FSL, as they used it to perform eddy current artifact correction and diffusion tensor fitting. Therefore, I’m not sure why they would not continue with the traditional pipeline, i.e. skeletonize the FA images using TBSS to ensure that misregistrations or differences in white matter tract size have not caused the observed FA differences. The authors themselves recognize that their approach has shortcomings (last sentence of discussion). It would be extremely easy and fast to perform the analysis again using TBSS, so I think the authors should do that or at least answer the question of why they did not use TBSS.

Minor Essential Revisions

3. I gather that English is not the native language for any of the authors, and if this is true then they have done a remarkable job of preparing the manuscript for publication in English. Even so, there are some areas where the manuscript requires the attention of someone a bit more fluent in English. These areas are
too numerous to mention, but here are some examples:

a. On page 4, the sentence, “Taken together, all the neuroimaging evidences have suggested an abnormality…” should be something more like, “Taken together, all the available neuroimaging evidence suggests an abnormality…”

b. On page 5, the sentence, “Then, 508 subjects whose SCARED scores…”, is unintelligible.

c. On page 6, the sentence, “For each participant, the b0 images was normalized…,” should be, “For each participant, the b0 image was normalized…,” or, “For each participant, the b0 images were normalized…”

4. I emphasize that these are not the only areas that need attention with regards to grammar. The entire manuscript should be reviewed by a fluent, ideally native English speaker.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests.