**Article Title: DECREASED WHITE MATTER VOLUMES IN YOUTH OFFSPRING OF BIPOLAR PARENTS: A MARKER OF RISK OR RESILIENCE?**

Background: The authors compare gray and white matter volumes of BD offspring and offspring of healthy parents using voxel-based morphometry. Bipolar offspring presented with decreased WM volumes in portions of the right hemisphere, including anterior cingulate and posterior frontal lobe compared with healthy offspring. No differences between groups were observed in GM volumes. When bipolar offspring were evaluated with regard to the presence of psychiatric symptomatology, those youth without psychiatric symptoms exhibited decreased WM volumes in largely these same brain regions as the whole group when compared with healthy offspring. Those youth with psychiatric symptoms demonstrated decreased GM volumes in left parietal lobe and no WM volume abnormalities when compared with healthy offspring. WM volumes decreases in anterior cingulate and posterior frontal regions are present in bipolar offspring prior to the development of mood episodes, and may be a correlate of risk or resilience to bipolar disorder. Small GM volume decreases in left parietal lobe might be a marker of incipient psychopathology rather than an endophenotype in youth at-risk for bipolar disorder.

**Comment:** I commend the authors for their successful work on offspring as recruitment, retention and MRI investigations often pose a challenge in these populations. Further, their approach in terms of analyses is robust as it addresses potential confounding effects related to psychophathology and comorbidities. This approach enables researchers to interpret differences in volumes in terms of resilience, protective factors and risk to the disease. Thus, the current findings have significant clinical relevance and deserve to be published in a timely fashion. I would like to recommend few minor changes that should be easy to address for the authors.

1. Abstract: Please provide mean ages and N of males/females for each group.
2. Methods: did the authors consider comparing children and adolescents?
3. The authors mention that they divided groups based on their K-SADS score. Did they consider comparing groups in relation of manic/hypomanic or depressive symptoms? If not do they think these factors may play a role?
4. As they included male and female adolescents did they consider covarying for stages of puberty? I can see a reference to the Tanner scale in Table 2 but it does not appear to be discussed in the manuscript.
5. How did the authors interpret the extremely high IQ of HC offspring?
6. Did the authors calculate potential correlations between IQ and WM/GM volumes in BD and HC offspring?
7. Cortical volumes are impacted upon by a range of genetic factors (Panizzou et al. 2009, Winkler et al. 2009/2010). Are subcortical volumes affected by genetic factors to the same extent? Could the authors discuss this and provide some future direction as to how and whether future studies in psychiatry could or should address this issue e.g. gene expression etc.? W