Title: Anxiety symptoms in bipolar offspring with the brain-derived neurotrophic factor (BDNF)

Val66Met genotype

*Review outcome:* accept, minor revisions

*Overall comment:* The authors explored the relationship between BDNF polymorphisms, anxiety symptoms and family support. The novel finding of this review is that the val/val polymorphism appears to be associated with greater anxiety in BD offspring. Further, family dysfunction moderates the interaction between the BDNF genotype and anxiety symptoms in BD. These results will help with early diagnosis and prevention in high-risk individuals and are fully within the scope of this journal.

*Abstract:* I would add a sentence on the statistical methodology and consider reviewing the title to include the role of family dysfunction.

*Minor comments:* Page 3. Decreased brain-derived neurotrophic factor (BDNF) levels have been implicated in both bipolar and anxiety disorders….it should be defined whether it is in the CNS or in the periphery.

Page 3. Offspring of parents with BD are biologically sensitive to…the authors should add example to define what *biologically sensitive* refers to.

Page 4. Add references for the following statement: “with a number of studies that have also found that the val/val allele also confers risk for anxiety or BD. This inconsistency across studies may be due to the heterogeneous nature of these disorders or unidentified moderating factors between the BDNF genotype and psychiatric symptoms”.

Page 12. …can affect the epigenetic regulation of BDNF genes…. Please define or add a sentence explaining what the authors refer to (BDNF expression? DNA methylation?).