

Comment (C): Please provide more details on the studies that investigate the single-nucleotide polymorphisms that are associated with the transcription of FKBP5. Also describe what are the populations included in each study, such as their race/ethnicity.

Response (R): We appreciate the reviewer's comment. We have included more details on this issue: "Binder et al. [8] evaluated the effect of rs1360780 variants in 294 subjects with mood disorders and 339 healthy controls, all of Caucasian ethnicity and more than 90% of German origin. They found that FKBP5 protein levels were 2-fold higher in carriers of the TT genotype of rs1360780. Likewise, in healthy controls, *FKBP5* mRNA levels in peripheral blood cells were higher in carriers of the TT genotype. These results are consistent with those subsequently found by Klengel et al. [21] from a cohort of African-American participants. In the latter research, of particular relevance in the field, the authors performed functional tests that corroborated the effect of the T-allele on transcription and chromatin structure, as well as its epigenetic regulation."

C: In line 119, please cite more papers.

R: We appreciate the reviewer's comment. In addition to the references of Klengel et al. 2013A and Klengel et al. 2013B, we have included Binder et al. 2004 and Pakinaaho et al. 2010.

C: In line 112, please provide more evidence on how rs1360780 is the SNP that most strongly associate with the mRNA expression.

R: We appreciate the reviewer's comment. In the second paragraph of point 3, we described the potential structural mechanism that explains the increased expression levels of *FKBP5*: "The presence of the T- allele is associated with structural DNA and chromatin modifications that play a crucial role in FKBP5 transcription. Sequences containing this variant have a higher affinity for the TATA-box binding protein, which facilitates direct contact of intron 2 with the transcription start site [21,22]. This interaction is mediated by specific three-dimensional chromatin configurations that promote gene expression [15,21,22]." We have incorporated further description of the studies obtaining these conclusions in the additional paragraph that was added as a reviewer's suggestion (third paragraph of point 3).