Reviewer's report

**Title:** Serotonin transporter gene polymorphisms and brain function during emotional distraction from cognitive processing in posttraumatic stress disorder

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**Reviewer:** Udo Dannlowski

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Morey et al. report novel data from a functional MRI study on N=42 trauma exposed subjects (divided into a PTSD and a non-PTSD group by means of a cutoff score in the DTS) genotyped for several polymorphisms in the serotonin transporter gene (SLC6A4), including the frequently studied length polymorphism 5-HTTLPR. Subjects underwent a working-memory task with trauma-related pictures as distractors. In a previous publication they reported group differences between the PTSD and the non-PTSD group regarding the neurobiological responses to combat-related pictures (vs. scrambled pictures). In the present study, they sought to investigate genetic effects on brain activation patterns in (functionally predefined) ROIs, involved in emotion processing and regulation.

The fMRI paradigm is interesting and well designed. The imaging methods seem excellent. The weaknesses of the study (e.g., small sample sizes, racial heterogeneity) were addressed by the authors. While I still think that small sample is a major problem for the interpretation of the data (Munafo et al. (2008) suggested at least N=70 subjects for detecting 5-HTTLPR effects on amygdala responsiveness), the study is interesting and definitely a contribution to the field. The manuscript is concise and well written. I just have a few thoughts and questions the authors might want to address:

#1 The authors correctly state that amygdala hyper-responsiveness has been repeatedly reported in PTSD patients. However, this doesn’t seem to be a very specific finding since studies in anxiety disorders (see Etkin et al. 2007 for a review) and major depression (e.g., Suslow et al., 2010) show similar results. The same holds for differences in PFC activation. The authors could mention these studies and provide their thoughts on this issue.

#2 Introduction: Surguladze et al. (2008) did not find differential amygdala responsiveness dependent on 5HTTLPR genotype (however, they report findings in the right ventrolateral PFC).

#3 It is a pity that the LaLa groups did not have sufficient cell sizes since most studies contrast the LaLa group with all other genotypes. Did the authors find an effect of the triallelic 5HTTLPR (LaLa vs. others) if the two diagnostic groups were collapsed? If not, please provide an effect size and discuss the lack of this repeatedly observed effect.

#4 Defining PTSD by a cut-off score is not really a standard procedure. A SCID
interview or other diagnostic interviews would be more acceptable. How about treating DTS as dimensional measure (i.e., as covariate)?

#5 A problem of the paradigm is that only negatively valanced pictures (and neutral pictures plus scrambled pictures) were employed. This means that valence and emotionality are confounded. In other words – how do the authors know that the genetic effects they observed have anything to do with combat-related material or just emotional pictures in general? I would suggest referring to findings of Heinz et al. (2005) and Dannlowski et al. (2010) who both reported a valence specific effect of 5-HTTLPR on amygdala responsiveness to negative but not positive stimuli.

#6 multiple comparisons: The authors corrected sufficiently for multiple SNPs. Did they also correct for multiple ROIs?

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**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