**Psychiatry research: neuroimaging**

*Relationship between the catechol-O-methyl transferase val108/158met genotype and brain volume in treatment naïve major depressive disorder: voxel-based morphometry analysis*

The authors revised the introduction and methodology as recommended and the quality of the paper has improved significantly. There are however a few issues to be addressed.

1. Abstract: please add 1-2 sentences to highlight take-home message of the paper (overall conclusions, clinical relevance)
2. Re genotyping description: could the authors please explain if they refer to mean direct sequencing of (DNA?) regions or what kind of regions? 2. Add references for choice of primers and technique (overall)
3. Authors should be clearer when describing Freesurfer: they say that it can segment subcortical regions but not analyze subcortical regions? Please rephrase.
4. Could the authors explain why they chose to focus on the ratio between caudate volume and total GM volume? This is still not clear.
5. Discussion: I would talk about neurodevelopmental delay or abnormalities rather than differences…what kind of a differences do the authors refer to? Please rewrite or clarify
6. Unclear what authors mean by “dopamine flux in the PFC indirectly has the opposite effect on downstream dopaminergic targets…”. Please rephrase
7. Stressful life events cannot be defined as leading to neurotoxic damage unless the authors mention underlying biological mechanisms or directly describe what they mean by it. Please reconsider the rationale of this paragraph and rewrite.
8. I asked how the authors corrected their results for intracranial volume differences but this question has not been addressed. Please clarify.
9. Unclear what authors mean by “an estrogen and a primary female sex hormone down-regulated the COMT expression. Please rephrase.
10. Discussion: please either delete the words “regarding the emotional regulation” or clarify link between reward related mechanisms and emotional regulation”.
11. Language: the newly added paragraphs in the introduction, methods and conclusions need to be proofread and re-written by a native English speaker (manuscript is not easily understandable if left as it). There are a number of syntax, grammar and spelling mistakes such as “the VBM using SPM”, “Freesurfer have also been used widely”, mononuclearcells). Please write subjects/individuals with MDD and not just “MDD underwent brain scan”. Please rephrase this sentence: we added the region of interest analyses regarding the caudate volume that observed the VBM analyses” and section starting with “In addition, our results…” and finishing with “….to caudate volume in MDD”.