Reviewer's report

Title: Multimodal functional and structural neuroimaging in major depressive disorder before and after treatment with duloxetine

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Reviewer: Thomas Frodl

Reviewer's report:

This is a very interesting paper by a highly respected group in the field. The sample of 32 currently not yet treated patients with MDD is large for such a study and the longitudinal control arm (healthy controls) is novel. Interestingly, the default mode network connectivity increased while increased posterior cingulate cortex activity during the emotional stroop task decreased. OFC connectivity predicted response to therapy.

The paper has several strengths, in particular the sample size and longitudinal design and adds to the current knowledge about depression and response.

I have some minor suggestions:

There is a missing literature link to an earlier publication of this kind on venlafaxine and mirtazapine treatment using fMRI in untreated patients with depression (Frodl et al. 2011, J Clinical Psychiatry, also Lisiecka et al. 2011/2012, J Psych Res), which further would add to the hypothesis of the current study and also found changes during therapy and predicted therapy response. The current study did follow-up patients for 12 weeks, whereas the previous studies only had a treatment duration of 4 weeks until a second scan was carried out.

Information on the previous course of depression should be included, e.g. number of previous episodes, previous response to therapy and it should also be indicated if these variables differed between responders and nonresponders to duloxetine.

The facial emotional task and the stroop task should be briefly described in the main text of methods as well, since it is not that easy often to access the online material of journals.

Please describe the difficulties in data acquisition that leaded to drop outs.

The fact that there were no significant time by group interactions in resting state and face task limits the results and this should be discussed as limitation as well. Interesting is that there was a significant group by time interactions in stroop task fMRI.

Level of interest: An article of outstanding merit and interest 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:

there is no conflict of interest