Reviewer's report

Title: The Effects of Psychotropic drugs On Developing brain (ePOD) study; objectives and methods of a neuroimaging study in adolescent patients with a psychiatric disorder

Version: 2

Date: 31 October 2013

Reviewer: Kathryn R. Cullen

Reviewer's report:

Minor Essential Revisions

The sentence at the second bullet point under General Design of the ePOD Project, in which the SSRI trial is described, is unclear and has poor grammar and needs to be re-written.

The first sentence of the following paragraph (after the 3rd bullet point) is incomplete.

Under Methods--Imaging parameters---fMRI, authors state that the effect of MPH or SSRI treatment on functional connectivity in either adults or children is not known. This is incorrect, there have been several studies published on this. For example see:

The effects of stimulant medication on working memory functional connectivity in attention-deficit/hyperactivity disorder.
Wong CG, Stevens MC.

Effects of methylphenidate on resting-state brain activity in normal adults: an fMRI study.

Methylphenidate normalises activation and functional connectivity deficits in attention and motivation networks in medication-naïve children with ADHD during a rewarded continuous performance task.
Rubia K, Halari R, Cubillo A, Mohammad AM, Brammer M, Taylor E.

The Effects of Pharmacological Treatment on Functional Brain Connectome in Obsessive-Compulsive Disorder.

JAMA Psychiatry. 2013 Apr;70(4):373-82.

It's unclear why the authors detail a plan to use both DTI and rsfMRI to examine effects of MPH on the brain but only DTI to study the effects of SSRI on the brain.

In the power analysis section, authors first state that they have only limited and indirect data to perform a sample size calculation, but then they go on to say that they will have enough power with sample sizes of 15 to detect 1.25 effect size. This seems off-base.

The authors do not include a limitation section. One limitation of the study that should be stated is that for the SSRI trial, the treatment provided to adolescents and adults is not the same: both will get SSRI but only the adolescents will get CBT. This will limit the conclusions when comparing effects on the brain between groups, since CBT can also change the brain. Another limitation of the study is that the conclusions drawn about long-term, within-individual effects will be limited, since the study does not follow treated (or untreated) depression or ADHD through into adulthood. The approach taken by the authors is an excellent step forward and is ethical, but the limitations about what can be concluded should be stated.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:
I declare that I have no competing interests.