Minutes 4th TC ENIGMA-ADHD, 28 Oct 2014

Attendees:
Janneke Dammers, Maarten Mennes, Paul Thompson, Patrick de Zeeuw, Steve Faraone, Jan Haavik, Annette Conzelman, Danny Brandeis, Sarah Medland, Marcel Zwiers, Barbara Franke, Annette Conzelmann, Sara Ambrosino, Tobias Banaschewski, Andreas Reif, Sarah Baumeister, Derrek Hibar, Boris Gutman, Jan Haavik, Kerstin Konrad, Neda Jahanshad**,** representative of George Karkashadze lab, Martine Hoogman (……..we missed a few additional people).

Agenda:

- **First results**
- **Cortical protocols**
- **How should we make the data available**
- **Other initiatives**

First results

- Effect sizes of our meta-analysis are similar to those of other working groups (BP, SZ, MDD). We will take a look at the heterogeneity values for the meta-analysis
- Mega analysis: the violin plots are not optimal and show differences between cases and controls in some brain regions. This means that we are not able to remove all site effects from the data, which hampers mega-analysis. However, the meta-analysis results resemble the mega-analysis results, so that is a good thing.
- The model for the mega analysis was kept similar to the meta analysis (including age, gender and ICV as covariates) but this seemed to be too simplistic. Age^2, age*gender, diagnosis*age and diagnosis*age^2 will be added into the model.
- Age analysis: by correcting for site, we are likely to take away some of the age variance as well, because age is not equally distributed over the sites. We will contact the SZ group, who are doing similar analyses (*MH: we contacted them, but they could not help us further*). It was also suggested to make age bins (which we already did in an earlier stage with an incomplete data set; this showed similar age effects as the current analysis)
- It was suggested to use empirical p-values by permuting instead of using a p-value for controls and cases separately
- It was suggested to look at the subtypes of ADHD and/or symptom ratings. This data, however, is not available for all the sites, similar to data on medication and co-morbidity)
- We could also look at left and right structures separately, and at asymmetry. However, there are some issues with flipping of hemispheres in some scans and registration software, which would require effort from individual groups to sort through the data again. Also, there is already an ENIGMA working group focusing on asymmetry measures, so we decide to leave it to them for now.
- Boris Gutman and Paul Thompson have done some very interesting work on the shape of the caudate. The protocols for this are available, and can be executed by individual sites. Boris might be pursuing this in a proposal.
- We are dealing with incomplete data for the medication and comorbidity data. For some we have data, but we are not sure whether for example someone doesn't have a depression in the past or whether it was not asked. Therefore, we might contact you again. For the medication analysis, it was suggested to do the primary case-control analysis also in only the medication-

naive cases. In addition, we could look at differences based on the percentage of medicated participants in a sample.

Cortical protocols

I will shortly send out a Google form, in which I'll ask about whether you want to be part of follow-ups to the current project on the subcortical analysis, which will analyze cortical measures (thickness, volume). I will ask whether you already have segmented your imaging data using FreeSurfer 5.3. As decided earlier, for the cortical analysis we want to have all the data segmented with FreeSurfer5.3. If you want to be part of the cortical measure analysis, but have not segmented your data, we can help you with that. You will be able to indicate that option in the Google form.

How should we make the data available

While you have provided your data for a first analysis of subcortical volumes in Nijmegen, it is clear that a lot of additional analyses can also be done for ADHD, like the proposed analysis of cortical volumes, an analysis of DTI etc. Different people –also outside of Nijmegen- should be given the opportunity to lead such work and/or carry out analyses contributing to papers. For this to be possible the data stored in Nijmegen would need to be shared with others. We talked about prerequisites for this. Researchers should first write a proposal, which we would send to all the collaborating sites. These sites could either indicate their willingness to participate, but they could also decide opt out for individual analyses. In the Google form, we will ask you how you feel about this and how this should be operationalized. Your ethics approval might be an important guideline for your decision in this. If you have additional thoughts about this issue, you can also let us know via the Google form.

Other initiatives

Additional analysis ideas for the working group that have come up already are an analysis of structural brain connectivity through DTI data, which would be supported by Neda Jahanshad. Also Thomas Frodl, who could not join us in the call today, contacted me to ask the group about the availability of childhood adversity data in your samples. I have included that in the Google form. Earlier mentioned is the idea of the shape analysis by Boris Gutman (see above).

To do next:

- Update of the presented analyses according to the suggestions collected today
- Circulation of a first draft of the paper by beginning in December
- A Google form will be sent out within the next few days. Please fill out the form to indicate: which additional data you have available for your sample (e.g. DTI), what your opinion is about data sharing for additional proposals, and information about cortical analysis