

ENIGMA-ADHD

Teleconference | Tuesday, June 23, 2015
7AM PST, 10AM Eastern, 3PM BST, 4PM CEST

Attendees:

- Barbara Franke
- Boris Gutman
- Christopher Whelan
- Danny Brandeis
- Derrek Hibar
- Yuliya Yoncheva
- Martine Hoogman
- Neda Jahanshad
- Sarah Durston
- Sara Ambrosino
- Paulo Mattos
- Philip Shaw
- Ruth Tuura
- Silvia Brem
- Andrew Schork
- Janneke Dammers
- ..

Actions:

- **All groups** to run cortical analyses using the ENIGMA (3) protocols
- **All** if you know potential reviewers for the subcortical paper, please let Martine know
- **All** If you know of any cohorts with older patients (>40 years), please let Martine know
- **Martine Hoogman** to run a preliminary analysis of available cortical data
- **Boris Gutman** to send everyone a link to shape analysis scripts
- **Neda Jahanshad** to perform beta-testing on Philip's cerebellar scripts
- **Philip Shaw and Martine Hoogman** to agree on a timetable for cerebellum study
- **Chris Whelan** to publicize Philip's proposed studies on the ENIGMA website
- **Neda Jahanshad** to circulate preliminary cross-disorders slides
- **Boris Gutman/Pamela Douglas and Philip Shaw** write formal proposal about their plans

Business:

1. Paper

- **Martine** thanked everyone for their constructive comments on the subcortical paper. More emphasis on mega-analysis; did not exclude meta-analysis but put them in to confirm heterogeneity between samples was not the reason for finding results. Age analysis received the most feedback... there is no way to treat these cross-sectional data as if they are longitudinal data. Three things are mentioned in the paper (i) Age*diagnosis is included in the regression analysis, and for illustrative purposes: (ii) moving averages have been included and (iii) polynomial analyses have been included.
- **Martine** asked the group if they can think of any reviewers for the paper
- **Martine** asked the group if they can think of any cohort with older ADHD patients (40 years or older).

2. New groups

- **Martine** updated attendees on three new groups from Germany, Russia and Switzerland and reminded everyone that we are still including new groups.

3. Cortical data collection

- **Martine** said that some all groups must have their cortical regions segmented already because this is incorporated in the FreeSurfer analysis that you have run for the subcortical data. For protocols please visit <http://enigma.ini.usc.edu/protocols/imaging-protocols/> (the ENIGMA3 header). The main thing for this analysis is actually to take a good look at the QC protocols from ENIGMA (http://enigma.ini.usc.edu/wp-content/uploads/2010/05/Cortical_QA_March2015.pptx)
- **Martine** emphasized that we need to decide if we have a hypothesis-driven or a hypothesis-generating approach. There are 34 cortical regions on each side, which will likely create issues of multiple comparisons. What's the groups' opinion - should we zone in on areas from previous studies?
 - **Derrek** mentioned that other groups (e.g. ENIGMA-SZ, ENIGMA-MDD) have chosen to do all of the cortical regions. Reviewers would want to know about all regions. At least in bipolar disorder, some of the regions you'd expect were certainly affected, but they also observed a very strong *global* effect across the cortex. FDR correction is typically implemented to correct for multiple comparisons. Or MEF could be applied.
 - **Philip and others** agreed that we should look across the entire brain, adopting a hypothesis-generating approach. Suggested to make an effect size heat map across the entire brain
 - **Barbara** suggested taking the left and right regions together, as per our subcortical analysis.
- **Martine** suggested a tentative deadline for inclusion of cortical data: **30th July 2015**.
 - **Derrek** gave other groups a timeline of several months... some got the processing done within a month whereas others with limited resources or more clinical backgrounds took longer.
 - **Neda** said people could zip up snapshots of their images into a package and we could help them with the QC.

- **Barbara** suggested **running a preliminary analysis on data we already have before August, when people go on vacation.**

4. Shape analysis - Boris Gutman and Pamela Douglas

- **Boris** sent everyone copies of his slides containing preliminary results.
- They ran shape analysis on data from a publicly available ADHD dataset (ADHD-200). Some of the results dovetail nicely with the group's subcortical results; caudate, thalamus, amygdala all show patterns of significant effects.
- **Boris** mentioned some of the practicalities of shape analysis:
 - Once FreeSurfer is already run, he provides the group with a set of additional scripts that take about 1 extra hour to run.
 - The QC scripts work through Matlab; Boris offered to look at snapshots if groups are not interested in running the quality analysis themselves.
- **Martine** asked how long it would take - 1 hour per subject?
 - Boris said it all depends on whether FreeSurfer has been run. It's one hour per subject if FreeSurfer has already been run.
 - Boris will **send everyone a link to the scripts on Dropbox.**
- **Martine** asked how Boris would like to move forward with the ADHD group.
 - Boris encouraged groups to download the scripts from Dropbox.
 - He can then help groups identify erroneous data and then obtain summary statistics.
 - It will start off as a meta-analysis, but mega-analysis is possible too.
 - Other groups who are running this analysis include: ENIGMA-SZ, ENIGMA-MDD.
- **Martine** asked what the images from Boris's slides mean...
 - Red areas have more influence from ADHD than blue areas (in terms of stretching in surface area).
 - Not clear whether this corresponds with functional sub-divisions of the subcortical regions.

5. Longitudinal data / cerebellum - Philip Shaw

- **Philip** took the group through two projects...
 - **1. Regional anatomy of the cerebellum in ADHD.** This project will ask whether cerebellar anatomy changes are consistent across groups or affected by medication? Their method '*Multiple atlas and template generation*' performs exceptionally well against manual segmentations. The QC is also relatively straightforward - visual QC across two raters (JPEG snapshots - 10 minutes per image). Philip asked whether anyone would be interested in piloting the project - he offered to give people access to the server at Montreal to process their data (1 hour per image). Two scholars will be working with Philip on the project.
 - **Neda** mentioned that **she would be willing to do some Beta testing for ENIGMA and create protocols if needed**
 - had some issues running the code locally a year ago

- Philip mentioned that now it can be run on a virtual machine, where data can be uploaded and deleted
- Philip said he can help anyone having problems running the protocols locally, i.e. with a weekly phone call.
- Barbara suggested that **Philip** and **Martine agree on a timetable.**
- **2. Longitudinal data.** This would be a subgroup within ADHD dedicated to longitudinal data only. Philip mentioned this very briefly, just to gauge interest.
 - **Chris** offered to publicize both new projects on the ENIGMA-ADHD website.

6. Cross disorders

- **Barbara** said processing is already completed for ADHD, MDD, SZ, BPD.
- **Neda** has a slide comparing results across these groups. **She will circulate**, although she emphasised that these results are preliminary.

7. Dimensional aspects of ADHD

- Dimensional aspects of ADHD - **Sarah Medland** proposed this project for healthy subjects but was not on the line. **Annette Conzelmann** has shown an interest in looking at symptom traits within the ENIGMA-ADHD dataset. Martine will contact her