To be distributed by Working Group PIs to their working groups

Summary of the ENIGMA Retreat, Thursday June 24 2016-Friday June 25 2016

[Please could each speaker write 5-8 lines BELOW on what they said, what points they would like people to know about the status of their group's projects. What is the N of the current analysis, maybe a key finding, and plans. Thank you!]

Chateau de Bossey, Geneva, Switzerland •Ÿ Thursday 23rd - Friday 24th June 2016
https://www.bossey.ch/en

- Day 1 -

Morning Reception

8.30am	**Registration and breakfast**
9:00am	**General introduction and overview of ENIGMA organization and working groups; introduction of new groups** Paul Thompson Paul Thompson introduced the meeting with 3 goals: (1) all the PIs meet each other and discuss "low-hanging fruit" collaborative opportunities, (2) share recent findings and challenges to help each other make decisions based on the available data, (3) discuss common themes, such as secondary proposals, genotyping, cross-disorder analyses, upcoming ENIGMA workshops, etc.

Genetics and General Updates

9:15am

ENIGMA GWAS (MRI + DTI Genomics) & polygenic scoring projects

Jason Stein & Neda Jahanshad & Derrek Hibar & Peter Kochunov & Janita Bralten

Three current projects conducting genome-wide association studies with human brain structure traits were discussed. The ENIGMA2-CHARGE Hippocampal volume and ENIGMA2-CHARGE ICV (N~33,000 for each) findings were discussed. These results are in submission for publication now. Genetic correlations with other neuropsychiatric diseases were shown. The most significant for hippocampal volume is with Alzheimer's disease. Preliminary results for ENIGMA3 cortical thickness and cortical surface area studies were shown. We encourage all groups who have yet to upload to please do so.

9:45am

ENIGMA-Schizophrenia

Jessica Turner & Theo van Erp

The ENIGMA-SZ working group published its subcortical volume meta-analysis findings based on ~4,500 subjects from 15 samples in June 2015. The findings were replicated by the Japanese COCORO consortium. The group is currently finalizing its cortical meta-analysis based on ~9,500 subjects from 39 world-wide samples. The analyses examine between-group effects for thickness and surface area both with and without global thickness/surface area correction, as well as diagnosis x age, diagnosis x sex, medication, age of onset, duration of illness, and symptoms severity effects. Study findings include lower global thickness and surface area in patients, compared to controls. Group differences in frontal and temporal lobe cortical thickness remain present when controlling for mean cortical thickness. Significant associations with standardized medication dosage and symptoms severity are also present. Numerous secondary projects are ongoing, including relationship with positive and negative symptoms, cortical shape measures, sulcal measures, longitudinal and family meta-analyses. ENIGMA-SZ enthusiastically collaborates with the ENIGMA-DTI, ENIGMA-Early Onset Psychosis, is planning collaborations with the ENIGMA Laterality working group, and is looking forward to cross working group analyses with the BD, MDD, and 22Q working groups. Finally, we are interested in examining the possible confounding effects of differential motion between patients and controls on structural imaging abnormalities; using proxy measures of motion, estimated from rsfMRI motion correction parameters (Pardoe et al., NeuroImage, 2016).

10:00am

ENIGMA-DTI Disease Working Group Results and Status

Sinéad Kelly, Anne Uhlmann, Laura van Velzen, Neda Jahanshad

Updates:

1. The DTI analyses have taken off in 8 disease working groups and we are finding very significant effects, helping us better fully understand the findings with structural MRI, including the subcortical and cortical findings.
2. The ENIGMA-SZ DTI manuscript (led by Sinead Kelly) is near completion and will be circulated to co-authors in the next week or two.
    a. Effect sizes are similar to those found with subcortical volumes from anatomical MRI
    b. Radial diffusivity (and mean diffusivity), not axial diffusivity, show significant effects
    c. FA shows higher effect sizes than diffusivity
3. The ENIGMA-MDD DTI group (led by Sinead Kelly) has recently taken off; initial meta-analyses show effect sizes ***larger*** than those seen with volumes.
4. The anterior *corona radiata* and corpus callosum show high effects in both disorders.
5. The ENIGMA-Addiction DTI (led by Anne Uhlmann) group is performing an initial analysis. All groups currently are open to sharing the data.
6. Groups including 22q.11DS, bipolar disorder, PTSD, addiction, HIV, OCD, and Epilepsy are also currently running the DTI analyses.
7. Individual groups interested in joining any of these efforts should contact the group PI. All DTI projects are currently accepting and welcoming new groups.
8. ENIGMA-DTI Genetics --
    a. Over the last 3 years, the ENIGMA-DTI working group has been testing the reliability and heritability of the DTI measures.
    b. Our work and others have shown that most regional measures are highly heritable and are now being used to test for specific genetic variants that affect FA.
    c. Several “candidate SNPs” were previously published to show effects on FA. ENIGMA-DTI tested these in a meta/mega analytical setting in a sample size of over 6,000 individuals to determine whether the results are robust. No statistically significant effects were found across the FA regions with these historical “candidate” psychiatric SNPs.
    d. The DTI GWAS is underway. Over 8,000 samples have been submitted. Initial GWAS results show a few genome-wide

significant loci across the regions of interest. So far, these do not survive corrections across the 21 GWASs.

10:20am

e. The GWAS group is looking for added contributions for the discovery sample, and will accept contributions until September.

Break
10 minutes

Disease Working Groups, Part 1

10:30am

ENIGMA-Major Depressive Disorder
Lianne Schmaal & Dick Veltman

Updates:

1. The subcortical meta-analysis paper was published last year in Molecular Psychiatry (2015): we found evidence for **smaller hippocampal volume** in MDD compared to controls, mostly driven by recurrent patients and early age of onset patients.
2. The cortical meta-analysis paper was accepted this year in Molecular Psychiatry (2016): we found intriguing results showing **thinner cortices of various frontal, temporal and cingulate regions in adult patients**, but no differences in surface area, whereas we observed global **surface area decreases in adolescent patients** but no thickness differences.
3. Following-up on the cortical results we are now extending to a mega-analysis to capture the full age range and investigate age*diagnosis interaction effects. We presented some preliminary results based on fractional polynomial analysis, but we are thinking of using alternative more model-free statistical models for the effects of age, which will be discussed with the MDD working group members in the short term.
4. There are many other ongoing projects within ENIGMA MDD: 1.The effects of childhood maltreatment on brain volumes (Thomas Frodl), 2. The effects of suicidal thoughts on brain volume (Miguel Renteria), 3. Investigating IRT methods to obtain standardized measures of symptom severity (Felix Fischer/Matthias Rose), 4. Examining hippocampal subfields in relation to MDD (Philipp Saemann, Lianne Schmaal), 5. ENIGMA MDD Subcortical Shape project (Boris Gutman, Sean Hatton), 6. ENIGMA MDD DTI project (Sinead Kelly, Laura van Velzen, Neda Jahanshad, Lianne Schmaal), 7. Brain structural correlates of

insomnia severity in depression (Eus van Someren, Lianne Schmaal, Dick Veltman), 8. Classification of MDD using Multi-site LASSO and EPIC (Paul Thompson)

0:45am **ENIGMA-Bipolar Disorder**

Ole Andreassen & Christopher Ching

Updates:

1) The subcortical paper was published in Molecular Psychiatry
2) Derrek received input from co-authors on the cortical manuscript and it will be submitted to Mol Psychiatry the coming month. Interesting findings were obtained with a **mega-analytical** approach.
3) Chris has been working on the subcortical shape analysis and presented preliminary findings from a meta-analysis of 534 BD and 1022 HC. Shape processing will be completed by the end of July at which point there will be a data freeze for preparation of the manuscript. If you are still interested in being part of the subcortical shape analysis please contact Chris Ching (cching47@gmail.com)
4) DTI processing and analyses are ongoing. Preliminary results indicate r**eductions in FA in a variety of regions for BD patients** relative to CN (no significant increases in FA). If you are interested in participating in the BD DTI analysis, contact Josselin Houenou (josselin.houenou@inserm.fr) and Melissa Pauling (mpauling@gmail.com)
5) Ongoing work, next projects:
    a) Finalize genotyping of whole sample
    b) Start **cross-disorder** analyses, aim for mega-analysis
    c) Plan extended TBI analysis with std ENIGMA protocol

Questions: Contact Ole: o.a.andreassen@medisin.uio.no
or Chris: (cching47@gmail.com)

10:55am **ENIGMA-ADHD**

Martine Hoogman & Barbara Franke

Updates:

6) We have **appealed** to Mol Psychiatry about the subcortical paper and were allowed to submit again. It is now out with reviewers again.
7) Cortical analysis is ongoing, we have **grown from 25 projects to currently 33 projects** contributing and currently have a sample size of nearly 4,200.

8) **Strongest finding is that total surface area is smaller in people with ADHD (Cohen's d = -0.23).** Significant regional findings after FDR correction are only for cortical thickness, for temporal pole, fusiform gyrus, precentral gyrus, entorhinal cortex, and parahippocampal gyrus, in all cases the thickness is smaller. In the age-stratified analysis, an additional result is observed, showing increased (!) thickness of the superior parietal lobule (d = 0.21).
9) First promising results have been obtained for a subsample of our working group in the cerebellum project of Phil Shaw, which is currently being extended.
10) Several secondary projects have been/are being started: the subcortical shape analysis is going on with Boris Gutman, and three researchers have proposed classification/prediction projects.

11.05am

ENIGMA-OCD

Odile van den Heuvel & Premika Boedhoe

1) Subcortical meta- and mega-analysis pediatric and adult OCD: **accepted for publication in Am J Psychiatry**. Results: bigger pallidum (related to early onset/disease chronicity) and smaller hippocampus (related to comorbid depression) in adults and bigger thalamus in children.
2) Cortical meta- and mega-analysis pediatric and adult OCD: analyses in progress. Discussed the preliminary results of meta-analysis in adult OCD. Lower cortical thickness in frontal and temporal brain regions in medicated OCD patients vs controls (not in unmedicated OCD vs co). Results are not consistent with OBIC mega-analyses (voxel-based VBM and vector-based FS). Plan: run mega-analyses with specific focus on clinical variables to understand medication findings, eventually also followed by vertex-based mega-analysis.
3) Update on secondary analyses plans that run in parallel: e.g. structural covariance (from the Korean group at SNUH) and DTI (work in progress)

11:15pm

ENIGMA-PTSD

Raj Morey & Emily Dennis

1. Subcortical analysis - **subcortical volume analysis has been completed in 1845 subjects from 21 sites**, paper is in preparation.

2. Subcortical Results: smaller hippocampal and amygdala volume in PTSD across whole group analyses.
3. Hippocampal effect **driven by women**. When M and F analyzed separately, smaller hippocampus only significant in F.
4. Results remain significant when controlling for alcohol abuse and childhood trauma, but these may be moderating factors.
5. More pronounced effect left hippocampus and in right amygdala.
6. Planned analyses: DTI, hippocampal subfields, cortical volume, cortical thickness.

Lunch

11.25pm **Lunch**

2 hour 35 minutes. Working groups can use this time for break-out sessions

Disease Working Groups, Part 2

2:00pm **ENIGMA-Addictions**

Scott Mackay, Hugh Garavan & Patricia Conrod

The Addictions WG presented an update on the mega analysis currently being conducted on 3,300 cases and controls. The current strategy includes linear mixed effects analyses with split-half validation to compare drug-using groups on cortical and subcortical brain measures. We are also testing a support vector machine classifier using all ROIs to dissociate different drug use groups. Analyses reveal both dependence-general as well as drug-specific effects. The most substantial effects are associated with alcohol dependence. Patricia Conrod also presented preliminary results from a meta-analysis and compared effect sizes to those reported by other disease working groups. While this is work in progress, **analyses revealed both dependence-general as well as drug-specific effects, particularly alcohol effects on subcortical and cortical regions.**

2:10pm **ENIGMA-Epilepsy**

Christopher Whelan & Sanjay Sisodiya

2:20pm

Chris Whelan and Sanjay Sisodiya (co-chairs, ENIGMA-Epilepsy) presented results of cortical and subcortical analysis from a worldwide study of epilepsy. A paper is being drafted for Lancet Neurology. This work won an award and a plenary talk at the OHBM meeting.

Visualizing ENIGMA results: Demo
Peter Kochunov
Univ. of Maryland group presented the pilot software for visualization of outcomes of ENIGMA pipelines for DTI, and MRI measures from cortical and subcortical analyses. The software will be hosted on www.enigma-viewer.org and source code is avaiilable at http://www.nitrc.org/projects/enigmaviewer_20. The proposed viewer will integrate GWAS information and **serve as the platform for distributing supplemental material.**

Genetics Planning Working Groups, Part 2

2:30pm

ENIGMA-CNV
Ole Andreassen & Ida Sønderby

1) Infrastructure and pipeline established for ENIGMA-CNV
2) Currently data from 10,500 individuals with both CNV and imaging (ENIGMA2 +/- ENIGMA3)-data.
3) Preliminary results: there is a borderline significant trend towards a dosage response on subcortical volumes for deletion and duplication carriers of the most abundant psychiatric CNV, 15q11.2 (20 deletions, 45 duplications and 8,444 controls from 28 scannersites).
4) The low frequency of psychiatric CNVs (<0.25%) makes every contribution valuable - your data could make the difference. Contributing is easy. So if you have genetics and imaging data, please contact: i.e.sonderby@medisin.uio.no and/or o.a.andreassen@medisin.uio.no for details.

2:40pm

ENIGMA Epigenetics Working Group
Sylvane Desrivieres & Miguel Rentería
Sylvane presented an update from the ENIGMA epigenetics group (also presented as a poster at OHBM).

2:50pm

Break
20 minutes

Genetics Planning Working Groups, Part 3

3:10pm

Opportunities and Common Themes arising across groups

1. **Cross-Disorder analysis - explanation of tomorrow's 2pm meeting**
2. **GENETICS (30 min)**
   I. polygenic risk score cookbooks

- plan for harmonized polygenic scoring across disease working groups, and enrichment and genetic overlap testing - 20 min.
- II. **update on options for genotyping** (Lianne, Jess, Theo, David G, others; 10 min.)

All Disease WG PIs

3:40pm

ENIGMA Connectomics Workshop (Oct 23-28, Utrecht) for Harmonization of DTI Connectivity

Martijn van den Heuvel, Marcel de Reus, & Neda Jahanshad

Neda Jahanshad, Marcel de Reus, Paul Thompson and Martijn van den Heuvel announce a **'10Kin1day' workshop for large-scale analysis of the structural connectome** (with diffusion imaging). Aim is to gather all ENIGMA DTI members into an energetic hands-on workshop, making brain network analysis easily and directly available to ENIGMA working groups. Large datasets encouraged. Let's hit that 10K!

Tentative date: 28-30 October (arrival for international on 27).
Location: Utrecht, The Netherlands
Requirements: DTI data (bval, bvec) + FreeSurfer T1 data (similar to other ENIGMA projects)

Seats: approximately 50 available, 250 euro per participant including the workshop, housing, food, coffee
Details & join 10Kin1day: http://www.myconnectome.nl/10Kin1day

Highlights:
* analysis of DTI to connectomes will all be performed during the workshop (no strong preprocessing needed before hand). Simple instructions to participate and upload data will be made available.
* user accounts and computer power from Dutch government Super Computer SURF (https://www.surf.nl/en)
* Connectome maps collected and distributed to individual working groups for additional group-analysis of brain network data. ENIGMA PIs are encouraged to take on these projects
* morning and afternoon sessions with hands-on workshops on how to 'run' and 'analyze' connectome data on individual and group level
* workshop sponsored by ENIGMA, NCU (Utrecht University) and SURF

4:10pm

Resting State fMRI - Harmonizing ENIGMA and the Human Connectome Project

Peter Kochunov (15 min talk + 15 min discussion / questions)

The leaders of the ENIGMA-DTI group, Neda Jahanshad and Peter Kochunov, propose to use the success of the ENIGMA-DTI pipeline to analysis of the resting state data. The preliminary data were presented from a three-site sample of schizophrenia patients and controls. The PIs are soliciting data sample to create a deformable brain atlas and samples that include related individuals. Please contact Peter at pkochunov@gmail.com for information on how to contribute the data.

Disease Working Groups, Part 3

4.40pm **ENIGMA-Autism**

Daan van Rooij & Jan Buitelaar

Updates were presented by Daan van Rooij on the ENIGMA-Autism group; pilot results are presented in an OHBM poster.

4:50pm **ENIGMA-22q11DS**

Christopher Ching

The group now includes 377 deletion patients, 15 duplication patients, and 249 healthy controls. Analyses on cortical and subcortical FreeSurfer measures, subcortical shape analysis, and DTI analysis are ongoing and yielding differences between 22qDel patients and controls. Neurobehavioral data is being requested from working group members to investigate associations between brain measures and neuropsychiatric outcomes. Preliminary cross-disorder comparisons are beginning to address the overlap between imaging markers in idiopathic psychosis and 22q11 deletion syndrome.

5:00pm **ENIGMA-HIV**

Neda Jahanshad & Ron Cohen

The current HIV analysis is being led by JP Fouche in Dan Stein's group in Cape Town, South Africa. Dan Stein and Ron Cohen (U Florida) are co-PIs of the ENIGMA-HIV working group, but Dan and JP could not make the meeting. A brief background on the neuropsychiatric effects of HIV were covered:

- Infection has high comorbidity with other disorders - schizophrenia, depression, alcohol and substance abuse and addictions
- Consistent effects of CD4+ counts on brain structure are being found and meta-analyzed across cohorts in ENIGMA-HIV worldwide

Early Dinner

Starting 7:00pm

ENIGMA Planning Dinner - Restaurant du Lac Versoix

http://www.restaurant-du-lac-versoix.ch

Paul has pre-paid for dinner and transportation is being arranged for the 60 attendees, to and from Chateau de Bossey. This is a closed dinner for ENIGMA Planning; Please consult Paul re significant others; for audit reasons we cannot have additional guests.

- Day 2 -

Quick Introductions to New Working Groups

9.00am

ENIGMA-Stroke Recovery

Sook-Lei Liew

1. ENIGMA Stroke Recovery was formed in October 2015, with a goal of n>3,000 for the first full analysis. We currently have n>1,800 committed from 14 sites and are actively seeking new collaborators! Contributors should use a T1-weighted MRI and a motor score (NIHSS, Rankin, Fugl-Meyer, Wolf, etc.). Email sliew@usc.edu if you or someone you know is interested.
2. Preliminary mega-analysis results from n=281 from 8 sites show hypothesized effects, with greater basal ganglia and thalamus volumes positively correlating with motor scores, and greater lateral ventricles (for us, a clear measure of atrophy) negatively correlating with motor scores. Individual sites (n=30-40) only show weak and inconsistent results across sites - suggesting the potential impact of this approach for greater robustness.
3. We aim to conduct subgroup analyses (e.g., left/right hemisphere, acute/subacute/chronic stroke, and mild/moderate/severe stroke), to examine neural correlates of recovery of motor impairment versus functional improvements, to examine both cross-sectional and longitudinal datasets, and to look at genetic/epigenetic effects.
4. To account for the lesion volume, we are manually marking the QCs for ROIs affected by the lesion volume, and we have started the ATLAS project to manually segment over 300 brains (potentially up to 3000) to develop better automated lesion segmentation methods for use in our analyses.

9:10am

ENIGMA-Anorexia Nervosa

Esther Walton & Stefan Ehrlich

ENIGMA-AN is a new working group dedicated to improving our understanding of structural brain changes in patients with anorexia nervosa (AN) and how those changes normalize during or after recovery. Reduction of GM has been

shown in acute AN but it is unclear if those reductions are global or local. Also the speed and completeness of GM rehabilitation with realimentation remains equivocal.
Twenty sites have joined so far: about 700 cases will be available. We are happy to welcome new cohorts at any time! Contact transden.lab@uniklinikum-dresden.de for more information on how to join.

1) Goal: case-control meta-analysis (prob. subcortical-cortical)
2) Planned covariates:
•age
•time between realimentation and MR scan
•AN subtype
•psychotropic medication
•duration of illness (DOI)
•age of onset
•BMI at scanning
•comorbid diagnoses? (if available) Challenges:
•How about (partially) refed patients?
•FreeSurfer not established at several sites
•FreeSurfer versions we will accept

3) Challenges
•How about (partially) refed patients?
•FreeSurfer not established at several sites
•FreeSurfer versions we will accept

4) Future prospects: Participation in cross-disorder comparisons and an analysis of the effects of BMI on brain structure across large samples was discussed.

9:20am **ENIGMA Studies of Family Members**

Neeltje van Haren

ENIGMA-Relatives aims to investigate brain abnormalities in (first-degree) relatives of patients. This project originated in the ENIGMA schizophrenia group and now includes relatives from both schizophrenia and bipolar disorder. Given that the relative risk to develop the disorder differs for different types of relatives, the goal of this group is to study the association between the extent of brain deficits and the relative risk to develop the disease.

Five sites sent in their data (N = 1971); parents, siblings, offspring, monozygotic and dizygotic cotwins, patients and healthy controls) and another

11 have agreed to join (total N = 4545). Preliminary results show the largest effects in the offspring for both schizophrenia and bipolar disorder. We are still including sites [please contact Sonja de Zwarte; s.m.c.dezwarte@umcutrecht.nl]!

ENIGMA-Parkinson's Disease

Ysbrand van der Werf & Boris Gutman

9:30am

9:40am

The ENIGMA-PD workgroup was launched on June 9, 2016 in the first telco. Currently, 15 sites in 10 countries have indicated wanting to collaborate with >1,000 PD and >1,000 control scans pledged; we are still keen to include more sites. Please email Ysbrand (yd.vanderwerf@vumc.nl) and/or Boris (bgutman@gmail.com) if you know of any sites, we are happy to supply more information.
Our first step will be to perform FreeSurfer (cortical and subcortical) analyses on each of the local cohorts followed by meta-analysis.

ENIGMA-Irritability

Robert Althoff

9:50am

The irritability WG presented the rationale for this new group, initially focusing on the pediatric population. The rationale is to examine irritability as a cross-diagnostic phenotype that is increasingly being studied as its own entity, related to ODD, MDD, bipolar disorder, PTSD, anxiety, and other diagnoses. Data were presented on a preliminary analysis within the IMAGEN dataset with both structural and GWAS findings using a quantitative phenotype of irritability. The WG is currently recruiting and has approximately 5500 samples pledged at this time with an initial plan of mega-analysis for structural associates. Groups with any irritability measure are encouraged to contact the working group.

ENIGMA-GCTA

Roberto Toro and JB Poline

This WG is gathering SNP data to get better estimates of brain structures / other phenotypes and testing new statistical methods to estimate heritability (Bonnet et al., BioRxiv; Zhou et al., in prep). We will be looking at functional partitions of SNP, genetic correlations, etc.

Healthy Variation Working Groups

10:00am

ENIGMA-Lifespan

Danai Dima & Sophia Frangou

Update: Current sample size of the Lifespan group is above 12,000. Subcortical and cortical analysis completed. The results in subcortical analysis due to be published in Human Brain Mapping (now under revision). Drafting of the cortical manuscript will proceed.

10:10am **ENIGMA-Laterality**

Clyde Francks & Tulio Guadalupe

ENIGMA Laterality: the first paper on effects of sex, handedness and age on subcortical volumetric asymmetries, in 52 healthy control or population datasets, is under review at Brain Imaging and Behavior (reviews just came back, July 2016). The group proposes a similar study of cortical asymmetries (global and regional surface and thickness asymmetries) in terms of healthy variation. Similarly, diagnosis effects will be investigated in separate partnerships with individual disease groups. A genetic study of superior temporal gyrus asymmetry, with an evolutionary context, is also underway.

10:20am **ENIGMA-Plasticity/Change**

Rachel Brouwer & Hilleke Hulshoff Pol

The ENIGMA plasticity working group has finished its first project on the heritability of longitudinal brain changes. Results include:

- Heritability of change in all global and most subcortical volume change in several cohorts throughout the lifespan and from across the world
- Longitudinal MRI is sensitive enough to pick up genetic signal on univariate annual change rate
- Genes for baseline volume are not always the same as genes for subsequent change.

Next step: GWAS on volumetric brain changes. We are currently writing a proposal and will reach out to groups that have longitudinal MRI and GWA available very soon. For more information, please contact Rachel Brouwer [r.m.brouwer-4@umcutrecht.nl].

10:30am **Break**

15 minutes

Methods Development Working Groups

10:45am **ENIGMA Shape Analysis - Protocols and Updates**

Boris Gutman & Christopher Ching

Boris Gutman gave an update on the results of ENIGMA Shape mapping initiatives in progress across 7-8 Disease working groups, and also in the GWAS Genomics working groups.

10:55am

ENIGMA Hippocampal Subfield Protocols
Philipp Saemann

13 of 22 candidate centers (participants of ENIGMA-MDD) are currently active in this project, which aims to localize hippocampal volume changes in MDD to specific subfields. Currently, 7 of 13 active centers have accomplished the subfield segmentation, awaiting specific instructions for quality control. This step has been identified as potentially critical to the eventual analysis, as mostly minor but also few major segmentation failures can be found. In the talk, both the general background and potential use of an MDD-related hippocampal subfield finding are explained and the QC problem is highlighted. While the algorithm proves generally stable on both 3 T and 1.5 T data, a set of (potentially) failed segmentations is demonstrated (spared areas in CA1 and CA3, discontinuous CA1, 'bulky CA1', incomplete/too large subiculum). Next steps include (a) contacting the centers for examples of qualitatively different examples to develop a more systematic 3-categories-scheme, and (b) discuss essential points with the developers.

11:05am

Cortical folds - In Depth Cortical Analysis (waiting for slides)
Neda Jahanshad & Jeff Mangin

Jeff Mangin and Neda Jahanshad showed a new in-depth cortical analysis that is giving a richer feature set for group analysis at the cortex, including detailed sulcal measures. Tests are underway in the ENIGMA Schizophrenia and Genomics Working Groups, showing good disease effect sizes and robust heirtability.

11:10am

Voxelwise genomics and fastGWAS
Habib Ganjgahi & Neda Jahanshad

Habib G. gave an update on his new methods for speeding up GWAS, which will be highly useful as the number of traits in ENIGMA increases to entire images.

General Discussion and Wrap-Up

11:15am

General Discussion (60 minutes)
Handling of Secondary Proposals - 10 min
Authorship and use of ENIGMA as a Consortium Author - 10 min
Updates on Handling Cross-Disorder Partnerships and Overlap - 10 min
Project Tracking and Management - 10 min
Proposed Training Workshops - 10 min
Mega vs Meta - fixed vs random effects (Habib Ganjgahi & Tom Nichols) - 10 min

Lunch

12.30pm

Lunch
90 minutes

14:00pm

Satellite meetings
If any group wants an hour to discuss their own things, they could have the room from 2pm onwards

In-depth planning of Cross-Disorder Analysis (90-min discussion led by Lianne Schmaal, Dick Veltman, and Disease Working Group PIs who have completed their Cortical Analysis).
Topics:

1. **Pairs of disorders to compare - e.g., SZ-BD-MDD (adult) and OCD-ADHD (adolescents)**
- **Comparing effect sizes (simple)**
- **Proper adjustment for site effects (mega-analysis possible?)**
- **Machine learning to distinguish 2 or more disorders (plan to start ML within each disease group first - ongoing in Addiction, MDD, ADHD)**

A follow-up call was held in July to discuss these issues in the SZ-BD-MDD Cross-Disorder group

2. **Choosing hypothesis-driven rather than data-driven analyses**
3. **Hippocampal shape (all of the above plus PTSD).**
4. **Dealing with secondary proposals that want data from more than one working group (WG PIs in the loop to monitor data sharing complies with agreements and proposal, avoid trouble/conflict)**
5. **Others**

The meeting was adjourned with thanks by Paul Thompson at 4:30pm Friday.