

Enhancing Neuroimaging Genetics through Meta-Analysis (ENIGMA)

Epilepsy Working Group



- *Memorandum of Understanding* -

21st April 2015

Introduction

Members of the ENIGMA-Epilepsy Working Group include investigators from different centers around the world who are actively engaged in neuroimaging research and who have contributed results from primary analyses of imaging, and/or genetic data, and/or algorithm development for the purpose of meta-analysis, replication, and/or algorithm testing in a collaborative manner. The Working Group's initial effort is to demonstrate the success of collaborative, systematic genome-wide image analyses across multiple centers to find and replicate genetic associations with neuroimaging phenotypes.

The ENIGMA-Epilepsy working group is expected to work collaboratively on a growing dataset of contributed results from brain phenotypes in several large samples. This database will likely be useful to investigators both within and outside of the Working Group who may request to use parts of the dataset for secondary analyses. In addition, the Working Group will likely conduct future primary analyses of different brain phenotypes, agreed in each case by contributors. This wealth of data requires (1) organization, (2) protection of authorship rights for contributors to the primary analyses, and (3) direction for future analyses.

In order to accomplish these three aims, the ENIGMA-Epilepsy working group's scientific initiatives and policies will be guided and overseen by the overall Working Group leaders: Professor Sanjay Sisodiya (UCL), Dr. Christopher D. Whelan (USC) and Professor Paul Thompson (USC). Each ENIGMA-Epilepsy subgroup will also appoint a subgroup leader: typically that sub-group's principal investigator. Subgroup leaders are responsible for ensuring that work is carried out in a timely manner, and within the appropriate ethical guidelines set down for research on human subjects. Part of this responsibility is to ensure that all sites have obtained approval from their local Ethics Committees, and that such assurances are updated regularly in accordance with Office for Human Research Protections (OHRP) regulations. Additionally, the Working Group and subgroup leaders will be responsible for oversight of authorship, determining whether a paper constitutes a Working Group Publication, and whether the scientific contributions of the sites have been correctly and fairly acknowledged in the publication.

Authorship and Publications

What Constitutes a Working Group Publication?

ENIGMA-Epilepsy Working Group publications are papers or abstracts based on investigations that: (1) rely on intellectual resources of the Working Group or (2) use data collected through the efforts of the Working Group, or (3) rely, in whole or in part, on information obtained through Working Group membership.

In agreeing to contribute MRI or GWAS results to a Working Group meta-analysis for a given phenotype, the ENIGMA-Epilepsy members at that site must also sign an agreement (below) that they will not publish or publicize (to the media or on the Internet) the results of the meta-analyses for that phenotype prior to the publication of the Working Group meta-analysis. Prior to publication, findings may be presented at conferences only after consulting in advance with the ENIGMA-Epilepsy support group. This consultation is designed to ensure that they comply with embargo policies of top-tier journals, protecting the interests of other Working Group members. In addition, secondary analyses based on the findings of the Working Group (for example, correlating structural MRI results with

neuropsychological findings in people with epilepsy), may not be submitted to journals for publication until after the Working Group paper is accepted for publication. This is intended to avoid the risk of duplicate submissions that may jeopardize a Working Group publication.

Any participating site may choose to publish and present the results of a GWAS or MRI study conducted at their own site, which does not contain analyses conducted as part of the ENIGMA-Epilepsy Working Group. These publications *do not* constitute Working Group publications. If a Working Group meta-analysis for a given phenotype is proposed and a group is already engaged in a meta-analysis for that same phenotype, the site agrees to disclose their participation in the ongoing project(s) for that phenotype if they wish to participate in the ENIGMA meta-analysis. This is also intended to avoid the risk of duplicate submissions that may jeopardize a Working Group publication.

Working Group publications may be classified as primary or secondary publications. Primary publications of the ENIGMA Working Group are those for which a meta-analysis is conducted for the first time by the Working Group on a phenotype of interest (for example a meta-analysis of GWAS results using hippocampal volume as a phenotype). Secondary publications are those that rely upon data collected in primary publications (for example re-analyzing the ENIGMA data using a novel meta-analysis technique or checking if a marker found in a separate case-control analysis is associated with the volume of the hippocampus).

Guidelines for Authorship on Primary Publications of the ENIGMA-Epilepsy Working Group

The ENIGMA-Epilepsy Working Group will be listed as an author on all Working Group publications, including manuscripts on which all contributing Working Group members are listed by name. The text “as the ENIGMA-Epilepsy Working Group” will appear the end of the author list.

Authorship credit should be based on substantial contribution to at least one of the following: (1) the generation of Genome Wide Association (GWA) results, or measurement of structural Magnetic Resonance Imaging (sMRI) phenotypes or genotypic data for the meta-analysis; (2) contributions or generation of data for replication of results obtained in the meta-analysis; (3) contributions to the conception, design, analysis and/or interpretation of the data; and (4) final approval of the manuscript version to be published. All co-authors are also expected to help draft the manuscript and/or revise it critically for important intellectual content.

Based upon the level of contribution, authorship at each site may vary from one publication to another. For each discrete publication, each site PI is responsible for preparing the authorship and acknowledgment list for their site. Each subgroup leader will have final responsibility to adjudicate who contributed enough to their respective group’s analysis to be considered a co-author.

Authorship for all Working Group papers will be weighted by current effort and contribution rather than on past contribution to ENIGMA Working Group research. Working Group members will be reasonable and self-critical in their claims for authorship. If a question arises regarding the appropriateness of authorship of a member(s), other Working Group members will be asked to advocate for these members in order to avoid putting members in the awkward position of having to advocate for themselves.

Guidelines for secondary analyses of and access to data collected during an ENIGMA-Epilepsy meta-analysis

Although the data contributed to the ENIGMA-Epilepsy Working Group consist of group-level summaries and post-estimation statistics rather than raw phenotype (and/or genotype data), there is theoretically a minute risk of determining whether a given individual participated in a study. While the re-identification of samples requires access to the raw phenotype or genotype data of the target individual and constitutes scientific misconduct, most groups have opted to appoint a gate-keeper approach rather than allowing full public access to the results of GWAS analyses or meta-analyses. Within the ENIGMA-Epilepsy Working Group, the subgroup leaders will act as the gate-keepers. Any Working Group member wishing to access the results of MRI or GWAS analyses or meta-analyses will be asked to complete a short proposal describing (in 1-2 paragraphs) why they wish to access the results files from each group. Non-Working Group members will be asked to complete a more detailed proposal and sign a Memorandum of Understanding regarding authorship and publishing.

The ENIGMA-Epilepsy subgroup leaders will screen proposals for scientific interest. The proposal will then be sent by email to all ENIGMA-Epilepsy Working Group members. ENIGMA-Epilepsy members will have 14 days from the time of the posting to opt-out of the analysis, ask for clarification, voice concerns or objections and/or give feedback to the proposal. No site data will be shared without the consent of the PI of the site, who may opt to impose specific conditions or limitations on the use of the data. If the author of the proposal agrees to the authorship and publication policies of the Working Group, the access request will be granted to the results files of those groups which have not opted-out of the analysis and one of the ENIGMA-Epilepsy subgroup leaders will be assigned as a project liaison. The ENIGMA-Epilepsy Working Group liaison will be responsible for providing the data and answering any queries relating to the project, and providing the contributing site PIs with updates.

Manuscripts using data obtained via this mechanism will be considered secondary Working Group publications. We will request that the 'ENIGMA-Epilepsy Working Group' and the liaison person will be listed as co-authors. The ENIGMA-Epilepsy Working Group on the byline will reference the PIs of each study, in addition to contributors at their site. In this way the authors contributing data to the Working Group will be appropriately acknowledged on any publication.

Genetic data

Sites without the availability of genetic data are welcome to participate in our initial meta-analyses on MRI data.

Sharing raw data

This memorandum of understanding only concerns meta-analyses on data processed by the individual sites, and not meta-analyses on pooled raw data. A separate MOU will be signed for those sites that are willing to share raw data for meta-analyses.

Participation in the ENIGMA-Epilepsy Working Group

Admitting New Sites as Members

Success of ENIGMA-Epilepsy phase 1 is anticipated to lead to a larger, longstanding Working Group. New Working Group members will sign a Memorandum of Understanding indicating that they agree with the policies listed here and that they have obtained the required ethical clearances to participate or send data.

Expulsion from the ENIGMA-Epilepsy Working Group

Expulsion from the Working Group will be considered when a site fails to uphold this Memorandum of Understanding, or does not contribute significantly to the work of the Working Group either in data collection, data analyses, or its goals. It is the responsibility of the Working Group subgroup leaders to assemble evidence and present the reasons for possible expulsion to the PIs. Expulsion from the Working Group will require a simple majority vote of the PIs.

A site may request to withdraw from the Working Group. Requests for withdrawal will be reviewed by the ENIGMA-Epilepsy support group. The withdrawing site will need to agree in writing to a moratorium on publication of any data that were obtained in the context of the Working Group work, or where the interpretation of the data relies in any part on unpublished Working Group work.

Working Group Membership is contingent upon signing the following statement:

I AGREE:

1. To consider participation in meta-analyses and secondary analyses proposed by the ENIGMA-Epilepsy Working Group, subject to constraints or limitations that I can impose in each case.
2. To abide by the guidelines for authorship and publication, and other guidelines described in this document.
3. Not to distribute or communicate any privileged information to individuals who are not members without consent of the entire Working Group. This includes any other existing collaborators who are not members of the ENIGMA-Epilepsy Working Group. Privileged information includes results of any unpublished analyses completed by members of the Working Group.
4. Not to distribute or copy any data collected by the Working Group without prior written consent of all Working Group members.
5. That the ENIGMA-Epilepsy subgroup leaders will review and evaluate future scientific opportunities, and will make recommendations regarding the needed expertise and research program to maximize those opportunities in the best possible way.
6. That failure to uphold this agreement may result in my expulsion from the Working Group (but I will still be bound by publication moratorium on Working Group work, as described above).

I, as subgroup leader of my site, consent to participate within the ENIGMA-Epilepsy Working Group with:

- MRI data for meta-analyses only (no sharing of raw MRI data)
- MRI and genetic data for meta-analyses only (no sharing of raw MRI and genetic data)

Signature

Date

Please print name

Institute
