

Enhancing Neuroimaging Genetics through Meta-Analysis (ENIGMA) Bipolar Disorder Working Group Memorandum of Understanding

Working Group Specifics

This memorandum of understanding (MOU) pertains to the ENIGMA Bipolar Disorder Working Group, hereinafter referred to as Working Group or WG.

This Working Group is chaired by Ole A. Andreassen and Christopher R. K. Ching, hereinafter referred to as Working Group Chairs or chairs.

The e-mail addresses of the Working Group Chairs are o.a.andreassen@medisin.uio.no and chris.ching@uci.edu.

The members of Working Group's support group and the participating sites and their PIs are listed on the ENIGMA Working Group website <http://enigma.uci.edu/ongoing/enigma-bipolar-working-group/bipolar-disorder-working-group-members/>, hereinafter referred to as *ENIGMA Working Group website*.

Individual subject level Working Group data will be stored at the University of Southern California only when approved by a participating working group member. This site is hereinafter referred to as the *Main Working Group Data Storage Site*. Individual subject level data may also be stored at sites with approved secondary proposals. Together these sites are hereinafter referred to as *Additional Working Group Data Storage Sites*.

In all publications that use the ENIGMA Working Group data, that are not able to list all contributing authors, the text "for the ENIGMA Bipolar Disorder Working Group", hereinafter referred to as "for the ENIGMA Working Group", will appear near the end of the author list.

The Overall ENIGMA PI is Dr. Paul M. Thompson.

Introduction

This document outlines the policies for participation in the ENIGMA Working Group, sharing data from the ENIGMA Working Group, and publication and publication credits for those who use or provide ENIGMA Working Group data. The intent of these policies is to facilitate the sharing of data, to encourage academic productivity, and to provide a mechanism for tracking and archiving data requests, intended analyses, and publications related to and resulting from ENIGMA WG data.

Members of the 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 and/or mega-analysis, replication, and/or algorithm testing in a collaborative manner.

The Working Group's initial effort is to demonstrate the success of collaborative, systematic neuroimaging analyses across multiple centers to clarify the effects of the working group's disease phenotypes on the brain.

This ENIGMA Working Group is expected to work collaboratively on meta-analyses and where feasible on growing a dataset of brain phenotypes and associated clinical data from consortium samples, which will be extended to include genetic data. This database will likely be useful to investigators both within and outside of this ENIGMA Working Group who may request to use parts of the dataset for secondary analyses. In addition, this Working Group will conduct future primary analyses of different brain phenotypes and their relation to genotypes, agreed in each case by contributors. This wealth of data requires (1) organization, (2) protection of authorship rights, and (3) direction for future analyses.

In order to accomplish these three aims, the ENIGMA Working Group's scientific initiatives and policies will be guided and overseen by group chairs. ENIGMA chairs are composed of a selection of principal investigators participating in the Working Group. ENIGMA chairs 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, when relevant. Part of this responsibility is to ensure that all sites have obtained approval from their local Ethics Committees for the ENIGMA-related analyses if needed, and that such assurances are updated regularly in accordance with Office for Human Research Protections (OHRP) regulations. In addition, ENIGMA chairs will be responsible for oversight of authorship, 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.

The Working Group chairs are listed in the section Working Group Specifics at the top of this document. The members of ENIGMA support group and the participating sites and their PIs are listed on the ENIGMA Working Group Website.

Projects and Publications

What Constitutes a Working Group Publication?

ENIGMA Working Group publications are papers or abstracts based on investigations that: (1) rely on intellectual resources of the Working Group, (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 data to an ENIGMA Working Group analysis for a given phenotype, the members at that site also agree that they will not publish or publicize (to the media or on the Internet) the results of the analyses for that phenotype prior to the publication of the Working Group analysis. Prior to publication, findings may be presented at conferences after consulting in advance with the ENIGMA Working Group chairs. 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 functional imaging correlates of a related brain structure found through an analysis by the ENIGMA Working Group), may not be submitted to journals for publication until after the original 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 brain imaging and /or imaging genetics analysis for a given phenotype conducted at their own site, which does not contain analyses conducted as part of the ENIGMA Working Group. These publications *do not* constitute Working Group publications.

If an ENIGMA Working Group analysis for a given phenotype and/or imaging genetics association is proposed and a group is already engaged in a 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 analysis. This is also intended to avoid the risk of duplicate submissions that may jeopardize a Working Group publication.

Guidelines for Primary Publications of the ENIGMA Working Group

ENIGMA Working Group publications may be classified as primary or secondary publications. Primary publications of the ENIGMA WG are those for which an analysis is conducted for the first time by the Working Group on a phenotype of interest (for example analysis of hippocampal subfields).

The ENIGMA Working Group will be listed as an author on all Working Group publications that cannot list all contributing Working Group members by name (e.g., conference abstracts for which the number of contributing authors is often limited). In these cases, the text “*for the ENIGMA Working Group*” (see Working Group Specifics section) will appear near the end of the author list.

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 authorship and acknowledgment lists for their site¹. The ENIGMA BD WG Chairs have created a simple protocol to better facilitate authorship approvals and include resources to properly contact site PI's to request their approval of the manuscript/abstract/symposia submission and indicated which members from their research team need to be listed as co-authors (see Authorship section below).

Authorship for all ENIGMA Working Group papers will be weighted by current effort and contribution rather than on past contribution to ENIGMA Working Group research. We recommend the guidelines for authorship from the International Committee of Medical Journal Editors (ICJME)¹. 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 members having to advocate for themselves.

¹ <http://www.icmje.org/recommendations/browse/roles-and-responsibilities/defining-the-role-of-authors-and-contributors.html>

Guidelines for secondary ENIGMA Working Group projects

Secondary publications are those that rely upon data collected in primary publications (for example re-analyzing ENIGMA Working Group data using a novel technique or focusing on different phenotypes).

Each proposal for a publication with ENIGMA WG data will be submitted to the ENIGMA WG chairs using the analysis plan form that can be requested from the ENIGMA WG chairs. All ENIGMA WG consortium members are encouraged to submit such proposals, which typically involve novel analyses, answering new questions, and may involve subsets of the available sites and/or the addition of new sites. Non-Working Group members can, after consultation with the ENIGMA WG chairs and members, also submit a proposal for data-analysis and publication and will be asked to sign the Memorandum of Understanding regarding authorship and publishing. The ENIGMA WG chairs will screen all proposals for scientific interest, quality, overlap with other plans, appropriateness and feasibility of the proposed timeline, and whether the proposed resources committed to the project are sufficient.

Analysis plans should include a proposal for publication of a specific scientific paper, not for multiple papers on a more general topic or for a "line of work". This implies that the analysis plan should include specific research questions and hypotheses and a detailed plan for data analysis to answer those specific research questions. To attempt to avoid overlap between papers resulting from different analysis plans, the data analyses and results reported in the manuscript are limited to those described in the analysis plan. For additional analyses not described in the analysis plan, a new analysis plan needs to be submitted. For any proposals concerning a similar topic but different data or different analyses on the same data, a new analysis plan also needs to be submitted.

When the analysis plan is approved by the ENIGMA WG chairs, the proposal will be circulated amongst ENIGMA WG members. ENIGMA WG members will have 14 days from the time of the posting to ask for clarification, voice concerns or objections, and/or give feedback to the proposal. Each analysis plan will be discussed during a conference call before the project can be initiated and the project leader can invite sites to participate. No site data will be shared without the consent of the PI of that site, who may opt to impose specific conditions or limitations on the use of the data. ENIGMA PIs and members are not required to take part in any proposed project, participation in all projects will be on an opt-in basis. The ENIGMA WG chairs will help enlist members who might be interested in collaborating and will assist in general coordinating tasks. Proposals will be discussed on ENIGMA WG calls and emails to encourage the broadest participation.

Submission of a proposal implies actual plans for a publication, which will be worked on within a reasonable time frame specified in the proposal. When within 6 months after submitting a proposal

there are no provable activities in that direction, the subject can be released for other interested parties.

Data sharing

Data sharing is not required for ENIGMA Working Group membership. For groups that can share de-identified subject-level data for the purposes of mega-analyses within or across working groups, the results and/or data files from each group will be housed at the *Main Working Group Data Storage Site*, and will not to be transferred or mirrored to other sites without permission from the site contributing the data because of privacy concerns. With permission from the site PI, data from a group may also be stored at *Additional Working Group Data Storage Sites* for analyses. Any Working Group member wishing to access the results of meta-analyses, group-level summaries and post-estimation statistics or individual subject level data will need to complete an analysis plan. The analysis plan will clearly state which variables will be included in the analysis, and thus what data is requested from each of the participating sites. The level of data-sharing will also be mentioned in the analysis plan, so that it is clear whether raw imaging, genetic, individual structural or functional imaging measures (hereinafter referred to as 'individual data') derived from software packages including, but not limited to, FreeSurfer, or group-level summaries and post-estimation statistics will need to be shared for the project.

The site PIs are responsible for ensuring de-identification/anonymization of their site's MR and phenotypic data. Both the site PIs who contribute data to the project as well as the project leader are responsible to comply with all relevant rules and regulations imposed by their institutions. This may mean that the project needs to be approved or declared exempt by a committee that oversees research on human subjects, e.g. a local IRB or Ethics Committee. Depending on the existing ethical approval and the level of data sharing required by the project, sites may need to obtain additional approval for sharing anonymized data with the project leader. The project leader of an approved analysis plan is required to keep track of ethical approval from each participating cohort when raw data or individual data needs to be shared for the project, will be able to provide this list when asked for, and will include relevant information in the subsequent publication.

The project leader of an approved analysis plan is not allowed to share the data of participating cohorts to third parties inside or outside the ENIGMA consortium. Individuals who will have access to the data during the project shall all be named in the Analysis Plan. In case of sharing raw or individual data, the project leader keeps a document stating who has access to these data. In case of a project using a mega-analytical approach, the location of data storage, the people who will have access to the data, and a timeline for finishing the project shall be stated in the analysis plan. If the project did not result in a publication and no extension is requested and approved, the project leader shall remove data from participating ENIGMA WG members from their local data storage at the end of the proposed timeline. If the project results in a publication, project data, analysis code, and results may be stored for archival purposes for a period allowed by the local institution to address any regulatory data audit request. The archived data shall not be used for any further data analyses or publications. Any new projects require a new secondary proposal and obtaining of a new set of data approved by each of the cohort PIs. Shall a cohort PI determine to withdraw from a project they had previously enrolled in and committed data towards, the project

leader will comply and remove the dataset in question from all future analyses. Prior to this, all efforts would be made by ENIGMA WG chairs to address any concerns the withdrawing PI may have and to determine if the project has deviated from proposed plans.

Authorship

The ENIGMA WG Chairs will provide each Project Leader with a set of publication resources including a step-by-step guide for submissions and resources for standardized authorship approval tracking.

Specific authorship policies for:

Manuscript:

1. All manuscripts resulting from approved analysis plans must be submitted to the ENIGMA WG chairs (see Working Group Specifics section) and all other co-authors for approval prior to submission to a journal.
 - a. Active approval of all authors on the article's content is required before it is submitted to a journal. It is required that the lead author maintain documentation of coauthors' approval of the final manuscript prior to submission and that this authorship approval documentation be made accessible to the WG Chairs. The WG Chairs will provide authorship guidelines to each project leader, including templates and assistance for authorship approval tracking.
 - b. Analysis results should be presented on a WG conference call prior to drafting the publication. This presentation is intended to ensure that provisions described in the analysis plan are correctly implemented and to avoid overlap with other ENIGMA WG proposals/manuscripts.
2. Authorship credit should be based on substantial contribution to: (1) the measurement of clinical and Magnetic Resonance Imaging (MRI) phenotypes and/or genotypic data for a ENIGMA WG analysis; (2) contributions or generation of data for replication of results obtained in the analysis; (3) contributions to the conception, design, analysis and/or interpretation of the data; (4) drafting the manuscript or revising it critically for important intellectual content. In addition, all co-authors need to (5) provide a final approval of the manuscript version to be published.
3. Individuals involved in the primary design, analysis and writing parts of the project will be listed as first (or joint first - denoted with an asterisk) and senior (last or joint last) authors. In addition, the ENIGMA WG chairs and all members of the ENIGMA Working Group who contribute data for this project and edit the manuscript will be listed as co-authors.
4. We request that the phrase "for the ENIGMA Working Group" (see Working Group Specifics Section) be included on the author line of the manuscript for any publication that is not able to list all of the contributing authors (e.g., conference abstracts). The ENIGMA Working Group website (see Working Group Specifics Section) can be used as the affiliation.
5. Funding by NIH will be acknowledged in the support acknowledgement section of the manuscript using language similar to the following: The *ENIGMA Working Group* gratefully

acknowledges support from the <grant name>, for example “NIH Big Data to Knowledge (BD2K) award (U54 EB020403 to Paul Thompson)”.

6. It is the responsibility of the first author that the authorship guidelines are followed, that the sample and the research-methodology are described correctly, and that references to former relevant ENIGMA Working Group publications where appropriate are made.

Conference poster and talk abstracts:

1. If the conference allows listing all contributing authors, please include all contributing authors on the author line. For most conferences additional names may need to be submitted to the conference separately.
2. If the conference has a hard limit on contributing authors (many do), include the project leaders, major contributors and, as co-authors, the ENIGMA Working Group chairs, overall ENIGMA PI, and the statement "for the ENIGMA Working Group" (see Working Group Specifics Section). For this ENIGMA Working Group, include at least FIRST AUTHOR (Presenter), the Working Group Chairs, the overall ENIGMA PI, LAST AUTHOR, and “for the ENIGMA Working Group” (see Working Group Specifics Section). Of course other important contributors can be included as well.
3. If not all authors can be listed, consider putting in the abstract "Contributing Authors are listed at ENIGMA Working Group Website."
4. Regardless of the names listed on the abstract, it is best to list all contributors on the conference poster and/or the conference acknowledgement slide. PDF copies of the conference abstracts can be used by all ENIGMA Working Group members to list abstracts on CVs.

Symposium submissions:

1. List the presenting author, and if possible, on behalf of the ENIGMA Working Group. Again, if possible, consider adding "Contributing Authors are listed at ENIGMA Working Group Website."
2. Regardless of the abstract, all contributors should be listed on the symposium talk acknowledgement slide.

Participation in the ENIGMA Working Group

Admitting New Sites as Members

New Working Group members will sign the Memorandum of Understanding (MOU) 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 Working Group

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

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

ENIGMA Working Group Membership is contingent upon signing the following statement:

I AGREE:

1. To consider participation in primary and secondary analyses proposed by this ENIGMA Working Group, subject to constraints or limitations that I can impose in each case.
2. To abide by the guidelines for data sharing, 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 ENIGMA Working Group. This includes any other existing collaborators who are not members of this ENIGMA WG. Privileged information includes results of any unpublished analyses completed by members of this ENIGMA WG.
4. Not to distribute or copy any data collected by this ENIGMA WG without prior written consent of all Working Group members.
5. That the ENIGMA WG chairs 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 this ENIGMA Working Group (but I will still be bound by publication moratorium on this ENIGMA WG's work, as described above).

Signature

Date

Please print name
