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Facilitating Big Data Meta-Analyses for Clinical Neuroimaging through ENIGMA Wrapper Scripts

Project URL: https://github.com/npnl/ENIGMA-Wrapper-Scripts

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1 Introduction

A vast number of clinical disorders may involve changes in brain structure that are correlated with cognitive function and behavior (e.g., depression, schizophrenia, stroke, etc.). Reliably understanding the relationship between specific brain structures and relevant behaviors in worldwide clinical populations could dramatically improve healthcare decisions around the world. For instance, if a reliable relationship between brain structure after stroke and functional motor ability was established, brain imaging could be used to predict prognosis/recovery potential for individual patients. However, high heterogeneity in clinical populations in both individual neuroanatomy and behavioral outcomes make it difficult to develop accurate models of these potentially subtle relationships.

Large neuroimaging studies ($n > 10,000$) would provide unprecedented power to successfully relate clinical neuroanatomy changes with behavioral measures. While these sample sizes might be difficult for any one individual to collect, the ENIGMA Center for WorldwideMedicine, Imaging, and Genomics has successfully pioneered meta- and mega-analytic methods to accomplish this task. ENIGMA brings together a global alliance of over 500 international researchers from over 35 countries to pool together neuroimaging data on different disease states in hopes of discovering critical brain-behavior relationships (http://enigma.ini.usc.edu) [1, 2]. Individual investigators with relevant data run ENIGMA analysis protocols on their own data and send back an output folder containing the analysis results to be combined with data from other sites for a meta-analysis. In this way, large sample sizes can be acquired without the hassle of large-scale data transfers or actual neuroimaging data sharing.

ENIGMA protocols were initially developed to harmonize processing methods of imaging researchers around the world and they require a moderate level of familiarity with several programming languages and environments. However, ENIGMA's recent success has attracted greater interest in collaborative neuroimaging and protocols must be adjusted to allow for all levels of experience, as, the success of this approach depends on individual collaborators running these ENIGMA protocols on their data. Here, we worked on simplifying these protocols so even a novice programmer could use them. In this way, we hope to expand the feasibility of collecting critical clinical data from collaborators who may have less experience with neuroimaging techniques.

2 Approach

The current ENIGMA protocols (http://enigma.ini.usc.edu/protocols/) for structural neuroimaging analyses consist of a number of different word documents with embedded links to different scripts and snippets of code that use R [3], Bash scripting [4], Matlab [5], FSL [6], and Freesurfer [7]. Each step must be run sequentially, costing the user time during the implementation to wait for each step to finish before beginning the next. In addition, the number of different scripts, programming languages and software environments can be challenging for a novice user and

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Table 1 Description of scripts.

Scripts	Description	Execution Time
1_enigma_runfreesurfer.sh	Runs freesurfer	12-16 hours per subject
2_extractsubcortical_volumes.sh	Extracts freesurfer data and runs the quality checks for subcortical analyses	30 min per 27 subjects
3_extractcortical_volumes.sh	Extracts freesurfer data and runs the quality checks for cortical analyses	30 min per 27 subjects

Table 2 User feedback.

User Level	EOU	Time	Notes
Novice 1	8	00:35:25	Required walk through support
Novice 2	8	00:52:55	Required support for basic terminal commands only; then was able to complete independently
Moderate 1	3	00:23:45	Required no support
Moderate 2	4	00:22:10	Required no support
Expert 1	3	00:11:34	Required no support
Expert 2 - DE	3	02:00:00	Getting scripts to run took several minutes but reorganizing data and troubleshooting with freesurfer took significant time
Expert 3 - DE	2	01:15:00	Required walk through support

EOU: Ease of Use score (1-10) 1 = easiest, 10 = hardest. Time: the time it took for the user to setup and learn to use the scripts. DE: User's expertise is with a different computational environment than the one required by the scripts.

introduces numerous instances where the individual may make errors in implementing the code. To address this, we created 3 easy-to-use wrapper scripts that automate the implementation of the ENIGMA protocols for both subcortical and cortical structural MRI analyses (see Table 1). These wrapper scripts reduce over 40 steps down to 3 quick steps for the user. We also created a user-friendly readme file that includes screenshots of the code implementation.

To examine the ease of use and time to implement the new scripts, we tested each of them on 7 users who had different levels of familiarity with programming and neuroimaging (novice users (no programming experience), moderate users (basic-to-intermediate programming experience), and expert users (extensive programming)). To explore additional factors relating to implementation, two of the expert users had to use the scripts in a different environment (e.g., organize the data, install the software, etc.).

3 Results/Discussion

Overall, moderate and expert level users found the scripts extremely easy to implement and required less than 25 minutes to get all three scripts running (excluding the run time of each script; see 2 for individual results). The two novice users required greater support to understand basic elements (e.g., what is a terminal), but with support, were able to complete all the steps in less than 1 hour. Finally, the expert users who implemented the scripts on their own environment found the most time-consuming steps to be installing and troubleshooting Freesurfer (e.g., install errors; troubleshooting a conflict between the preset Freesurfer subjects directory and the output directory required by the scripts) and reorganizing data into a format for the scripts (e.g., putting the data into an organized format with main_folder/subject_folder/subject.nii.gz). Once these steps were complete, each expert user reported about 10 minutes for script implementation.

The wrapper scripts made the implementation of the ENIGMA protocols quick and feasible even for novice users. However, there were still three main barriers to participation that required significant time, computational resources, and some expertise: 1) data organization (depending on previous data structure), 2) running freesurfer (~12 hrs/subj), and 3) installation of the required software (e.g., Freesurfer, FSL, R). Future projects may look at ways to streamline these areas for a more seamless user experience in order to facilitate greater sharing of clinical neuroimaging data through ENIGMA.

All scripts and user guides can be found at: https://github.com/npnl/ENIGMA-Wrapper-Scripts

Author's contributions
Eric Kan, Julia Anglin, and Sook-Lei Liew wrote the wrapper scripts. Neda Jahanshad and Paul Thompson developed the original ENIGMA protocols and provide guidance/support for ENIGMA working groups. Michael Borich, Julia Anglin, and Sook-Lei Liew tested and edited the wrapper scripts. All authors contributed to the creation of the manuscript.

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