Approaches and Challenges for Across-Site Harmonization of Structural, Functional, and Diffusion MRI

Janine Bijsterbosch Co Organizer
Washington University in St Louis
Saint Louis, MO
United States

Wei Zhang Co Organizer
Washington University in St Louis
Saint Louis, MO
United States

Michael Harms, Ph.D. Organizer
Washington University in St Louis
Saint Louis, MO
United States

1253
Symposium

Neuroimaging is entering an era in which large sample sizes are necessary for a number of reasons, including the study of individual differences, the generation of sufficient power to study complex questions related to genetics, behavior, and psychopathology, the application of deep learning approaches, and the realization that large samples promote more robust and replicable science. Obtaining such large samples in practice often involves data collection at multiple sites, across different scanner models and manufacturers, possibly with acquisition protocols that may differ considerably. Thus, there is a critical need for post-acquisition MRI data 'harmonization' tools and approaches that reduce the unwanted variance across subjects, sites, and scanners that is introduced by these factors, while still retaining individual difference effects of interest. In this symposium, we will provide a broad overview of the nascent, but growing, literature and approaches to data harmonization in a variety of MRI modalities, including structural (morphometric), functional (fMRI), and diffusion MRI. The talks will also cover a variety of approaches, including ComBat (and extensions thereof), direct intensity/contrast harmonization of T1w images, rotation invariant spherical harmonics, retrospective and prospective (i.e., traveling subject) approaches, and deep learning approaches. We will also discuss the challenges inherent to 'harmonizing' MRI data, given that (1) different MRI modalities have very different properties and that (2) a very wide variety of downstream measures are used to quantify and compare subjects, both of which make it challenging to develop "universal" approaches to harmonization. At the conclusion of the symposium, participants will have an understanding of the current "state-of-the-art" regarding MRI data harmonization, and be better equipped to employ harmonization to aggregate samples for their particular research questions of interest.

Objective

1. Participants will develop an integrated understanding of current approaches for MRI data harmonization.

2. Participants will learn how different MRI modalities and research questions may need fundamentally different approaches to harmonization, and be able to assess what sort of harmonization is most necessary and appropriate for their study.

Target Audience

We anticipate broad interest because data harmonization challenges affect many or all of us. For example, the audience is expected to include the "Open Science" community, clinical researchers who often collaborate across sites for patient recruitment, and individual researchers with an interest in combining data across multiple studies performed within the same laboratory.

Presentations

Statistical Harmonization Methods for Next Generation Neuroimaging Studies

With the increasing needs for big data analytics in medical imaging, pooling and integrating data from multi-site studies has become critical. Yet site differences attributed to various sources including differences in scanner manufacturers, acquisition and preprocessing protocols are known to exist and might have substantial impact towards the analytic results. Recently, batch-effect correction methods from other biomedical applications have been successfully adapted to remove scanner and site differences in neuroimaging data and applied in many large-scale studies such as ABCD and ADNI. This talk will provide an overview on a series of efforts in developing novel statistical methods for imaging harmonization led by members of the Penn Statistics in Imaging and Visualization (PennSIVE) Center at the University of Pennsylvania. We will begin by introducing the published work on statistical harmonization modeling on imaging data from multiple modalities, including structural, functional, and diffusion MRI. In particular, we will emphasize ComBat (Combating Batch Effects), initially proposed in Johnson et al. (2007) and demonstrate its use on diffusion tensor imaging data (Fortin et al., 2017), cortical thickness measurements (Fortin et al., 2018), and functional connectivity matrices (Yu et al., 2018). The method removes unwanted sources of variability in mean and scale (i.e., variance) of the imaging outcomes via an empirical Bayes framework, while preserving biologically-relevant variations by accounting for related covariates in the model. We will then discuss some ongoing development of further harmonization methods. In particular, ComBat-GAM (Pomponio et al., 2019) was developed to merge a large-scale LIFESPAN dataset of 10,477 structural brain MRI scans from 18 different studies to simultaneously remove site differences and quantify nonlinear age trajectories over a large set of anatomical regions and cortical structures. A web-based visualization interface was generated to display the resulting age trends and serve as reference data for comparisons with future studies in brain development and aging. Furthermore, a longitudinal ComBat has been proposed (Beer et al., 2019) to appropriately handle harmonization and estimation of within-subject changes in longitudinal data. Lastly, existing harmonization methods have mostly focused on correcting the mean and scale shifts for univariate data. We demonstrate that site differences could remain in covariance patterns using existing harmonization techniques and would potentially hinder the performance of multivariate pattern analysis (MVPA). Critically, we propose CovBat (Chen et al., 2019), a novel approach that extends the ComBat methodology combined with variance decomposition to remove the spatially-dependent site deviations in the covariance patterns of structural data. Future efforts will focus on developing robust automated methods for imaging quality control and data harmonization for large-scale multimodal imaging datasets collected under various study designs and extracting clinical meaningful imaging biomarkers from the harmonized data.

Presenter

Haochang Shou, University of Pennsylvania philadelphia, PA
United States

Multi-Site Data Harmonization during Childhood and Adolescence: an ABCD Study Perspective

The Adolescent Brain Cognitive Development (ABCD) Study is the largest long-term study of brain development and child health in the United States, tracking 11,875 participants from childhood through adolescence to young adulthood. The full baseline neuroimaging data was released in April 2019 encompassing structural (T1-weighted, T2-weighted), diffusion (diffusion tensor imaging and restriction spectrum imaging), resting state and task-based fMRI data. Half of the 2 year follow-up neuroimaging data will be released mid-2020. During this age range, it is important to distinguish between rapid neurological development and non-biological factors. This talk will discuss the challenges and solutions for harmonization between scanners (vendor/model, head coils, acquisition protocols) and over time. To correct for structural MRI intensity differences biased by scanner manufacturer and acquisition protocol, a novel T1/T2 intensity normalization approach will be previewed. For diffusion MRI, there will be a preview of a dynamic DTI atlas that adjusts for age, sex and scanner manufacturer for improved population registration while offsetting scanner bias. The presentation will also touch on tools for confirming that baseline and follow-up scans are from the same individual, and discuss the challenge of accounting for task fMRI practice effects within a two year follow-up window (i.e., delineating improvements in cognition from repeating a practiced cognitive task).

Presenter

Sean Hatton, University of California San Diego La Jolla, CA
United States

Retrospective and Prospective Diffusion MRI Data Harmonization for Site-Independent Analysis

Large collaborative efforts have led to “Big-Data” initiatives, aimed at improving the poor reproducibility of small neuroimaging studies and gaining statistical power to detect subtle changes in neuropsychiatric disorders. However, scanner induced bias, especially in diffusion-MRI (dMRI) signal, limits direct pooling of the multi-site dMRI data. “Harmonization” of multi-site dMRI datasets can dramatically increase the statistical power of neuroimaging studies and enable comparative studies pertaining to several brain disorders (Tax et al., Neuroimage, 2019; Cetin-Karayumak et al., Neuroimage, 2019; Mirzaalian et al., MICCAI, 2015; Fortin et al., Neuroimage, 2017). In this talk, we will present novel strategies we have developed for harmonization of multi-site diffusion MRI data, which is essential for consistent microstructural, tractography and connectivity comparisons across studies. To minimize the effects of preprocessing as well as subsequent data modeling, we apply harmonization as early as possible, at the signal level (i.e., prior to diffusion modeling). Two primary approaches have been proposed by our group, both based on rotation invariant spherical harmonic (RISH) features, which represent the different angular frequencies of the diffusion signal and are used for successful mapping of one site to another while preserving the anatomical orientation of the fiber tracts: (i) Retrospective harmonization, for use where data has already been acquired without traveling subjects (Cetin-Karayumak et al., Neuroimage, 2019). Briefly, RISH templates are computed to learn the voxel-wise linear mapping using matched controls from each site, and those

templates are later used to harmonize all subjects. This approach was selected as the best performing method in the Multi-shell Diffusion MRI Harmonization (MUSHAC) challenge (Ning et al., MICCAI, 2018; Ning et al., ISMRM, 2019). (ii) Prospective harmonization, which requires traveling subjects scanned at each site to create a within-subject overlap cohort. Although the approach in (i) can also be used in this design, more advanced non-linear strategies such as deep learning can be used for harmonization or image quality enhancement across scanners (Cetin-Karayumak et al., MICCAI, 2018; Cetin-Karayumak et al., ISMRM, 2019). We will discuss our application of retrospective harmonization to a large schizophrenia database consisting of 1092 subjects (600 schizophrenia patients and 492 controls, age-range=[14,65] years), derived from 13 sites (Cetin-Karayumak et al., Mol. Psychiatry, 2019). The scanner-related differences were removed after harmonization, which allowed us to characterize lifespan trajectories of white matter pathology in schizophrenia. Additionally, this approach is going to be used for joint large-scale harmonization of diffusion MRI brain imaging data (30,000+ subjects) as part of an NIH grant (PI: Dr. Rathi), to improve our understanding of the human brain in health and disease. We will also show new results and validation using the prospective design, in which deep learning approaches (deep convolutional neural networks and cycle generative adversarial networks with segmentation loss) were used to harmonize multi-shell diffusion MRI data acquired with different magnetic strengths (3T and 7T) on 150 subjects scanned on both scanners (Cetin-Karayumak et al., MICCAI, 2018; Cetin-Karayumak et al., ISMRM, 2019). We will conclude with practical suggestions for others seeking to harmonize dMRI data.

Presenter

Suheyla Cetin-Karayumak, Brigham and Women's Hospital and Harvard Medical School
Psychiatry
Boston, MA
United States

DeepHarmony: Structural Harmonization through Deep Learning

T1-weighted imaging is the workhorse of modern-day structural neuroimaging; it is used for everything from determining differences in brain structure to identifying foci in functional imaging. Unfortunately, there is no universal standard for how T1-weighted images (or any other structural image) are acquired. Differences in acquisition protocol, manufacturer-specific implementation, and improvements over time all contribute to variation in the quantitative analysis of structural MRI. One solution is to acquire data for a given study on a single scanner, but this is not feasible for large-scale or long-term longitudinal studies. To tackle this problem, we explored the use of supervised deep image synthesis (which uses the popular U-Net neural network architecture to generate synthetic images) to create a harmonized image set that was indistinguishable in terms of quantitative analysis. The technique, called DeepHarmony, utilizes a prospectively collected overlap cohort with scans acquired on two scanners within 30 days. This dataset was used for training of a set of deep neural networks, which transforms data from both scanners into a consistent, harmonized version of each structural contrast. These harmonized images can then be used in downstream processing to extract quantitative metrics without the additional confound of scanner. In this talk, we will briefly introduce the concept of deep MRI synthesis and how it allows for the creation of harmonized images, given a set of target images and an appropriate training data set. We will also discuss the feasibility of structural harmonization with limited training data for applications to multi-site harmonization, where it is logistically and financially intractable to collect a large training data set. Finally, we will discuss the importance of multi-contrast data and how deep learning allows for the improvement of individual contrasts by borrowing information from other co-acquired images.

Presenter
Blake Dewey, Johns Hopkins University Baltimore, MD
United States