Image Processing in the A2CPS Project

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Introduction

Typically, the pain of an acute injury goes away after it heals. But sometimes, the pain of an injury, surgery, or disease can linger, eventually becoming chronic. Currently, a high proportion of people in the United States transition to chronic pain after an acute event, but the causes of this transition remain unknown. A new project aims to study the transition: the Acute to Chronic Pain Signatures (A2CPS) initiative[1,2]. The study aims to collect neuroimaging data on over 2800 participants who will undergo an incident of acute pain—surgery for either total knee replacement or thoracic surgery. Information collected includes psychosocial, omics, quantitative sensory testing, and brain magnetic resonance imaging data (Figure 1a). The project aims to test candidate biomarkers, assemble putative biomarkers into biosignatures, and furnish novel biomarkers or biosignatures. Here, we present the first release of the brain imaging data, quality control procedures, and analysis pipelines.

The A2CPS imaging protocol allows collection of several candidate biomarkers (Figure 1b), including volumetric and gray matter density differences in individual regions of interest, structural connectivity, fractional anisotropy, evoked responses, functional connectivity measures, graph theoretic measures, and multivariate signature responses. The scan protocols are based on those from the Adolescent Brain Cognitive Development study and were tailored to the study and to the scanner hardware of participating collection sites.

Study Design

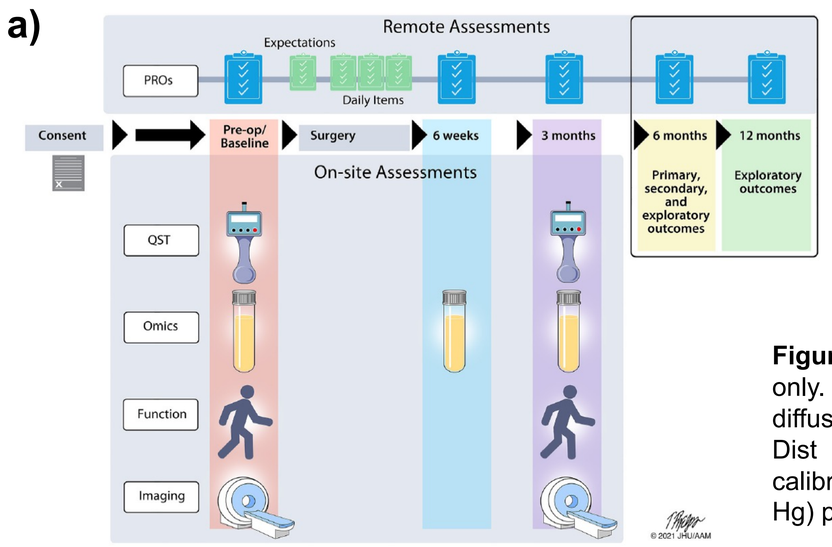


Figure 1 a) A2CPS Study Timeline. Release 1 includes pre-surgical data only. **b)** MRI Acquisition. The scanning session includes structural (sMRI), diffusion (dMRI), resting state (rfMRI), task (tfMRI), and fieldmap data (EPI Dist Corr). During the task runs, a cuff is maintained at a pressure calibrated to induce pain 4 out of 10 (first) or a standard intensity (120 mm Hg) pressure (second).

Raw Data QC

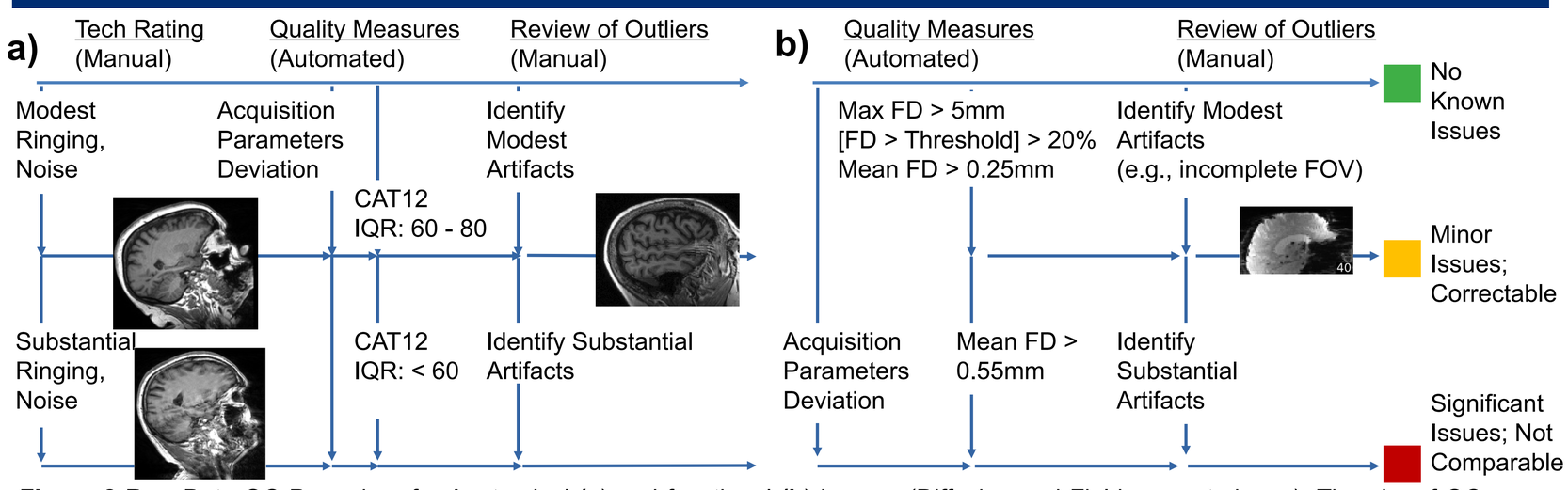
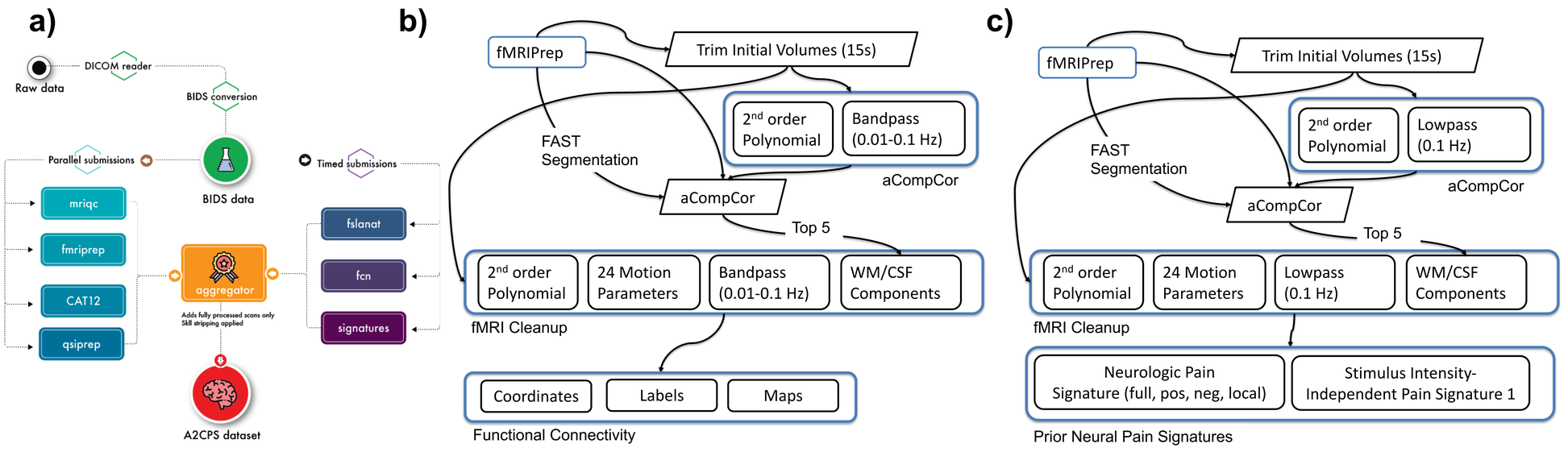


Figure 2 Raw Data QC Procedure for Anatomical **(a)** and functional **(b)** images (Diffusion and Fieldmap not shown). The aim of QC was a straightforward, three-tier quality rating assessing comparability. Scans start with a "green" rating but can be downgraded by combinations of automated metadata checks (e.g., adherence to acquisition parameters), standardized visual review (e.g., checks for eye spillover), and automated thresholds on measures extracted from the data (e.g., average framewise displacement).

Processing Pipelines

Figure 3 Image Processing Pipelines **a)** Overview. Analyses comprise three stages. First, the data are indexed and organized according to the Brain Imaging Data Structure (BIDS). Afterwards, the data are sent through a series of pipelines, including both established (MRIQC, fMRIPrep, FreeSurfer, QSIprep, fsl_anat, CAT12, brainageR, NeuroMark) and custom-made **(b)** Functional Connectivity (fcn) and **(c)** Prior Neural Signatures (signatures) Pipelines. Lastly, pipeline outputs are aggregated, de-identified, and stored with data from other modalities. Pipeline inclusion and configuration was guided by both pre-specified biomarkers and the aim of facilitating discovery of novel biomarkers.



Data Release 1 Contents Overview

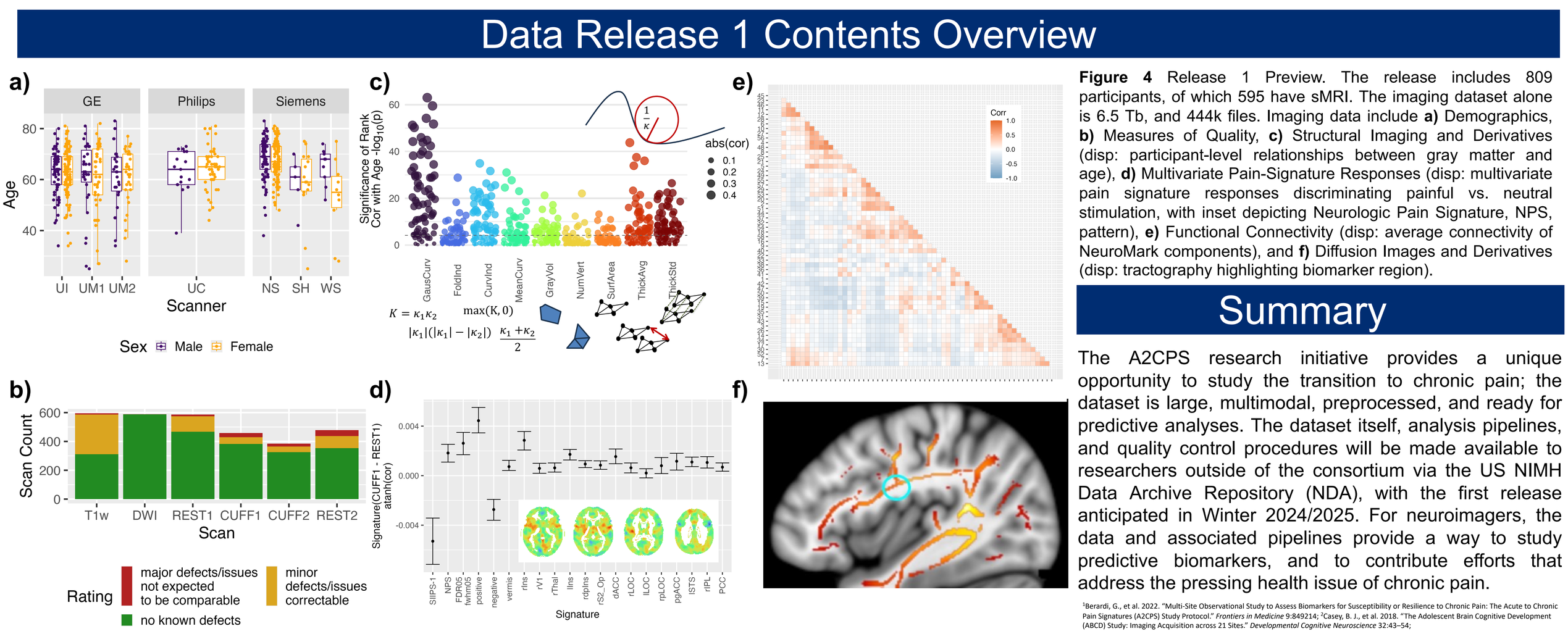


Figure 4 Release 1 Preview. The release includes 809 participants, of which 595 have sMRI. The imaging dataset alone is 6.5 Tb, and 444k files. Imaging data include **a)** Demographics, **b)** Measures of Quality, **c)** Structural Imaging and Derivatives (disp: participant-level relationships between gray matter and age), **d)** Multivariate Pain-Signature Responses (disp: multivariate pain signature responses discriminating painful vs. neutral stimulation, with inset depicting Neurologic Pain Signature, NPS, pattern), **e)** Functional Connectivity (disp: average connectivity of NeuroMark components), and **f)** Diffusion Images and Derivatives (disp: tractography highlighting biomarker region).

Summary

The A2CPS research initiative provides a unique opportunity to study the transition to chronic pain; the dataset is large, multimodal, preprocessed, and ready for predictive analyses. The dataset itself, analysis pipelines, and quality control procedures will be made available to researchers outside of the consortium via the US NIMH Data Archive Repository (NDA), with the first release anticipated in Winter 2024/2025. For neuroimagers, the data and associated pipelines provide a way to study predictive biomarkers, and to contribute efforts that address the pressing health issue of chronic pain.

[1]Berardi, G., et al. 2022. "Multi-Site Observational Study to Assess Biomarkers for Susceptibility or Resilience to Chronic Pain: The Acute to Chronic Pain Signatures (A2CPS) Study Protocol." *Frontiers in Medicine* 9:849214; [2]Casey, B. J., et al. 2018. "The Adolescent Brain Cognitive Development (ABCD) Study: Imaging Acquisition across 21 Sites." *Developmental Cognitive Neuroscience* 32:43–54;