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fMRIPrep: a robust preprocessing pipeline for functional MRI

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SUPPLEMENTARY NOTE 1: PREPROCESSING OF FMRI IN A NUTSHELL

Head-motion correction (HMC). Functional MRI (fMRI) data are usually acquired with echo-planar imaging (EPI) or other fast MR acquisition techniques in order to estimate the timecourse of blood oxygenation signals. During that time, the blood-oxygen-level dependent (BOLD) signal is measured at a pre-specified frequency called repetition time (TR), typically selected in a range of 300ms for the fastest sequences and 3s for the legacy, traditional acquisitions. Even at the shortest TRs and scanning the most cooperative participants, the position of the head with respect to the scanner will change to some degree. Head motion occurs as a slow drift from the original position or suddenly when triggered, for example, by swallowing, task responses or involuntary movements of both healthy and pathological subjects. Motion causes a spatial misalignment in the source of the BOLD signal measured in all voxels at a certain TR and its neighbors in the time-series. The effect is particularly noticeable at the brain edges, where the signal may fall inside or outside the brain mask computed on the spatial average of the time-series.

Susceptibility distortion correction (SDC). Magnetic susceptibility of tissues locally disturbs the B_0 field. Even though the tissue susceptibility is quite homogeneous across the brain parenchyma, those regions near air-filled cavities such as sinuses or the ear-canals may induce variations on the field. In addition, one limitation of fast MR acquisitions like EPI is the reduced bandwidth on the phase-encoding (PE) direction. The so-called *susceptibility distortion* renders as a warping along the PE direction of the registered BOLD signal, and deformation is proportional in magnitude to the inhomogeneity of the field at that point in space. Several techniques to estimate the variance of the field that induces the distortion have been proposed, such as field mapping techniques¹, the acquisition of several reference images with different PE directions that allow for estimating the field map through intra-modal image registration^{2,3}, using multi-modal image registration to a structural, “anatomically-correct” scan of the same subject (e.g. a T2-weighted (T2w) image⁴, a T1-weighted (T1w) image⁵), or surface-driven registration⁶. Once the field map is estimated, the distortion can be computed⁷ as a nonlinear map of displacements along the PE direction (oftentimes called voxel-shift map).

Slice-timing⁸ correction (STC). The MR schemes commonly utilized to acquire BOLD signal work with staggered scanning of 2D slices. Although all 2D slices are acquired very closely to one another, the hemodynamic response is sampled at different points in time. This effect is alleviated but still present in multi-band acquisitions that are able to acquire several 2D slices in parallel. To correct for slice timing it is necessary to record the relative time each slice is registered with respect to the first one and fit the hemodynamic response to then interpolate the signal at the reference TR⁸. Slice timing effects interact with head motion, raising the question of which one should be accounted for. Some correction methods are able to tackle both issues simultaneously by merging both interpolation processes⁹.

Intra-subject registration. Head motion also occurs between the acquisition of the different MR sequences defined in the protocol, especially when the experiment involves running different sessions. In order to allow fusing information from the different runs in the protocol, an image registration process between them is necessary. A further complication to the image registration process is the fact that the different MR sequences utilized in the protocol pose a multi-modal registration problem.

Spatial normalization. In order to enable group comparisons, it is necessary to find a spatial mapping that aligns the subject-space into a common space, generally defined using an atlas. After spatial normalization, the information given by the different images in subject-space (after all intra-subject registrations have been calculated) can be analyzed as *if all the participants shared the same underlying anatomy*.

Surface sampling. Although most studies have analyzed fMRI analysis in the three-dimensional volume, it is increasingly common to analyze the data on the cortical surface e.g.^{10,11}. The cortical surface of the brain is reconstructed from the anatomical (T1w and optionally T2w) images. Using the alignment described previously (intra-subject registration), these surfaces are mapped to the BOLD scan space and

the signal is sampled at the vertices of the surface.

Subspace projection denoising. A family of techniques for denoising BOLD time-series project the data into a low-dimensional *subspace* in search for signal *components* or *factors* that can be classified as noise or signal of interest. Signal separation is generally done through principal components analysis (PCA), independent components analysis (ICA), factor analyses, etc. Prominent examples of this approach are *CompCor*¹² and automatic removal of motion artifacts (ICA-AROMA¹³).

Other preprocessing elements. Other preprocessing tasks include the **spatio-temporal smoothing** of the signal, the **detection of spikes** and their removal, the identification of **nonsteady state** (strong T1 contrast at the beginning of the time-series), **frame scrubbing or censoring** in resting-state fMRI, the **calculation of masks and regions-of-interest (ROIs)**, the **calculation of confounds**, etc. see^{14,15}.

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SUPPLEMENTARY NOTE 2: THE BIDS ECOSYSTEM

The Brain Imaging Data Structure (BIDS¹) is a standard for organizing, describing and annotating neuroimaging datasets in a machine readable way. It promotes a consistent set of standardization efforts to make neuroimaging research shareable and eases the implementation of new software tools and resources. The element at the center of the BIDS ecosystem is the overarching principle of reaching out to the neuroimaging community driving the elaboration of the specifications by the agreement of experts. The adoption of BIDS brought down several fences limiting the standardization of neuroimaging tools. In particular, the initial BIDS proposal ensures the reusability of original (raw) data, fundamentally because the datasets are machine-readable. That feature allowed to generate software tools like pybids to query datasets in a consistent, systematic, and easy way. As a result, the source code necessary to access the datasets can also be reused and thus written only once (minimizing software development and support costs and/or dissolving the burden on a community of researchers). Moreover, the standardized access to data simplifies the identification of inhomogeneities and conflicts on the dataset (e.g. missing a particular run from one subject) and protects against data rot with the use of automated validation tools like the BIDS-Validator. A practical corollary is that BIDS dramatically flattens the learning curve for researchers to write software that adapts to the particular irregularities of all datasets and avoids manual intervention (e.g. accessing crucial metadata elements automatically instead of manually setting values). Following the consolidation of the organization scheme for raw data, a full ecosystem of standardization schemes around BIDS is blooming. The first extension to BIDS was called BIDS-Apps, addressing the common architecture of neuroimage processing tools, software execution paradigms (e.g. first- and second- level analyses), versioning, and continuous testing of the tools. Finally, the question about how to organize the results of processing to make them shareable emerged almost simultaneously to the proposal of BIDS. The working groups for the BIDS-derivatives extension are currently developing the standards to organize processed neuroimaging data.

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Box SN3.1. The citation boilerplate

Results included in this manuscript come from preprocessing performed using *fMRIPrep*^{1,2} version 1.0.8, a Nipype^{3,4} based tool. Each T1-weighted (T1w) volume was corrected for intensity non-uniformity (INU) using N4BiasFieldCorrection⁵ v2.1.0 and skull-stripped using *antsBrainExtraction.sh* v2.1.0 (using the OASIS template). Brain surfaces were reconstructed using *recon-all*⁶ from FreeSurfer v6.0.0, and the brain mask estimated previously was refined with a custom variation of the method to reconcile ANTs-derived and FreeSurfer-derived segmentations of the cortical gray-matter of Mindboggle⁷. Spatial normalization to the ICBM 152 Nonlinear Asymmetrical template⁸ version 2009c was performed through nonlinear registration with the *antsRegistration*⁹ tool of ANTs v2.1.0, using brain-extracted versions of both T1w volume and template. Brain tissue segmentation of cerebrospinal fluid (CSF), white-matter (WM) and gray-matter (GM) was performed on the brain-extracted T1w using *fast*¹⁰ (FSL v5.0.10). “Fieldmap-less” distortion correction was performed by co-registering the functional image to the same-subject T1w image with intensity inverted^{11,12} constrained with an average fieldmap template¹³, implemented with *antsRegistration* (ANTs). This was followed by co-registration to the corresponding T1w using boundary-based registration¹⁴ with 9 degrees of freedom, using *bbregister* (FreeSurfer v6.0.0). Motion correcting transformations, field distortion correcting warp, BOLD-to-T1w transformation and T1w-to-template (MNI) warp were concatenated and applied in a single step using *antsApplyTransforms* (ANTs v2.1.0) using Lanczos interpolation¹⁵.

Physiological noise regressors were extracted applying CompCor¹⁶. Principal components were estimated for the two CompCor variants: temporal (tCompCor) and anatomical (aCompCor). A mask to exclude signal with cortical origin was obtained by eroding the brain mask, ensuring it only contained subcortical structures. Six tCompCor components were then calculated including only the top 5% variable voxels within that subcortical mask. For aCompCor, six components were calculated within the intersection of the subcortical mask and the union of CSF and WM masks calculated in T1w space, after their projection to the native space of each functional run. Frame-wise displacement¹⁷ was calculated for each functional run using the implementation of Nipype. Many internal operations of *fMRIPrep* use Nilearn¹⁸, principally within the BOLD-processing workflow. For more details of the pipeline see <https://fmriprep.readthedocs.io/en/latest/workflows.html>.

SUPPLEMENTARY NOTE 3: THE PREPROCESSING WORKFLOW OF *fMRIPREP*

The general overview and details of processing are thoroughly documented

During the workflow set-up, *fMRIPrep* applies a set of heuristics to determine the appropriate processing operations for the input dataset (see Main Document, *Figure 1*). All available sub-workflows implementing individual processing steps that can be combined in the final processing pipeline are described in the [documentation website](#)^a. *Figure SN3.1* shows how the right-hand side of *Figure 1* (Main Document) translates into the pipeline graph, as implemented with Nipype.

Particular processing elements of *fMRIPrep*

Generating blood-oxygen-level dependent (BOLD) references for image registration. Although generating realignment and co-registration references may seem like a clerical task, doing so reliably for any dataset is not trivial. *fMRIPrep* integrates a BOLD reference generation workflow that adapts to the contrast of the input image. The workflow was tested to generate over ten thousand binary brain masks, of which two thousand were screened to ensure they did not exclude extensive areas of the brain nor included substantial background volumes. *Figure SN3.2* describes the workflow and provides further details on the generation of BOLD references.

^a<https://fmriprep.readthedocs.io/en/latest/workflows.html>

Fieldmap-less susceptibility distortion correction (SDC). This workflow takes a skull-stripped T1w image and reference BOLD image, and estimates a field of displacements that compensates for the warp caused by susceptibility distortion. The tool uses ANTs' `antsRegistration` configured with symmetric normalization (SyN) to align a fieldmap template¹³ and applies the template as prior information to regularize a follow-up registration process. The follow-up registration process also uses `antsRegistration` with SyN deformation, with displacements restricted to the phase-encoding (PE) direction. If no PE direction is specified, anterior-posterior PE is assumed. Based on the fieldmap atlas, the displacement field is optimized only within regions that are expected to have a >3mm (approximately 1 voxel) warp. This technique is a variation on previous work^{11,12}.

The Brain Imaging Data Structure (BIDS¹⁹) structure is hierarchically queried to discover whether extra acquisitions containing field map information are available. BIDS prescribes how the different native formats for field maps and corresponding metadata should be harmonized (see section 8.3.5 of the BIDS specification, version 1.1.1). The highest priority is given to the “PE-Polar” (phase-encoding POLARity) approach. In this case, in addition to the BOLD time-series, an extra echo-planar imaging (EPI) image is acquired with all parameters matching those of the BOLD data, except for the PE direction. Changing either the axis or (more often) the polarity of the PE results in a different realization of the distortion. “PE-Polar” methods establish a highly constrained registration framework between the two images of the same object with different distortions to estimate the underlying field map. If extra EPI scans for “PE-Polar” approaches are not available, then *fMRIPrep* queries for actual field mapping acquisitions. Typically, two gradient-recalled echoes can be acquired. Measuring the phase drift between the two echoes, and knowing the time delta between them, it is possible to map the inhomogeneity of the field. Once the field map is estimated, distortion is proportional to the inhomogeneity. In the last resort, when no field map information was acquired, *fMRIPrep* may run the “fieldmap-less” correction option (when enabled). The three methodologies will compensate for the low-frequency components of the distortion. However, current BOLD acquisitions are very fast at the cost of accepting the complete deletion (drop-out) of signal in particular regions. These regions are typically located around the orbitofrontal lobe (due to the proximity of the sinuses) and the temporal lobes (near the ear canals).

Organization of preprocessing results. The results from preprocessing with *fMRIPrep* follow the “Derivatives Extension” of BIDS. BIDS-Derivatives is inspired by the original BIDS for raw data. Therefore, results are sorted by subject in folders under the `fmrip/` folder. In each subject folder, two folders contain the derivatives from processing the anatomical reference (under the `anat/` folder) and the functional data (`func/` folder). Results are generally 3D or 4D brain data objects (represented with brain icons in the filesystem tree of *Figure SN3.3*). They also contain one “<derivative_prefix>_confounds.tsv” corresponding to each functional MRI (fMRI) run. These *confounds files* contain specific regressors for different noise sources that can be included in analysis. The full description of *fMRIPrep*'s outputs is documented in fmriprep.readthedocs.io/en/latest/outputs.html.

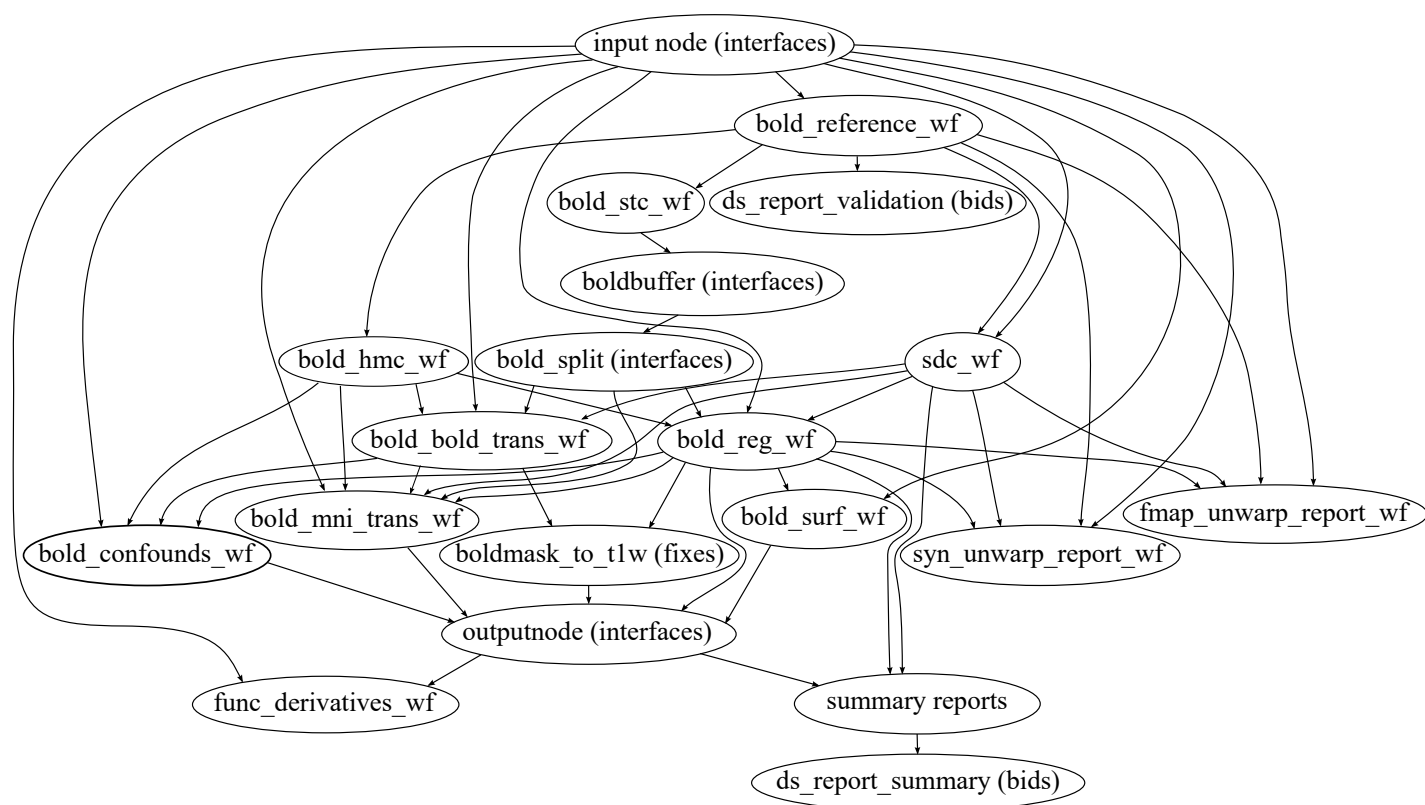


Figure SN3.1. The overview of *fMRIprep*'s workflow for functional preprocessing. The graph corresponding to the BOLD processing workflow of a dataset with slice-time information, one of the possible choices of field maps and surface reconstruction enabled in the anatomical processing branch (not shown in this graph representation). The graph also shows that BOLD data will be resampled into both MNI space and the subject's corresponding T1w space. This is a raster flow chart automatically generated by Nipype. For individual visualization, a high-resolution version is available at <https://doi.org/10.6084/m9.figshare.6809927>.

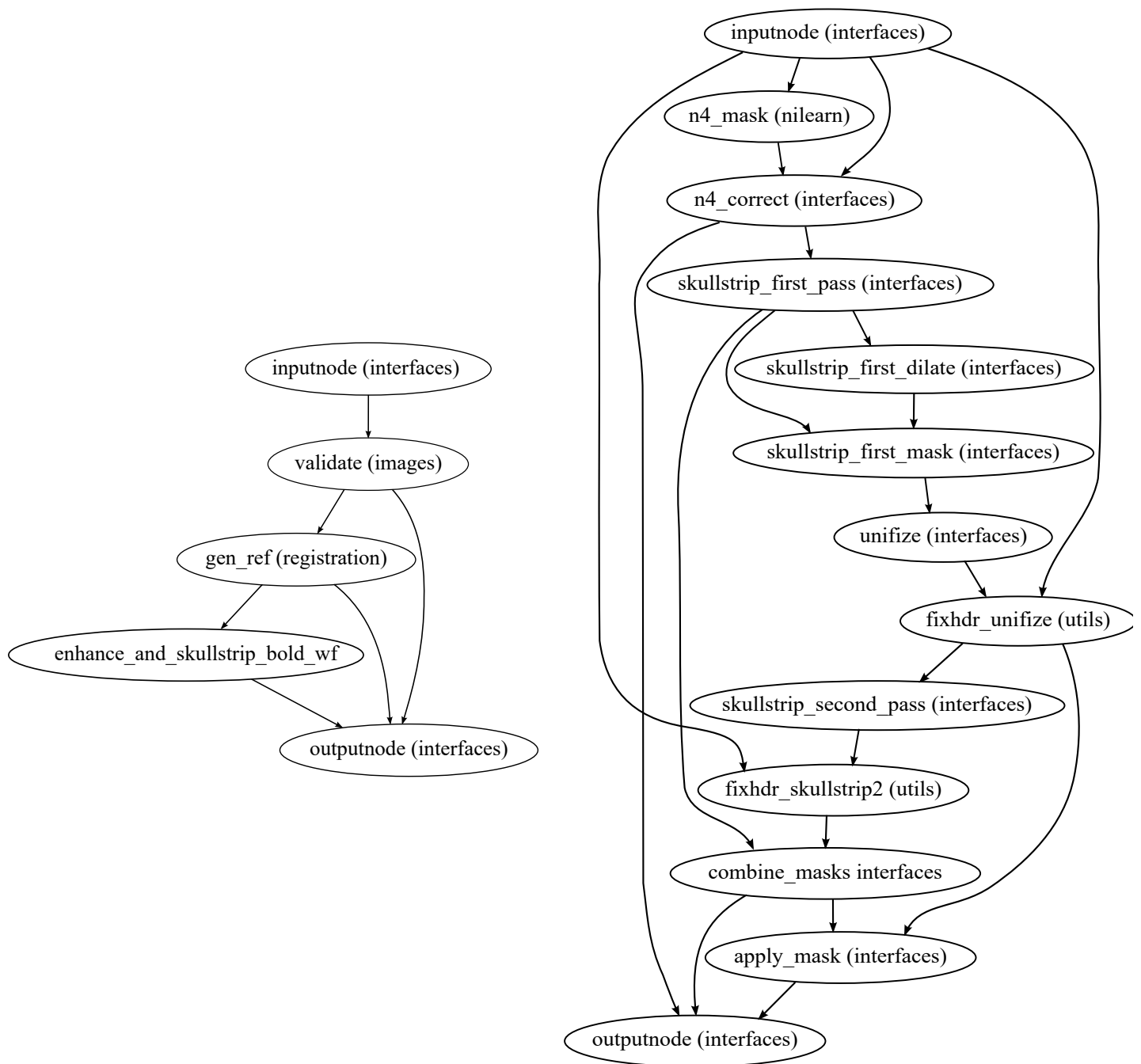


Figure SN3.2. Left | Workflow for the generation of a BOLD reference. The input BOLD image is first validated and the *xform* information (q-form and s-form matrices) are checked. Then, volumes with substantial T1 contrast derived from nonsteady states of the scanner (typically found in the beginning of EPI schemes) are identified, realigned, and averaged to generate a reference (within the node labeled *gen_ref*). That reference is then contrast-enhanced and a brain mask is calculated by the *enhance_and_skullstrip_bold_wf* workflow, presented on the right. **Right | Workflow for enhancement and skull-stripping of the BOLD reference.** The reference undergoes several interim masking and contrast enhancement processes to robustly find the outline of the brain from the BOLD average. The process involves the use of ANT's *N4BiasFieldCorrection*⁵, FSL's *bet*²⁰, Nilearn's *compute_epi_mask*¹⁸, AFNI's *3dAutomask*²¹, and *in-house* image enhancement heuristics. These are raster flow charts automatically generated by Nipype. For individual visualization, corresponding high-resolution versions are available at <https://doi.org/10.6084/m9.figshare.6809927>.

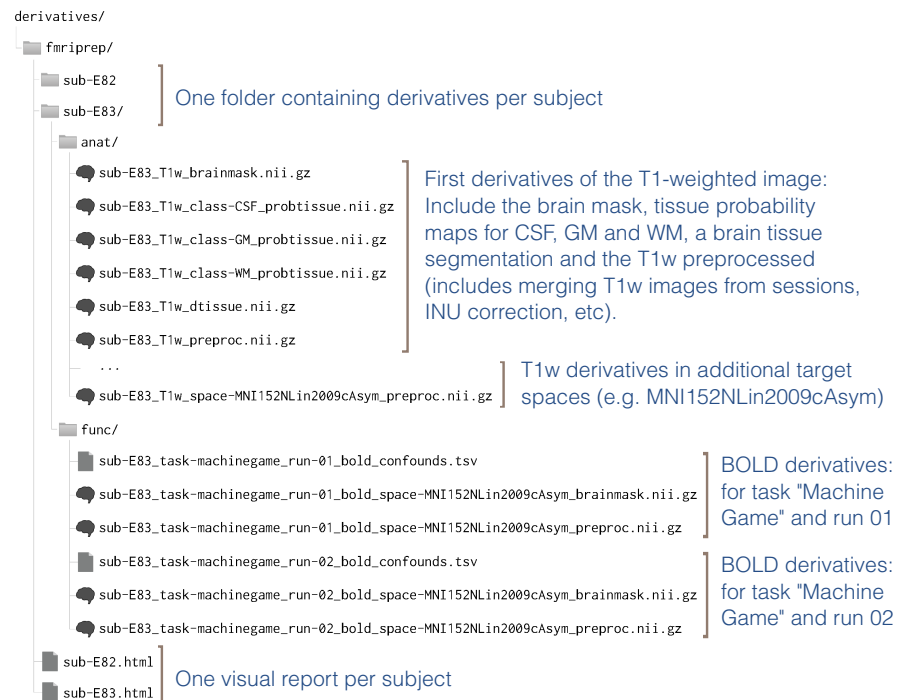


Figure SN3.3. Example of the organization of *fMRIprep*'s processing outcomes. The *BIDS-Derivatives* draft describes how the results from preprocessing can be organized. In this figure, imaging data are represented with brain icons, while additional text metadata and the visual reports are represented with a paper sheet.

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SUPPLEMENTARY NOTE 4: COMMUNITY-CENTERED, PEER-REVIEWED DEVELOPMENT, AND ADOPTION OF fMRIPREP

Community-building to ensure a sustainable impact

Inspired by the *rOpenSci* experience¹, the development of *fMRIPrep* has been driven by open-source principles, with a strong focus on community building from the start. To measure how much a given project depends on just a few individuals, Avelino et al. proposed the so-called *bus- or truck-factor*². As they define it, the truck-factor “is a measure of concentration of information in individual team members” and it “designates the minimal number of developers that have to be hit by a truck (or quit) before a project is incapacitated”², conveying that community-building is fundamental for open-source projects to ensure survival. Over 30 researchers have already contributed with code, reported issues, or with communications through the GitHub platform. GitHub is an effective platform for sharing code and information built atop the Git versioning system. An instance of its effectiveness to discuss and drive the progress of *fMRIPrep* is presented here^a. A larger number of researchers has also engaged within the community through the [NeuroStars](https://neurostars.org/tags/fmriprep) forums^b. Statistics about current adoption and usage of *fMRIPrep* are given below.

Peer-reviewed development

GitHub provides with a powerful tool to easily screen the quality of code changes by contributors called “pull-requests”. Pull-requests have a dedicated forum accessible via web, where collaborators can interact, enabling the necessary conversation and oversight to ensure the quality of contributions. Collaborators are aided by a review template to ensure all relevant aspects of the feature have been properly implemented and documentation has been included. The review template and the process of pull-request review are inspired by those of The Journal of Open Source Software³. An example is available here^c.

Continuous integration, a technique for recurrent, unsupervised assessment of software

Leveraging the free tier of CircleCI (<https://circleci.com>) for open source projects, *fMRIPrep* has an established test and deployment framework. With every iteration of the code development (a bug fix, a new feature), a new test cycle (*Figure SN4.1*) is triggered automatically. The test cycle first builds the software, assessing the correct packaging and containerization. Then, using substantially sub-sampled data for tests, three variants of the *fMRIPrep* workflow are run. The first variant runs *fMRIPrep* without surface reconstruction on one participant from DS000005. A second variant runs with surface reconstruction re-using pre-calculated results, on one participant from DS000054. A third variant runs the workflow without surface reconstruction on a multi-echo dataset (DS000210). These three full executions of *fMRIPrep* are completed with a complete rebuild of the documentation pages, and some unit-tests. By adding code coverage collection to the continuous integration tests, we expect to identify those sections of *fMRIPrep* that should be more tested. Finally, when a new version of *fMRIPrep* is being built, the continuous integration workflow finishes with the upload of new Python packages and container images to their corresponding repositories.

Current usage of *fMRIPrep*

Since the inclusion of a monitoring code with *fMRIPrep* version 1.0.12 (May 3, 2018), the tool has been invoked over 15,000 times (~5,000/month) by researchers around the globe, illustrating its fast adoption. These trends on adoption are also suggested by the number of unique, worldwide visitors to the documentation website (see *Figure SN4.2*) and more than ten thousand *pulls* of *fMRIPrep*’s Docker image^d. On [OpenNeuro](https://openneuro.org), *fMRIPrep* has accumulated more than 240 run requests, accounting for the

^a<https://github.com/poldracklab/fmriprep/issues/817>

^b<https://neurostars.org/tags/fmriprep>

^c<https://github.com/poldracklab/fmriprep/pull/1170#pullrequestreview-135163343>

^d<https://hub.docker.com/r/poldracklab/fmriprep/>

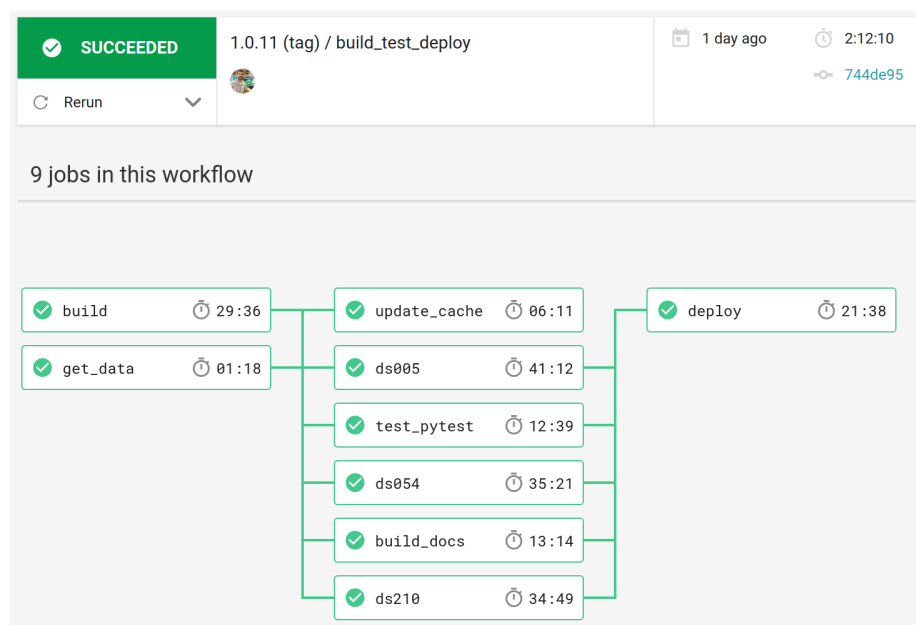


Figure SN4.1. Continuous Integration testing and deployment. Every code iteration adding features or fixing defects triggers a battery of automated tests. The full documentation website is regenerated, some unit tests are performed and *fMRIprep* is also run on three datasets from [OpenfMRI](#) (i.e. *DS000005*, *DS000054*, and *DS000210*). In order to ease the computational load on the continuous integration service, the three datasets were fixed for Brain Imaging Data Structure (BIDS⁴) errors (in particular *DS000210*), reduced to a single-participant and heavily down-sampled, after downloading from [OpenfMRI](#). The figure shows the current deployment workflow at [CircleCI](#). Only after all tests (middle column) passed successfully, the “deploy” job pushes the Docker image to the Docker Hub repository and the Python package is uploaded to the Python Package Index (PyPI).

~40% of all analyses requested so far in the platform. Some of these requests were executed on data uploaded by users – not found in [OpenfMRI](#).

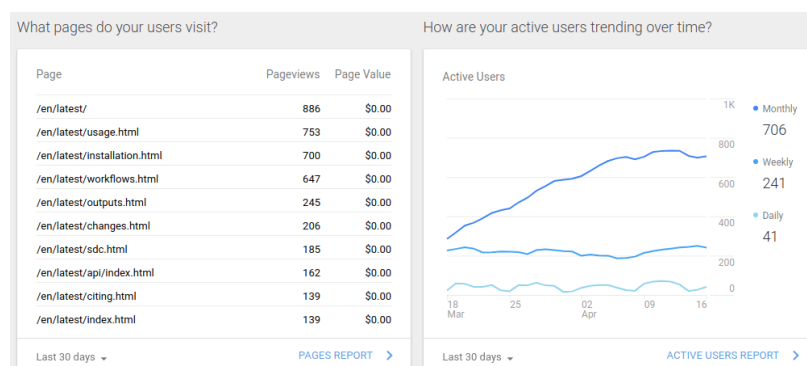


Figure SN4.2. Unique visitors to the *fMRIprep*’s documentation site. Clip from Google Analytics Panel showing tracking results for the documentation website <http://fmripred.org>.

We have incorporated *fMRIprep* in the processing workflow of all datasets in our laboratory. One example of the robust performance of *fMRIprep* on idiosyncratic datasets is presented in **Supplementary Figure 5**. *fMRIprep* performed with high-accuracy on a challenging dataset with simultaneous electrocorticography (ECoG) recordings. We have successfully applied *fMRIprep* on multi-band data, although some improvements such as the use of the single-band reference (“SBRef”) as co-registration target are scheduled for evaluation and inclusion within the tool^e. Artifacts inherent to this type of acquisition are

^e<https://github.com/poldracklab/fmripred/issues/449>

not particularly addressed by the tool, as a consensus on particular preprocessing steps for these images has not been yet reached.

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- 3 Katz, D. S., Niemeyer, K. E. & Smith, A. M. Publish your software: Introducing the Journal of Open Source Software (JOSS). *Computing in Science Engineering* **20**, 84–88 (2018). doi:[10.1109/MCSE.2018.03221930](https://doi.org/10.1109/MCSE.2018.03221930).
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SUPPLEMENTARY NOTE 5: RELATED FMRI PREPROCESSING WORKFLOWS

The most comprehensive neuroimaging packages –AFNI, FSL and SPM in particular– include graphical user interfaces (GUIs) (see *Figure SN5.1*) and workflows for functional MRI (fMRI) preprocessing. AFNI (*Analysis of Functional NeuroImages*) offers a general purpose GUI and `afni_proc.py`, a single-subject, single-run preprocessing workflow for fMRI. The `afni_proc.py` pipeline is complemented by a GUI (`uber_subject.py`) and `align_epi_anat.py`, an image alignment tool (including several intra-subject registration schemes: fMRI-to-anatomical, anatomical-to-anatomical, fMRI-to-fMRI and anatomical-to-atlas). AFNI is completely open-source, and user feedback is utilized to improve the tool and users can contribute with bugfixes and features through <https://github.com/afni/afni>. FSL (*FMRIB's Software Library*) possesses the most extensive GUI, covering a number of MRI processing and analysis workflows, not limited to fMRI. One of the available tools is *FEAT FMRI Analysis*, a GUI that creates a single-subject, single-run preprocessing and analysis workflow. Execution of the workflow can be delayed by writing one script file in the FSL internal format, generally referred to as `design.fsf`. Users can manually modify the file to analyze different subjects and runs. The user is responsible for manually executing other elements of the pipeline, such as anatomical preprocessing or susceptibility distortion corrections (SDCs) other than fieldmap-based. SPM (*Statistical Parametric Mapping*) offers a GUI for the different processing and analysis tasks in the workflow and the users can combine them manually. Particular processing elements can be introduced using *plug-ins*, for instance to include a susceptibility distortion correction (SDC) step. Finally, SPM allows *plug-outs* to create workflows and batch scripts to run over several subjects. Both FSL and SPM are open-source, although they follow a more traditional development model less open to third-party contributions.

Interoperability between these three main software packages is low, since their internal processing and analysis elements are highly coupled. Although *Nipype*¹ provides a homogeneous interface that enables the decoupling of these components (and effectively allows one to mix-and-match these tools), most researchers have been historically attached to one of the options. Their custom processing workflows are generally based off of one single package. In other words, their *ad hoc* pipelines are variations of `afni_proc.py`, FSL `feat` or SPM's batch scripts.

Human Connectome Project (HCP²) Pipelines constitute a different type of solution to this challenge. They propose a very comprehensive ensemble of workflows for preprocessing and analysis of “HCP-like” datasets. HCP Pipelines are built combining (mainly) FSL and FreeSurfer to perform fMRI surface analysis (among other anatomical and diffusion MRI analyses). The development of HCP Pipelines is open-source and collaborative through <http://github.com>.

Finally, C-PAC³ (configurable pipeline for the analysis of connectomes) integrates AFNI and FSL tools through *Nipype* for preprocessing and analysis of resting-state fMRI connectomes. C-PAC offers a GUI that generates an extremely detailed configuration file where all the processing steps and all the necessary parameters are defined. Additional strengths of C-PAC are the open-source and collaborative development, and up-to-date and thorough documentation.

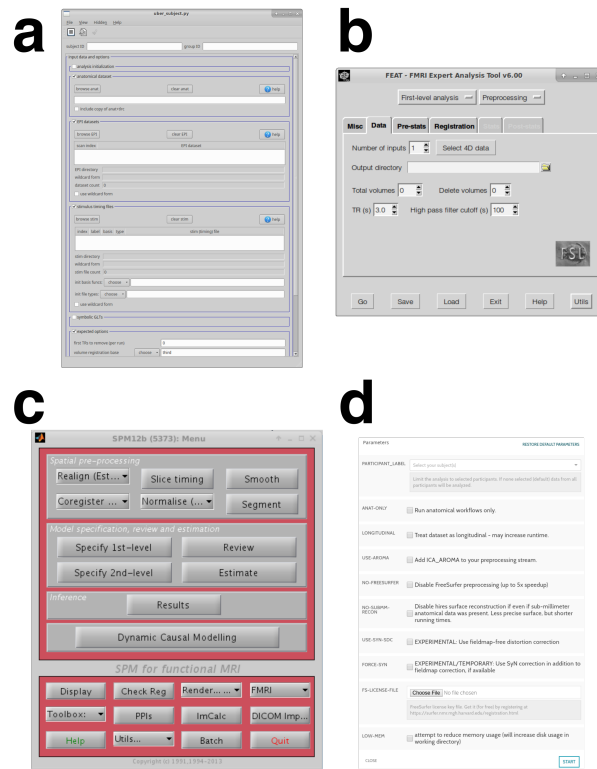


Figure SN5.1. **a** | AFNI's `uber_subject.py` GUI. **b** | FSL's `feat` GUI. **c** | SPM's fMRI analysis GUI. **d** | *FMRIPrep*'s GUI at [OpenNeuro](https://openneuro.org).

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SUPPLEMENTARY RESULTS 1: EXAMPLES OF BUG FIXES (EXTENSION TO SUPPLEMENTARY FIGURE 2)

During the Evaluation Phase I, some ubiquitous problems arising from the data or the integration of software tools were identified. The first example present in Main Document, *Figure 3* shows how the consistency of NIfTI headers is crucial. Software packages have inconsistent implementations of the two possible coordinate systems (s/q-form matrices or “x-forms”) of the NIfTI format. For instance, ANTs¹ will only make use of the q-form matrix when available (because it uses the *Insight Toolkit*² –ITK– to read images). Particular settings of these matrices may introduce alignment errors. To address this issue, *fMRIPrep* checks the headers early and sanitizes the x-forms consistently. Several heuristics are applied in order to extract the most plausible and consistent x-form matrices configuration, setting appropriate x-form matrix. If no x-form information is set, *fMRIPrep* creates a default one with “LAS” (left-to-right, anterior-to-posterior, superior-to-inferior) orientation and the voxel spacing information.

The second example in Main Document, *Figure 3* shows how some blood-oxygen-level dependent (BOLD) scans failed at the brain extraction step. The origin of the issue was identified as a problematic contrast of the BOLD reference image due to strong intensity non-uniformity (INU). Some examples of datasets showing this problem are DS000116, DS000133 and DS000157. This intensity non-uniformity (INU) field precluded the calculation of a brain mask for the time-series. As a result, the brain mask was too conservative, leaving out substantial areas of the brain. The problem was solved with a more robust BOLD reference calculation and a less conservative mask calculation. Currently, we are in the process of integrating a specific unit test to protect from regressions of this problem on new datasets^a.

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- 2 Yoo, T. S. *Insight into Images: Principles and Practice for Segmentation, Registration, and Image Analysis* (Taylor & Francis, 2004).

^a<https://github.com/poldracklab/fmripred/pull/1074>

SUPPLEMENTARY RESULTS 2: COMPARISON TO FSL FEAT

***fMRI*Prep achieved higher spatial accuracy**

Supplementary Figure 4 shows the variability maps obtained with both preprocessing pipelines, and suggests that results from *feat* are smoother. These maps reveal a superior anatomical accuracy of *fMRI*Prep over *feat*, likely reflecting the combined effects of a more precise spatial normalization scheme, the single-shot interpolation that uses the more accurate sinc kernel (Lanczos interpolation), and the application of the “fieldmap-less” susceptibility distortion correction (SDC) methodology. *fMRI*Prep outcomes are particularly better aligned with the underlying anatomy in regions typically warped by susceptibility distortions such as the orbitofrontal lobe, as demonstrated by the close-ups on the lower panel of **Supplementary Figure 4**.

First-level and group-level modeling did not show substantial differences

The results and figures associated to this experiment are fully reported using [Jupyter Notebooks^a](#). For example, we observed that the distributions of *t*-values for the second-level (group) activation maps are very similar for both tools. **Figure SR2.1** shows the distribution of nonzero *t*-values for the two groups of size 50 participants across all the repetitions, for both *fMRI*Prep and *feat*. The *t*-value distribution has a heavier tail on the negative effect side for *feat*, with and without smoothing. However, when we applied the 5mm FWHM smoothing kernel at the entry point of the first-level analysis, the resulting distributions are nearly identical. The fact that smoothing increased group level statistical values aligns well with the literature¹, and supports the claim that *fMRI*Prep allows for a better control over the smoothness of data.

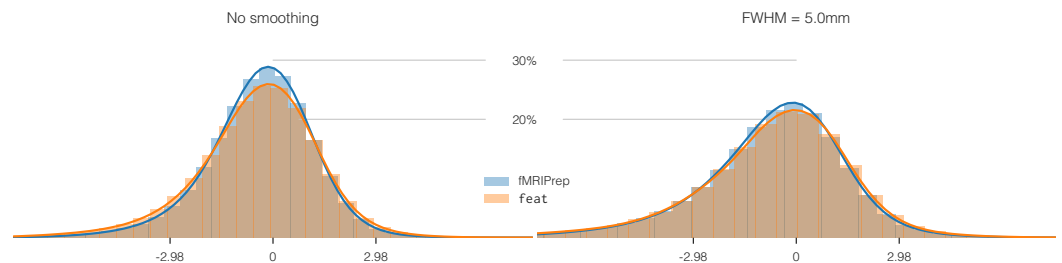


Figure SR2.1. The distributions of *t*-values resulting from the group-level analysis are similar between tools, and almost identical when a smoothing step was implemented in the beginning of the first-level analysis.

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^a<https://github.com/poldracklab/fmripred-notebooks/tree/783eb2aa867ef779a49e14fccb67e078753320e>

Summary

Reports start with an overview of the dataset, as identified using BIDS.

Anatomical processing

Several panels allow for quality control of the anatomical workflow. Brain tissue segmentation, spatial normalization and surface reconstruction (if requested) can be inspected using these visualization panels.

Fieldmaps processing

When the dataset contains any of the supported alternatives to estimate the deformation map corresponding to susceptibility distortions, these panels help assess these images were correctly processed.

Functional processing

Each BOLD run across the different tasks and sessions will be presented at different quality control points.

First, when fieldmaps were found, some mosaics will show the alignment of those maps to the BOLD reference. The block ends with a dynamic plot showing how images are unwarped.

The report also shows processing in native BOLD space plotting the brain mask calculated from the functional MR signal and the regions-of-interest (ROIs) where the CompCor confounds are calculated.

Finally, the alignment between same-subject T1-weighted and that specific BOLD run is presented.

Errors

FMRIPrep is explicit about errors, and any problems encountered along the processing will be listed at the end of the report, with collapsible panels containing the specific detail of each error.

T1-weighted reference, brain mask, intensity inhomogeneity and brain tissue segmentation panel. A static mosaic allows the assessment of these four crucial steps of pre-processing anatomical images.

Spatial normalization. A dynamic mosaic that transitions between the target atlas space and the T1w-reference aligned into that space allows checking the accuracy of this image registration process.

Susceptibility distortion correction. If fieldmap information was found or the "fieldmap-less" correction is requested, the step is assessed with a dynamic mosaic that transitions between the unwarped ("after") and original ("before"). Contours of the white-matter are also presented as anatomical cue.

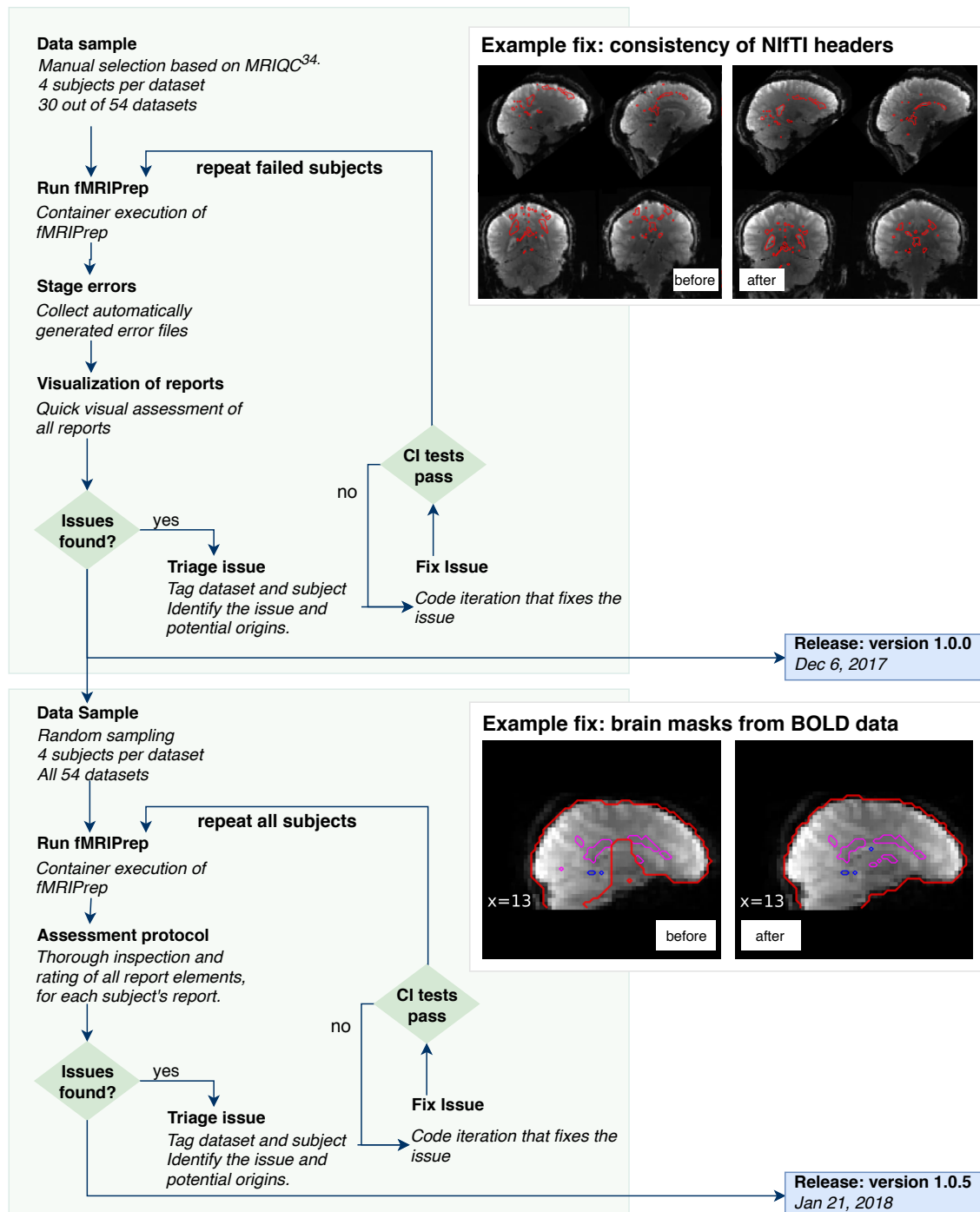
BOLD mask and CompCor ROIs. The final BOLD signal is presented, with contours representing the outline of the brain mask, and two regions-of-interest (ROIs) where CompCor confounds are estimated.

Alignment of BOLD and the T1w reference. The correct alignment to the anatomical reference is assessed with a dynamic mosaic that renders the reconstructed surfaces over the BOLD reference.

Supplementary Figure 1.

The visual reports ease quality control and help understand the processing flow.

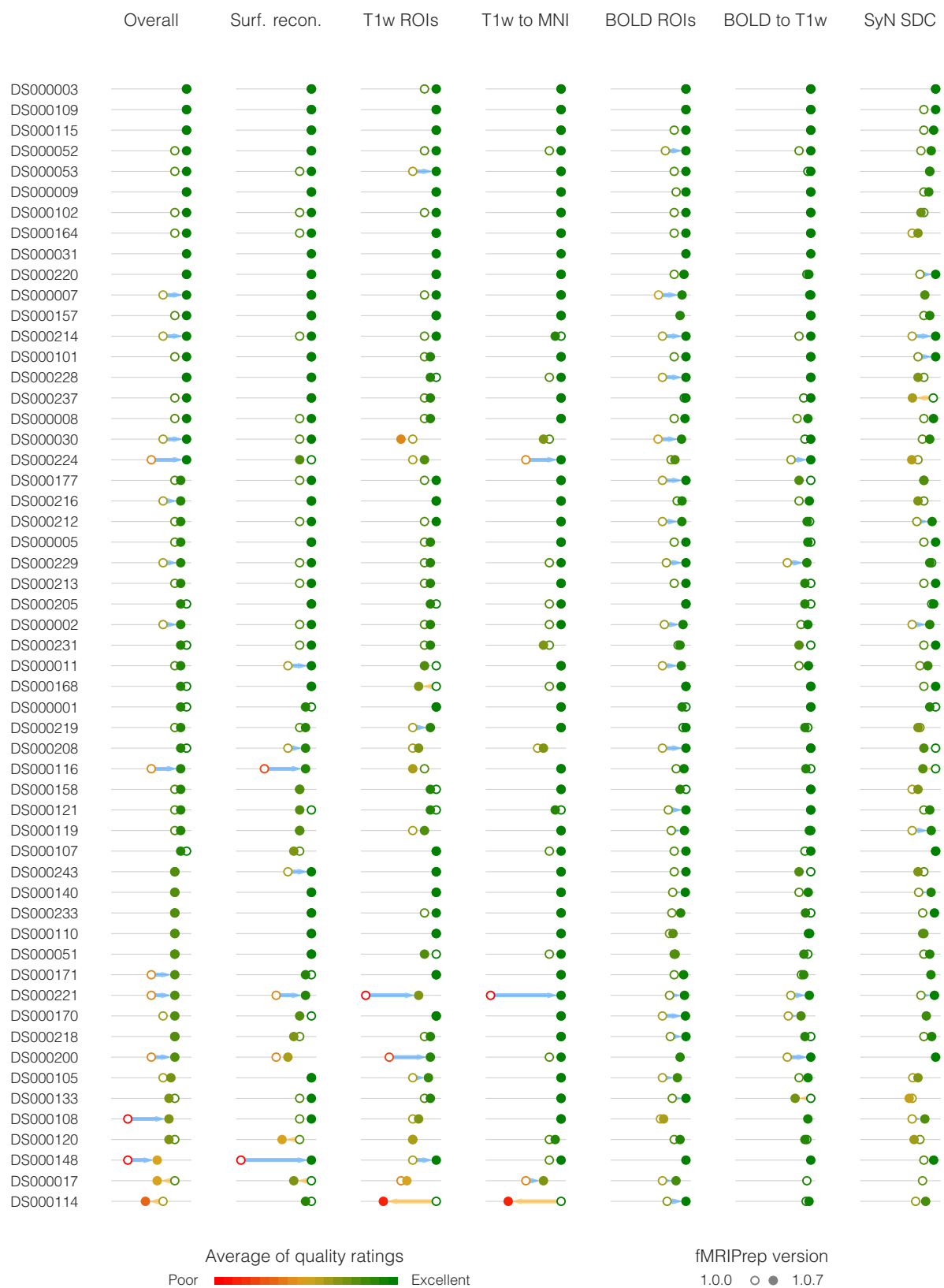
The visual reports facilitate the assessment and curation of the results, optimizing the process of visual inspection. They also contribute to the "glass-box" philosophy with which the software was developed; rather than hiding a complex set of operations within a monolithic black box. *FMRIPrep* exposes interim results at multiple steps to encourage active engagement by the scientist.



Supplementary Figure 2.

Combining visual assessment within the software testing flow.

We complement well-established techniques for software integration testing with manual assessment of the outputs. The evaluation framework is designed with two subsequent testing phases. Phase I focuses on fault-discovery and visual reports are used to better understand the issues found. The top box (Example fix 1) shows an example of defect identified and solved during this testing cycle. After addressing a total of 21 issues affecting 7 datasets, and the release of *fMRIprep* version 1.0.0, the next testing stage is initiated. Phase II focuses on increasing the overall quality of results as evaluated visually by experts. Following an inspection protocol, reports from 213 participants belonging to 58 different studies were individually assessed. We found 12 additional issues affecting 11 datasets that have been addressed with the release of *fMRIprep* version 1.0.3 on January 3, 2018. The bottom box (Example fix 2) illustrates one of these issues, which produced errors in the brain extraction process from blood-oxygen-level dependent (BOLD) data. In **Supplementary Results 1**, both examples and the corresponding solutions are described in detail.



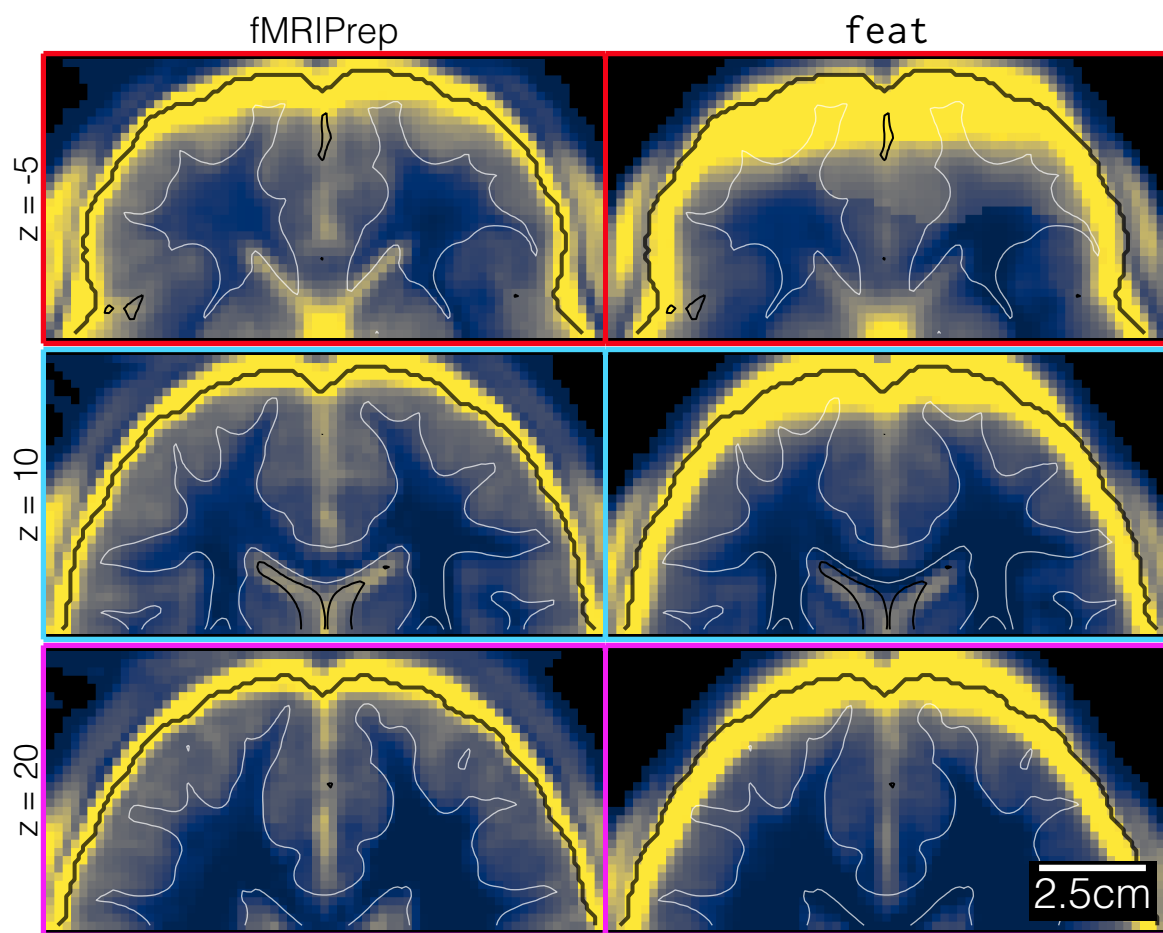
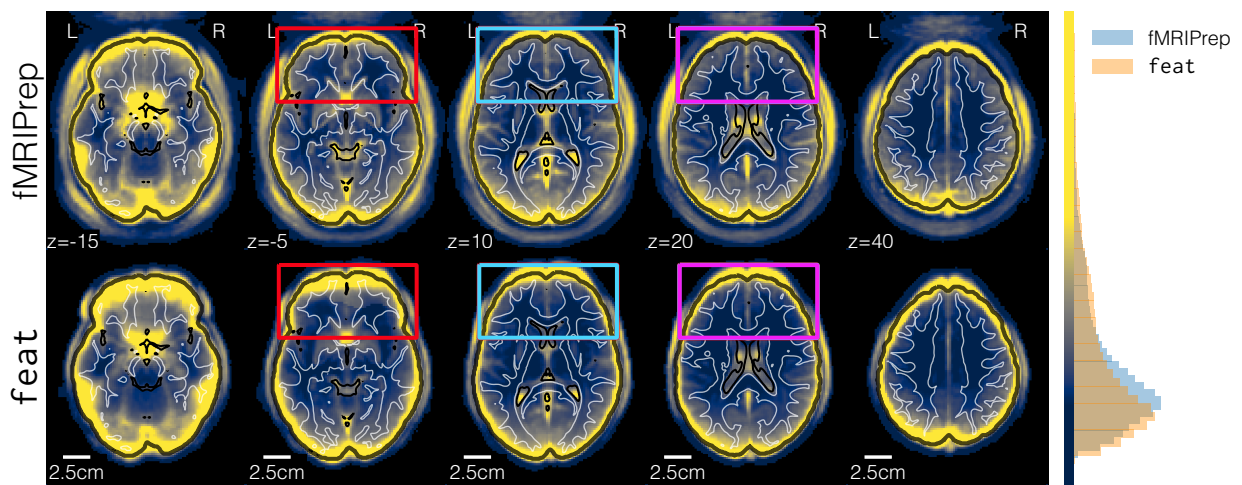
Supplementary Figure 3.

Visual assessment of all datasets under test, arranged by the mean overall rating.

Each column of the diagram represents one out of the seven quality control points in the Phase II assessment described in **Online Methods, sec.**

Validation of fMRIprep on diverse data. Colors encode the average rating assigned by the experts, across all runs and participants for each dataset.

The filled or hollow markers represent the fMRIprep version being assessed (1.0.7 or 1.0.0, respectively).

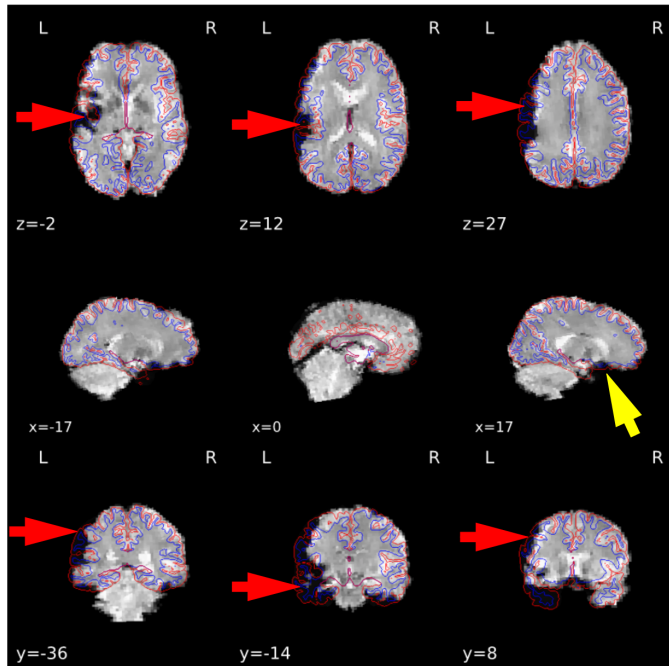
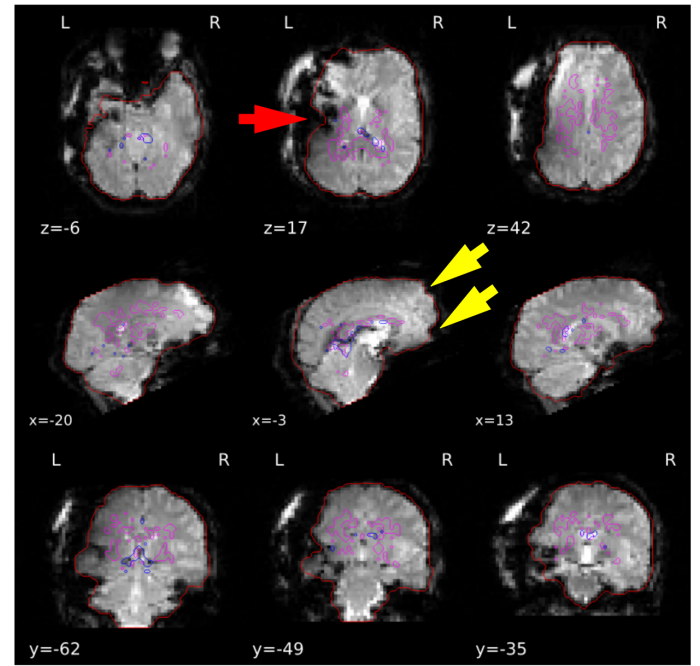


Variability mappings presented in this figure are derived from N=257 biologically independent participants

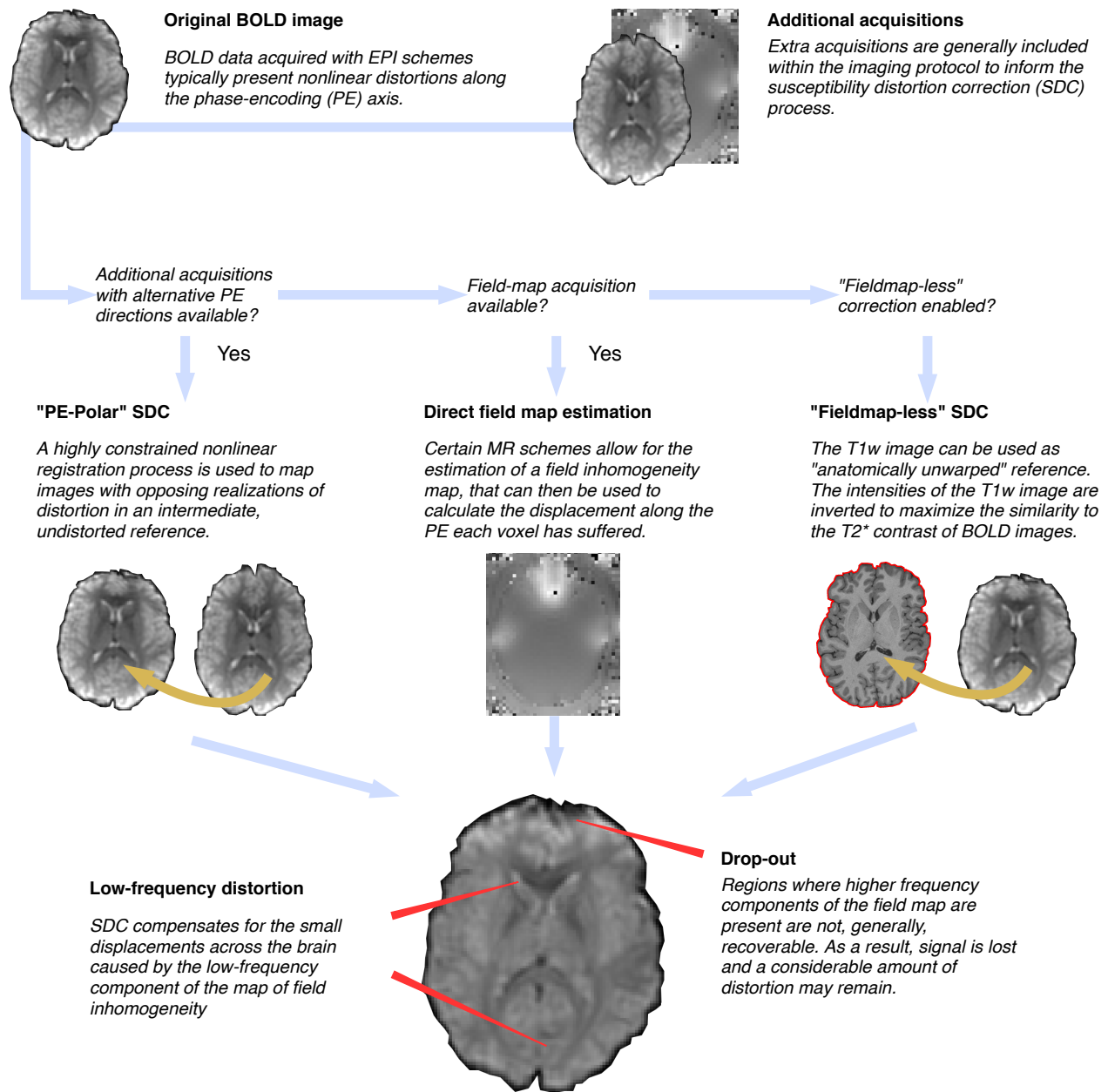
Supplementary Figure 4.

Maps of between-subjects variability of the averaged BOLD time-series resampled into MNI space.

The top box of the panel extends the number of views presented in **Figure 3**. The histogram at the right side plots the normalized frequency of variability (arbitrary units) for both maps, within the brain mask. The color bar maps the bins of the histogram to the corresponding colors that are used in the mosaic of panel B. The heavier tail of *feat* in the distribution of variability is compensated in the case of *fMRIprep* by the peak in voxel-counts located at a higher variability than that of *feat*. Such peak in *fMRIprep*'s distribution corresponds to variability in cortical gray matter regions. As demonstrated in the lower box of the panel, *fMRIprep*-preprocessed images keep a higher spatial detail, especially on those regions affected by susceptibility-derived distortions.

A**B****Supplementary Figure 5.****Successfully processing functional MRI (fMRI) data with intracranial electrodes.**

FMRIprep successfully processed some datasets acquired with simultaneous electrocorticography (ECoG) recordings. For ECoG, electrodes are placed directly on surfaces of the brain surgically exposed. As described previously, the exposed areas introduce large steps of magnetic susceptibility across the imaged volume, that lead to large distortions and signal drop-out (marked by red arrows). Yellow arrows point at distortions typically found in regular BOLD data. **A | Performance of co-registration.** Despite the wide areas of signal completely lost, boundary based registration performed accurately. **B | Delineation of regions-of-interest (ROIs).** *FMRIprep*'s heuristics and workflow for BOLD skull-stripping performed correctly (red contour). Moreover, regions where data are sampled to calculate *CompCor*¹⁰ (blue and magenta contours) do not include any cortical regions.



Supplementary Figure 6.

The overview of *fMRIprep*'s workflow for susceptibility distortion correction (SDC).

The Brain Imaging Data Structure²¹ (BIDS) structure is hierarchically queried to discover whether extra acquisitions containing field map information are available. BIDS prescribes how the different native formats for field maps and corresponding metadata should be harmonized (see section 8.3.5 of the BIDS specification, version 1.1.1). The highest priority is given to the "PE-Polar" (phase-encoding POLARity) approach. In this case, in addition to the BOLD time-series, an extra echo-planar imaging (EPI) image is acquired with all parameters matching those of the BOLD data, except for the phase-encoding (PE) direction. Changing either the axis or (more often) the polarity of the PE results in a different realization of the distortion. "PE-Polar" methods establish a highly constrained registration framework between the two images of the same object with different distortions to estimate the underlying field map. If extra EPI scans for "PE-Polar" approaches are not available, then *fMRIprep* queries for actual field mapping acquisitions. Typically, two gradient-recalled echoes can be acquired. Measuring the phase drift between the two echoes, and knowing the time delta between them, it is possible to map the inhomogeneity of the field. Once the field map is estimated, distortion is proportional to the inhomogeneity. In the last resort, when no field map information was acquired, *fMRIprep* may run the "fieldmap-less" correction option (when enabled). The three methodologies will compensate for the low-frequency components of the distortion. However, current BOLD acquisitions are very fast at the cost of accepting the complete deletion (drop-out) of signal in particular regions. These regions are typically located around the orbitofrontal lobe (due to the proximity of the sinuses) and the temporal lobes (near the ear canals).

Supplementary Table 1. Data from OpenfMRI used in evaluation. *S*: number of sessions; *T*: number of tasks; *R*: number of BOLD runs; Modalities: number of runs for each modality, per subject (FM indicates acquisitions for susceptibility distortion correction); Part. IDs (phase): participant identifiers included in testing phase; *N*: total of unique participants; *TR*: repetition time (s); #*TR*: length of time-series (volumes); Resolution: voxel size of BOLD series (mm).

DS000XXX	Scanner	S	T	R	Modalities	Part. IDs (Phase I)	Part. IDs (Phase II)	N	TR	#TR	Resolution
001 ³⁵	SIEMENS	1	1	21	1 T1w, 3 BOLD	02, 03, 09, 15	01, 02, 07, 08	7	2.0	6300	3.12×3.12×4.00
002 ³⁶	SIEMENS	1	3	48	1 T1w, 6 BOLD	01, 11, 14, 15	02, 03, 04, 10	8	2.0	9510	3.12×3.12×5.00
003 ³⁷	SIEMENS	1	1	6	1 T1w, 1 BOLD	03, 07, 09, 11	02, 09, 10, 11	6	2.0	956	3.12×3.12×4.00
005 ³⁸	SIEMENS	1	1	21	1 T1w, 3 BOLD	01, 03, 06, 14	01, 04, 05, 15	7	2.0	5040	3.12×3.12×4.00
007 ³⁹	SIEMENS	1	3	46	1 T1w, 5 BOLD	09, 11, 18, 20	03, 04, 08, 12	8	2.0	8205	3.12×3.12×4.00
008 ⁴⁰	SIEMENS	1	2	38	1 T1w, 5 BOLD	04, 09, 12, 14	10, 12, 13, 15	7	2.0	6808	3.12×3.12×4.39
009	SIEMENS	1	4	48	1 T1w, 6 BOLD	01, 03, 09, 10	17, 18, 21, 23	8	2.0	10528	3.00×3.00×4.00
011 ⁴¹	SIEMENS	1	4	41	1 T1w, 5 BOLD	01, 03, 06, 08	03, 09, 11, 14	7	2.0	8041	3.12×3.12×5.00
017	SIEMENS	2	2	48	4 T1w, 9 BOLD	2, 4, 7, 8	2, 5, 7, 8	5	2.0	8736	3.12×3.12×4.00
030 ^{34,42}	SIEMENS	1	8	30	1 T1w, 7 BOLD		10[440,638,668,855]	4	2.2	6254	3.00×3.00×4.00
031 ⁴³	SIEMENS	107	9	191	29 T1w, 18 T2w, 46 FM, 191 BOLD		01	1	1.2	79017	2.55×2.55×2.54
051 ⁴⁴	SIEMENS	1	1	54	2 T1w, 7 BOLD	03, 04, 05, 13	02, 04, 06, 09	7	2.0	10800	3.12×3.12×6.00
052 ⁴⁵	SIEMENS	1	2	28	2 T1w, 4 BOLD	06, 08, 12, 14	05, 10, 12, 13	7	2.0	6300	3.12×3.12×6.00
053	SIEMENS	1	3	32	1 T1w, 8 BOLD		002, 003, 005, 006	4	1.2	10712	2.40×2.40×2.40
101	SIEMENS	1	1	16	1 T1w, 2 BOLD	06, 08, 16, 19	05, 11, 17, 20	8	2.0	2416	3.00×3.00×4.00
102 ^{46–48}	SIEMENS	1	1	16	1 T1w, 2 BOLD	05, 19, 22, 23	08, 10, 16, 20	8	2.0	2336	3.00×3.00×4.00
105 ^{49,50}	GE	1	1	71	1 T1w, 11 BOLD	1, 2, 3, 6	1, 4, 5, 6	6	2.5	8591	3.50×3.75×3.75
107 ⁵¹	SIEMENS	1	1	14	1 T1w, 2 BOLD	02, 05, 20, 29	05, 36, 39, 47	7	3.0	2315	3.00×3.00×3.00
108 ⁵²	GE	1	1	41	1 T1w, 5 BOLD	01, 03, 07, 17	03, 10, 24, 26	7	2.0	7860	3.44×3.44×4.50
109 ⁵³	SIEMENS	1	1	12	1 T1w, 2 BOLD	02, 10, 39, 47	02, 11, 15, 39	6	2.0	2148	3.00×3.00×3.54
110 ⁵⁴	GE	1	1	80	1 T1w, 10 BOLD	07, 09, 17, 18	01, 02, 03, 06	8	2.0	14880	3.44×3.44×4.01
114 ⁵⁵	GE	2	5	70	2 T1w, 10 BOLD	01, 05, 07, 08	02, 03, 04, 07	7	5.0	10626	4.00×4.00×4.00
115 ^{56,57}	SIEMENS	1	3	24	1 T1w, 3 BOLD	31, 68, 77, 78	04, 33, 67, 79	8	2.5	3288	4.00×4.00×4.00
116 ^{58–61}	PHILIPS	1	2	36	1 T1w, 6 BOLD	02, 08, 10, 15	08, 12, 15, 17	6	2.0	6120	3.00×3.00×4.00
119 ⁶²	SIEMENS	1	1	31	1 T1w, 3 BOLD	10, 51, 59, 74	11, 26, 56, 58	8	1.5	7564	3.12×3.12×4.00
120 ⁶³	SIEMENS	1	1	11	1 T1w, 2 BOLD		04, 05, 08, 24	4	1.5	2376	3.12×3.12×4.00
121 ⁶⁴	SIEMENS	1	1	28	1 T1w, 4 BOLD	01, 04, 05, 20	01, 18, 22, 26	7	1.5	5656	3.12×3.12×4.00
133 ⁶⁵	PHILIPS	2	1	24	2 T1w, 6 BOLD		06, 21, 22, 23	4	1.7	3480	4.00×4.00×4.00
140 ⁶⁶	PHILIPS	1	1	36	1 T1w, 9 BOLD		05, 27, 32, 33	4	2.0	7380	2.80×2.80×3.00
148	GE	1	1	12	1 T1w, 1 T2w, 3 BOLD		09, 26, 28, 33	4	1.8	3162	3.00×3.00×3.00
157 ⁶⁷	PHILIPS	1	1	4	1 T1w, 1 BOLD		04, 21, 23, 28	4	1.6	1485	4.00×4.00×3.99
158 ⁶⁸	SIEMENS	1	1	4	1 T1w, 1 BOLD		064, 081, 122, 149	4	2.0	1240	3.00×3.00×3.30
164 ⁶⁹	SIEMENS	1	1	4	1 T1w, 1 BOLD		006, 012, 019, 027	4	1.5	1480	3.50×3.50×3.50
168 ⁷⁰	SIEMENS	1	1	4	1 T1w, 1 BOLD		08, 27, 30, 49	4	2.5	2112	3.00×3.00×3.00
170 ^{71–73}	GE	1	4	48	1 T1w, 12 BOLD		1700, 1708, 1710, 1713	4	3.0	2160	3.44×3.44×3.40
171 ⁷⁴	SIEMENS	1	2	20	1 T1w, 5 BOLD		control0[4,8,14], mdd03	4	3.0	2066	2.90×2.90×3.00
177 ⁷⁵	SIEMENS	1	1	4	1 T1w, 1 BOLD		04, 07, 10, 11	4	3.0	920	3.00×3.00×3.00
200 ⁷⁶	SIEMENS	1	1	4	1 T1w, 1 BOLD		2004, 2011, 2012, 2014	4	2.5	480	3.28×3.28×4.29
205 ⁷⁷	SIEMENS	1	2	12	1 T1w, 3 BOLD		01, 05, 06, 07	4	2.2	4103	3.00×3.00×3.00
208 ⁷⁸	SIEMENS	1	1	4	1 T1w, 1 BOLD		27, 45, 56, 69	4	2.5	1200	3.44×3.44×3.00
212 ^{79,80}	SIEMENS	1	2	40	1 T1w, 10 BOLD		07, 13, 20, 29	4	3.0	5808	3.12×3.12×4.00
213 ⁸¹	SIEMENS	1	1	4	1 T1w, 1 BOLD		06, 10, 12, 13	4	2.0	1120	3.00×3.00×3.99
214 ⁸²	SIEMENS	1	1	4	1 T1w, 1 BOLD		EES0[06,31,33,34]	4	1.6	1364	3.44×3.44×5.00
216 ⁸³	GE	1	1	16	1 T1w, 4 BOLD (ME)		01, 02, 03, 04	4	3.5	2688	3.00×3.00×3.00
218 ⁸⁴	PHILIPS	1	1	12	1 T1w, 3 BOLD		02, 07, 12, 17	4	1.5	6709	2.88×3.00×2.88
219 ⁸⁴	PHILIPS	1	1	14	1 T1w, 3 BOLD		04, 09, 10, 12	4	1.5	7807	2.88×3.00×2.88
220 ⁸⁵	PHILIPS, SIEMENS	3	1	12	3 T1w, 3 BOLD		tbi[03,05,06,10]	4	2.0	1728	3.00×3.00×4.00
221	SIEMENS	2	1	15	1 MP2RAGE, 9 FM, 3 BOLD		010[016,064,125,251]	4	2.5	9855	2.30×2.30×2.30
224 ⁸⁶	SIEMENS	12	6	399	4 T1w, 4 T2w, 10 FM, 79 BOLD	MSC[05,06,08,09]	MSC[05,08,09,10]	5	2.2	88528	4.00×4.00×4.00
228	SIEMENS	1	1	4	1 T1w, 1 BOLD		pixar[001,017,103,132]	4	2.0	672	3.06×3.06×3.29
229 ⁸⁷	SIEMENS	1	1	12	1 T1w, 3 BOLD		02, 05, 07, 10	4	2.0	4680	3.44×3.44×3.00
231 ⁸⁸	SIEMENS	1	1	12	1 T1w, 3 BOLD		01, 02, 03, 09	4	2.0	4548	2.02×2.02×2.00
233 ⁸⁹	PHILIPS	1	2	80	2 T1w, 10 BOLD	rid0000[12,24,36,41]	rid0000[01,17,31,32]	8	2.0	15680	3.00×3.00×3.00
237 ⁹⁰	SIEMENS	1	1	41	1 T1w, 5 BOLD	03, 08, 11, 12	01, 03, 04, 06	7	1.0	19844	3.00×3.00×3.00
243 ⁹	SIEMENS	1	1	13	1 T1w, 1 BOLD	012, 032, 042, 071	023, 066, 089, 094	8	2.5	2884	4.00×4.00×4.00
Total				2176		120	325	304		551769	