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Mindcontrol: A Web Application for Brain Segmentation Quality Control

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Abstract

Tissue classification plays a crucial role towards the understanding of normal neural development, brain-behavior relationships, and the disease mechanisms of a number of psychiatric and neurological illnesses. Ensuring the quality of tissue classification is important for the translation of imaging biomarkers to clinical practice. Because the accuracy of segmentation must be assessed with the human eye, quality assurance becomes more difficult at a large scale - a problem of increasing importance as the number of data sets is on the rise. To make this process more efficient, we have developed Mindcontrol, which is an open-source web application for the collaborative quality control of neuroimaging processing outputs. Mindcontrol consists of a dashboard to organize data, descriptive visualizations to explore the data, an imaging viewer, and an in-browser annotation and editing toolbox for data curation and quality control. Mindcontrol is flexible and can be configured for the outputs of any software package in any data organization structure. Example configurations for three large, open-source datasets are presented; they are the 1000 Functional Connectomes Project (FCP), the Consortium for Reliability and Reproducibility (CoRR), and the Autism Brain Imaging Data Exchange (ABIDE) Collection. These demo applications link descriptive quality control metrics, regional brain volume and thickness scalars to a 3D imaging viewer and editing module, resulting in an easy to implement quality control protocol for large and small studies alike.

1. Background

The imaging biomarkers derived from MRI play a crucial role in the fields of neuroscience, neurology and psychiatry. Estimates of regional brain volumes and shape features help track

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the disease progression of several neurological and psychiatric diseases, including Alzheimer's disease (Dickerson et al. 2009) (Vemuri and Jack 2010), Parkinson's disease (Mangia 2013), schizophrenia (Shenton et al. 2001), depression (Meisenzahl et al. 2011), autism (Brambilla et al. 2003), and multiple sclerosis (Filippi et al. 1995), to name a few. Assuring the quality of these biomarkers is crucial as we scale their production, given recent increases in data collection to accommodate modern precision-medicine approaches.

Multiple semi-automated programs have been developed to estimate such MRI biomarkers. While these programs are efficient, errors in regional segmentation frequently occur, stemming from multiple sources. First, the quality of the MRI scan itself due to motion artifacts or scanner instabilities could blur and distort anatomical boundaries (Blumenthal et al. 2002) (Pardoe et al. 2016) (Reuter et al. 2015) (Savalia et al. 2016). Differences in MRI hardware, software, and acquisition sequences also contribute to contrast differences and gradient distortions that affect tissue classification, which makes combining datasets across sites challenging (Keshavan et al. 2016). An additional source of error comes from parameter selection for segmentation algorithms, where varying parameter choices give different results (Han et al. 2006). Furthermore, if MR segmentation algorithms were developed and tested on healthy adult brains, using the algorithm on brain images of children, the elderly, or those with pathology, may violate certain assumptions of the algorithm, resulting in drastically different results.

Several quality assurance strategies exist to address these segmentation errors. Researchers could flag bad quality scans before analysis by viewing the data before input to tissue classification algorithms. However, often this is not straightforward, and gets too time consuming for large datasets. By running the Preprocessed-Connectomes Project's Quality Assurance Protocol (PCP-QAP) (Shehzad et al. 2015), researchers can view summary statistics that describe the quality of the raw data going into the algorithm and automatically remove subpar images. However, these metrics are limited because segmentation may still fail even if the quality of the scan is good. Another quality assurance strategy is to plot distributions of the segmentation output metrics themselves and remove any outlier volumes. However, without manual inspection, normal brains that naturally have very small or large estimates of brain size or pathological brains with valid segmentations may be inappropriately removed. Ideally, a link would exist between scalar summary statistics and 3D/4D volumes. Such a link would allow researchers to prioritize which images to implement quality control (QC) procedures, to collaborate and organize QC procedures, and to understand how scalar quality metrics, such as signal to noise ratio, relate to the actual image and segmentation. In this report, we propose a collaborative and efficient MRI QC solution that links group-level descriptive statistics with individual volume views of MRI images.

We propose an open source web-based brain quality control application called Mindcontrol, which is a dashboard to organize, QC, annotate, edit, and collaborate on neuroimaging processing results. Mindcontrol provides an easy-to-use interface for examining distributions of descriptive measures from neuroimaging pipelines (e.g., surface area of right insula), and viewing the results of segmentation analyses using the Papaya.js volume viewer (https://github.com/rii-mango/Papaya). Users are able to annotate points and curves on

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the volume, edit voxels, and assign tasks to other users (e.g., to correct the segmentation of a particular image). The platform is pipeline agnostic, meaning that it can be configured to QC any set of 3D volumes regardless of what neuroimaging software package produced it. In the following sections, we describe the implementation details of Mindcontrol, as well as its configuration to three different open-source datasets, with three different types of neuroimaging pipeline outputs.

2. Materials and Methods

Mindcontrol was developed with several design constraints. Platform independence is essential so that QC can occur on any computer or device, like a tablet. Because most tablets cannot store whole neuroimaging datasets, Mindcontrol requires cloud-based data storage. For efficient storage of annotations and voxel editing, Mindcontrol should only store the changes to files, rather than whole file information. Researchers should be able to QC outputs from any type of neuroimaging software package, so Mindcontrol should be flexible to any file organization structure, with configurable "modules" that contain any type of descriptive statistics and 3D images. Mindcontrol configuration and database updates should require minimal Javascript knowledge, since Matlab/Octave, Python, R and C are primarily used in the neuroimaging community for data analysis. Finally, changes to the database, like the addition of new images, changes in descriptive measures, and new edits/annotations, should be reflected in the application in real-time to foster collaboration.

2.1. Implementation Details

Mindcontrol is built with Meteor (http://www.meteor.com), which is a full-stack javascript web-development platform. Meteor features a build tool, a package manager, the convenience of using one language (javascript) to develop both the front- and back-end of the application, and an abstracted implementation of full-stack reactivity. Data is transferred "over the wire" and rendered by the client, (as opposed to the server sending HTML), which means that changes to the database automatically trigger changes to the application view. For example, as soon as a user finishes implementing QC procedures on an image and hits "save", all other users can see the changes. A diagram of this process is provided in Figure 1.

The user interface consists of a dashboard view and an imaging view, as shown in Figures 2 and 3. The primary dashboard view consists of processing module sections, a query controller, data tables, and descriptive statistic visualizations. The processing modules are defined by the user in the JSON structure, which describes the module names and columns to display in the data table below. Each entry in the table is a link that, when clicked, filters all tables on the page. The filters or queries can be saved, edited, and loaded in the query controller section shown in Figure 5.

Descriptive statistics are visualized using the D3 library (https://d3js.org/). Currently, two visualization are provided: a histogram of calendar dates that shows the number of exams collected on a given day and 1D histograms with dimensions that are swappable using a dropdown menu, as shown in Figure 2. Both histogram plots interactively filter the

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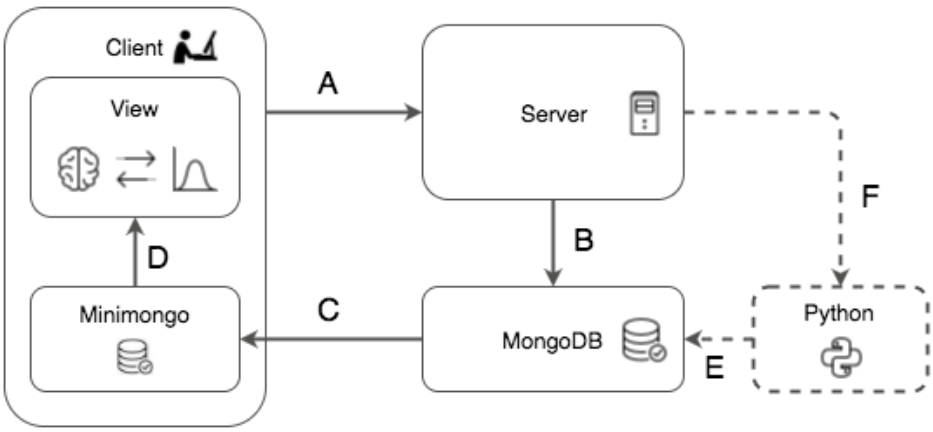

Figure 1: This diagram shows the different components of the Mindcontrol application. A) The client sends information, such as annotations and edits, to the server. B) The server calls a method that updates the mongoDB backend. C) When the back-end MongoDB database changes, these changes are automatically pushed to the minimongo database on the client. D) Changes on the minimongo database automatically re-renders the view on the client. E) Users can optionally push changes to the client view via the MongoDB with Python MongoDB drivers. Drivers for C, C++, Scala, Java, PHP, Ruby, Perl, and Node.js are also available through MongoDB. F) Developers can optionally write server methods to launch and Python or command line processes that use user annotations and edits to re-process images, and update the MongoDB with new results.

data tables below. Clicking on a particular date on the date-histogram plot filters all tables by the exams collected on that particular date. Users are able to "brush" section of the histogram to filter all tables with exams that meet values within that range.

The imaging view is shown in Figure 3. The left-side column includes a section to mark an image as "Pass", "Fail", "Edited", and "Needs Edits" and provide notes. The status bar at the top-left portion updates instantaneously, with information on which user checked the image, the quality status of the image, and when it was last checked. Users are also able to assign edits on other users on the system, for example, if the image needs to be edited by someone else. On the right hand side, the Papaya.js viewer (http://rii-mango.github.io/Papaya/) is used to display the NifTI volumes of the original data and FreeSurfer segmentations. Images must be hosted on a separate server or a content delivery network (CDN) and the Mindcontrol database must be populated with URLs to these images.

Annotations of points and curves are shown in Figure 6. Using the *shift* key, users may click on the image to annotate points or select the "Logged Curves" toolbar. By *shift+click and dragging*, users can draw curves. Keyboard and mouse shortcuts provided by the Papaya.js viewer, along with Mindcontrol include toggling overlays (*zz*) and undoing annotations (*dd*). Figure 7 shows the editing ("Painter") panel of the imaging view. Users set paintbrush values and *shift+click and drag* to change voxel values. For point and curve annotations and voxel editing, the images themselves are not changed, but world x,y,z coordinates along with annotation text or paintbrush values are saved to the mongo database

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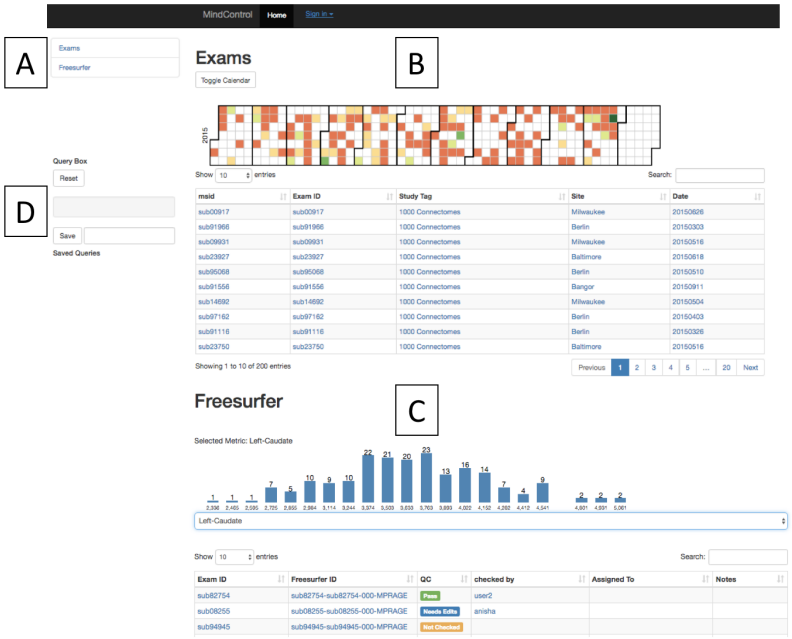

Figure 2: This figure shows the Mindcontrol layout configured to quality check Freesurfer outputs from the 1000 Functional Connectomes Project (FCP). Part A shows the module navigator, which links to the different processing modules on the dashboard. Part B shows the different exams and the dates they were acquired, as a heatmap, where green is larger and orange is smaller. For demonstration purposes, the dates depicted here do not reflect the actual dates the data were collected for the FCP, since this information was not provided at the time. Clicking on data in any of the columns of the table below filters the data by the column. For example, clicking the site "Milwaukee" reduces both the "Exams" and the "FreeSurfer" tables to only show subjects who were from Milwaukee. Part C shows the Freesurfer table and regional volume distribution of the left caudate. A drop down menu allows users to switch the descriptive metric. Clicking on a value in FreeSurfer ID column brings the user to the imaging view, shown in Figure 3 where users can mark the quality status of the image. The value of the label in the "QC" column changes instantaneously due to Meteor's built in full-stack reactivity.

when the user clicks "save". Custom offline functions may be written to apply editing to images, for example, to implement pial surface edits from FreeSurfer.

2.2. Applications

Mindcontrol configurations were developed for selected data from the 1000 Functional Connectomes project (FCP), the consortium for reliability and reproducibility (CoRR), and the Autism Brain Imaging Data Exchange (ABIDE) Collection I. The FCP consists of 1414 resting state fMRI and corresponding structural datasets collected from 35 sites around the world (Biswal et al. 2010), which has been openly shared to the public. The purpose of the FCP collaboration is to comprehensively map the functional connectome, understand genetic influences on brain's structure and function, and understand how brain structure and function relate to human behavior (Biswal et al. 2010). Segmentation of 200 selected anatomical images from FCP from Baltimore, Bangor, Berlin, ICBM, and Milwaukee was

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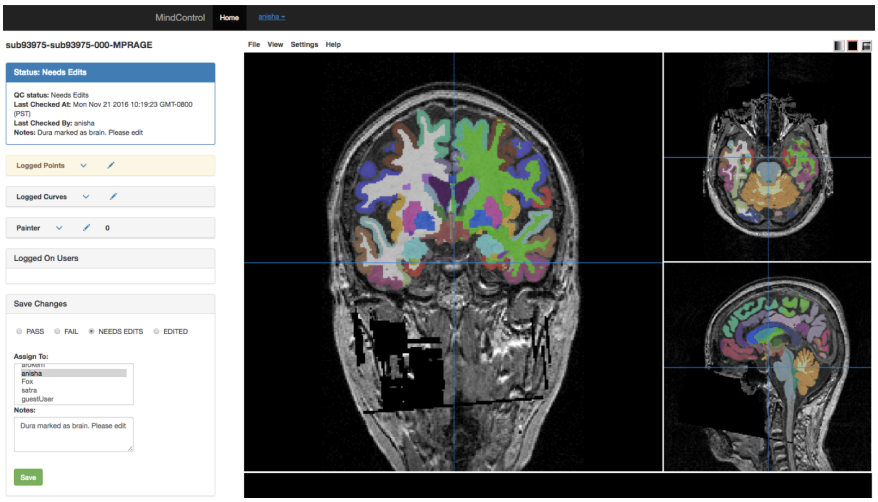

Figure 3: The imaging view of mindcontrol consists of a left-hand panel of the QC status, a point annotation menu, a curve annotation menu, a voxel editing menu, and a QC status, notes, and editor assignment panel. On the right hand side, the base MRI anatomical MPRAGE image is displayed with an overlay of the segmentation outputs of Freesurfer, using the same colormap of FreeSurfer using the Papaya.js viewer.

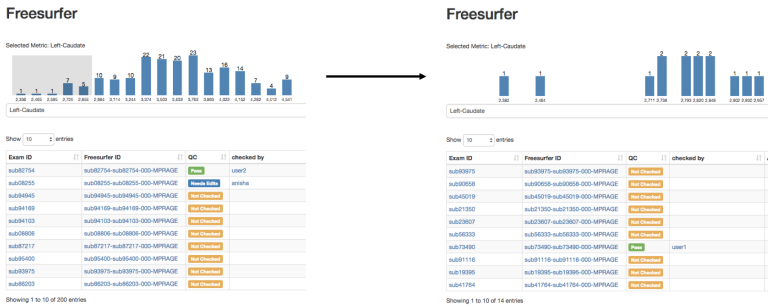

Figure 4: This demonstrates the interactive brushing feature of Mindcontrol histograms. On the left, the user has brushed the tail end of the distribution of left caudate volumes from Freesurfer, and on right, the histogram has been redrawn with data from the brushed range, and the table beneath has been filtered from 200 entries to 14 entries, based on the brushed caudate volumes.

performed with Freesurfer (recon-all) version 5.3.0 (Fischl et al. 2002) using the RedHat 7 operating system on IEEE 754 compliant hardware. Regional volumes of subcortical and cerebellar regions were computed. Cortical volumes, areas and thicknesses were also computed and averaged across hemispheres. Scan dates were simulated in order to demonstrate the date histogram shown in Figure 1B. The original, anonymized, T1-weighted images, along with the aparc+aseg output from Freesurfer, were converted to the compressed NifTi (.nii.gz) format and uploaded to Dropbox for the purpose of visualization within Mindcontrol. The Mindcontrol database was populated with URLs to these images, along with their

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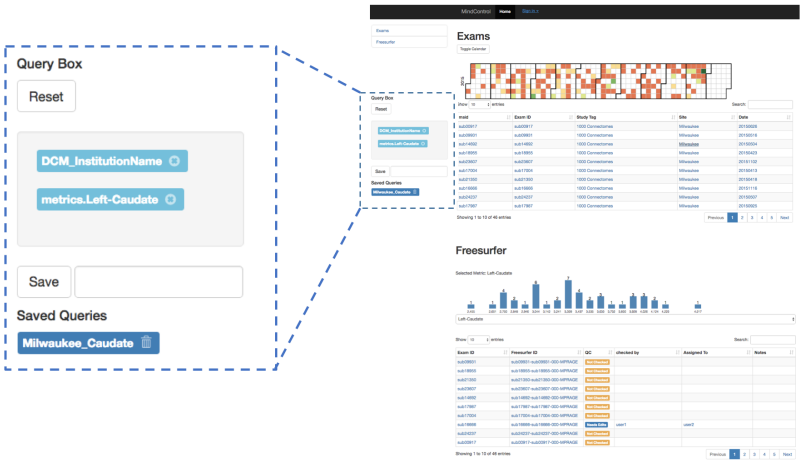

Figure 5: The query controller shows the different filters that have been applied to the dataset. In this example, the exams have been filtered by institution ("Milwaukee") and by a range of left caudate volumes (brushed from the histogram). Clicking the "x" next to the filter removes it, and the view updates. Queries can be saved and reloaded by providing a name in the text-entry box. "Reset" removes all filters to show the whole dataset.

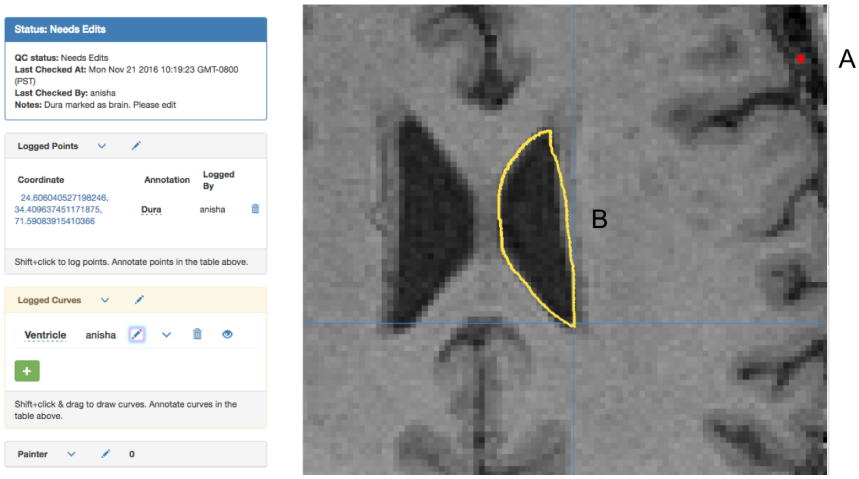

Figure 6: The annotations panel allows for the annotation of a single point (shown in red, part A) and annotating curves (shown in B). When annotating points, the user is shown the selected x,y,z world coordinates and is able to name the annotation. In the curve annotation panel on the left sidebar, the user is able to name the curve and add/remove curves. Keyboard shortcuts, "dd" removes the previous annotation and "zz" toggles the segmentation overlay.

corresponding FreeSurfer segmentation metrics.

The purpose of CoRR is to provide an open-science dataset to assess the reliability of functional and structural connectomics by defining test-retest reliability of commonly used MR metrics, to understand the variability of these metrics across sites, and to establish

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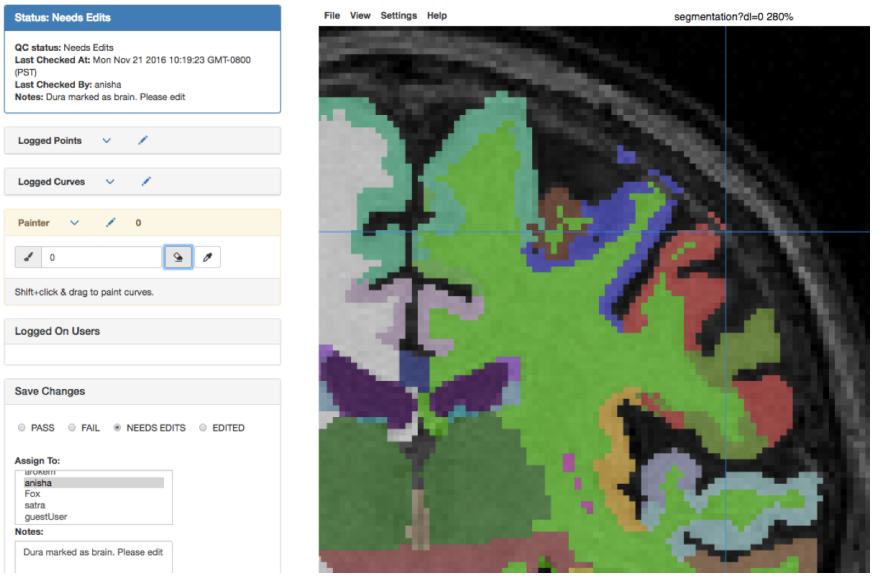

Figure 7: The editing panel on the left shows the "Painter" toolbox in yellow, where users can input brush values or use the eyedropper tool to set the value to that of a clicked label. The eraser icon sets the brush value to 0, to delete or erase voxels. In the image above, the Freesurfer segmentation is being edited by erasing the voxels missclassified as dura.

a standard benchmark dataset to evaluate new imaging metrics (Zuo et al. 2014). The Preprocessed-Connectomes Project's Quality Assurance Protocol (PCP-QAP) software was developed to provide anatomical and functional data quality measures, in order to detect low quality images before data processing and analysis (Shehzad et al. 2015). PCP-QAP normative data for the CoRR study was downloaded from https://github.com/preprocessed-connectomes-project/quality-assessment-protocol. The Mindcontrol database was populated with pointers to 2,963 CoRR structural images residing on an Amazon S3 bucket along with their corresponding PCP-QAP metrics. Some metrics include contrast-to-noise ratio, signal-to-noise ratio, voxel smoothness, percentage of artifact voxels, foreground-to-background energy ratio, and entropy focus criterion (Shehzad et al. 2015).

The overarching goal of the ABIDE initiative is to expedite the discovery of the neural basis of autism by providing open access to large, heterogeneous collection of structural and functional neuroimaging data, collected from over 23 institutions (Martino et al. 2013). The preprocessed connectomes project provides cortical thickness measures from the ANTs software package (Avants et al. 2009) of the ABIDE dataset, along with summary statistics across regions of interests (ROIs) defined by the Desikan-Killiany-Tourville (DKT) protocol (Klein and Tourville 2012). The Mindcontrol database was populated with pointer URLs to S3-hosted cortical thickness images and their corresponding ROI summary measures, along with PCP-QAP metrics. The FCP, CoRR and ABIDE Mindcontrol configurations are currently hosted on Heroku (https://www.heroku.com/)

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3. Implementation

The demo of the FCP data is located at `http://mindcontrol.herokuapp.com`. The demo of the CoRR dataset with PCP-QAP metrics is hosted at `http://mindcontrol-corr.herokuapp.com`. The demo of the ABIDE dataset with ANTS cortical thickness metrics is located at `http://mindcontrol-abide.herokuapp.com`. The Mindcontrol codebase is hosted on GitHub at `http://github.com/akeshavan/mindcontrol` along with installation instructions. The Mindcontrol configuration of the FCP data is located on the master branch of the GitHub repository, and the configurations for CoRR and ABIDE are located at `http://github.com/akeshavan/mindcontrol_configs` along with configuration documentation.

4. Discussion

Mindcontrol is a configurable neuroinformatics dashboard that links study information and descriptive statistics with scientific data visualization, MRI images, and their overlays (segmentation or otherwise). The three example configurations in this report demonstrate the link between MRI quality metrics and raw data, the link between Freesurfer regional volumes and segmentation quality, and the link between ANTS cortical thickness summary statistics and segmentation/thickness estimates on the volume. The platform is configurable, open-source, and software/pipeline agnostic, enabling researchers to configure it to their particular analyses. The dashboard allows researchers to assign editing tasks to others, who can then perform edits on the application itself.

There have been considerable efforts in this field to ensure data quality on a large scale. The human connectome project's extensive informatics pipeline, which includes a database service, QC procedures, and a data visualization platform, has been key to the project's success in collecting a large, high quality dataset (Marcus et al. 2013). The Allen Brain Atlas offers a comprehensive genetic, neuroanatomical, and connectivity web-based data exploration portal, linking an MRI viewer with data tables (Sunkin et al. 2012). The open-source LORIS web-based data management system integrates an imaging viewer with extensive QC modules (Das et al. 2012). Mindcontrol supplements these efforts by providing a lightweight and extensible data management and visualization system with the added ability to perform edits and curate annotations within the application.

Mindcontrol is actively being used at UCSF to study imaging biomarkers of multiple sclerosis (MS) disease progression in a 12-year longitudinal cohort of over 500 patients. MRI plays a crucial role in the diagnosis of MS due to its sensitivity to the white matter lesions characteristic of this disease (Ge 2006). Both the location and number of lesions are used in the diagnostic criteria of MS (McDonald et al. 2001); their evolution over time is considered a proxy for disease progression, and is closely monitored as a key outcome measure in clinical trials (Ge et al. 2000). Researchers have identified numerous imaging biomarkers of disease progression, including cortical atrophy (Fisher et al. 2008) and sensitive lesion quantification methods from FLAIR sequences (Schmidt et al. 2012).

Currently, Mindcontrol is being used as a data management dashboard and plays a role in the semi-automated identification of multiple sclerosis lesions. The Lesion Segmentation

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Toolbox (LST) automates the detection of FLAIR hyper-intense lesions, which is useful because it prevents user-bias of the lesion boundary (Schmidt et al. 2012). However, because our acquisition protocols sufficiently differ from those of the LST developers, manual intervention by neuroradiologists is often necessary to correct false positives and false negatives in our dataset. Mindcontrol's point annotation feature is used by neuroradiologists to mark the center of a false positive lesion. The curve annotation feature is used to roughly and quickly note the outline of a false negative lesion. Custom Python scripts use these annotations to produce a corrected lesion segmentation map, which is then used to tune the parameters of the LST. This method avoids biasing the lesion boundary and saves time by allowing users to quickly mark lesions with one click instead of the traditional method of coloring the full lesion volume. Distributions of the lesion count and lesion volume are used by the researchers to prioritize the more intensive edits from the relatively simple edits.

Mindcontrol is also being used at UCSF to coordinate a large scale brain mask editing effort of all >4000 exams in the MS cohort, by using a Microsoft Surface Pro 4 tablet with stylus. Using Mindcontrol's voxel editing or "painting" feature, multiple research assistants are erasing voxels incorrectly marked as brain and painting brain voxels that were not identified. These edits are done with a stylus, which feels more natural and is quicker than using a mouse. Researchers assign more complicated edits to the experts in the lab, write questions and comments in the "notes" section, and mark the brain as "Edited" once they are complete. A nightly cron-job applies their edits to the brain masks and assigns a reviewer to do one last QC. All brains marked with a "Pass" are added to a set of brain masks to be used as a training set for the mincbeast brain extraction algorithm (Eskildsen et al. 2012). Leveraging Mindcontrol as a semi-automated segmentation utility has made our processing methods more efficient, organized, and precise.

5. Future Directions

Mindcontrol is being actively developed with new features. New information visualizations to detect outliers are being developed, in the form of scatter plots to compare two metrics against each other, and a longitudinal view for the trajectory of single subject for a given metric. New scientific data visualizations are planned, by using using the BrainBrowser library (Sherif et al. 2015) to display cortical surfaces. There is a beta version of real-time collaborative annotations, where two users can annotate the same image and see the edits of the other user as they occur.

Currently, configuring Mindcontrol involves creating a JSON file to describe the different modules and another JSON file to populate the Mongo database with pointers to images and their scalar metrics. In the future, this process could be streamlined by creating a Mindcontrol configuration for datasets with a standardized folder structure, like the Brain Imaging Data Structure (BIDS) (Gorgolewski et al. 2016) and their derivatives (Gorgolewski et al. 2016). Further development of Mindcontrol will include the flexible importing of additional scalar metrics, such as measures of structural complexity, calculated by third-party toolboxes developed to complement standard analysis pipelines (Madan and Kensinger 2016) (Madan and Kensinger 2017). This will enable researchers to collaborate on the same

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dataset by uploading metrics from their newly developed algorithms, and will allow them to explore their relationship with metrics contributed by others. Finally, Mindcontrol has the potential to be a large-scale crowd-sourcing platform for segmentation editing and quality checking. We hope the functionality, ease-of-use, and modularity offered by Mindcontrol will help to improve the standards used by studies relying on brain segmentation.

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References

Dickerson BC, Bakkour A, Salat DH, and others (2009) The cortical signature of Alzheimer's disease: regionally specific cortical thinning relates to symptom severity in very mild to mild AD dementia and is detectable in asymptomatic amyloid-positive individuals.. Cereb Cortex 19:497–510.

Vemuri P, Jack CR (2010) Role of structural MRI in Alzheimer's disease. Alzheimers Res Ther 2:23. doi: 10.1186/alzrt47

Mangia PJTS (2013) Magnetic Resonance Imaging (MRI) in Parkinson/s Disease. Journal of Alzheimer's Disease & Parkinsonism. doi: 10.4172/2161-0460.s1-001

Shenton ME, Dickey CC, Frumin M, McCarley RW (2001) A review of MRI findings in schizophrenia. Schizophrenia research 49:1–52.

Meisenzahl E, Koutsouleris N, Reiser M, and others (2011) Structural MRI correlates for vulnerability and resilience to major depressive disorder. Journal of psychiatry & neuroscience: JPN 36:15.

Brambilla P, Hardan A, di Nemi SU, and others (2003) Brain anatomy and development in autism: review of structural MRI studies. Brain research bulletin 61:557–569.

Filippi M, Horsfield MA, Tofts PS, and others (1995) Quantitative assessment of MRI lesion load in monitoring the evolution of multiple sclerosis. Brain 118:1601–1612. doi: 10.1093/brain/118.6.1601

Blumenthal JD, Zijdenbos A, Molloy E, Giedd JN (2002) Motion Artifact in Magnetic Resonance Imaging: Implications for Automated Analysis. NeuroImage 16:89–92. doi: 10.1006/nimg.2002.1076

Pardoe HR, Hiess RK, Kuzniecky R (2016) Motion and morphometry in clinical and nonclinical populations. NeuroImage 135:177–185. doi: 10.1016/j.neuroimage.2016.05.005

Reuter M, Tisdall MD, Qureshi A, and others (2015) Head motion during MRI acquisition reduces gray matter volume and thickness estimates. NeuroImage 107:107–115. doi: 10.1016/j.neuroimage.2014.12.006

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Savalia NK, Agres PF, Chan MY, and others (2016) Motion-related artifacts in structural brain images revealed with independent estimates of in-scanner head motion. Human Brain Mapping. doi: 10.1002/hbm.23397

Keshavan A, Paul F, Beyer MK, and others (2016) Power estimation for non-standardized multisite studies. NeuroImage 134:281–294.

Han X, Jovicich J, Salat D, and others (2006) Reliability of MRI-derived measurements of human cerebral cortical thickness: The effects of field strength scanner upgrade and manufacturer. NeuroImage 32:180–194. doi: 10.1016/j.neuroimage.2006.02.051

Shehzad Z, Giavasis S, Li Q, and others (2015) The Preprocessed Connectomes Project Quality Assessment Protocol: A resource for measuring the quality of MRI data. Frontiers in Neuroscience. doi: 10.3389/conf.fnins.2015.91.00047

Giedd JN, Rapoport JL (2010) Structural MRI of pediatric brain development: what have we learned and where are we going?. Neuron 67:728–734.

Biswal BB, Mennes M, Zuo X-N, and others (2010) Toward discovery science of human brain function. Proceedings of the National Academy of Sciences 107:4734–4739.

Fischl B, Salat DH, Busa E, and others (2002) Whole brain segmentation: automated labeling of neuroanatomical structures in the human brain. Neuron 33:341–355.

Zuo X-N, Anderson JS, Bellec P, and others (2014) An open science resource for establishing reliability and reproducibility in functional connectomics. Scientific Data 1:140049. doi: 10.1038/sdata.2014.49

Martino AD, Yan C-G, Li Q, and others (2013) The autism brain imaging data exchange: towards a large-scale evaluation of the intrinsic brain architecture in autism. Molecular Psychiatry 19:659–667. doi: 10.1038/mp.2013.78

Avants BB, Tustison N, Song G (2009) Advanced normalization tools (ANTS). Insight J 2:1–35.

Klein A, Tourville J (2012) 101 Labeled Brain Images and a Consistent Human Cortical Labeling Protocol. Front Neurosci. doi: 10.3389/fnins.2012.00171

Marcus DS, Harms MP, Snyder AZ, and others (2013) Human Connectome Project informatics: Quality control database services, and data visualization. NeuroImage 80:202–219. doi: 10.1016/j.neuroimage.2013.05.077

Sunkin SM, Ng L, Lau C, and others (2012) Allen Brain Atlas: an integrated spatio-temporal portal for exploring the central nervous system. Nucleic Acids Research 41:D996–D1008. doi: 10.1093/nar/gks1042

Das S, Zijdenbos AP, Harlap J, and others (2012) LORIS: a web-based data management system for multi-center studies. Front Neuroinform. doi: 10.3389/fninf.2011.00037

Ge Y (2006) Multiple sclerosis: the role of MR imaging. American Journal of Neuroradiology 27:1165–1176.

McDonald WI, Compston A, Edan G, and others (2001) Recommended diagnostic criteria for multiple sclerosis: guidelines from the International Panel on the diagnosis of multiple sclerosis. Annals of neurology 50:121–127.

Ge Y, Grossman RI, Udupa JK, and others (2000) Glatiramer acetate (Copaxone) treatment in relapsing–remitting MS Quantitative MR assessment. Neurology 54:813–817.

bioRxiv preprint doi: https://doi.org/10.1101/090431; this version posted November 29, 2016. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC 4.0 International license.

Fisher E, Lee J-C, Nakamura K, Rudick RA (2008) Gray matter atrophy in multiple sclerosis: a longitudinal study. Annals of neurology 64:255–265.

Schmidt P, Gaser C, Arsic M, and others (2012) An automated tool for detection of FLAIR-hyperintense white-matter lesions in Multiple Sclerosis. NeuroImage 59:3774–3783. doi: 10.1016/j.neuroimage.2011.11.032

Eskildsen SF, Coupé P, Fonov V, and others (2012) BEaST: brain extraction based on nonlocal segmentation technique. NeuroImage 59:2362–2373.

Sherif T, Kassis N, Rousseau M-

Gorgolewski KJ, Auer T, Calhoun VD, and others (2016) The brain imaging data structure a format for organizing and describing outputs of neuroimaging experiments. Scientific Data 3:160044. doi: 10.1038/sdata.2016.44

Gorgolewski KJ, Alfaro-Almagro F, Auer T, and others (2016) BIDS Apps: Improving ease of use, accessibility and reproducibility of neuroimaging data analysis methods. bioRxiv 079145.

Madan CR, Kensinger EA (2016) Cortical complexity as a measure of age-related brain atrophy. NeuroImage 134:617–629. doi: 10.1016/j.neuroimage.2016.04.029

Madan CR, Kensinger EA (2017) Age-related differences in the structural complexity of subcortical and ventricular structures. Neurobiology of Aging. doi: 10.1016/j.neurobiolaging.2016.10.023