ANIMA: A data-sharing initiative for neuroimaging meta-analyses

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ABSTRACT

Meta-analytic techniques allow cognitive neuroscientists to pool large amounts of data across many individual task-based functional neuroimaging experiments. These methods have been aided by the introduction of online databases such as Brainmap.org or Neurosynth.org, which collate peak activation coordinates obtained from thousands of published studies. Findings from meta-analytic studies typically include brain regions which are consistently activated across studies for specific contrasts, investigating cognitive or clinical hypotheses. These regions can be subsequently used as the basis for seed-based connectivity analysis, or formally compared to neuroimaging data in order to help interpret new findings. To facilitate such approaches, we have developed a new online repository of meta-analytic neuroimaging results, named the Archive of Neuroimaging Meta-analyses (ANIMA). The ANIMA platform consists of an intuitive online interface for querying, downloading, and contributing data from published meta-analytic studies. Additionally, to aid the process of organizing, visualizing, and working with these data, we present an open-source desktop application called Volume Viewer. Volume Viewer allows users to easily arrange imaging data into composite stacks, and save these sessions as individual files, which can also be uploaded to the ANIMA database. The application also allows users to perform basic functions, such as computing conjunctions between images, or extracting regions-of-interest or peak coordinates for further analysis. The introduction of this new resource will enhance the ability of researchers to both share their findings and incorporate existing meta-analytic results into their own research.

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Introduction

Functional neuroimaging, like many other scientific fields, is faced with the daunting task of managing an ever-increasing amount of data (Poldrack and Gorgolewski, 2014). Online databases such as Brainmap.org (Laird et al., 2011), Neurovault.org (Gorgolewski et al., 2015), and Neurosynth.org (Yarkoni et al., 2011) provide access to data from hundreds of published task-based fMRI studies, in standard coordinates (recently reviewed by Fox et al., 2014). In addition to extensive meta-analyses based upon manual search techniques, these platforms have facilitated a growing number of meta-analytic studies of the neural correlates of specific cognitive functions, using methods such as multilevel kernel density analysis (MKDA;

Wager et al., 2007) and activation likelihood estimation (ALE; Eickhoff et al., 2009, 2012). Meta-analysis entails the pooling of data over tens to thousands of individual studies, and thus provides: (1.) greater sensitivity and specificity to detect "true" effects; (2.) a means of determining core groups of brain regions subserving a specific task or characterizing a specific disease; and (3.) a method for formal comparison of different subfacets of a cognitive domain. This approach has been used, for instance, to demonstrate the neural correlates of sustained attention (Langner and Eickhoff, 2013), investigate face processing areas in autistic subjects (Nickl-Jockschat et al., 2014), and identify key regions subserving supervisory attentional control (Cieslik et al., 2015).

Results from meta-analyses can be subsequently used as robust prior information in the design of task-based fMRI studies, and as regions-of-interest (ROIs) for connectivity methods based on functional correlations (e.g., Müller et al., 2014; Schilbach et al., 2014), or virtually any other type of seed-based analysis. This includes topical meta-analytic

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approaches such as ALE and MKDA, as well as methods which use meta-analysis to infer functional connectivity, such as meta-analytic connectivity modelling (MACM; Etkin and Wager, 2007; Kober et al., 2008; Robinson et al., 2010), in which functional coactivations are assessed across all tasks in the database (see also Xue et al., 2014). Additional meta-analytic approaches include the parcellation of the brain into functionally distinct subregions, such as coactivation-based parcellation (CBP; Chang et al., 2012; Eickhoff et al., 2011; Northoff et al., 2006). A typical ALE analysis, for example, will result in a distinct ROI or set of ROIs that are associated with a particular psychological or clinical feature (see Box 1). These results are then commonly used as seed regions for further analysis of these features (e.g., zu Eulenburg et al., 2012). Given their utility, results from meta-analytic studies are becoming increasingly popular as starting points for future analyses, and are hence commonly requested from the authors. However, this mode of data exchange typically requires a time delay for locating, organizing, packaging, and sending data, and can be complicated further by confusion over the way data are named, the type of information they represent, and data formats in which they are stored. Moreover, use of these data in published articles would benefit from the ability to reference a specific and permanent online location, as well as provenance tracking, particularly for purposes of validation and replication. These considerations present a need for a more standardized, easily accessible means of sharing meta-analytic results, which has motivated the creation of a new online data resource called the Archive of Neuroimaging Meta-Analyses (ANIMA). This database can be accessed at http://anima.fz-juelich.de.

The concept behind the ANIMA database is simple: to provide the results of published meta-analyses and coactivation-based parcellations to interested parties, in the form of statistical maps or labels, encoded as image files. This approach has a number of important requirements. Firstly, data should be easily citable if reused for further analyses, and thus full information about the source of the results must be provided

with them. In addition to metadata about the article itself (reference details, cross-links to PubMed entries, abstract information, etc.), there should be sufficient information provided to identify the data represented by each image file, including its associated figure, if applicable. Secondly, data retrieved from the database should be simple to organize, visualize, and use. A user should be able to peruse the web interface, query and select studies of interest, download these to their local machine, and immediately browse and utilize the data they have retrieved. Thirdly, in order for the database to expand and provide a thorough sampling of the literature, it is important to provide a convenient interface through which researchers can submit data from their own studies.

With the ANIMA database, we have provided solutions to each of these requirements. In what follows, we will describe our databasing approach, which includes an intuitive online interface for querying, downloading, and submitting data, as well as a stand-alone, cross-platform desktop tool for easily browsing, visualizing, and performing common computations, such as obtaining a conjunction between images. This new resource will provide researchers with a straightforward means of including meta-analytic results in their studies, both as ROIs for future analyses and as a point of comparison against new results. The initial release of the database will include data from 25 published meta-analytic studies, but is intended to grow in order to incorporate the increasing number of studies being added to the literature.

Database overview

ANIMA is designed to serve a number of functions. Firstly, it is a searchable online repository for the results of published neuroimaging meta-analyses. Data are organized as individual studies, along with information essential for describing these studies (authors, title, journal, date, abstract, etc.). Included with each study is a set of "study elements", which refer to individual files storing an important aspect of the study's findings. These will typically be individual volume files, stored in NIFTI format. However, other types of data can be uploaded, including text files containing useful descriptions, image files, or Volume Viewer session files, which store multiple images, along with information on how they should be visualized (see description below). Each study element is also associated with a set of metadata which describe its contents (title, figure captions, type of information, full-text PDF, etc.).

A second function of ANIMA is the ability to submit one's own study to the database. The online interface includes a "Submit" page, which allows registered users to define their study and upload files. If a researcher would like to share results from a meta-analytic study that has been published in peer-reviewed journal, we encourage them to do so via this interface. The general philosophy of this approach is the concept of "open data". For reasons of security and data integrity, submitting a study requires that a user register with the database, and that each submitted study is first vetted for completeness and validity by the database administrators. However, the process of submitting one's data to ANIMA is designed to be a straightforward process.

Finally, ANIMA was designed with the idea that, once retrieved, data should be simple to organize and query on one's desktop. Accordingly, we have developed a desktop application called Volume Viewer, which interacts seamlessly with the ANIMA interface. Volume Viewer is open source Java-based software tool, built on the ModelGUI API (http://www.modelgui.org), and both the program and its source code are freely available online (https://launchpad.net/volumeviewer). The interface allows data to be organized within a "library" framework, in which individual studies can be represented. The data retrieved from ANIMA is already organized according to this framework, so downloaded ANIMA studies can be immediately imported and viewed in Volume Viewer. Furthermore, if a study includes Volume Viewer session files, predefined sets of image composites, with custom colour mapping and template or atlas

Box 1
Common methodologies used in ANIMA studies.

Four common approaches used in ANIMA studies are described below.

Activation likelihood estimation (ALE): This is a meta-analytic approach through which peak activation foci, reported in standard MNI or Talairach coordinates, are used to inform Gaussian probability models of activation. This *topical* approach addresses the sparse information provided by activation foci, as is used to estimate smooth statistical distributions associated with particular psychological or clinical features.

Multi-kernel density analysis (MKDA): A topical approach which is similar in principle to ALE, MKDA uses a spherical instead of Gaussian kernel, and statistical analysis is performed on the number (density) of activation peaks within a given radius.

Meta-analytic connectivity modelling (MACM): This approach models the probability that brain regions are active simultaneously with a particular seed region. MACM is typically performed across many experimental paradigms, providing a meta-analytic estimate of functional connectivity.

Coactivation-based parcellation (CBP): CBP is a parcellation method derived from co-activation profiles obtained via the MACM approach. CBP uses clustering approaches such as hierarchical or k-means clustering to identify subregions within a larger ROI that are distinct from each other in terms of their connectivity profiles.

layers, can be viewed with little effort on the part of the user. Importantly, this tool also implements a number of utilities which allow users to combine their data with ANIMA data, create new ROIs for analyses, report peak coordinates, or quantify the overlap between different distributions.

What data are available?

At the time of writing, ANIMA contains data from 25 meta-analytic studies (both topic-based ALE meta-analyses and coactivation-based parcellations), as summarized in Table 1. We intend to expand this number considerably, both by requesting and adding new studies from authors, as well as by encouraging authors to submit their own studies through the online interface. The majority of the data available represent statistical maps which are produced through common meta-analytic approaches, including ALE, CBP, and MACM. Box 1 provides an overview of these methods. In many cases, these data are directly related to a figure in the article, but we also encourage authors to submit supplemental data, if desired. Since the database is based on meta-analyses, no demographic or phenotypical data are directly available, although these can generally be determined by reference to the individual articles. However, the database does provide searchable keywords and sample sizes (number of primary studies, experiments, and subjects) associated with individual articles. Finally, studies in ANIMA each have a unique uniform resource locator (URL), which displays the available data and metadata, along with the date the study was last modified. This URL, along with the modification date, can be used for precise citation of any data used in a new publication. ANIMA keeps a history of any changes to the data that has been made publicly available, such that the exact archive used in a study can be retrieved for purposes of validation or replication.

Data in ANIMA are freely available, although their use is conditional on acceptance of a Data Usage Agreement (DUA). The general terms of this agreement are provided in Box 2. Any redistribution of ANIMA data requires consent from the authors whose data are redistributed, as well as the database owners. Additionally, the DUA specifies that attribution for use of the data must include reference to both the database and the specific studies used. Both database users and contributors must agree to the terms of the DUA in order to use or contribute to the database, respectively.

Accessing, viewing, and using ANIMA data

Fig. 1 shows the online interface for browsing studies in ANIMA (http://anima.fz-juelich.de/query). Notably, querying and downloading is a fully open process with no registration required. Studies are listed in tabular format, with each entry showing the title of the study (in the form of the lead author and publication year), a brief description, the size of the archive, and links to download the study, view its PubMed page, or download its associated full-text PDF. At the top of the page, a search bar allows the user to search by author, publication year, or journal. More detailed information about individual studies can be accessed by clicking on the study's title. Here, abstract, keywords, and version information are displayed, as well as a list of individual study elements (Fig. 2). It is also possible to view image elements, using the Javascript-based Papaya viewer (http://github.com/rii-mango/Papaya), by clicking on the eye icon for an individual

Table 1
Studies for which data are available in the ANIMA database at the time of writing. *Abbreviations:* ALE, activation likelihood estimation; MACM, meta-analytic connectivity modelling; CBP, coactivation-based parcellation; RS-fMRI, resting-state fMRI connectivity.

Study	Description	Methods
Amft et al. (2014)	Characterized an extended social-affective default network through coactivation-based parcellation	MACM, RS-fMRI, CBP
Bzdok et al. (2011)	Performed meta-analysis to investigate the localization of facial judgments of trustworthiness and attractiveness	ALE
Bzdok et al. (2012b)	Performed ALE meta-analysis on morality, theory of mind, and empathy	ALE
Bzdok et al. (2013a)	Investigated the structural, connectional, and functional subspecialization of the amygdala	MACM, CBP
Bzdok et al. (2013b)	Investigated parcellation, connectivity, and functional decoding of the temporoparietal junction	MACM, RS-fMRI, CBP
Caspers et al. (2010)	Performed meta-analysis to investigate the localization of action observation and imitation in the human brain	ALE
Cieslik et al. (2013)	Derived a coactivation-based parcellation of the dorsolateral prefrontal cortex	MACM, RS-fMRI, CBP
Cieslik et al. (2015)	Identified three key regions for supervisory attentional control, using meta-analysis	ALE
Clos et al. (2013)	Used coactivation-based parcellation to divide Broca's area into five clusters, each having distinct functional profiles	MACM, CBP
Friebel et al. (2011)	Performed an ALE meta-analysis of experimentally induced and chronic persistent neuropathic pain	ALE
Goodkind et al. (2015)	Combined meta-analysis of VBM studies across psychiatric disorders, with three parallel connectivity analyses	ALE, MACM
Hardwick et al. (2013)	Performed meta-analysis to investigate the localization of motor learning in the human brain	ALE
Hoffstaedter et al. (2014)	Compared functional connectivity derived from RS-fMRI and MACM, for the anterior mid-cingulate cortex	MACM, RS-fMRI
Keuken et al. (2014)	Used meta-analysis to characterize the brain regions associated with perceptual decision making	ALE
Kohn et al. (2014)	Performed an ALE meta-analysis and MACM analysis of cognitive emotion regulation	ALE, MACM
Krall et al. (2015)	Performed an ALE meta-analysis to investigate the role of the right temporoparietal junction in both attention and social interaction	ALE
Kurth et al. (2010)	Performed an ALE meta-analysis to investigate the functional differentiation and integration of the human insula	ALE
Langner and Eickhoff (2013)	Conducted a meta-analytic review of the neural mechanisms of vigilant (sustained) attention	ALE
Müller et al. (2014)	Investigated the influence of gray matter volume, functional connectivity and trait impulsivity on cognitive flexibility	ALE
Nellessen et al. (2014)	Performed an ALE meta-analysis on 28 task-based fMRI studies, in patients with mild cognitive impairment or Alzheimer's disease	ALE
Nickl-Jockschat et al. (2014)	Investigated the neural correlates of face processing in subjects with autism spectrum disorder (ASD), using ALE meta-analysis	ALE
Reid et al. (2015)	Compared MACM, RS-fMRI, and structural covariance to investigate the convergence of connectivity estimates for the anterior lateral prefrontal cortex (aLPFC)	MACM, RS-fMRI
Rottschy et al. (2012)	Investigated the neural correlates of working memory using ALE meta-analysis	ALE
Schilbach et al. (2012)	Used ALE meta-analyses to study the neural correlates of emotional processing, social & default mode cognition	ALE
zu Eulenburg et al. (2012)	Used meta-analysis to localize activations corresponding to a vestibular stimulus, and evaluated functional connectivity of these regions using RS-fMRI	ALE, RS-fMRI

Box 2
Summary of the data usage agreement for the ANIMA database.

- Data are provided "as is", with no guarantee whatsoever
- Data can be used for any non-commercial purpose, with the exception that redistribution of the data can only be done if written consent is obtained from the database owners, and only for studies whose authors have approved redistribution.
- Any public use of ANIMA data must provide attribution, specifically by reference to the database itself, and the primary article associated with those data
- The owners of ANIMA do not claim any copyright over the data archived in the database

element. This will overlay the image on the non-linear ICBM-152 anatomical template, and is accessible from any modern web browser.

The web page allows a user to download single studies, or select and download multiple selected studies at once. The download will be a compressed tar archive, which can be decompressed and either used directly in one's analyses, or viewed and queried using the Volume Viewer tool (Fig. 3). This is facilitated through the inclusion of XML-format files which store study metadata and a list of study elements, along with the actual data. Image files are stored in NIFTI format (although Volume Viewer can also read MINC or MGZ format images). Volume Viewer provides a convenient dialog for automatically interpolating images which have been registered to the same space, but which do not have the same size or orientation as the current volume. This allows comparison of multiple images without having to preprocess them in advance. The process of downloading and visualizing a study is illustrated in Fig. 4.

Volume Viewer currently supports a number of useful features which provide supplemental utility to the ANIMA online interface. These include:

- The ability to overlay and compare images. This allows a user, for instance, to compare the results of a new analysis with those of published meta-analyses in ANIMA.
- The ability to save the current configuration as a single Volume Viewer session file (".vvs" extension), which can be uploaded to ANIMA via the online interface, and viewed by all users who download a given study. The session includes all images, templates, and atlases, the way they are arranged and composited, and the currently selected viewing planes.
- The ability to compute a conjunction image, and quantify the degree of overlap between two images. This feature also yields ROIs that can be immediately used for further analysis.
- The ability to obtain peak coordinates from smoothed maps, for reporting in an article, or use as seed points in further analyses.
- The inclusion of standard template and atlas images, which allow data to be cross-referenced against anatomy or well-known parcellation schemes. A dialogue for defining new atlases is also provided.

Submitting your study to ANIMA

ANIMA provides an intuitive online interface for submitting a study for inclusion in the database (http://anima.fz-juelich.de/submit). The submission process follows a series of tabs, as shown in Fig. 5. The first tab ("Login") allows a new user to register with the database, which is necessary to submit data. Registration allows the administrators of ANIMA to associate a name and institution with a particular study, and provides a level of security by ensuring users provide a valid email address. The email address will not be accessible to the public, and will only be used to contact the user in case of issues related to the study. Registered users can also log in using this tab. The next step of the process (the "Study" tab) requires the user to enter meta-data about the study. This includes author and publication information, a brief description (for browsing purposes), and a full-text PDF, if desired

Fig. 1. The query page of the ANIMA online interface. Studies can be filtered by keyword, author name, journal, or publication date. Single studies can be downloaded using the icons at the right of each entry, and multiple studies can also be selected and downloaded together using the check boxes at left.
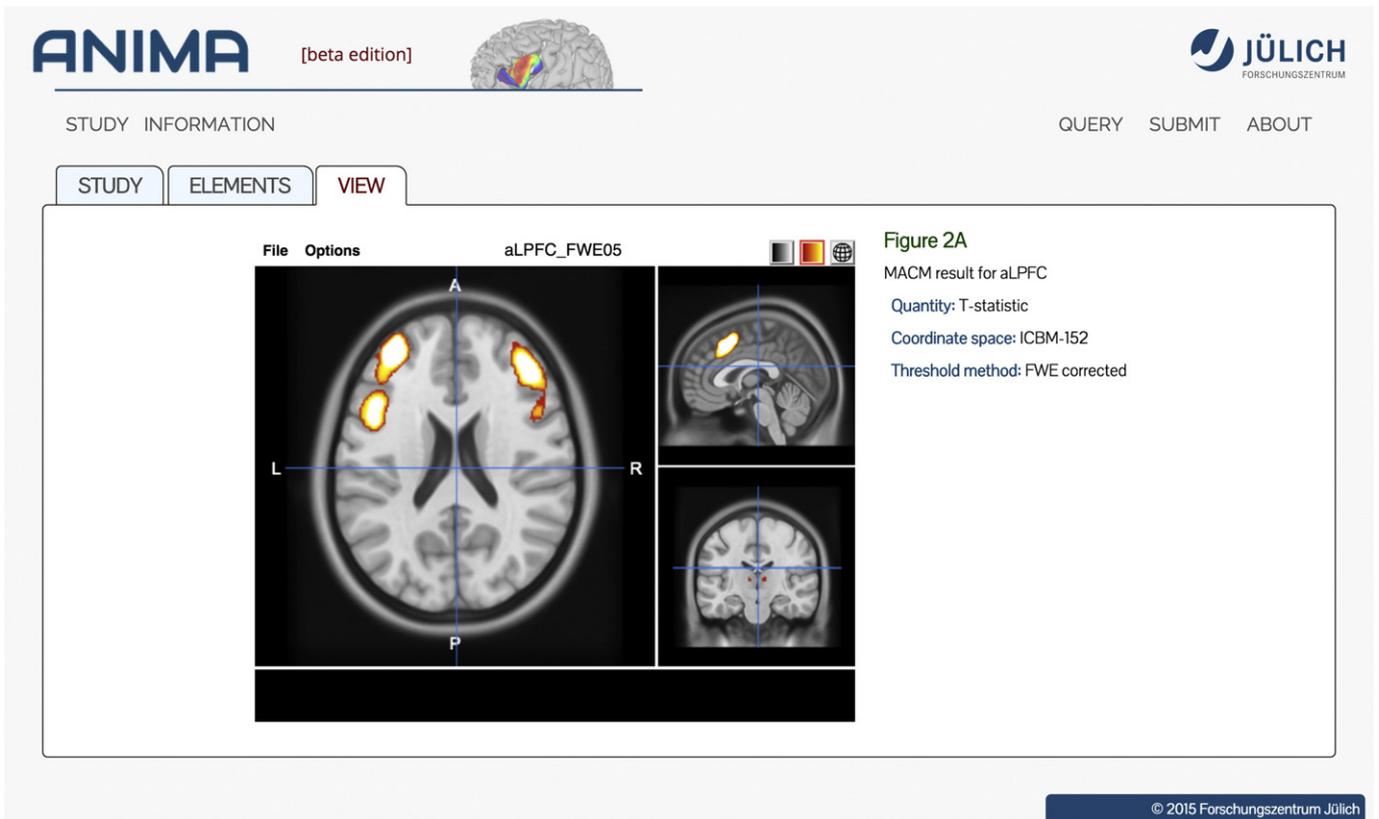
Fig. 2. The single-study information page of the ANIMA online interface, showing the Papaya viewer. This page displays more detailed information about a study, including a list of individual study elements and their associated captions.
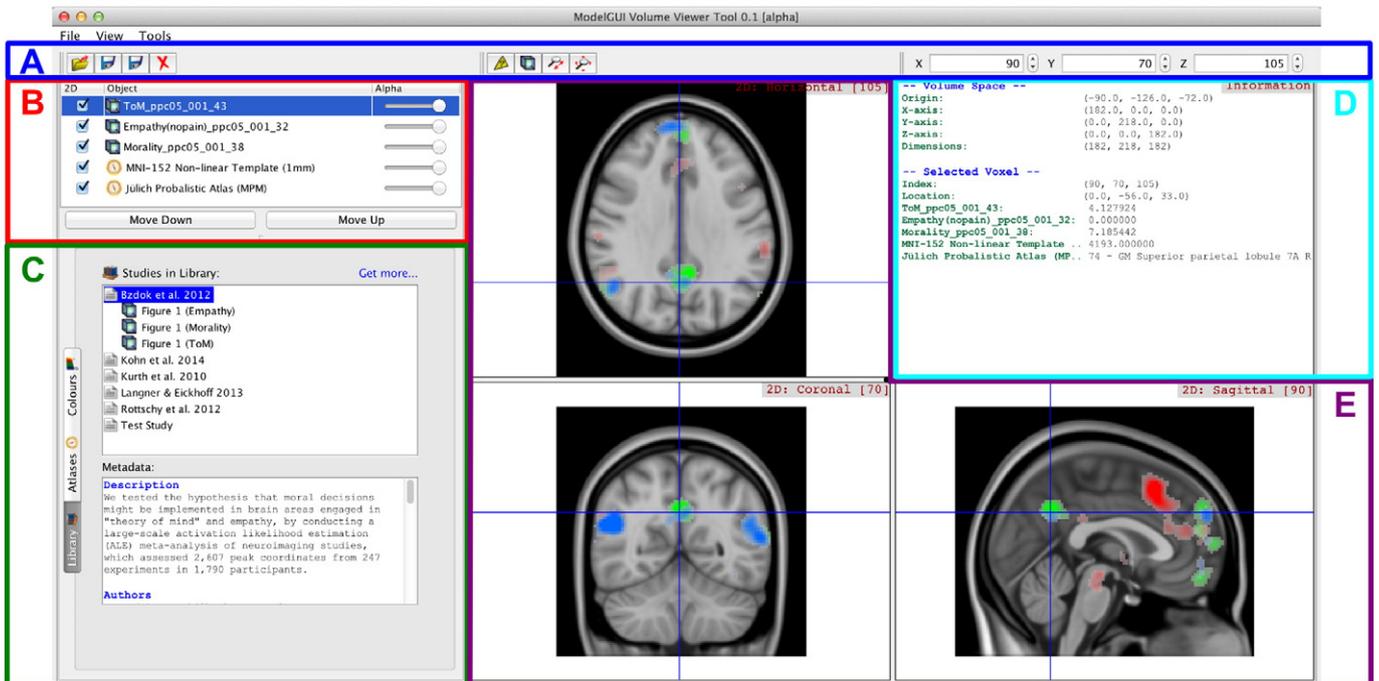

Fig. 3. Screenshot of the stand-alone desktop application Volume Viewer. A. The toolbar, which allows individual images or Volume Viewer sessions to be loaded or saved, or removed from the current session. Buttons in the middle of the panel allow the user to set the mouse behaviour (zoom or query mode). At far right, the current voxel coordinates are display and can be modified. B. The image selection list, which allows the visibility of individual layers to be toggled, their order to be modified, and their transparency (alpha) to be set. C. The Library Panel, which lists the user's local library of studies which have already been downloaded. Individual study elements (images or entire Volume Viewer sessions) can be loaded via this panel. Two other panels are also selectable in this space: (i) the Atlases panel, which allows individual standard atlas or template images to be loaded; and (ii) the Colours panel (shown in inset), which allows a predefined colour map to be applied to the currently selected image layer. D. The Information Panel, which displays information about the current volume space, as well as the voxel defined by the currently viewed sections. Values can be queried for numeric data, while text representations are shown for atlases (here the Maximum Probability Map of the Jülich Probabilistic Atlas). E. The 2D rendering panels, which show the three standard orthogonal planes of the loaded images (horizontal/transversal, coronal, and sagittal). These can be zoomed, panned, and queried with the mouse.
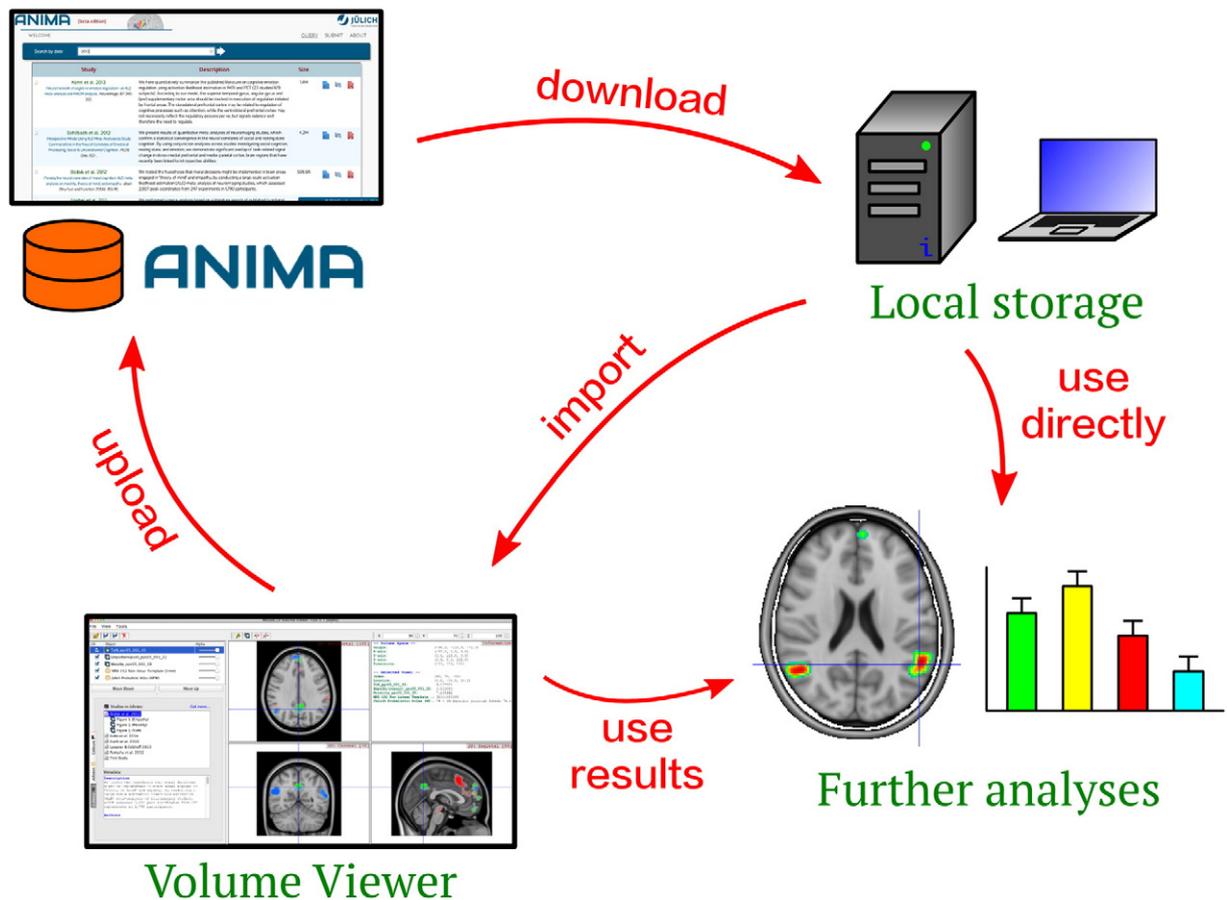
Fig. 4. Overview of typical database usage, illustrating the process of querying, selecting, downloading, and importing the data into the Volume Viewer library. Study data is *downloaded* from the ANIMA online interface into local storage, where it can be *imported* into Volume Viewer or *used directly* for further analysis. Data can also be first processed by Volume Viewer, for instance to extract conjunction ROIs, *before being used* in further analyses. Volume Viewer can also be used to defined sessions, which can be *uploaded* to the database.

and permitted. The subsequent tab ("Elements") provides a means of uploading the study elements (i.e., data files), and associated titles and captions. Five types of files can be uploaded, as shown in Table 2. The final tab ("Submit") provides a preview of the study as entered, and allows the user to verify all information before submitting it to the database.

Upon submission, a message will be sent to the database curators, who will review the submission for validity, completeness, typographic errors, and any other issues. If issues are encountered, an email will be sent with instructions to the submitter on how to update them. Otherwise, the study will be accepted and a confirmation email will be sent. This curation design ensures that only valid, published data are made available through ANIMA, and that the uploader has the right to share data on behalf of the associated authors. Notably, once a study is submitted, it is always associated with the submitter. Modifications can then be made to the study only by the submitter or a database administrator. ANIMA provides a "subscribe" feature, which allows the submitter (as well as any registered user) to request a notification whenever a specific study is modified. Any modifications made to the study (including edits, additions, subtractions, or removal) will result in subscribers being automatically notified of the change via email. Additionally, ANIMA implements a simple versioning policy, which ensures that any major modifications to existing studies are captured as new *versions* of the study. This feature is important, since any publication using ANIMA data should be able to point to the precise version of a data element used for its analysis.

Metadata

The use of metadata to precisely define individual neuroimaging results is an important consideration for any online database, and is essential for both understanding individual database elements, and facilitating further meta-analyses (Poldrack and Gorgolewski, 2014). For the ANIMA database, all such metadata are encoded in XML format, which allows them to be easily extended as necessary. In its present state, the database provides metadata for whole studies (including citation details, keywords, abstracts, and DOIs), as well as single study elements. Study element metadata include a caption which describes the element, and – specifically for image data – further details such as the quantity represented, how the image is thresholded, and the coordinate space (standard or native) in which it is expressed.

Future plans

The platform described above was designed to provide simple, efficient access to results of a specific type of study (meta-analyses), in a standard way. Moreover, the inclusion of a stand-alone desktop application provides a useful means of visualizing, querying, and manipulating data for use in future studies. However, both the online and standalone components of this platform are also generic enough to be used with other types of studies as well. All data is stored as XML files, which can be easily extended or modified, depending on the type of data required. One potential future development will be to host other types of study results using the ANIMA interface.

Fig. 5. Online interface for submitting a new study to ANIMA. A. After login, the "Study" tab becomes visible. Entering the study name and a unique identifier, and pressing "Save" will start the ball rolling, and enable the remaining tabs. In the "Study" tab, you upload a full-text PDF file, a concise description of the study, and other information about the article. B. The "Elements" tab allows the user to upload individual data elements, and describe them with a caption. C. The "Submit" tab provides a summary of the project, as it will appear on the Query page. This can be used to verify that the study is correctly entered. Finally, clicking the "Submit my Study" button will submit the uploaded data for validation by the database administrators.

Ideally, this will involve exposing the database code as a documented and supported open-source project, and providing an online REST interface accessible to registered users (Masse, 2011). As an extension of this, ways in which ANIMA could be integrated with existing databases will also be pursued. Specifically, we plan to implement a REST API in order to allow a database such as Neurovault.org (Gorgolewski

Table 2
File types which can be uploaded to ANIMA.

File type	Description	Extensions
Volume File	A 3D brain image file, typically containing statistical maps such as t-, z-, or p-scores, which indicate the result of a specific analysis. These should be in NIFTI format.	nii, hdr, nii.gz
Volume Viewer Session File	An XML-format file containing all data and metadata specifying a Volume Viewer session. This can be used to pre-define a set of composite images, templates, atlases, and their colour mapping.	vvs
Volume Viewer Point Set File	An XML-format file specifying a list of 3D coordinates, along with associated data which can be used to specify and label individual points of interest in a study.	pointset
Image File	A standard 2D image file, which could represent an informative figure, schematic, or other useful information pertaining to the study.	png, jpg, gif, tif, etc.
Text File	A text file, which can contain additional free descriptions or other information about the study and its elements.	txt, rtf

et al., 2015) to access ANIMA data, for inclusion in large-scale meta-analytic approaches.

Another important consideration is how the database will be maintained and managed in the future. The organization of the database ensures that its management is minimal, but it is still important to have a team of administrators who can evaluate submissions, respond to feedback about data quality, and provide support to users of the database. We intend to assume this role for the foreseeable future. As an extension of this, additional support for ANIMA will be provided in terms of documentation, and an online support forum which can be used to ensure that common issues can be answered once, and a means of reporting bugs, which can be of great assistance to the database developers.

The Volume Viewer tool is based on the ModelGUI API, which is an open-source project hosted on http://www.launchpad.net/modelgui (an online platform designed to be scalable, and which supports projects as large as the Ubuntu community). We intend to provide Volume Viewer also as an open-source project, such that it can be freely obtained and developed by interested members of the neuroscience community. A number of future improvements are planned for Volume Viewer, including: the ability to specify named voxels and ROIs; the ability to extract peaks from a smoothed image map; the addition of 3D volume and surface rendering; easy transfer of data between surfaces and volumes; rendering of network graphs for the visualization of connectivity information; and layout and printing features.

Summary

We present a new database which provides free and convenient online access to the results of published neuroimaging meta-analyses. Data can be used for comparison with one's own results, or as a starting point for new analyses, and the ANIMA interface provides a set of simple tools which greatly facilitates this process. This interface includes a search function, a form for submitting new studies, and an open-source stand-alone software tool for visualizing and organizing study data, and generating ROIs for further analysis. It is our hope that the ANIMA database will improve the way in which the results of meta-analytic neuroimaging studies will be used in the future, and encourage researchers to incorporate these important results into their research approaches.

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