SchizConnect: Mediating neuroimaging databases on schizophrenia and related disorders for large-scale integration

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Abstract

SchizConnect (www.schizconnect.org) is built to address the issues of multiple data repositories in schizophrenia neuroimaging studies. It includes a level of mediation—translating across data sources—so that the user can place one query, e.g., for diffusion images from male individuals with schizophrenia, and find out from across participating data sources how many datasets there are, as well as downloading the imaging and related data. The current version handles the Data Usage Agreements across different studies, as well as interpreting database-specific terminologies into a common framework. New data repositories can also be mediated to bring immediate access to existing datasets. Compared with centralized, upload data sharing models, SchizConnect is a unique, virtual database with a focus on schizophrenia and related disorders that can mediate live data as information is being updated at each data source. It is our hope that SchizConnect can facilitate testing new hypotheses through aggregated datasets, promoting discovery related to the mechanisms underlying schizophrenic dysfunction.

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Introduction

Schizophrenia is a complex psychiatric disease with heterogeneous clinical, behavioral, cognitive and genetic manifestations, and the literature, especially on neuroimaging studies, has yet to achieve a state of consistency and reproducibility. As a result, multi-site consortia have been created to coordinate the collection of large datasets in order to address these issues (Turner, 2014). Consortia such as the Functional Biomedical Informatics Research Network (FBIRN) (Friedman et al., 2008; Helmer et al., 2011a; Keator et al., 2008), the Mind Clinical Imaging Consortium (MCIC) (Gollub et al., 2013), North American Prodrome Longitudinal Study Consortium (NAPLS) (Addington et al., 2012) and Bipolar-Schizophrenia Network for Intermediate Phenotypes (B-SNIP) (Keshavan et al., 2011; Thaker, 2008) have led to the improvement of our understanding of brain circuitry, brain function and genetic variability in schizophrenia (Allen et al., 2011; Arnold et al., 2015; Cannon et al., 2015; Castro et al., 2014; Chen et al., 2012; Chen et al., 2013; Ehrlich et al., 2014; Hass et al., 2015a, 2015b; Kim et al., 2009; Kim et al., 2010; Mathew et al., 2014; Potkin et al., 2009). These efforts were successful in part because they were created with data sharing in mind, and they anticipated many of the difficulties in combining data from multiple sites in their design and schema. Yet, in building data repositories, many decisions were made that were specific to that particular repository or study, about what they would call different data types. In one study's data a structural MRI scan may be listed informatively as “T1-weighted scan”, or something...
as complex as “5MPRAGE-AVG” or just “scan1”. Combining data from datasets that do not share the same protocols and data structures is challenging and it remains a barrier to aggregating mega-datasets. When combining data across different sources, individual investigators face the difficult and costly process of understanding the different imaging, subject, assessment, meta-data content (definitions, formats, organizations) and converting the data into standardized terms. A critical and unmet need exists to automate and virtualize this process so that appropriate data can be retrieved and combined from different databases regardless of differences in their structure and terminology.

In this paper, we describe the initial deployment of “SchizConnect” (publicly available at http://www.schizconnect.org/), a new resource aimed at establishing mega-datasets (Wang et al., 2014). Building on the success of previous consortia efforts, SchizConnect creates a resource that supports structured querying and retrieval of neuroimaging and related data across these consortia repositories.

Methods

SchizConnect architecture

SchizConnect follows the classical virtual data integration framework (Florescu et al., 1998; Halevy, 2001; Lenzerini, 2002; Ullman, 1997; Wiederhold, 1992), which saw its initial theoretical application on schizophrenia neuroimaging data within the FBIRN consortium (Ashish et al., 2010). A distinct feature of this framework is that the data can reside at and be maintained at the original data sources in their original formats and schemas (i.e., their own ways to define the structure, content, and semantics of data). SchizConnect consists of the following three fundamental components (Fig. 1): 1) the data sources that provide the data, structured according to native schemas; 2) the mediation software (i.e., mediator) that reconciles the semantic differences in the data across the different sources through domain modeling and inter-schema mapping; and 3) the web portal that provides a user-friendly interface for querying and downloading data.

The typical data flow begins with a user query constructed by dragging and dropping terms in a graphical user interface (GUI) at the SchizConnect web portal. The graphical query is translated to SQL and passed to the SchizConnect mediator. The mediator then relies on the SchizConnect domain model and inter-schema mappings to translate the user query into source-specific terms, and then queries each data source directly and concurrently, using the available source-specific query mechanisms, languages and variables. The results from the sources are collated and joined together by the mediator and provided to the SchizConnect web portal as a unified result table containing the mediated (harmonized) variables. The SchizConnect web portal then interacts with the user for further processing, including signing of data use agreements and data download.

![SchizConnect Architecture & Data Flow Diagram](https://schizconnect.org/)

**Fig. 1.** SchizConnect architecture & data flow. The SchizConnect architecture has the following 3 components: the federated data sources, the SchizConnect mediator, and the SchizConnect.org web portal. After the user builds the query at the SchizConnect web portal, the query command is passed to the SchizConnect mediator engine. The mediator engine then relies on the SchizConnect domain model to translate the incoming query into source-specific schemas, and queries each data source directly and in parallel, using source-specific query mechanisms, languages, and variables. The returns from the sources are handled by the mediator engine, which provides the SchizConnect web portal with a unified results table. The SchizConnect web portal then interacts with the user for further processing, including signing of data use agreements and data download.

Please cite this article as: Wang, L., et al., SchizConnect: Mediating neuroimaging databases on schizophrenia and related disorders for large-scale integration, NeuroImage (2015), http://dx.doi.org/10.1016/j.neuroimage.2015.06.065
use agreements and data download. Below we describe each of the components in detail.

The data sources

SchizConnect accesses the data available at each of the sources in real time. It maintains a library of connectors (wrappers) to common source types, including relational databases, XML (Extensible Markup Language) or JSON (JavaScript Object Notation) databases, SOAP (Simple Object Access Protocol) or REST (Representation State Transfer) web services, or flat files. For previously unseen source types, the architecture is extensible to program new connectors. Each source runs their own server platforms with their own database schemas, formats and application programming interfaces (APIs). SchizConnect imposes no requirements on data sources with regard to databaseing or access methods, but is flexible to special needs (see results below for special case example).

SchizConnect mediator

The SchizConnect mediator is built on the BIRN mediator (Ashish et al., 2010; Helmer et al., 2011b). The core idea is to define a common domain schema and inter-schema mapping rules that map between the domain schema and the different source schemas. The domain model defines an integrated view of the shared data in the application domain (i.e., SchizConnect). This concept is closely related to that of an ontology, but it is more limited in scope, in the sense that it only models the part of the application domain that is relevant to integrating a set of sources (Ashish et al., 2010). It can be viewed as an incremental, data-driven, pragmatic approach to domain ontology development. Inter-schema mappings are logical formulas, or rules, that relate the data models at each of the sources with the domain model, reconciling their semantic differences in the description of the data. The SchizConnect domain model consists of terms that are pertinent to schizophrenia neuroimaging research (such as those related to imaging protocol, disease severity or cognitive functioning). Definitions of these terms are provided via downloadable documents available on the SchizConnect web portal. During development, we have aligned the SchizConnect domain model terms with the standards provided by the ontology community: XCEDE (XML-Based Clinical Experiment Data Exchange Schema, http://www.xcede.org/XCEDE.html) (Gadde et al., 2012), NeuroLEX (the Neuroscience Lexicon, http://neurolex.org/) (Larson and Martone, 2013), NIF (the Neuroscience Information Framework, http://incf.org/) (Bjaalie and Grillner, 2007; De Schutter, 2009), wherever appropriate. The domain terms with links to existing ontology can be found on the SchizConnect website documentations page. For example, the Positive and Negative Symptom Scale (PANSS) has an entry on NeuroLex (birmlex_3032, http://neurolex.org/wiki/Category:Positive_and_Negative_Symptom_Scale). In cases where no accepted ontology has been defined, such as the UPSA (University of California Performance-based Skills Assessment), we work with the neuroimaging and neuroinformatics community to define them. Although such effort is ongoing, since there doesn’t yet exist a standard process for ontological term contribution, we will work with data contributors and the neuroinformatics community on a case-by-case basis.

The mediator performs two core functions. First, it uses the inter-schema mappings to rewrite the user query, e.g., “T1 images from individuals with schizophrenia older than 30 years old,” from the domain schema to the formats and languages specific to each source. It currently uses GAV (global-as-view) mappings (Ashish et al., 2010; Florescu et al., 1998; Halevy, 2001; Lenzerini, 2002; Ullman, 1997; Wiederhold, 1992), wherever appropriate. The domain terms with links to existing ontology can be found on the SchizConnect website documentations page. For example, the Positive and Negative Symptom Scale (PANSS) has an entry on NeuroLex (birnlex_3032, http://neurolex.org/wiki/Category:Positive_and_Negative_Symptom_Scale). In cases where no accepted ontology has been defined, such as the UPSA (University of California Performance-based Skills Assessment), we work with the neuroimaging and neuroinformatics community to define them. Although such effort is ongoing, since there doesn’t yet exist a standard process for ontological term contribution, we will work with data contributors and the neuroinformatics community on a case-by-case basis.

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source connector (which wraps the source APIs). Results from source queries are collated and joined together in the mediator, and served to the SchizConnect web portal as a unified table organized using the domain schema terms.

The query execution engine used by the mediator for source-level query evaluation is based on the Open Grid Services Architecture Data Access and Integration (OGSA-DAI) and Distributed Query Processing (OGSA-DQP) services (http://www.ogsadai.org.uk/) (Antoniolietal., 2005; Grant et al., 2008; Lynden et al., 2009; Lynden et al., 2008). OGSA-DAI is a streaming workflow engine in which data resources and web services are wrapped through a library of connectors. OGSA-DQP is a query engine that optimizes and implements the query evaluation plan as an OGSA-DAI workflow, which accesses the multiple data sources.

The SchizConnect domain query language is SQL expressed on the domain model terms. Each data source query is wrapped as an OGSA-DAI resource through its library of connectors to common data sources such as PostgreSQL, MySQL, or XML. For additional details on the mediator architecture, see our previous work on the BIRN mediator (Ashish et al., 2010).

SchizConnect web portal

SchizConnect has been conceptualized as a one-stop resource for querying and retrieving neuroimaging and related data from distributed, heterogeneous repositories. SchizConnect is therefore set up to facilitate user registration and compliance with data use agreement (DUA) with each data source. To maximize the usage and efficiency, while complying with NIH policies and best practices, the SchizConnect web portal is structured to have two query modes. The first is a preliminary search, for example, for the number of male subjects between the ages of 20 and 60 with diffusion MRI scans. This mode is completely open to the public, allowing for anyone to browse and immediately obtain useful, current information on a current summary count of available data without having the need to register. However, no subject-level data at this point are downloadable. In the second mode, the user registers and signs in, and with the same query is able to view subject-level data, sign DUAs and download the data. Only data for which DUA has been signed are downloadable. Signed DUAs are forwarded to each respective data source administrator for reviewing and filing. The administrators at SchizConnect as well as each data source will work with each user’s institution for data use and institutional review board (IRB) terms upon request. Regarding participant privacy, we require that it is the responsibility of the data source to ensure that data are shared in accordance to rules and regulations set forth by their IRB. The responsibility of SchizConnect is to confirm with each data source that they agree to this responsibility.

Results

The initial deployment of SchizConnect makes available data on 1129 subjects from its contributing sources. Sample demographics can be found in Table 1 as well as on the SchizConnect web portal (http://schizconnect.org/#subject-stats). Of these subjects, 1029 have scan data, which include structural MRI (sMRI), resting-state functional MRI (fMRI), task- and paradigm fMRI, and diffusion MRI (dMRI) scans, totaling 21,309 volumes (Tables 2 and 3). Demographic, neuropsychological measures, and clinical assessments are either available or in the process of becoming available. As the data sources take in new subjects/scans, they can automatically become available for querying through SchizConnect, depending on the source data repository’s policies. At the writing of this manuscript, SchizConnect has 49 users and 37 downloads, and that statistic is steadily growing (http://schizconnect.org/#user-stats).

SchizConnect data sources

Current data sources include the following schizophrenia-related datasets, which are all publicly available themselves and have been extensively curated, documented, and subjected to quality assurance. Detailed explanations of data can be found in the accompanying special papers describing the data source repositories, as well as the following papers: (Cetin et al., 2014; Glover et al., 2012; Gollub et al., 2013; Wang et al., 2013).

- **FBIRN Phase II dataset @ UCI** (http://fbirnbdr.nbirn.net:8080/BDR/)1 (Glover et al., 2012; Potkin and Ford, 2009), containing cross-sectional multisite data from 251 subjects, each with two visits. (See paper on FBIRN data in this special issue.) Data include sMRI and fMRI scans collected on a variety of 1.5 T and 3 T scanners, including Sternberg Item Recognition Paradigm (SIRP) and Auditory Oddball paradigms, breath-hold and sensorimotor tasks. The underlying database is HID (Keator et al., 2009; Ozyurt et al., 2010) in PostgreSQL using the relational data model. Access is provided via Java database connectivity technology (JDBC), a database-access API for the Java programming language. Results from the query are returned to the Mediator as an SQL ResultSet.

- **NUSDAST @ XNAT Central** (http://central.xnat.org/REST/projects/NUDataSharing) (Wang et al., 2013), containing data from 368 subjects, the majority with longitudinal data (~2 years apart). (See paper on NU data in this special issue.) Data include sMRI scans collected on a single Siemens 1.5 T Vision scanner. The underlying database is XNAT (Marcus et al., 2007), using the XML data model. Access is provided via XNAT REST API. The mediator constructs a query XML document conforming to the XNAT search web service specification. Results from the query are returned to the Mediator as an XML document.

- **COBRE & MCICShare @ COINS Data Exchange** (http://coins.nmr.mrn.org/) (Bockhoff et al., 2010; Scott et al., 2011; Wood et al., 2014), containing data from 198 and 212 subjects from COBRE (Cetin et al., 2014) and MCICShare (Gollub et al., 2013) projects, respectively. (See paper on COINS data in this special issue.) Data for COBRE include sMRI and rest-state fMRI scans collected on a single 3 T scanner. Data for the multisite MCICShare include sMRI, rest-state fMRI and dMRI scans, collected on 1.5 T and 3 T scanners. COINS data required special handling in order to satisfy SchizConnect’s needs because the native COINS architecture involves dynamic data packaging following the query, which does not allow for data to be immediately returned to the query engine.2 With

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1. This link will be replaced by the SchizConnect web portal in the near future.
2. On the COINS website, after user builds a query, data are packaged offline and a link is provided for downloading. Therefore the user never sees the actual data until the data are downloaded via the link.
permission from the COINS executive committee, an API was built to enable SchizConnect to extract domain-model defined variables (see below) from the COINS databases and to duplicate them at the Mediator site. The database underlying the duplicated MCICShare/COBRE data is MySQL using the relational data model. Access is provided via JDBC to the MySQL server. Results from the query are returned to the Mediator as an SQL ResultSet.

**SchizConnect mediator**

The SchizConnect mediator domain schema defines the following concepts: project, subject, imaging, cognitive, and clinical, described in detail below.

- **Project** contains the name and description of the 4 projects from 3 data sources for which data are collected (Fig. 2A).

![Fig. 2. SchizConnect mediator (Virtual) domain Schema and Inter-schema Mappings.](image)

**Please cite this article as:** Wang, L., et al., SchizConnect: Mediating neuroimaging databases on schizophrenia and related disorders for large-scale integration, *NeuroImage* (2015), [http://dx.doi.org/10.1016/j.neuroimage.2015.06.065](http://dx.doi.org/10.1016/j.neuroimage.2015.06.065)
Subject contains demographic and diagnostic information for individual participants, including "subject id", "age", "sex" and "diagnosis" (Fig. 2B). Current diagnosis categories are: "no known disorder" (for healthy controls), "bipolar disorder," "schizophrenia broad," which includes "schizophrenia strict" and "schizoaffective." We note that the precise definition of "control" may depend on specific studies and...
study populations, we did not use the term “control” to label the healthy comparison subjects provided by each data source. Instead, the term “no known disorders” is used.

- Imaging Protocol (MRI) contains information on MRI scanner platforms and imaging protocols. “Imaging protocol” consists of “structural,” “functional,” “perfusion,” and “field mapping” categories. Both “structural” and “functional” protocols are subdivided for further distinctions, e.g., “T1,” “T2,” “resting state,” and “task paradigm” (Fig. 2C).

- Cognitive domain contains neuropsychological assessments. The domain model uses the MATRICS Consensus Cognitive Battery (Nuechterlein et al., 2008) terms whenever appropriate, which are “attention,” “executive function,” “learning,” “working memory,” “episodic memory,” “intelligence,” “language,” “motor,” “premorbid functioning,” “processing speed,” “social cognition,” and “visuospatial” (Fig. 2D).

- Clinical domain contains full demographics, assessments of symptoms and functional capacity, and medical information. Demographic
information includes "Race," "Ethnicity," "Education," "SES (socioeconomic status)," and "Handedness." Symptom measures include "PANSS (Positive and Negative Symptoms Scales)," "SAPS (Scale for the Assessment of Positive Symptoms)," "SANS (Scale for the Assessment of Negative Symptoms)," using the Unified Medical Language System (UMLS) terms whenever appropriate. Symptom measures also include "Depression," "Mood," "Suicide Ideation," and "Extrapyramidal Symptoms." Medical information includes “Medical History/ Medication,” “SCID (Structured Clinical Interview for DSM Disorders),” and “Nicotine Addiction/Dependence” (Fig. 2E).

The SchizConnect mediator relates the above domain model concepts to the terms in the source schemas using inter-schema

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mappings (see Fig. 2F for sample mappings). For example, subject data for the NUSDAST source is obtained by calling the XNAT search web service and joining with a diagnostic code mapping table to harmonize the diagnoses; normalized diagnosis of Strict Schizophrenia for the subjects in the HID source is computed on the fly, by first joining three HID tables with subject and assessment data, then selecting the subjects according to a predefined algorithm on assessment values.

Currently, the SchizConnect model comprises 7 domain predicates, 17 source predicates (from the 4 sources HID, NUSDAST, COBRE and MCICShare, a local database that contains value mapping information, and utility functional sources), and 18 inter-schema mappings (10 for HID, 4 for NUSDAST, and 4 for COBRE/MCICShare). It is worth noting that since the inter-schema mappings are specified in a declarative rule language, the mediator is easily extensible to incorporate additional sources by writing the appropriate inter-schema mappings.

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At the http://www.schizconnect.org/ web portal, the operating statuses of the data sources are displayed (Fig. 3A). Queries are performed only on data sources that are operational. Data queries are constructed using a drag-and-drop GUI, in which a series of logical “AND” and “OR” operators can be concatenated filtering on domain model terms. An example query is shown in Fig. 3B, C, with summary return information presented Fig. 3D. Additional sample queries are listed in Table 3. Upon signing in, detailed subject-level information returned from the query is presented to the user as an on-screen table (Fig. 3E). This table lists sortable domain model variables including provenance, age, sex, and scan parameters for each subject with downloadable images. The user can review and use this information to decide whether to further refine the query. The user also has the ability to modify, save...
and retrieve queries. A data download button is available that leads to the DUA page (Fig. 3F). The user must sign the SchizConnect DUA, and has the option of choosing which participating source DUs agree with, and receives data only from data sources with which the DUs have agreed been.

For downloading, the imaging data resulting from the queries are transferred out of the data sources and staged at the SchizConnect.org host, together with the returned meta-data table of the mediated variables. Transfer is performed via gridFTP, REST API, HTTP, or others, depending on the specific data transfer protocol at each source. Imaging data files are compressed and packaged into 10-GB easily reconstructible, individual 7-zip (http://www.7-zip.org/) segments, available for the user to download within a specified limited time period (currently 2 weeks). Depending on the size of the requested imaging data, it can take up to a few days for all data to be staged for download. These data files contain the original and/or preprocessed imaging data shared by each source, in DICOM, Analyze, or NIFTI formats. Links to these files along with unpacking instructions are sent to the user via email. The links are also available on the “My SchizConnect” page of the web portal (Fig. 3G, H). Documentation for descriptions of imaging formats and directory structures can be found on the SchizConnect website (http://www.schizconnect.org/documentation). All cognitive and clinical data (see model description above) can be included in the download package along with the download imaging data. On the documentation page, the user can find useful information including: Tutorials on how to use the website, DUs of all data sources, data descriptions, data dictionaries, and peer-reviewed journal papers related to the data. Since not all neuroimaging data (such as scan sequence parameters) have been modeled into the SchizConnect domain hierarchy, it is important to provide technical information on our website to facilitate research. In the data description section, the NUSDAST description lists structural parameters (e.g., 3D MPRAGE: TR = 9.7 ms, TE = 4 ms, flip = 10°, ACQ = 1, 256 × 256 matrix, 1 × 1 mm in-plane resolution, 128 slices, slice thickness = 1.25 mm, 5:36 min scan time each) and the COBRE description lists resting-state parameters (resting state scans consisting of 149 volumes of T2*-weighted functional images, acquired using a gradient-echo EPI sequence: TR = 2 s, TE = 29 ms, flip = 75°, slice thickness = 3.5 mm, slice gap = 1.05 mm, field of view = 240 mm, matrix size = 64 × 64, voxel size = 3.75 mm × 3.75 mm × 4.55 mm). In the Publications section, we have provided a link to a peer-reviewed journal publication that provide detailed technical descriptions on each data source. For example, Gollub et al. (2013) describes the “MCIC collection: a shared repository of multi-modal, multi-site brain image data from a clinical investigation of schizophrenia.” Similar papers describing all the other data sources currently participating in SchizConnect can be found here.

Discussions and future plans

These initial results demonstrate that SchizConnect allows combining of neuroimaging data from different databases via mediation to form compatible mega-datasets with accuracy and fidelity. In SchizConnect, data remains with the source rather than warehoused in a central repository. Providers maintain control of their data and do not need to modify them for sharing. The user query is done over a single, consistent, well-defined model that is translated to the schemas of the sources. This approach unburdens the user and each source from having to make contact and helping to interpret the data each time, especially when new data are being continuously added to the data source repository. The web portal is user-friendly and intuitive, appearing to the user as a single, virtual database with real-time query and download performance. As an on-going project, we are continuing to define additional domain model terms for neuropyschological and psychopathological variables, make available additional imaging modalities and subjects, and identify and evaluate potential new data sources. Work is also under way integrating with clinical research databases such as Research Electronic Data Capture (REDCap) (Harris et al., 2009) where clinical and cognitive assessment data are stored, further enhancing the functionality of SchizConnect by searching across imaging and non-imaging databases for the same subject.

SchizConnect shows considerable potential for overcoming current barriers for creating large-scale datasets to increase statistical power, accelerating the testing of new hypotheses and methods, and creating a resource for developing advanced techniques to better integrate disparate data at low cost. As a proof-of-concept for combining datasets, we compared SAPS/SANS and neurocognition across the current data sources. For SAPS/SANS, we found that while fewer schizophrenia subjects in the NU data scored 2 or higher, the distributions were not statistically different between sites. For neurocognitive measures, we computed z-scores on episodic memory, working memory, attention and executive function domains using each site's own controls as reference sets. No statistical difference between sites was observed (NU range: −1.23 to −0.71, FBIRN: −1.28 to −0.65), indicating that schizophrenia subjects across both consortia exhibit similar degrees of psychopathology and cognitive impairment. Nonetheless, subtle differences in cohort make up may still exist upon closer inspection, but users will have the opportunity to explore the sources of potential heterogeneity and use such differences to benefit in developing new hypotheses.

SchizConnect was aimed at combining across different types of data repositories, and its current data sources are examples of classic types of data repository: The HHD that houses the FBIRN data is a multisite study repository with prospectively collected data using pre-determined protocols; The COINS Data Exchange that houses the MCICShare and COBRE data, and the XNAT Central that houses the NUSDAST data, are centralized data repositories where data from unrelated studies are uploaded and stored, and the database platforms provide the user with queryable data structures and interfaces. When owners of these datasets are willing to share subject-level data (i.e., scans, assessments), SchizConnect is designed to interact with such data repositories for mediation. When investigators are only willing to share measures, meta-analysis efforts such as the ENIGMA (Gupta et al., 2014; Thompson et al., 2014; van Erp et al., in press; Wright et al., 2015) will be an excellent alternative for data sharing.

During the initial implementation of SchizConnect using the current data sources as test beds, we have established a series of domain models and their translations to the initial data source models. The SchizConnect mediation approach simply translates user queries into the query language of each data source (i.e., equivalent to the user performing the same query at the individual data source’s own web portal). The SchizConnect data models can be extended easily to accommodate new data structures of a new data source while placing no restrictions on what the data source wants to share. Although the process of domain understanding and data modeling can be labor intensive, we have laid the foundation for extending SchizConnect to other schizophrenia neuroimaging data sources, which will build on the existing schemas. A limitation of the current domain model work is that the understanding and modeling of source data remains a manual step. In SchizConnect, this data mediation process starts with domain understanding by experts on the specific data that is being integrated so that we have a clear knowledge on the data terms and their definition. The data mediation experts can then integrate this new knowledge into existing SchizConnect models to enable the data to be accessed without requiring it to be modified. We have provided a questionnaire on the SchizConnect.org web portal that can initiate the process, http://schizconnect.org/questionnaires/1/responses/new. It is important as a next step for us to develop approaches that learn from existing data to facilitate more automated procedures for inclusion of new data sources (e.g., following our previous work [Knoblock et al., 2012]). Another limitation is query evaluation in the virtual integration approach, is generally slower than query evaluation on a warehouse-model database.

Finally, SchizConnect is the only data finder (data broker) of its kind for researchers interested in combining neuroimaging data on
schizophrenia and related disorders from disparate sources. Existing data portals such as the COINS, FBIRN, and XNAT Central, data sources used in this project, contain schizophrenia data but serve as repositories of these types of data. When users intent to combine data across these sources, harmonization of data terms and mediation of these terms remain a critical challenge and barrier. SchizConnect is fulfilling this critical need, and the data mediation framework that SchizConnect created can be readily extended to other clinical domains including Bipolar Disorder. Recent developments on data harmonization have led to the creation of the Research Domain Criteria Database (RDoCdb) at the National Institute of Mental Health (NIMH) and its associated data repository, the National Database for Autism Research (NDAR) (Hall et al., 2012). It should be noted that SchizConnect is a virtual database that can mediate data sources that make ongoing updates to their repositories, and SchizConnect is focused on schizophrenia and related disorders. Administratively, the SchizConnect web portal is hosted at Northwestern University, the SchizConnect mediator is hosted at the Information Science Institute of the University of Southern California. For inclusion into SchizConnect, new data sources will be evaluated on completeness, quality, and enthusiasm to collaborate. The focus of the initial expansion will be the quickest return for the research community, so that larger, richer datasets that have been carefully collected and checked for completeness and quality (e.g., already analyzed and published) would be of the highest priority. Data repositories based on XNAT, or those already in COINS can be more readily integrated, up to any new data models and new querying news. For valuable datasets without a database platform, we can help develop an XNAT database for schizophrenia and related disorders. It is our hope that SchizConnect can facilitate the testing of new hypotheses that are hitherto not possible, thus greatly promote discovery related to the mechanisms underlying schizophrenia. We aim to expand to repositories on psychosis and related disorders, thus facilitating large-scale dimensional research. We hope that SchizConnect will become the prototype for the study of psychiatric disorders, serving as a model for broader efforts for the integration and sharing of biomedical information across the greater scientific community.

Acknowledgment

This work was supported in part by NIH grants U01 MH097435, 1R01 MH084803, P05 MH071616, R01 MH056854, U24 RR025736-01, U24-RR021992, U24GM10420, P20 GM103472.

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