Hypothesis-Exploring Methods for Automated Meta-Analyses of Brain Imaging Literature

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Abstract

The PORTAL-DOORS system (PDS) has been designed as a resource metadata management system intended to support applications such as automated searches of online resources and meta-analyses of published literature. We present a methodological approach with a PDS-compliant concept-validating registry and hypothesis-exploring ontology that organizes focal-onset dementias including Sensory-Onset, Language-Onset and Motor-ONset (SOLOMON) dementias with novel classifying and relating concepts. This approach facilitates semantic search of resources and exploration of hypotheses related to neurodegeneration. SOLOMON interoperates with other PDS registries and ontologies including BrainWatch, ManRay and GeneScene.

Objectives

Within the framework of the PORTAL-DOORS System (PDS), we have maintained the goal of supporting tools that facilitate automated searches of online resources and meta-analyses of the published literature. Ontologies used by PDS serve as critical components that determine the scale and scope of these searches and meta-analyses. Our objectives here are to develop the informatics tools and systems required for supporting automated meta-analyses of the brain imaging literature with the capability of exploring biomedical and scientific hypotheses relevant to neurodegenerative disorders and dementias.

Methods

Software development has been continued within the informatics framework of the PORTAL-DOORS System (2,4) enabling lexical and semantic search across different problem-oriented and topic-focused specialty domains including nuclear medicine, radiopharmaceutics and molecular imaging with the ManRay ontology (1), brain imaging with the BrainWatch ontology (5) and now neurodegenerative disorders and dementias with the SOLOMON ontology. This new OWL ontology organizes focal-onset dementias, including Sensory-Onset, Language-Onset and Motor-ONset (SOLOMON) dementias, with novel classifying and relating concepts expressed as RDF triples, that facilitate exploration of biomedical and scientific hypotheses of neurodegeneration. These hypotheses attempt to explain the initial onset and subsequent progression of heterogeneous brain disorders (6) that share the common characteristic of neurodegeneration. An automated smart agent has been developed to search and find online resources, including peer-reviewed articles, that report clinical trials and basic research for brain imaging studies. Resources found are added as records to the BrainWatch, ManRay and SOLOMON registries. These records are then able to be analyzed by automated meta-analysis tools or curated further by human experts.

Table 1: Onset types with example diseases, protein aggregates and anatomical regions

Onset Type	Disease	Protein	Region
Memory	Alzheimer's Disease	Beta-amyloid	Hippocampus
Sensory	Posterior Cortical Atrophy	Beta-amyloid	Visual cortex
Language	Primary Progressive Aphasia	Tau	Insular cortex
Motor	Parkinson's Disease Dementia	Alpha-synuclein	Substantia nigra
Focal	Any of the above	Any of the above	Any of the above

Fig 1: PET brain scans of focal onset dementias

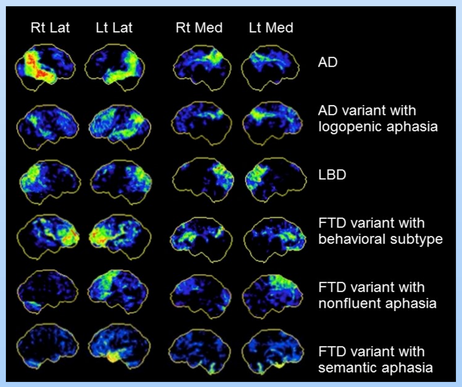

Fig 2: Onset type relationships with other concepts

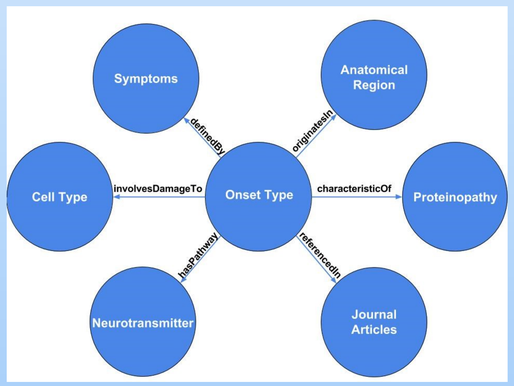

Fig. 3: PDS resource metadata server networks

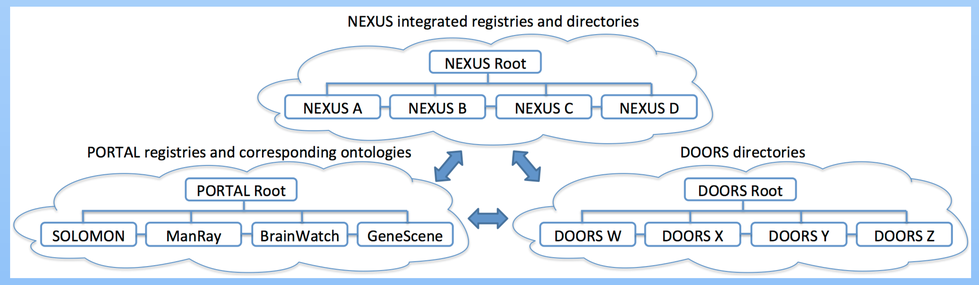

Table 2: Design principles guiding development of the SOLOMON ontology

Principle	Benefit
PDS compliance	resource discovery through the PORTAL-DOORS System
Modularity	coverage of domain of interest, ease of use and maintenance
Interoperability	discovery of resources tagged with well-established ontologies
Concept-validating (lexical and semantic side)	relevance of resources registered with PORTAL registry
Thesaurus-interfacing (lexical side)	discovery of resources employing synonyms of the target terms
Ontology-interfacing (semantic side)	discovery of resources employing target concepts in the desired context
Hypothesis-exploring (lexical and semantic side)	ease of use for biomedical end-users interested in the hypothesis space

Results

The SOLOMON project implements a PDS PORTAL registry and ontology for focal-onset neurodegenerative disorders and dementias with a focus on brain imaging research studies related to hypotheses involving the proteinopathies including tauopathy, amyloidopathy, and synucleinopathy. A prototyped smart agent has been created to search and find relevant resources. The website https://www.BrainHealthAlliance.net hosts SOLOMON and other PDS registries with their schemas, ontologies and resource records. Examples of focal-onset dementias are listed in Table 1 and displayed in Figure 1 for which relationships with other entities are shown in Figure 2. Onset type is related to the associated disease, proteinopathy, and anatomical region of the brain; ontology relationships also shown include cell type, symptom, neurotransmitter, and literature research article.

Conclusions

Continuing development of ontologies, such as SOLOMON, BrainWatch and ManRay as open standards for the organization, classification, analysis and interoperable exchange of data involving nuclear medicine, brain imaging, and the dementias remains an important approach to managing the continuing growth of published data and information from basic research and clinical trials. When supported with tools that enable automated search for resources and automated meta-analyses of the literature, the SOLOMON, BrainWatch and ManRay ontologies will facilitate the exploration of hypotheses that address neurodegeneration, brain imaging, and nuclear medicine. These ontologies and associated software applications will serve as necessary components of a knowledge engineering workbench for brain imaging and the study of dementias.

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