PROCEEDINGS
Towards an Ontology of Mental Functioning workshop

Medical University of Graz

Introduction

Mental functioning includes all the faculties of the mind, e.g., perception, planning, language, memory, emotion, and self-representation. The study of these processes cuts across disciplines such as psychology, neuroscience, and biomedicine. These disciplines have seen remarkable progress and have brought complementary methods to bear in understanding mental processes and their biological bases.

However, translating the results of such research across disciplinary boundaries in order to achieve a holistic view of the current state of the art, to faciliate knowledge discovery and to enable the translation of research results into benefits to patients, remains a challenge. Ontologies are increasingly used to annotate and organise primary data in each of these disciplines, and ontologies are also widely used to enable interdisciplinary research in other fields. The primary objective of this workshop is to enable such translational benefits for existing annotation efforts through the creation of a strategy for interlinking and aligning mental functioning ontologies.

There remain important gaps in representation of mental functioning entities across disciplines, reflected in differences in ontologies such as the Gene Ontology, Neural ElectroMagnetic Ontology, Cognitive Paradigm Ontology, and the Mental Functioning and Disease ontologies. In some cases, mental processes have been interpreted in different — even incommensurate — ways. In other cases, there are transparent relationships between ontologies. Finally, some differences reflect different, and highly complementary, levels of analysis (e.g., neuronal vs. systems-level representation of memory changes in the brain); this case may present the most interesting challenge. The objective of the workshop is to bring together scientists, ontology developers and users interested in the domain of mental functioning and to generate a targeted discussion of gaps and challenges in harmonization and representation.

Schedule

Time	Session	Speaker
8:30-9:00	Arrivals, Registration, Coffee	
9:00-9:30	Welcome, Introduction, Workshop Overview	Janna Hastings, Gwen Frishkoff
9:30-10:00	Mental Functioning and Semantic Search in the Neuroscience Information Framework	Maryann Martone
10:00-10:30	Representing mental functioning: Ontologies for mental health and disease	Janna Hastings
10:30-11:00	========COFFEE BREAK========	
	Ontology and Neuroscience	
11:00-11:30	Mental Functioning IS Neural Functioning: Towards a Unified Ontology of Mind, Brain, and Behavior	Gwen Frishkoff
11:30-12:00	What is the relationship between cognitive experiments and cognitive processes?	Jessica Turner, Angela Laird
12:00-12:30	GROUP DISCUSSION: Relating mind and brain	Moderator: BS
12:30-13:30	========LUNCH BREAK=========	
	Ontology and Biological Investigations	
13:30-14:00	Mental Functioning in the Gene Ontology and Annotations	Jane Lomax
14:00-14:30	Mental Functioning and the Ontology of Language	Barry Smith
14:30-15:00	GROUP DISCUSSION: Integrating MF research across disciplines using ontologies	Moderator: JH
15:00-15:30	========COFFEE BREAK=========	
	Applications in Psychology, Neuroscience and Medicine	
15:30-16:00	Annotating affective neuroscience data with the Emotion Ontology	Janna Hastings
16:00-16:30	Ontologies for the Study of Neurological Disease	Mark Jensen
16:30-17:00	GROUP DISCUSSION: Applications, Canonical and non-canonical functioning: representing disease and dysfunction	Moderator: GF
17:00-17:30	Workshop closing: Gaps, publication strategy and action points	Moderator: JH & GF

Ontologies for the Study of Neurological Disease

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ABSTRACT

We have begun work on two separate but related ontologies for the study of neurological diseases. The first, the Neurological Disease Ontology (ND), is intended to provide a set of controlled, logically connected classes to describe the range of neurological diseases and their associated signs and symptoms, assessments, diagnoses, and interventions that are encountered in the course of clinical practice. ND is built as an extension of the Ontology for General Medical Sciences — a high-level candidate OBO Foundry ontology that provides a set of general classes that can be used to describe general aspects of medical science. ND is being built with classes utilizing both textual and axiomatized definitions that describe and formalize the relations between instances of other classes within the ontology itself as well as to external ontologies such as the Gene Ontology, Cell Ontology, Protein Ontology, and Chemical Entities of Biological Interest. In addition, references to similar or associated terms in external ontologies, vocabularies and terminologies are included when possible. Initial work on ND is focused on the areas of Alzheimer's and other diseases associated with dementia, multiple sclerosis, and stroke and cerebrovascular disease. Extensions to additional groups of neurological diseases are planned.

The second ontology, the NeuroPsychological Testing Ontology (NPT), is intended to provide a set of classes for the annotation of neuropsychological testing data. The intention of this ontology is to allow for the integration of results from a variety of neuropsychological tests that assay similar measures of cognitive functioning. Neuropsychological testing is an important component in developing the clinical picture used in the diagnosis of patients with a range of neurological diseases, such as Alzheimer's disease and multiple sclerosis, and following stroke or traumatic brain injury. NPT is being developed as an extension to the Ontology for Biomedical Investigations.

1 INTRODUCTION

The field of neurology deals with a diverse domain of diseases related to the functioning of the nervous system in all its aspects, including diseases resulting from disorders of the central, peripheral, and autonomic nervous systems. Neurological diseases may exhibit both acute and chronic courses, affect a variety of cell types and anatomical regions of the body. They are manifested via a variety of mechanisms, including cell-autonomous disorders, unregulated protein aggregation, autoimmune conditions, and vascular pathology, which, depending on the disease, may occur alone or together in various combinations (Ropper *et al*., 2005; Merritt and Rowland, 2000). At a different level of granularity we see neurological diseases that affect cognitive as well as mental functioning. Following Ceusters and Smith (2010), we maintain that mental diseases are (at least primarily) special kinds of neurological diseases in the sense that the disorder, which serves as the material basis for the disease, is a part of an anatomical structure in the organism responsible for producing and maintaining cognitive representations and behavior. For example, a variety of neurological conditions result in dementia, such as Alzheimer's and Parkinson's disease, and many of the late-onset leukodystrophies.

We have recently begun building a new ontology for the domain of neurological diseases – the Neurological Disease Ontology (ND). ND is an ongoing project that aims to accurately represent every facet of neurological diseases in as much detail as possible. This includes their clinical presentation, diagnosis, treatment, physical manifestation, course of development, genetic and physical bases, and more. ND is still in the early stages of development, but is rapidly growing to include more of these facets. While our ultimate goal in developing ND is to provide a comprehensive account of all neurological diseases, it has three initial areas of focus: Alzheimer's disease (AD), multiple sclerosis (MS), and stroke and cerebrovascular events. At this time, the most progress has been made on AD and other diseases that result in dementia, but work is currently under way on representing MS and associated demyelinating diseases as well as on representing stroke and cerebrovascular disease.

As a corollary to ND, we have begun development of the NeuroPsychological Testing Ontology (NPT) to represent neuropsychological assessments such as the Folstein Mini-Mental State Examination (MMSE), the Trail- Making Test, the Hopkins Verbal Learning Test, and the Wechsler Memory Scale. These standardized assessments are useful for identifying the presence and degree of cognitive impairment in patients (Lezak *et al*., 2004). An initial goal of the NPT project is to test hypotheses about the diagnosis of AD based on the results of neuropsychological assessments. Part of the development of NPT necessitates reference to aspects of cognitive functioning. For example, MMSE produces scores that are indicative of impairment in certain functional cognitive domains such as language, executive function, or memory. A challenge we have encountered is how to connect these commonly described cognitive domains to functioning on the side of the organism. We see this as an ex-

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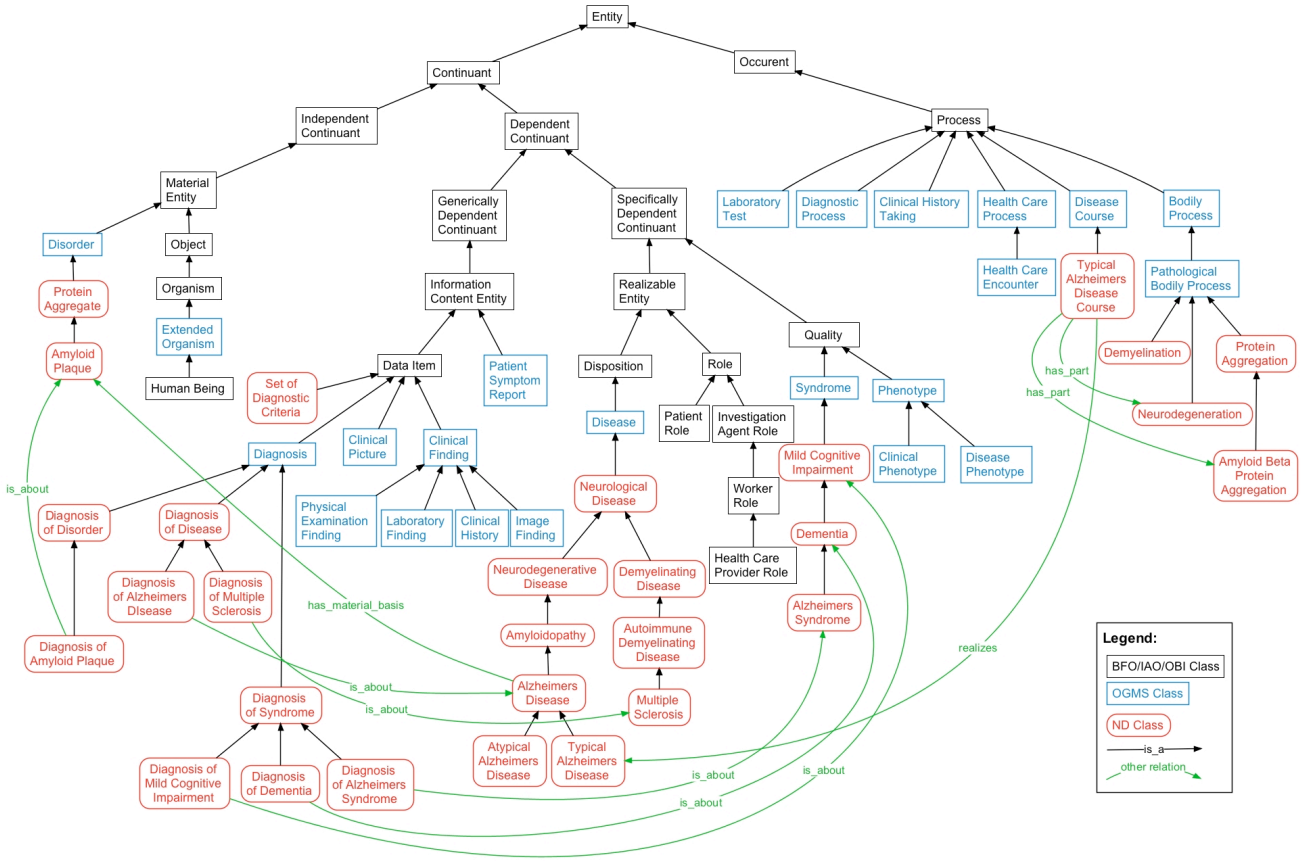

Figure 1: A subset of OGMS and ND and some connections to external ontologies.

cellent opportunity to connect ND and NPT with work in the Mental Functioning Ontology (MF) as well as with the Mental Disease Ontology (MD). Ideally we hope to drive development in both. For example, an extension of MD that represents dementia from the perspective of it being a mental disease or syndrome could then be linked via logically defined relations to classes in ND.

We plan to build ND over the long-term in a collaborative manner with other groups focused on representing particular neurological diseases as modules within ND. Our work is intended to be OBO-Foundry compliant and builds upon the paradigm established by Ontology for General Medical Sciences (OGMS) for the representation of entities in the domain of medicine and disease (Scheuermann et al. 2009).

2 METHODS

ND and NPT are being curated using both top-down and bottom-up approaches to the creation of classes within the ontology. A major aspect of the top-down approach for ND has involved analyzing what types of neurological diseases exist and how they ought to be represented within the ontology according to their relevant characteristics. Of some concern is how our strategy will fit with other disease ontologies. A key element includes deciding what other types of entities should be represented in ND in order to accurately represent the neurological diseases as well as how the relationships between these classes should be represented. For instance, the class 'neurological disease' currently includes 'neurodegenerative disease', 'infectious neurological disease', 'demyelinating disease', and 'vascular neurological disease' as four of its subclasses. The inclusion of these subclasses was driven by our decision to focus, as much as possible, on representing neurological diseases from the perspective of their etiology. For example, it is part of the logical definition for 'neurodegenerative disease' that all realizations of these diseases involve some process of neurodegeneration. This top-down approach provides ND with its primary structure.

Due to the complex nature of neurological diseases, as well as the diversity of perspectives from which they are studied and classified, we have also included additional immediate subclasses of 'neurological disease'. For example, 'central nervous system disease' and 'peripheral nervous system disease' are included as subclasses of 'neurological disease'. Currently we do not explicitly assert any disease

as a subclasses of these classes, however ND is being built using axioms that will allow an ontological reasoner to automatically create an inferred hierarchy of neurological disease types based on anatomical structure or genetic basis. This approach allows ND more versatility without committing it to a single perspective or creating confusion by switching between perspectives within the asserted hierarchy. Another example of this approach is creation of the defined class 'disease resulting in dementia', which has a limited number of asserted subclasses, and was created to provide a reference class from which to allow a reasoner to infer a hierarchy of all diseases that result in dementia.

While the top-down aspect of the project is essential to shaping the development of ND, it is the bottom-up aspect of the project that provides the bulk of the information. In particular, it is this approach that results in the creation and refinement of the definitions for terms in ND. We have consulted primary research articles, review articles, medical professionals, and other sources to inform the development of ND. This process has led to the inclusion of new terms in ND as well as more detailed classifications of particular neurological diseases. Both approaches are necessary for the completion of the project.

Development of NPT is based upon analyses of neuropsychological tests to drive the development of classes for the representation of neurological assays and their results. Many neuropsychological tests have multiple subtests, and these are being captured within the ontology as well. Neuropsychological tests assay domains such as verbal and visual-spatial memory, executive function, and linguistic functions. NPT is being developed to allow the integration of scores from different neuropsychological tests and subtests so that results for patients who have been tested using different protocols can be queried and grouped appropriately.

ND and NPT are built using Protégé 4.1 as OWL2 ontologies. The importation of classes from other ontologies according to the MIREOT standard has been achieved using OntoFox (Xiang, 2010).

Both ND and NPT are being developed according to OBO Foundry principles (Smith *et al.*, 2007) and is being done in cooperation with the related efforts to develop ontologies for representing Mental Disease (MD) and Mental Functioning (MF) (Hastings *et al.* 2012a and 2012b).

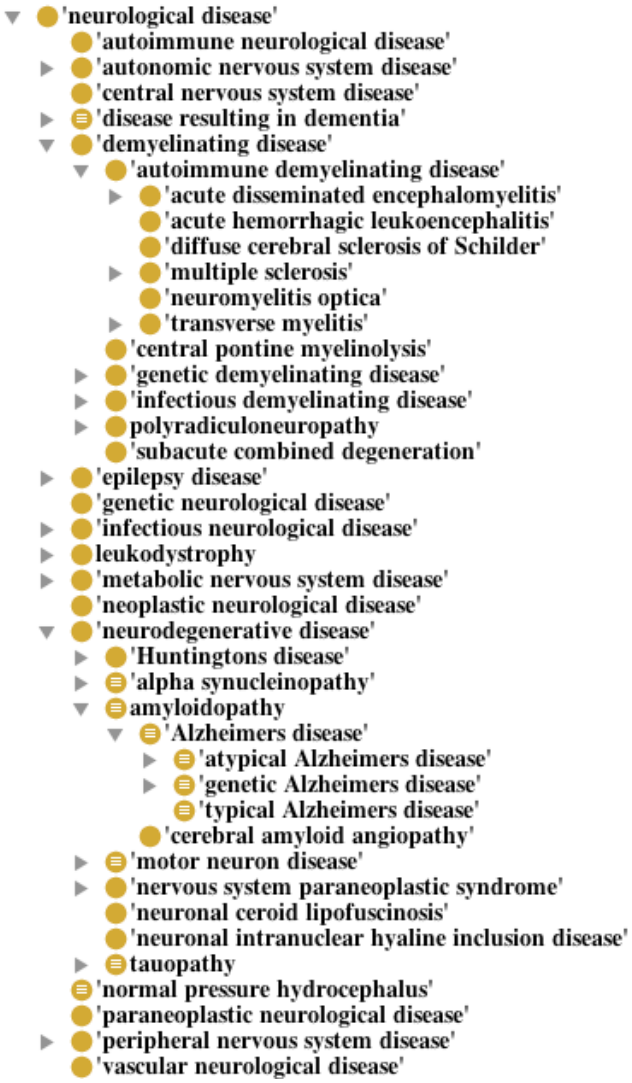

Figure 2: A portion of the ND disease hierarchy.

3 RESULTS

The Neurological Disease Ontology is being built according to OBO Foundry principles as an extension of OGMS, which provides a set of general reference classes related to diseases, their patients, and diagnoses (Scheuermann *et al.* 2009). OGMS follows the paradigm of the Basic Formal Ontology (BFO). Figure 1 illustrates the layers of granular-

Ontology Name	Use in ND
Basic Formal Ontology (BFO)	Top-level reference ontology
Ontology for General Medical Sciences (OGMS)	Mid-level reference ontology
NIF-Dysfunction *and* Disease Ontology (DO)	Externally referenced disease classes
Relation Ontology (RO)	Imported relation types
Protein Ontology (PR)	Select classes for proteins imported via MIREOT
Foundational Model of Anatomy (FMA)	Select classes for anatomical structures imported via MIREOT
IAO, PATO, ChEBI, GO, CL, and OBI	Select classes imported via MIREOT

Table 1. External ontologies used by the Neurological Disease Ontology.

ity captured by the relations between ND, OGMS, and BFO as well as IAO and OBI. Furthermore, we are ensuring that ND is compliant with the pre-release revised version of BFO – BFO 2.0, and the revised version of OGMS that is also compliant with BFO 2.0.

In building ND, we have relied upon a number of sources, including reference works, review articles, and other ontologies, such as NIF-Dysfunction and the Disease Ontology (DO) (Bug *et al.,* 2008; Larson & Martone, 2009). Based on these sources we have curated a high-level disease hierarchy that we believe presents a useful initial approach to categorizing neurological diseases, a section of which is shown in Figure 2. We go beyond earlier efforts at creating disease ontologies by providing textual definitions for every disease class and by incorporating logical definitions in order to relate classes for diseases and other entities in ND to other classes in ND and to separate ontologies (See Table 1 for a summary).

These high level disease classes provide a framework for the in depth curation of ND ontology modules intended to represent neurological diseases in extensive detail. At the University at Buffalo, our initial efforts are focused upon the areas of Alzheimer's disease and other diseases resulting in dementia, multiple sclerosis, and stroke and cerebrovascular disease. As an early stage ontology development project, ND currently contains approximately 400 classes; about 250 classes have textual definitions; more than 50 classes have logical definitions; more than 150 classes have external references; and there are nearly 200 children of the class 'disease'. In addition to disease classes, ND has a heavy focus on diagnosis, syndrome, disorder, and protein classes among others in order to fully represent all of the various aspects of neurological diseases.

In building NPT we have relied upon source tests, such as the Folstein Mini-Mental State Exam, as well as upon textbooks and articles about particular neuropsychological tests (Lezak *et al*., 2004; Mitrushina *et al.*, 2005). NPT is built using the schema for representing assays that has been developed in OBI and consequently currently imports all of OBI. At a later point, we will rely upon a slimmed (MIREOTed) version of OBI. At the moment, there are more than 250 NPT specific classes, but we expect this to grow quickly as we add representations of additional neuropsychological tests. Figure 3 shows a portion of NPT for the representation of the MMSE.

4 DISCUSSION

Our use cases in building these ontologies include annotation of clinical studies in neurology as well as annotation of patient records. Particularly for the latter case we expect ND and NPT to complement each other, with ND providing terms for representing the diagnoses of patients based on their signs and symptoms, and associated phenotypes. NPT will provide a very detailed set of classes for annotation of neuropsychological measures that may be used in the formation of a patient's clinical picture, which is used to reach a diagnosis. These diagnostic conclusions are annotated as an

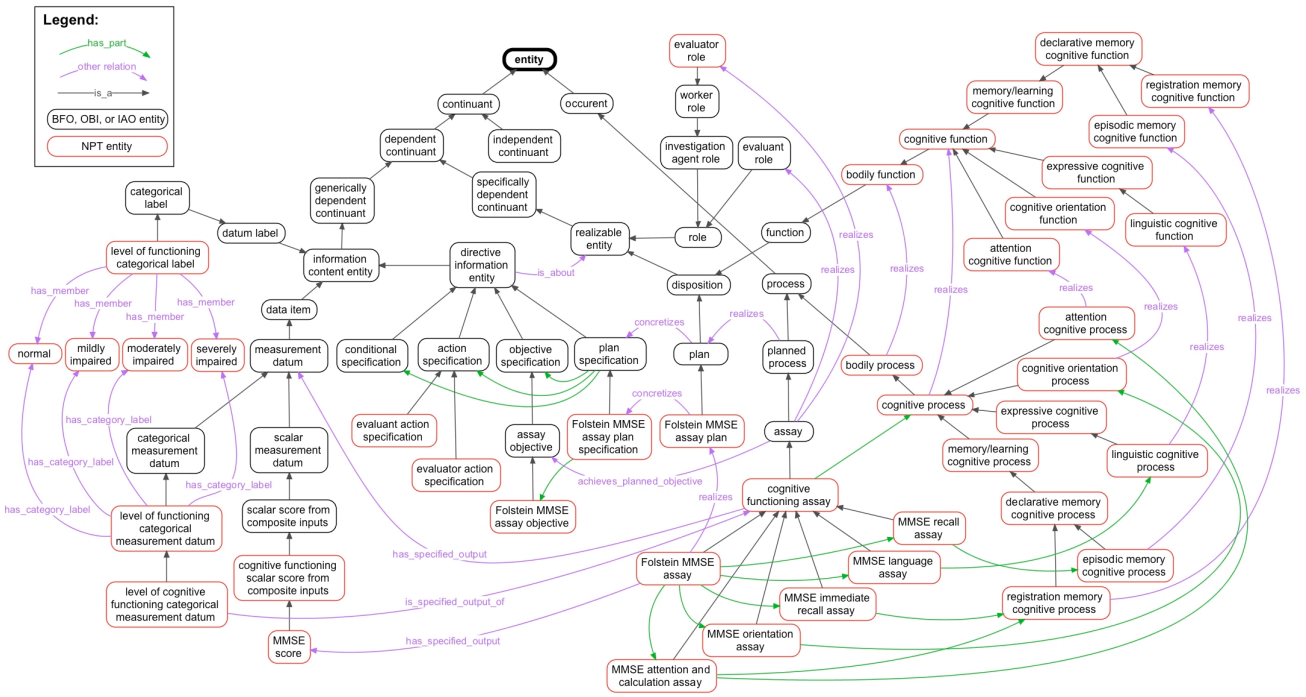

Figure 3: A portion of the representation of the MMSE assay in NPT.

instance of a diagnosis class in ND. The diagnosis classes are linked to the disease classes in ND, which themselves link via their logical definitions to other classes in ND such as the disorder which serves as the material basis of the disease, and then, in turn, to other ontologies such as PR.

In developing ND and NPT we recognize the need to coordinate with other ontology development efforts in related domains. In Ceusters and Smith (2010), for instance, the framework for what are now named the Mental Functioning Ontology (MF) and the Mental Disease Ontology (MD) was presented. Neurological diseases by their very nature often affect cognitive and mental functioning, for instance in any disease that results in dementia, such as Alzheimer's disease, and often lead to mental diseases, such as depression in MS or epilepsy patients. In developing ND we will need to ensure representation of conditions such as dementia or depression are coordinated with MF and MD, such that a class representing a clinical phenotype of "depression in conjunction with multiple sclerosis" may have a parent class of "depression" in MD. Moreover we feel that our work can aid in a bottom-up approach to developing MD and MF.

Furthermore, we believe our work on NPT will be valuable for the annotation of neuropsychological data not just for patients with neurological disease, but also for studies of general mental functioning and in testing in patients with mental diseases. Thus, our work on NPT will hopefully prove of value for a number of related domains in addition to that of neurological diseases, and will eventually be complemented by ontologies for other types of assessments of nervous system function and anatomy, such as an MRI imaging ontology.

ACKNOWLEDGEMENTS

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What is the relationship between cognitive experiments and cognitive processes?

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ABSTRACT

Human neuroimaging such as PET and fMRI are used to study cognitive function in human subjects. The Cognitive Paradigm Ontology builds on the experience of the BrainMap database in describing and storing cognitive neuroimaging experiments, to present a basic ontology of experimental paradigms, conditions, stimulus types, and related terms. The relationship between the cognitive experiment and the behavioural domain or cognitive process under study, however, is left undefined. We present some considerations about this possible relationship, based on the fact that an experiment is an operationalization of many levels of inference. Cognitive experiments have hypotheses about cognitive process, the physical conditions of the experiment which in part operationalize those hypotheses, results which summarize the physical outcomes, and interpretations which link the physical outcomes to the models of cognitive processes. Pragmatically, this complexity has led to experimental databases tagging experiments as being "about" various cognitive domains and behaviours, while leaving the precise relationship open-ended.

1 INTRODUCTION

Cognitive neuroscience is an experimental discipline that establishes correspondences between brain structure and brain function through the integrated application of experimental psychology, human neuroscience, and non-invasive neuroimaging. Cognitive neuroscience is a highly productive, rapidly growing research field that aims to localize the underlying neural systems in virtually every mental domain. In the last two decades, research in cognitive neuroscience has resulted in an enormous amount of functional magnetic resonance imaging (FMRI) and positron emission tomography (PET) data. Functional brain mapping is being pursued in healthy populations, as well as patients with neurological or neuropsychiatric disorders.

This scientific enterprise has spawned several efforts to facilitate integrating the vast array of results and publications regarding brain function under different conditions and diseases. The BrainMap database (www.brainmap.org, (Fox et al., 2005; Laird, Lancaster, & Fox, 2005)) is one of the oldest and best-curated of the efforts to pull together human neuroimaging results for ease in comparison across papers. It has developed a basic, hierarchical tagging schema for experimental results which has evolved into a data model of experiment, contexts, and behavioral domains. This model formed the backbone for the Cognitive Paradigm Ontology (CogPO; (Turner & Laird, 2012)). CogPO builds on BrainMap by making explicit the experimental paradigm terms, definitions, and their relationships.

CogPO works within the context of BFO, RO, and the Information Artifact Ontology (IAO); the full details are explained in (Turner & Laird, 2012). In summary, the model is that a *Behavioral Experimental Paradigm* is a *planned process* which has_part at least two *Behavioral Experimental Paradigm Conditions*. The subclasses of paradigms are often well-known, named experimental paradigms such as the Stroop experiment, the Sternberg experiments, Auditory Oddball, etc. An experimental condition consists of the stimulus type presented to the subject (e.g., a dimly flashing light or moving random dots), the response the subject is supposed to give (e.g., pushing a button), and the instructions given to the subject for that condition (e.g., lie quietly or make a decision about the stimulus). Each stimulus and response also has a modality, such as the visual modality for a dimly flashing light, and the use of the hand or foot to push a button.

The BrainMap schema includes all the CogPO terms as annotations for the papers and results it includes. While not explicit in CogPO, the relationship between the data and the experiment can be modeled as in the Ontology of Biomedical Investigations (OBI; (Brinkman et al., 2010)); the data are the outcome of the planned process. There has not been a need to date to model that relationship more thoroughly (see, however, the NEMO model for a more explicit representation; http://nemo.nic.uoregon.edu/).

With relevance to mental function, however, BrainMap also includes an initial taxonomy of behavioral domains, or cognitive processes (see Figure 1). Each experiment in the database is related to a behavioral domain, based on the judgment of the human curators; the behavioral domains and subdomains have evolved both from a priori understanding of cognitive science, and as needed by the literature. It is neither complete nor fully defined, and is open for expansion if new experiments do not fit these categories. Each experiment is tagged with one or more of these behavioral domains. The precise relationship between the experiment and the cognitive process under study, however, is not currently defined in CogPO or other ontologies. At the moment, the best guess is that the data from that experiment

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"is about" that behavioral domain, with no further constraints. In attempting to make that relationship more precise, several issues arise.

2 COGNITIVE EXPERIMENTS

Cognitive experiments do not arise in a vacuum; they are designed to answer a scientific question, usually. That scientific question assumes a certain framework for thinking about cognitive processes. A basic example from psychophysics is an experiment to measure how bright a light has to be before someone can see it. This is a basic sensory perception example about the limits of the visual system: a light of varying intensity in a dark room, a human with a button to indicate whether or not they saw it--the experiment doesn't get much simpler. But questions exactly like that have spawned decades of development in signal detection theory, because the link between internal processes and external behavior is convoluted. In cognitive neuroscience, where we include the covert physiological response of the brain in the experiment, in concert with the individual's overt response, the links become even more complex.

2.1 Cognitive processes and behavior

In the psychophysical example above of the limits of light detection, a classic experiment would be to have a healthy human subject sit in a completely dark room for 15 minutes or more; then with their head fixed, so that the light was always aimed at their eye, lights of varying intensity would be flashed, and the subject would indicate if they saw the light. Assuming a subject who is not malevolent but actually trying to do the task, the proportion of times the subject reports seeing each light level is an increasing function of the intensity of the light. At very low levels, the subject will never report seeing the light; at very high levels, they can't miss it and will always report seeing it. In the middle, there is uncertainty—from the subject's point of view, many times they aren't sure if they saw it or not, and they have to guess. And that is where the link between external measures (did they report detecting the light) and internal processes (they actually perceived it) becomes complicated. It becomes a probabilistic relationship.

The actual "threshold of detection" is usually inferred to be the light level at which subjects are reporting seeing it 50% of the time. But that threshold can be manipulated with incentives; the subject can be induced experimentally to be very conservative and only report detection when they are very sure the light flashed, or to be biased to be much more willing to indicate detection. The threshold has to be noted as being measured using a certain experimental design and biasing system (for review, see (Macmillan & Creelman, 2004)). The context of the experiment can move the measured threshold; so we have to update our model of the links between external measurement and internal detection threshold to take that into account.

2.2 Cognitive processes and physiology

Within an fMRI experiment, the relationship between behavior and the cognitive process is often assumed, while the relationship between the cognitive process and brain metabolism (highly indirectly measured, by the Blood Oxygenation Level Dependent or BOLD signal) is what is being studied. Often the connection is fairly straightforward: Within some limits, the BOLD signal increases with increasing light intensity in primary visual areas (Goodyear & Menon, 1998), and with increasing rate of finger-tapping in the motor cortex (Rao et al., 1996), and with increasing number of items to remember, in the dorsolateral prefrontal cortex (Potkin et al., 2009). However, in many other cases it is less clear: In an auditory oddball task, for example, the subject hears a stream of repeating tones, and every so often a different, target tone occurs (the oddball), to which the subject is supposed to respond by pushing a button. The auditory cortex BOLD signal usually increases for the target or oddball tone; in patients with schizophrenia, however, that BOLD signal increase is consistently reduced. Their performance in responding to the oddball tones is equivalent to healthy subjects, indicating they hear the tone. But the link between internal perception and the BOLD signal is broken, and the precise nature of that relationship is of course the subject of research.

2.3 The cognitive experimental framework

2.3.1 Hypotheses

An experiment usually is cast having a hypothesis, or at least a question, about the cognitive process being studied. We want to know the limits of visual sensitivity, or the effects of emotional shock on memory, for example; the questions we ask are formed within the context of current scientific understanding, and our models of cognitive processes. It does not make any sense to ask about how different odors are processed visually, for example; within the framework we use to understand how sensory cognition works, odors are not included in visual processing. They can affect emotions, they can drive memory retrieval, they can enhance attention to visual detail; but they are not part of the accepted model of visual processing. The relationship between the experiment and cognitive processes is formed in part by how we model cognitive processes.

2.3.2 Operationalizing

The experimental conditions are the embodiment of the test of the hypothesis. We have a hypothesis, e.g., that short-term memory is impaired in emotional situations. We create several conditions of various emotional and non-emotional situations, and we ask people to do something—Push this button if this is an item you've seen before (memory). The

implicit assumption is that the number of correct responses will be decreased, or the speed of the response will be slower, or both, when memory is impaired; that is the operationalization of impairment. That operationalization works off the assumption that the emotional situation does not affect visual processing, for example, but that the results are specific to memory function. For the effects of emotional manipulations on behavioral domains other than memory, we might ask something else--Respond as quickly as possible when the arrow appears (attention). Name the color, don't read the word (executive function). Choose which person you'd rather talk to (social cognition). In each case, we measure the overt behavior against the variation experimental conditions which we control, and within our assumed framework about how that links to cognitive processes, we use those results to draw conclusions about the processes we are studying.

2.3.3 Analysis

The "use" of the results, the next step after data collection, is a formative step in linking experiments to cognitive processes. Few cognitive experimental papers simply report results by subject, without attempting to summarize the data in some way. The simple choice of whether to report a mean or a median reflects what kind of response the subjects were asked to give and our understanding of what kind of scale that response should be measured on, and what is the best measure of central tendency for that response (Stevens, 1946). That theoretical framework is just part of what underlies the choice of statistical summaries and analyses we do on the results, even if it is an unquestioned, standard analysis that many research groups use.

2.3.4 Interpretation

The final step is linking the results back to the cognitive processes: In the emotion and memory example, suppose the number of correct responses in the emotional situation was less than in the non-emotional situation, and under the assumptions used in the analysis, it was a difference that is unlikely to have arisen by chance. Or using a non-parametric approach such as bootstrapping, the difference was again fairly extreme and unlikely to have happened randomly. The conclusion would likely be written up for scientific publication as evidence that short-tem memory is impaired in emotional situations—with a long list of caveats, limitations on the interpretations, and suggestions for follow-up experiments (i.e., new hypotheses), all of which reflect our understanding of cognitive processes, their characteristics, and the links between external observables and internal processes.

3 DISCUSSION

The question in the title is really asking ontologists to summarize all of the scientific method in one simple relationship. Our underlying model of cognitive processes, their characteristics, limitations, and connections to external observables such as behavior and physiology, is certainly not captured by a simple taxonomy of the sort that BrainMap uses. Hence, we simply tag experiments with behavioral domains or cognitive process labels and a catch-all relationship "is about". The full modeling of the context of cognitive experimental design requires considering hypothesis identification, operationalization, analysis, and interpretation, and will have to develop in concert with the modeling of our understanding of the characteristics of and relationships among cognitive processes.

Fig. 1. The current behavioral domains and their subtypes as used in the BrainMap schema.

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Representing mental functioning: Ontologies for mental health and disease

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ABSTRACT

Mental and behavioral disorders represent a significant portion of the public health burden in all countries. The human cost of these disorders is immense, yet treatment options for sufferers are currently limited, with many patients failing to respond sufficiently to available interventions and drugs. High quality ontologies facilitate data aggregation and comparison across different disciplines, and may therefore speed up the translation of primary research into novel therapeutics.

Realism-based ontologies describe entities in reality and the relationships between them in such a way that - once formulated in a suitable formal language - the ontologies can be used for sophisticated automated reasoning applications. Reference ontologies can be applied across different contexts in which different, and often mutually incompatible, domain-specific vocabularies have traditionally been used. In this contribution we describe the Mental Functioning Ontology (MF) and Mental Disease Ontology (MD), two realism-based ontologies currently under development for the description of human mental functioning and disease. We describe the structure and upper levels of the ontologies and preliminary application scenarios, and identify some open questions.

1 INTRODUCTION

Mental disorders are common in all countries, representing a significant portion of the public health burden. In the US, about one in four adults is diagnosed with a mental disorder in a given year, and about one in seventeen is thought to suffer from a serious and disabling mental illness. Mental disorders are the leading cause of disability in the United States and Canada for persons aged 15 to 44 (National Advisory Mental Health Council Workgroup, 2010). The cost of these disorders is immense, affecting not only patients but also their caregivers, rendering adults unable to work productively, destroying relationships and increasing the financial burden on society. Treatment options for sufferers are currently limited, with many patients failing to respond sufficiently to currently available interventions, which include psychotherapeutic, somatic, and pharmacological actions. And, while there is enormous variance in individual responses to therapeutic agents, there is often little alternative for the clinician other than trial and error in determining the best treatment strategy for the patient's genetic, physiological, or behavioral profile.

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The volume of data, information and knowledge, both in patient records and in scientific literature, is steadily increasing. Computer-based methods able to harness such data are mandatory for supporting decision-making processes in the treatment of individual patients as well as in the interpretation of scientific findings. Whereas, traditionally, most relevant information has only been available as free text, machine processing increasingly requires the adherence to terminological standards (Freitas *et al.*, 2009). This need has been addressed by the development of controlled vocabularies such as SNOMED CT (International Health Terminology Standards Development Organization, 2012), and classification systems such as the International Classification of Diseases (World Health Organization, 2012) and the Diagnostic and Statistical Manual of Mental Disorders (DSM) (APA, 2000). DSM provides not only a classification of disorders but also guidance as to the diagnostic criteria for these disorders in the form of checklists of symptoms, with counts of how many symptoms of a various sort are required for the condition to be diagnosed. The DSM is currently in its fourth revision, but the fifth revision is scheduled for release in May 2013 (Regier *et al.*, 2009), and a draft version of the revisions have been released for public review at `www.dsm5.org`. Some issues that the revision will try to address are a high occurrence of co-morbidity of disorders according to the diagnostic criteria and the high use of 'catch-all' categories such as 'not otherwise specified'. To address these, the revision is expected to emphasize dimensional measures of symptoms that cross diagnostic category boundaries.

Terminology systems and controlled vocabularies address some of the requirements of computational support for data management, but in recent years a more powerful solution has become available in the form of formal ontologies. Realism-based ontologies are formalized descriptions that are based on scientific theories about the nature of entities in reality and the relationships between them (Smith, 2008; Munn and Smith, 2009; Rubin *et al.*, 2008). These ontologies may be expressed in a formal language and enhanced with standard identifiers, labels and definitions that are intended to facilitate unambiguous interpretation and annotation. A key advantage that such ontologies confer, over and above the mere standardization of terminologies, is that their underlying logical formalisms are natural language-independent and formally rigorous. This allows these ontologies to form the backbone of sophisticated automated reasoning applications, and to be applied across contexts

in which multiple competing domain-specific vocabularies have traditionally been used (Stenzhorn *et al.*, 2008). Especially in the domain of biomedicine, ontologies have found a broad acceptance.

In the next section, we will describe the structure and upper levels of the Mental Functioning (MF) and Mental Disease (MD) ontologies. Thereafter, we provide a preliminary listing of possible application scenarios for these ontologies. Finally, we identify some open questions in the ontology of mental functioning.

2 ONTOLOGY STRUCTURE AND CONTENT

2.1 Mental Functioning Ontology

Based on the Basic Formal Ontology (BFO, Grenon and Smith (2004)) and being developed in the context of the OBO Foundry (Smith *et al.*, 2007) library of interrelated modular domain ontologies, the Mental Functioning Ontology (MF, (Hastings *et al.*, 2012)) is a modular domain ontology aiming to represent all aspects of mental functioning, including mental processes such as cognitive processes and qualities such as intelligence. MF grounds mental functioning entities in an upper level ontology, and gives a framework within which mental functioning can be related to ontological descriptions of related entities in other domains such as neuroanatomy and biochemistry. Modules of MF that are actively under development are those for cognition, perception and emotion.

Figure 1 illustrates the upper levels of the ontology, based on the framework laid out in (Ceusters and Smith, 2010a), together with the alignment to BFO. At the top level, BFO introduces a distinction between continuants and occurrents. Occurrents are processes and other entities that unfold in time, i.e. entities that have temporal parts. Continuants, on the other hand, are those things that exist in full at all times that they exist, have no temporal parts, and continue to exist over an extended period of time. This distinction can be seen in the context of mental functioning between, for example, an organism, or a part of an organism's *anatomy*, that continues to exist over time (thus is a continuant), and an organism's *thinking process* that spans over a few minutes (unfolding in time) before it is completed (thus is an occurrent). Within continuants, BFO further distinguishes between those entities that are independent and those that are dependent. Independent continuants can exist by themselves, while dependent continuants are those sorts of things that need a "bearer" in order to exist, such as colours, social roles, or behavioral dispositions that are realized in behavior, an occurent entity. 'Functioning' is defined as the realization of a function, where a function is a special type of disposition that is realized in end-directed activity that is appropriate for the kind or kinds of contexts for which the bearer is designed or in which the bearer has evolved (Arp and Smith, 2008). In the domain of the mental, therefore, mental functionings are those mental processes that are realizations of functions; processes that have been positively selected for by human evolution. While cognition, remembering, and emotion can all be examples of mental functionings, examples of mental processes that are not functionings include the auditory perception involved in tinnitis and, contentiously, possibly dreaming (if dreaming realizes a function at all, which function it realizes is disputed).

The illustrated upper levels of MF show several important distinctions in the framework to annotate and describe mental functioning allowing interrelationships across a wide variety of different levels of description. The organism is the fundamental independent continuant in which mental functioning takes place. A mental

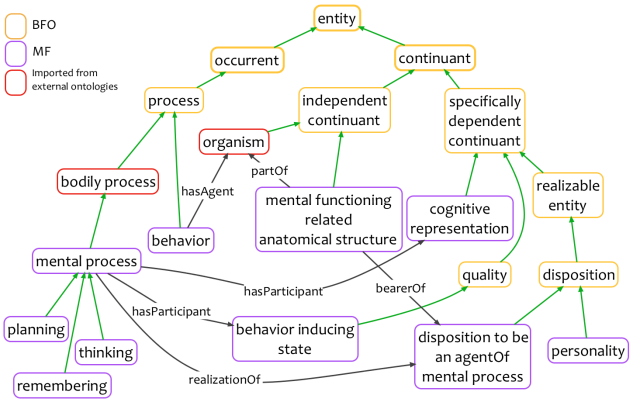

Fig. 1. The Mental Functioning Ontology upper level aligned to BFO. Unlabelled arrows represent subsumption relations.

functioning related anatomical structure is that part of an organism that bears a disposition to be the agent of a particular mental process. So, for example, the particular neuronal and biochemical configuration (i.e. the bona fide group of receptors and neurotransmitters (Ceusters and Smith, 2010b)) that gives rise to a particular person's feeling of sadness is a mental functioning related anatomical structure. Neurons and brain chemistry are themselves described as continuants in other ontologies such as CHEBI for the neurotransmitters, the Protein Ontology (PR, Natale *et al.* (2011)) for the receptors, and NeuroLex and BIRNlex (Bug *et al.*, 2008) for neurons and neuronal systems. These components can be linked together as parts of the corresponding mental functioning related anatomical structure, the boundaries of which are to be determined with the advance of our understanding of the neurobiology and neurochemistry of the physical basis of the various mental processes involved. The links from entities in MF to the known biochemical and neurobiological bases will be maintained in bridging modules, ensuring that different levels of granularity and description can be separately maintained. References to other vocabularies such as ICD and BIRNlex will be annotated in the ontology where applicable.

Dispositions are properties that inhere in their bearers and consist in the potential for certain processes in the bearer to occur when this bearer comes into the right circumstances, for example, a glass breaking when it is dropped onto a hard surface. An example of a disposition in the domain of mental functioning is human personality. Personality (or character) is the kind of thing that is realized in the behavioral interactions of a human being with the external world, along with characteristic patterns of thought, such as in task performance when learning new things. Personality may be measured by standardised tests (which are information content entities concretized in, for example, the paper assessment questionnaires handed out to subjects). Such tests - ideally - can be linked using something like a 'measures' relation to the representation of personality in MF.

On the side of occurrents beneath BFO, MF includes mental processes, which are defined as the processes that bring into being, sustain or modify cognitive representations. Cognitive representations are dependent continuants that specifically depend on the cognitive structures of an organism and contain cognitive content which can take the form of thoughts or memories, representing such

things as tables, people, smells, and colors. Mental processes – manipulating those cognitive representations – include all of the standard processual examples of mental functioning such as thinking, planning and learning or remembering. This is not say it is straightforward to formalize these common notions of the entities of mental functioning, but MF will focus as a major point of its development on providing the most accurate representation for these entities possible and appropriate at this level of description.

MF is being developed modularly, allowing different teams with different core areas of expertise to focus on the extension of the overall ontology to describe the entities relevant to their scientific area. One such extension is the Emotion Ontology (Hastings *et al.*, 2011), describing entities of relevance to all aspects of affective science. Another extension covers the domain of mental disease.

2.2 Mental Disease Ontology

The Mental Disease Ontology (MD) is a separate ontology module that aims to describe and categorize mental disorders based on the strategy outlined in (Ceusters and Smith, 2010a). MD extends not only the MF but also the Ontology for General Medical Science (OGMS). OGMS is designed to interrelate ontologies in the medical domain to support research on Electronic Health Record (EHR) technology and on the integration of clinical and research data. It provides definitions for 'disease', 'diagnosis' and 'disorder', among others, based on the terminology in (Scheuermann *et al.*, 2009).

Following OGMS, a mental disease is defined as a disposition to undergo pathological mental processes. A mental disease is a clinically significant deviation from mental health. Mental health is conformity of perception, emotion, and behavior internally and in relation to the external real-world environment. In contrast, pathological mental processes are those that hinder well-being. Thus, mental disease is a deviation from mental health that hampers the bearer in his or her mental well-being (Ceusters and Smith, 2010a). Figure 2 shows an extract of entities from MD for the domain of substance addiction, a mental disease characterised by substance use and phenomena such as tolerance, craving and withdrawal.

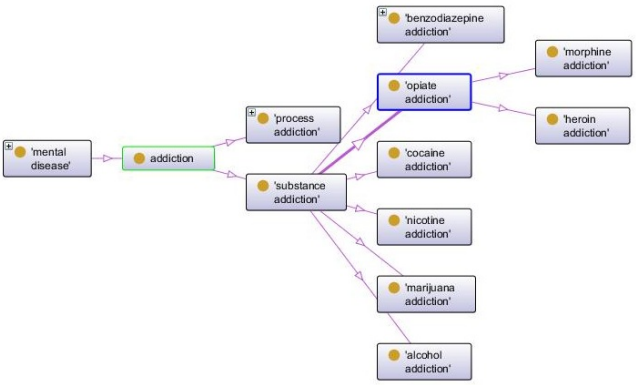

Fig. 2. Addiction in the Mental Disease Ontology.

For each mental disease, the ontology contains representations of the symptoms and signs that are manifested in the disease course, including pathological behavior. By differentiating a disease from a disease course and by explicitly representing symptoms and signs within a logically rigorous ontological framework that includes a definition for mental disease, MF aims to address some of the challenges that have been observed with the DSM approach, such as high levels of co-morbidity and the use of catch-all 'not otherwise specified' placements. The DSM approach, termed 'descriptive psychiatry', focuses on symptom assessment and confers disorder status on specified thresholds of symptoms in terms of counts of symptom types and tokens and durations of symptom episodes. For example, a major depressive episode is stated to be diagnosable if five of a set of nine symptoms are found to obtain within the same two-week period. Symptoms include 'insomnia or hypersomnia nearly every day' and 'fatigue or loss of energy nearly every day'. (Notice how these are not likely to be mutually exclusive.) The DSM-5 proposal has also been criticised for promoting medicalisation of *normal human experiences*: grief, a normal human emotion in response to bereavement, has been proposed as a type of depression, a mental disorder (Cacciatore, 2012).

One symptom of substance addiction, for example, is a preoccupation with use of the substance in question, a kind of non-canonical (i.e. not in accordance with the environment, not conducive to well-being) thinking process (since the organism is not able to control the thinking process as they would in canonical thinking processes). Furthermore, pathological (or non-canonical) processes are related to the canonical versions of those processes. This interlinking of symptoms to diseases and to canonical related processes in a computable framework allows bridging from research involving different diseases to research exploring ordinary functioning or underlying mechanisms. It also allows hypotheses of mechanisms underlying diseases to be made explicitly testable in terms of supporting data.

3 APPLICATIONS OF THE ONTOLOGIES

3.1 Standardisation

Ontologies are already widely used to facilitate *standardised database annotations* throughout the biomedical sciences. To be truly successful, this use case necessitates adoption of the principles of the OBO Foundry such as the use of semantics-free stable unique identifiers and the annotation of clear textual definitions for each entity in the ontology. Databases containing data that could potentially be annotated with mental functioning terminology include those in neuroscience such as BrainMap (Laird *et al.*, 2005), a curated database of functional neuroimaging research studies. Many more neuroscience databases are aggregated in the NIF webpages (Gardner *et al.*, 2008)). Beyond neuroscience, mental functioning annotations are of increasing relevance in systems biology contexts such as the BioModels database (Li *et al.*, 2010). Mental functioning is also particularly relevant for defining chemical influences in biological systems, as done in ChEBI (de Matos *et al.*, 2010).

An additional context where standardisation is of paramount importance is in the organisation and maintenance of biobank data in which human samples are stored for purposes of clinical research (Krestyaninova *et al.*, 2011). Often, in order to research underlying mechanistic factors in rare diseases, samples from patients bearing the condition may need to be sourced from multiple biobanks in multiple countries or regions. Traditional systems which use local (language and country-specific) terminologies to annotate the sample databases will certainly not be straightforward to integrate and search across different sample collections. It is even more difficult to interrelate sample data with EHR data and with known indicators

in medical and biological knowledgebases such as those collecting annotated genetic sequence information.

3.2 Behavioral and Cognitive Testing

Neuropsychological and psychometric tests are designed to obtain information about brain functioning through behavioral expressions to determine the kind and dimension of dysfunction present in a subject. These tests have putative links to various cognitive domains like attention, language, episodic or semantic memory, executive function, as well as general intellectual functioning, etc. (Lezak *et al.*, 2004). Tests are typically used as part of the clinical picture that a physician develops to make a diagnosis in cases of patient injury, neurodegenerative diseases like Alzheimer's disease and related dementias or deliriums, or paradigmatic mental diseases such as dissociative or autistic spectrum disorders. The Neuropsychological Testing Ontology (NPT) is currently under development to represent many of these test procedures by describing the stimuli, methods and responses, along with associated plan specifications (Cox *et al.*, 2012). These need to refer to mental functioning.

3.3 Population research: clinical questionnaires

Genetic and psychiatric population-wide research often relies on diagnostic interviews which standardise the collection of data into aspects of psychiatric functioning such that the data can be compared and aggregated across large groups of patients. In the domain of mental functioning, this is a particularly pressing problem since many aspects of mental functioning are not directly observable, and the assessment of mental functioning therefore relies on the subjective assessment of the trained practitioner and on self-reports by the patient, who of course has no access to alternative experiences of mental functioning other than his/her own. Standardised questionnaires are thus an essential element of population research into mental functioning. An example of such a questionnaire is the Diagnostic Interview for Genetic Studies (Nurnberger *et al.*, 1994), a questionnaire used in clinical interviews to assess major mood and psychotic disorders and related spectrum conditions. Linking the symptoms assessed in such questionnaires to ontologies of mental functioning provides the capability to standardise the collected data across multiple such questionnaires. Furthermore, it allows multi-level aggregation, rather than only aggregation at the level of whether a particular disorder is diagnosed or not – which in some cases may obscure rather than illuminate shared underlying mechanisms and pathologies.

A concrete example here is a project funded by the National Institutes of Health (NIH) designed to obtain better insight into the complexity of pain disorders, specifically concerning the assessment of different pain types in the orofacial region, as well as into pain-related disablement and its association with mental health and quality of life. Five existing data collections compiled independently from each other have been made available for this study. The data collections cover the same domain, but are distinct in various respects: (1) some variables are identical across collections, others involving, for instance, somatization, depression and anxiety, are different because measured with in total 22 distinct assessment instruments; (2) these instruments contain each between 50 and 500 unique assessment items, but, although frequently sharing intent, do not share a similar presentation across forms, supporting detail, instructions regarding the sources of information that can be used to complete each item, or severity/frequency response scales that are comparable across instruments; (3) because of their distinct origins, the data collections incorporate cultural influences related to pain report that have an impact on the comparability of the collections, despite the use of common instruments. One specific aim of the project is to make these data collections comparable by building a realism-based reference ontology for pain-related disablement, mental health and quality of life (OPMQoL) following the principles of Ontological Realism (Ceusters, 2012).

3.4 Translational research

Increasing the speed and throughput of the translation of primary research in brain and mind science into novel therapeutic agents, and ultimately clinical interventions, has been highlighted as a pressing current concern for mental health research and practice (National Advisory Mental Health Council Workgroup, 2010). However, this effort is hindered by the disconnect between the different communities involved in primary research and the different levels needed for the translation into therapeutics. Understanding the processes involved in mental disorders requires research and integration of knowledge across all the different levels of life science, from the most fundamental such as genetic and biomolecular, through medical, brain and neurosciences, to the psychological and psychiatric perspectives which focus on the behavioural and functional aspects. Recent breakthroughs in basic science in all of these different levels have the potential to be exploited towards novel interventions and therapeutics, but severe obstacles remain in the path of translation, and there is still a resulting shortage of new agents and approaches in the therapeutic pipeline (National Advisory Mental Health Council Workgroup, 2010). Most importantly, ontologies offer a common language that enables automated bridging between different disciplines, facilitating translation as research becomes increasingly interdisciplinary. Furthermore, sophisticated querying and hypothesis testing frameworks are able to be developed around the ontologies.

4 OPEN QUESTIONS

A core open question for any effort to create an ontology for mental functioning is in how to relate descriptions at the level of the *brain* with descriptions at the level of the *mental functioning*. While most modern biomedical researchers reject extreme views such as mind-body dualism or outright eliminativism in favour of some form of pragmatic embodied cognition, nevertheless the question of the nature of the ontological relationship between mental functioning entities and the purported corresponding brain processes is disputed. The realism framework that MF is based on does not imply physicalist reductionism, since we allow that there are mental functionings which can be experienced in the first person, and which are first-class entities in their own right.

The precise nature of the physical and neural basis for a mental process is the subject of neuroscientific research, an appropriately empirical question. MF aims to offer a framework within which different types of empirical data can be compared as evidence for different theoretical models. The problem of linking different levels becomes more detailed when different levels of brain description are considered – there is brain anatomy, brain activity as measured by various different technological platforms, neuronal systems, neuronal, and synaptic electrical and biochemical activity. Each of these

different levels of description need to be categorised and related to the description of the mental functioning of which they are a part.

Our approach follows that of (Ceusters and Smith, 2010a) in that the definition of mental disease as "a clinically significant deviation from mental health [...] that hampers the bearer in his or her mental well-being." Determining what counts as a clinically significant deviation from mental health can be challenging, as this can differ depending on the environmental context. Another open challenge is that it is not possible to straightforwardly link symptoms, such as behaviour, to the diseases that they are indicative of, since such symptoms are usually not necessary conditions for the disease (except in the case of markers). A challenge for MD and MF will be to provide bridging modules that reconcile these aspects.

5 CONCLUSION

The ontology efforts that we have described aim to place mental functioning in a central role within a broader evolving biological and medical scientific context. Ontologies show great potential for addressing many of the challenges of data management and data-driven research in the post-genomic age of computer-assisted science. However, to be successful such ontologies have to be adopted by a wide, diverse community of users across different but overlapping domains. We have highlighted some use cases where adoption of the ontologies described could lead to benefits, and raised some open questions where we believe interdisciplinary discussions would contribute to the evolution of the framework.

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Annotating affective neuroscience data with the Emotion Ontology

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ABSTRACT

The Emotion Ontology is an ontology covering all aspects of emotional and affective mental functioning. It is being developed following the principles of the OBO Foundry and Ontological Realism. This means that in compiling the ontology, we emphasize the importance of the nature of the entities in reality that the ontology is describing. One of the ways in which realism-based ontologies are being successfully used within biomedical science is in the annotation of scientific research results in publicly available databases. Such annotation enables several objectives, including searching, browsing and cross-database data integration. A key benefit conferred by realism-based ontology is that suitably annotated research results are able to be aggregated and compared in a fashion that is based on the underlying reality that the science is studying. This has the potential of increasing the power of statistical analysis and meta-analysis in data-driven science. This aspect has been fruitfully exploited in the investigation of the functions of genes in molecular biology.

Cognitive neuroscience uses functional neuroimaging to investigate the brain correlates of areas of mental functioning such as memory, planning and emotion. The use of functional neuroimaging to study affective phenomena such as the emotions is called 'affective neuroscience'. BrainMap is the largest curated database of coordinates and metadata for studies in cognitive neuroscience, including affective neuroscience (Laird *et al.*, 2005). BrainMap data is already classified and indexed using a terminology for classification, called the 'Cognitive Paradigm Ontology' (CogPO), that has been developed to facilitate searching and browsing. However, CogPO has been developed specifically for the BrainMap database, and the data are thus far not annotated to a realism-based ontology which would allow the discovery of interrelationships between research results across different databases on the basis of what the research is about. In this contribution, we describe ongoing work that aims to annotate affective neuroscience data, starting with the BrainMap database, using the Emotion Ontology. We describe our objectives and technical approach to the annotation, and mention some of the challenges.

1 INTRODUCTION

Research in affective science faces the need to integrate results obtained on the basis of subjective reports with those obtained through different sorts of scientific experimentation, and to compare results across disciplines. Even within each discipline and methodological paradigm, data are distributed across multiple databases and the primary literature. Efforts to harmonize the schemas and vocabularies used to describe such data have thus far not been very successful (Derrfuss and Mar, 2009).

Currently, therefore, it is impossible to automatically retrieve and reconcile data relevant to a given research question across multiple data sources. Such integration depends on the existence of (1) a shared, disambiguated and clear reference terminology for the domain (Frijda and Scherer, 2009; Scherer, 2005), and (2) a realism-based reference ontology that provides a formal description for how terms in the terminology relate to entities in reality (Smith and Ceusters, 2010). To address this requirement, we are developing the Emotion Ontology, a specialization of the Mental Functioning Ontology (MF, Hastings *et al.* (2012). MF is an overarching modular domain ontology that aims to represent all aspects of mental functioning, including mental processes such as thinking and mental qualities such as intelligence. It is based on the Basic Formal Ontology (BFO) (Grenon and Smith, 2004) and is being developed in the context of the OBO Foundry (Smith *et al.*, 2007), following the principles of Ontological Realism (Smith and Ceusters, 2010).

Ontologies are widely used for database annotation to enable searching, browsing and cross-database integration (Stevens and Lord, 2009; Smith *et al.*, 2007). A key benefit conferred by realism-based ontology is that suitably annotated research results are able to be aggregated and compared in a fashion that is based on the underlying reality that the science is studying. This has the potential of increasing the power of statistical analysis and meta-analysis in data-driven science, an aspect that has been particularly fruitful in the investigation of the functions of genes in molecular biology (Azuaje *et al.*, 2006; Hill *et al.*, 2008). We believe that the annotation of research results in affective neuroscience with the Emotion Ontology will similarly yield the potential for novel ontology-based analysis methods to be developed. This contribution describes our ongoing efforts towards realizing this objective.

The remainder of this introduction gives an overview of the Emotion Ontology and the BrainMap database for which annotations are initially being proposed. Thereafter, in our Methods section, we describe the structure of the proposed ontology annotations, present a synopsis of the experimental methods used in affective neuroscience investigations, and describe how these will be used to determine the ontology type to which results are annotated. Finally, we highlight some open issues.

1.1 The Emotion Ontology

The Emotion Ontology (MFO-EM) is a module that extends the Mental Functioning Ontology (MF) with representations of those types that belong to the domain of emotions and, more broadly, affective phenomena. Figure 1 illustrates the upper levels of the ontology beneath relevant MF and BFO entities. Definitions of core

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terms are reproduced in the figure, but for reasons of space the interested reader is referred to (Hastings *et al.*, 2011) for a fuller description of the ontology structure and core terms.

Each aspect of the ontology from this upper level is then developed further with specific subtypes annotated and defined beneath them. Table 1 shows representative lower levels for some of the entities in the ontology. For example, specific subtypes of 'emotion occurrent' include 'anger' and 'grief'; specific subtypes of 'subjective emotional feeling' include 'feeling in control' and 'feeling energetic'; specific subtypes of 'appraisal' include 'appraisal of dangerousness' and 'appraisal of pleasantness'.

Emotion Occurrent	Subjective Emotional Feeling	Appraisal
anger	feeling alert	appraisal of causal agency
anxiety	feeling at ease	appraisal of causal intent
compassion	feeling bad	appraisal of dangerousness
contempt	feeling calm	appraisal of expectedness
despair	feeling energetic	appraisal of familiarity
disappointment	feeling good	appraisal of goal importance
disgust	feeling in control	appraisal of justice
embarrassment	feeling nervous	appraisal of loss
fear	feeling out of control	appraisal of pleasantness
grief	feeling restless	appraisal of predictability
guilt	feeling strong	appraisal of social attention
happiness	feeling tired	appraisal of suddenness
hate	feeling weak	appraisal of urgency
...	...	...

Table 1. Example expanded subtypes of upper level entities 'emotion occurrent', 'subjective emotional feeling' and 'appraisal'

Emotion types such as fear show enormous variance across instances, just as do anatomical types such as ear or jaw. Realism-based ontologies represent what is always the case. Thus, much of what is known about the different emotion types cannot be straightforwardly expressed in these ontologies, since they do not always occur in every emotion instance of that type. Not all persons experiencing fear have fearful facial expressions, not all instances of fear cause raised heart rate, and so on. To address this issue, following the strategy of the Foundational Model of Anatomy (Rosse and Mejino, 2003), we introduce 'canonical' emotion types, which represent the standard, normal or prototypical instance of a particular emotion type. As discussed in (Smith *et al.*, 2011) for the case of pain, canonical mental processes are congruent with their function, i.e. the purpose for which humans evolved to have processes of that type. Canonical fear thus involves an appraisal of dangerousness, while non-canonical fear, such as that caused by flowers in persons suffering from *anthophobia*, may obtain even in cases where the person is absolutely aware that the eliciting object is not dangerous, or that the potential danger of the eliciting object does not warrant the level of fear. 'Canonical fear' is thus a subtype of 'fear' in the ontology. The canonical emotion type can then be augmented with what is known about that emotion in terms of its components: canonical fear is associated with appraisals of dangerousness that are appropriate to the actual level of dangerousness of the situation or object elicitor, with action tendencies involving 'fight or flight' responses, with physiological responses such as feeling cold or sweating, and with characteristically fearful facial expressions. Each of these aspects of the canonical emotion confer an evolutionary advantage on the bearer, thus resulting in the development of the emotion in the way that it has developed. Note that appraisals in our ontology need not be strictly higher-order cognitive acts, that is, we allow for canonical fear also in animals such as primates and dogs (as described in Hastings *et al.* (2011), see also Robinson (2005)).

1.2 BrainMap

BrainMap is a curated database of functional neuroimaging research results, including functional and structural neuroimaging experiments with coordinate-based results (Laird *et al.*, 2005). Other such databases include SumsDB (Van Essen *et al.*, 2005) and the Brede database (Nielsen, 2003). These databases can be contrasted with automated approaches such as used by the NeuroSynth project (Yarkoni *et al.*, 2011), which harvests activation coordinates from the literature and associates them with the most frequent words appearing in the publication. This can lead to odd results, such as the word 'indeed' being significantly associated with a brain region. We have chosen to begin our annotation project with BrainMap as it is at present the largest and most comprehensively annotated of these functional imaging databases (Derrfuss and Mar, 2009).

The BrainMap database is curated from the primary literature. The curation involves capturing the activation coordinate results of neuroimaging experiments into the database together with the literature reference. BrainMap also provides supporting software and tools for sharing and analysing neuroimaging results. The primary objective of the database is to enable meta-analysis studies, and BrainMap is one of the projects that is at the forefront of the effort to share and redistribute neuroscientific research results as open data. The goal is to promote greater reuse and reproducibility of the results of publicly funded neuroscience research.

BrainMap is supported by a classification of experimental paradigms, the Cognitive Paradigm Ontology (CogPO) (Turner and Laird, 2012). Research paradigms in cognitive neuroscience are repeatedly applied across multiple experiments, in order to render the experimental results comparable, just as assay designs are repeatedly applied in chemical biology across multiple laboratories (Lane and Nadel, 2002). CogPO includes representations of such paradigms, including the stimuli presented (e.g. sounds, images), the instructions given (e.g. count to 10, try to discern the gender of a face in a photograph), and the responses requested (e.g. press a specific button). It also includes some terminology referring to some emotion types, e.g. 'anger' and 'fear', beneath 'behavioural domain'.

Since the domain of CogPO is experiments, its authors have attempted to align its upper levels to the Ontology of Biomedical Investigations (OBI) (Brinkman *et al.*, 2010). Despite this, CogPO is currently not being developed following the principles of ontological realism used by BFO and MF. One shortcoming, from this perspective, of the CogPO classification in its current form, is that it incorporates definitions for classes that are not true for all instances. For example, 'response' is defined as 'The overt or covert behavior which is elicited from the subject in an experimental condition'. At the same time, various behaviors such as blinking and swallowing are classified as 'overt response', thus as instantiating a type of response, yet many instances of such behaviors (indeed, the majority of instances) do not take place as responses in any kind of experiment. Another shortcoming is evident in that 'behavioral experimental paradigm' is classified as a planned process (i.e. an occurrent), yet the definition given for this term classifies paradigms as descriptions: paradigms are said to "describe ...

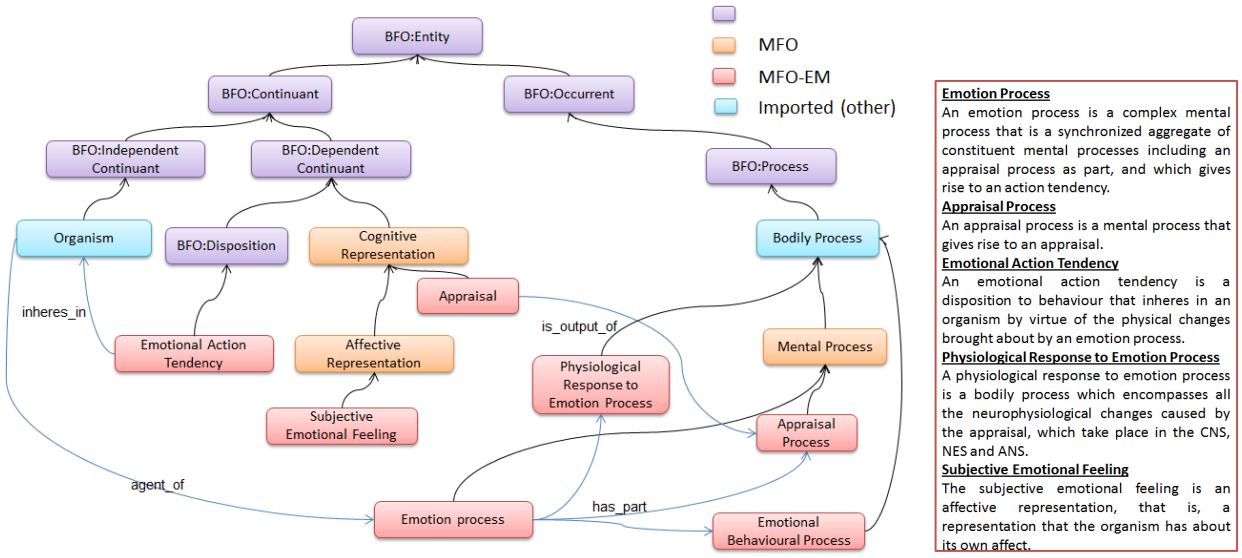

Fig. 1. An overview of the Emotion Ontology. Unlabelled arrows represent subsumption relations. For further detail, refer to (Hastings *et al.*, 2011).

behavioral aspects of the experiment". This indicates a confusion between information and what it is about. The focus of CogPO on experiments rather than on mental functioning, together with the mentioned shortcomings, render our effort in annotation of affective neuroscience information with the Emotion Ontology non-redundant. Furthermore, the implicit assumption behind the design of CogPO is that mental processes are not first-rate citizens in the ontology since they are unobservable. Our ontological realism admits mental processes as entities in their own right on the basis of the fact that they are first-person experienceable. The annotation of BrainMap with CogPO and with EM can, we believe, complement each other for the purposes of useful search and indexing of functional neuroimaging data.

2 METHODS

2.1 Structure of ontology annotations

Annotations of gene products (such as proteins) to the Gene Ontology types encode statements about the functions, processes and locations of those gene products, based on various types of evidence including experimental assays, scientific literature, textbook knowledge and algorithmic prediction (Hill *et al.*, 2008). The Gene Ontology annotations are curated by multiple research groups internationally, but are amassed in the central Gene Ontology Annotation (GOA) database (Camon *et al.*, 2004).

An ontology annotation consists of three components: a `<database-record-id>`, an annotation of `<evidence>` and lastly the `<ontology-entity>` that the annotation is about. Annotations are not themselves part of the ontology, but can be used in conjunction with the ontology in analysis tasks. For the current project, the `<database-record-id>` will be an identifier for an entry in the BrainMap database, which links to the coordinate data showing areas of statistically significant brain activation that have been reported in the study corresponding to that identifier. The `<evidence>` for the assertion will be the citation to the scientific literature that has been curated into that record in the database. And the `<ontology-entity>` will refer to an appropriate entity within the emotion ontology, as described further below.

2.2 Methods in affective neuroscience

As a preliminary survey to assess the feasibility of our approach, we sampled 14 studies from the BrainMap database that investigated affective topics such as anger and fear, spanning a date range from 1998 to 2009. In particular, we analysed the methods employed in the experimental part of the research in order to evaluate which representational unit (Smith *et al.*, 2006) in the Emotion Ontology would best correspond to what the subjects in the investigation were undergoing at the time that their brains were being imaged. For example, in one study (Morris *et al.*, 1998) the subjects were asked to determine the gender of the persons whose face was depicted, while being shown faces with various degrees of angryness and happiness and fearfulness depicted. The researchers were not interested in the gender recognition - they tricked the subjects - but rather in whether the angry/non-angry faces activate distinct brain parts. The recognition of gender in pictures of facial expressions is chosen as a task in order that the same task can be performed in the display of emotional faces as in the display of control (neutral) faces, and the resulting brain activity compared, with statistically significant differences in activity then ascribed to the difference in conditions, i.e. the emotional content of the picture rather than any other aspects. The facial expressions were generated at different intensities by computerised 'blending' of different facial expressions representing neutral, happy and fearful faces. The images used were sourced from a standard library of emotional facial expressions. One of the findings of the paper was that the amygdala was statistically significantly implicated in the processing of fearful facial expressions. Another study (Onur *et al.*, 2009) involved subjects viewing video clips with emotional content (happy, neutral, fearful) while being

exposed to either a placebo or to reboxetine, a norepinephrine reuptake inhibitor. It was found that the active substance reboxetine was able to induce an amygdala response bias towards fear signals that did not appear in the subjects given the placebo.

Dominant paradigms for investigating neural correlates of emotion processing included the display of visual stimuli such as emotional faces or video clips with emotional content, the presentation of auditory stimuli with emotional content (such as screams or sounds of disgust, as used in (Phillips *et al.*, 1998)), and the use of personal scripts to evoke memories of emotional experiences in subjects. A particularly innovative paradigm used professional actors as the subjects of the investigation, hypothesising that actors would be better at evoking occurrent emotional responses within the experimental context than ordinary subjects (Pelletier *et al.*, 2003).

2.3 Strategy for creating annotations

Guided by the extensive annotation in BrainMap, for each combination of study design characteristics in which a different mental phenomenon is induced in the study participants, we will create an *annotation template* that specifies the association between that study design and the best Emotion Ontology term with which to perform the annotation. This will be the term that represents the mental process type that is instantiated in the patient during the experiment. In the case of one of the oldest and most widely used affective neuroscience research paradigms, subjects are shown a display of pictures containing emotional facial expressions. In this case, the mental process that the subject is undergoing is *visual perception of a static image*, and the object that is represented in the image being perceived is a human face bearing an emotional facial expression. During experimental designs in which the patient is being shown a video with emotional content, the subject is undergoing *visual perception of a video*, with the video as the relevant object. In both of these cases, the relevant ontology type is MF:*visual perception*, and these types may be specialized into subtypes for the case where the object of the perception is static (a picture) or moving (a video).

There is an important further dimension of relevance for affective neuroscience researchers which pertains to the representational content of the image or video itself. This may be angry facial expressions in some cases and fearful facial expressions in others; it may show actors expressing disgust in some videos and loving interactions in others. These differences are very important for annotation of research results in affective neuroscience, since it is known that brain activity varies with differences in the representational content of the object of perception – that is, the brain reacts differently to pictures of angry faces compared to how it reacts to pictures of fearful faces. However, the distinction is not significant in terms of the underlying mental process to the extent that the ontology would be augmented with terms such as *perception of a picture of an angry facial expression*, since that would lead to a combinatorial explosion in the number of ontology entities and ultimately an unmanageable hierarchy, a well-known problem with old-style classification systems and controlled vocabularies (Rector *et al.*, 1994).

Our strategy to accommodate annotation to these complex composite redundant entities will be to introduce a separate module extending the ontology with *defined classes* which are about 'portions of reality' in a way similar to how the representational units in a realism-based ontology denote universals (Smith and Ceusters, 2010). These defined classes will be described with full logical definitions specifying the mental process as well as the object, which in the case of these perceptual processes are information artifacts of different sorts (Ruttenburg *et al.*, 2012). It can be convenient in some application contexts to assign identifiers or names to such defined classes for engineering purposes, such as for ease of storing ontology annotations in this case, but they are not *bona fide* ontology entities in their own right. We will use the Web Ontology Language (OWL) for this effort, version 2 (Grau *et al.*, 2008), which is supported by logic-based automated reasoners that are able to compute the classification of such defined classes within the ontology proper.

The defined class labelled with *perception of a picture of an angry facial expression* would be fully logically defined, according to the conventions described in (Ceusters and Smith, 2010), as:

MF:*visual perception* `and`
  has-participant `some` (
    IAO:*picture* `and` is-about `some`
      MFOEM:*characteristic angry facial expression*)

(Manchester syntax, Horridge and Patel-Schneider (2009).)

This composite term would be assigned as the annotation target in the annotation template for the experimental design using pictures of angry faces. Each annotation template can then be programmatically applied multiple times to records in BrainMap. The results of this process will form the EM annotations to BrainMap.

3 OPEN ISSUES

The design of suitable paradigms for the investigation of brain correlates of mental processes is well known to be a challenging aspect of cognitive and affective neuroscience, since the need to perform experiments within the confines of brain imaging equipment means that the full range of human experiences is not available to the experimenter. The so-called 'cognitive paradigms', or characteristic experimental designs, represent a proxy for the real research subject. Paradigms may be rather sophisticated: the use of professional actors who are trained in self-induction of emotional states in order to effect emotional performances is a case in point. Much work goes into the development and validation – across multiple experiments – of novel paradigms (Turner and Laird, 2012). But it is nevertheless not straightforward to assert in an ontology annotation that a particular study result using a paradigm for studying fear that involves perception of pictures of fearful faces represents brain activation for *canonical fear*. Indeed, the reaction to viewing a picture of an angry face may well be, appropriately, *fear* rather than anger. Our approach to annotation using templates based on the mental phenomena induced in the study participant during the experiment therefore is not sufficient to motivate an annotation for that study to the emotion type that is, in some sense, the "subject" of the investigation. The subjects may be perceiving angry faces but not experiencing anger, even though anger is the subject of the investigation as intended by the experimenter. Additional evidence may augment scientific knowledge about the mental phenomena experienced by the subjects to the extent that additional annotations are possible. For example, there is some evidence that empathetic emotional reactions may harness the same brain circuitry as the canonical emotions (Iacoboni, 2009). This, together with further evidence that, e.g., perception of pictures of angry facial expressions elicits empathetic anger as a response, would motivate creating an annotation to the ontology entity *empathetic anger*, a subtype of anger, for those experiments that involved perception of angry facial expressions. This matter is currently an open question that will be the subject of future research.

4 CONCLUSION

The increasing trend towards interdisciplinary research into all aspects of human functioning necessitates a new and broader focus on what the research is about, transcending the historical boundaries between disciplines. Realism-based ontology is designed specifically to facilitate this objective through categorising and describing not only scientific investigations themselves but also the entities in reality that are the subject of such investigations across different disciplines, in a way that allows research results to be unified through data annotation and automated integration. This is particularly pertinent in the case of research into complex human functioning such as the emotions, where the ordinary scientific method of objectivity and reproducibility is difficult to secure. We have described ongoing work to harness the Emotion Ontology in the annotation of research results in affective neuroscience contained in the BrainMap database. The work we have described is in a preliminary stage and much remains for future work, including creating the implementation for the annotation strategy described herein and making the results available in a database.

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Mental Functioning is Neural Functioning: Towards a Unified Ontology of Mind, Brain, and Behavior

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ABSTRACT

In order to develop a formal ontology for representing mental processes, it will be important to consider two questions: (1) What *is* mental functioning, and (2) How does it relate to bodily and brain function? In the present paper I offer a straightforward answer to both questions: Mental functioning is neural functioning. While this idea has met with a variety of criticisms through the years, it may be the only solution that can support a unified theory of mind, brain, and behavior. Moreover, it has the advantage of providing a transparent explanation for a variety of psychiatric conditions, as well as their biological basis. I propose an implementation of this view within the BFO/OBO framework and discuss some alternative views.

1 INTRODUCTION

In recent years, the health sciences have seen rapid grown in the development and application of bio-ontologies. These informatic resources span a number of domains, such as cellular and molecular biology (GO [8], [21]), experimental and measurement protocols (OBI [1], RadLex [15], cogPO [19], BirnLex [2]), behavior (cogPO [19], BirnLex [2]), phenotypes (PATO [6]) and neuronal structure (GO [8], [21], FMA [14], and NIF [2]) and function (NIF [2], NEMO [5]). As these resources mature, and as the community works to enable interoperability among them, it is increasingly possible to envision a formal, multi-level account of biological structures and functions, as well as their relevance for human health.

Scientific knowledge of how the mind works has an important role to play in this undertaking. Issues surrounding mental health, in particular, call for a systematic treatment of mental processes. A formal ontology could accelerate this work by providing an explicit, machine-readable framework for classifying and integrating relevant data, leading to greater confidence in diagnosis and treatment of mental illness [9].

Curiously, to date there is no reference ontology for cognitive or mental[1] functioning (although some work in this area has recently emerged ([9], [12]).

From a theoretical standpoint, this gap may reflect the uncertain status of the Mind within the biological sciences, recalling age-old questions about the relationship between mind and brain. These are thorny questions that have traditionally been consigned to philosophy. However, in order to develop a formal ontology for this domain, two questions seem unavoidable: (1) What *is* mental functioning, and (2) How does it relate to bodily and brain function?

In this paper I propose a straightforward answer to both questions: mental functions are neural functions. I show how this view could be implemented within the Basic Formal Ontology (BFO [7]), and I contrast alternative views. Finally, I suggest that this proposal is not as radical as it appears. On the contrary, it may be the only approach that can lead to a coherent and cross-disciplinary view of mind, brain, and behavior.

2 DECADE OF THE MIND

The 2010s may come to be viewed as the "Decade of the Mind." Previously, we have seen the official designation of the 1990s as "The Decade of the Brain," recognizing the extraordinary progress in neuroimaging over the past half century (http://www.loc.gov/loc/brain/). The following decade (2000-2009) was deemed the "Decade of Behavior," stressing the importance of social-behavioral issues such as education, healthcare, poverty, and barriers to economic and political justice (http://www.decadeofbehavior.org/).

A decade of the mind would seem a natural successor: The study of mind is inherently linked to the biological (brain) and the social-behavioral sciences. Indeed, recent discover-

[1] I use the term "cognitive" and "mental" interchangeably throughout this paper. Likewise, "mind" and "cognition" are used interchangeably. In reference to functions such as executive attention, decision-making, and language, I use the term "higher cognition" to emphasize the role of prefrontal cortex and other recently evolved cortical structures.

ies in social science and neuroscience have prompted reconsideration of the very foundations for defining mental function and dysfunction, leading to the first major revision of the Diagnostic and Statistical Manual of Mental Disorders, or DSM, in over three decades (http://www.dsm5.org). A quick search of "headlines in health" within the past year will show that discussions of proposed changes to the DSM have been remarkably heated, raising debates over the role of biological markers in mental health diagnosis, as well as educational, economic, and social consequences of proposed changes to DSM categories such as autism, dyslexia, and depression.

At the core of the DSM debate is the question of how to define mental functioning. There are many sources that can inform this question, including studies of the brain, cognitive processing, development of behavioral and brain systems, and latent dimensions of mood and temperament (i.e., personality). However, the core question comes down to this: What ***kind of thing*** is a mental function. That is, what is its superclass?

3 WHAT IS A MENTAL FUNCTION?

Attempts to define "mind" and "mental function" within a scientific context have stirred up controversy since the early 20th century. In certain areas of British and American psychology, it was famously taboo to use words such as "feeling," "belief," or even "memory" or "consciousness." While behaviorism is now viewed by many as a radical misstep, some of its core principles have survived and continue to inform scientific psychology.

Perhaps the defining principle is that "*we cannot observe the mind*." According to this view, we can observe and measure physical entities (e.g., button presses, vocalizations) and neural activity (e.g., changes in hemodynamics, electroencephalograms). By contrast, the Mind is an impenetrable black box, whose contents are private and therefore beyond the reach of scientific study. For this reason, cognitive psychologists are often careful to say that, technically speaking, they do not study cognition, but rather the behavioral and brain processes that are "associated with" (or "map to" or "subserve") cognitive functions. In one sense, this is a very sensible position: methodological behaviorism tends to promote a rigorous approach to experimental design, and it avoids sticky philosophical issues.

If we cannot observe mental functions, however, this presents a challenge in developing formal ontologies of cognition. What are mental processes if they are not observable, material entities? How can we develop a cognitive ontology that is compatible with realist principles [7] and is also grounded in scientific knowledge? What is it, exactly, that behavioral and brain processes are supposed to map to?

These questions inevitably raise the Mind-Body (or Mind-Brain) problem, that is, the problem of how the mind is related to the brain and to overt (observable) behavior, the two aspects of human functioning that we can describe in concrete, scientific terms. This problem been the subject of many books, and it is impossible to do justice to arguments for and against different positions. However, for practical purposes, it can be boiled down to some relatively straightforward choices.

The Basic Formal Ontology (BFO [7]) and the Ontology for Biological Investigations (OBI [1]) are rigorous upper ontologies that are widely adopted in the bioinformatics community. They provide a set of basic distinctions that can help us frame our questions more analytically. To begin, "mind" is an ambiguous term: it can refer to a mental ***process*** (or function[2]), a mental ***state***, or a mental ***representation***. These three concepts can be characterized as follows:

- ***Process***. A process[3] is an occurrent, that is, an entity that exists in four dimensions and that "unfolds itself in time," i.e., has temporal parts ([7]: p. 140).
- ***State*** — A state is a type of dependent continuant. It is a continuant because it endures through time ([7]: p. 151), and it is dependent, because it requires the existence of another, substantive or "independent" entity to exist (*ibid*.). More specifically, a state is a kind of realizable entity[4] that "inheres in" a substantive entity.
- ***Representation*** — Representation is not defined within BFO. It can be defined as an information content entity,[5] since the defining feature of a representation is that it is "about" something else.

While these distinctions may seem burdensome, Smith and colleagues have shown that ontologies are at risk of committing errors — sometimes serious (e.g., false reasoning over medical data) — unless the terms of natural language rigorously defined [3]. Further, the use of an upper ontology can facilitate ontology integration for closely related domains, such as scientific paradigms, neuroimaging results, and health-related applications.

[2] Technically, "function" is distinct from "process," within BFO. However, for the sake of simplicity, I do not discuss the more complex concepts of "function" and "dysfunction." See Smith & Ceusters (2010) for a discussion of this topic.

[3] http://www.ifomis.org/bfo/1.1/span#Process

[4] http://www.ifomis.org/bfo/1.1/snap#RealizableEntity

[5] http://purl.obolibrary.org/obo/IAO_0000030

4 HOW ARE MIND AND BRAIN RELATED?

Below are three views of how to represent mental processes, vis-a-vis neural processes. BFO. Once we address this issue, it is fairly simple to work out the relations between mental and brain processes, states and representations within the BFO/OBI framework.

> **View #1**: A mental process is a process (but it is not necessarily a bodily process).

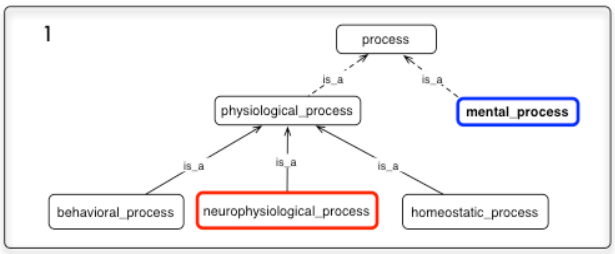

Figure 1. Mental processes are (nonphysical) processes.

View #1 is consistent with folk psychology: It explicitly defines mind as something other than brain or body. In philosophical terms, it assumes a dualist worldview: there is physical stuff, and there is nonphysical stuff. Mind is part of the nonphysical stuff, according to this view.

The problems with this position are well-known. Most important: it is difficult, if not impossible, to explain how the mind and brain interact. This is unacceptable for a biologically based theory of mental function.

Views #2 and #3 both suggest the opposite, that mind is part of the physical world (a materialist position). Materialism has met with several objections. One objection is that the mind cannot be reduced to the brain, because it "makes no sense" to say "My brain felt like having a nap." Thinkers sometimes use the term "category error" to describe this supposed misstep. However, as Churchland notes, "one person's category error is another person's deep theory about the nature of the universe" ([4]: p. 273). Theories about nature — and the idioms that are used to express them — do change over time. Therefore, this argument appears weak.

Two other arguments concern the "aboutness" of mental representations, and subjective experience, which are both claimed to be incompatible with physical entities. This may not be the case. For instance, Figure 4 suggests a way to represent the "aboutness" of mental representations, and the claim that purely physical entities cannot have subjective experience appears circular, much like the argument based on natural language and folk psychology of mind and brain.

The following two views both represent mental processes as physiological processes. However, there is an important difference: View #3 explicitly states that Mind=Brain. View #2 is agnostic on this point.

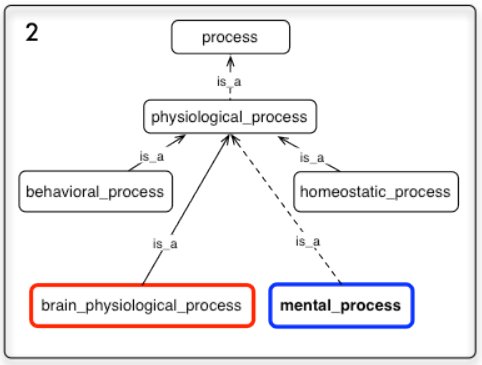

Figure 2. Mental process defined as a physiological process.

> **View #2**: A mental process is a bodily process (but not necessarily a brain process).

In other words, View #2 leaves open the possibility that some mental processes are not brain processes. There could be a rationale for this position if "mental" were defined to include functions outside the central nervous system (e.g., processes within the heart, the respiratory system, the digestive tract, and so forth). However, this would be an unusual (and perhaps over-extended) use of the term "mental."

> **View #3**: A mental process is a brain (i.e., a neurophysiological) process.

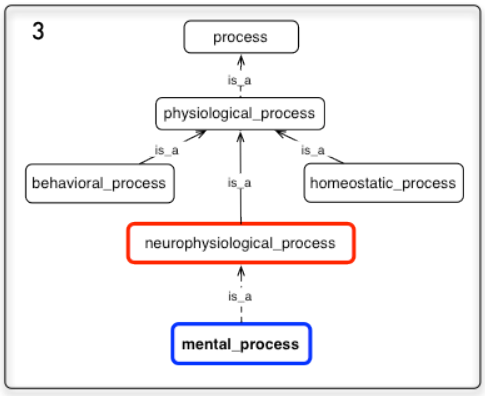

Figure 3. Mental process defined as a brain (i.e., neurophysiological) process.

Finally, View #3 defines mental processes as brain processes. There are two major advantages in adopting this view:

(1) Defining mental processes with respect to basic subdivisions of the brain will make it easier to describe mappings of core functions, such as sensation, action, and memory, across species [11].

(2) Our knowledge of the brain and its structural and functional subdivisions can provide a framework fro understanding different kinds of mental processing, and how they are related (see Fig. 4).

The first point is important, because a key goal within the bio-ontology community is to develop resources that can be used together, to integrate data and knowledge across domains. Comparative neurobiology has a critical role to play in bridging the domains of biology, neuroscience, and experimental psychology. Therefore, it may be useful to consider the semantic foundations for a cognitive ontology and whether they can support cross-species mappings of behavioral and brain systems.

The second point gets at the explanatory power of the view that mind is brain. The brain is undeniably complex. However, it is not infinitely complex. In fact, there are relatively straight-forward mappings between types of behavior and parts of the central nervous system, brain, and cortex (Table 1; see also [10], [17]).

In conclusion, View #3 (mental processing is neural processing) is most compatible with our larger aim: to develop a mental functioning ontology that is scientifically plausible and consistent with a realist framework.[6]

5 LEVELS OF BRAIN, LEVELS OF MIND

Table 1 summarizes four categories of mental processing, their primary functions, and the corresponding parts of the nervous system, brain, and cortex. From a neuropsychological view, all of human behavior (including covert as well as overt processes) can be explained with respect to one or more of these basic processes [17]. One advantage of this organizing framework is that mental processing can be viewed at different levels of analysis: with a focus on observable behavior (motor output), or on patterns of neural activity within different regions of cortex, brain, and nervous system.

Another virtue of considering the functional architecture of the brain is that it affords clear predictions about different kinds of mental and behavioral disorder [10]. For example, damage to parts of the motor control system (e.g., within cortico-striatal circuits) result in predictable symptoms, such as the slowed and uneven gestures that are characteristic of Parkinson's Disease (PD). Even more interesting, some PD patients exhibit linguistic disorders that resemble those of Broca's aphasics: i.e., difficulties with processing of natural language syntax [20]. While it may be possible to explain this comorbidity without reference to the brain, it is much easier to predict when we consider the connections between the basal ganglia and regions of left inferior prefrontal cortex. In general, understanding the distributed networks that relate different regions of the brain and body could help to explain clusters of psychological and behavioral symptoms, and when and why they occur.

Table 1. Mental processes (left-most column), major functions associated with these processes, and key regions of the body and brain that give rise these processes (right-most columns).

Process	Function	Region of Body (NS)	Region of Cortex
Sensory (somatic)	Afferent connections to **outer world** (input)	Peripheral NS	Unimodal (V1, A1, etc.)
Motor (somatic)	Efferent connections to **outer world** (output)	Peripheral NS	Unimodal (M1)
Affective (visceral)	Sensory-motor processing of **internal milieux** (self)	Autonomic NS	Polymodal (Limbic/Paralimbic Regions)
Cognitive (central)	Association & integration of sensory-motor, affective processes	Central NS (brain)	Polymodal (Association Areas)

[6] I do not discuss "idealist" views (brain and body are reducible to mind or consciousness), because most biological workers assume that the physical world is real. By contrast, there is no consensus on how to define mental phenomena within a biological context (other than use of "operational," that is, experiment-specific, definitions). The Mind-Body question is usually avoided in standard textbooks on behavioral and biological psychology.

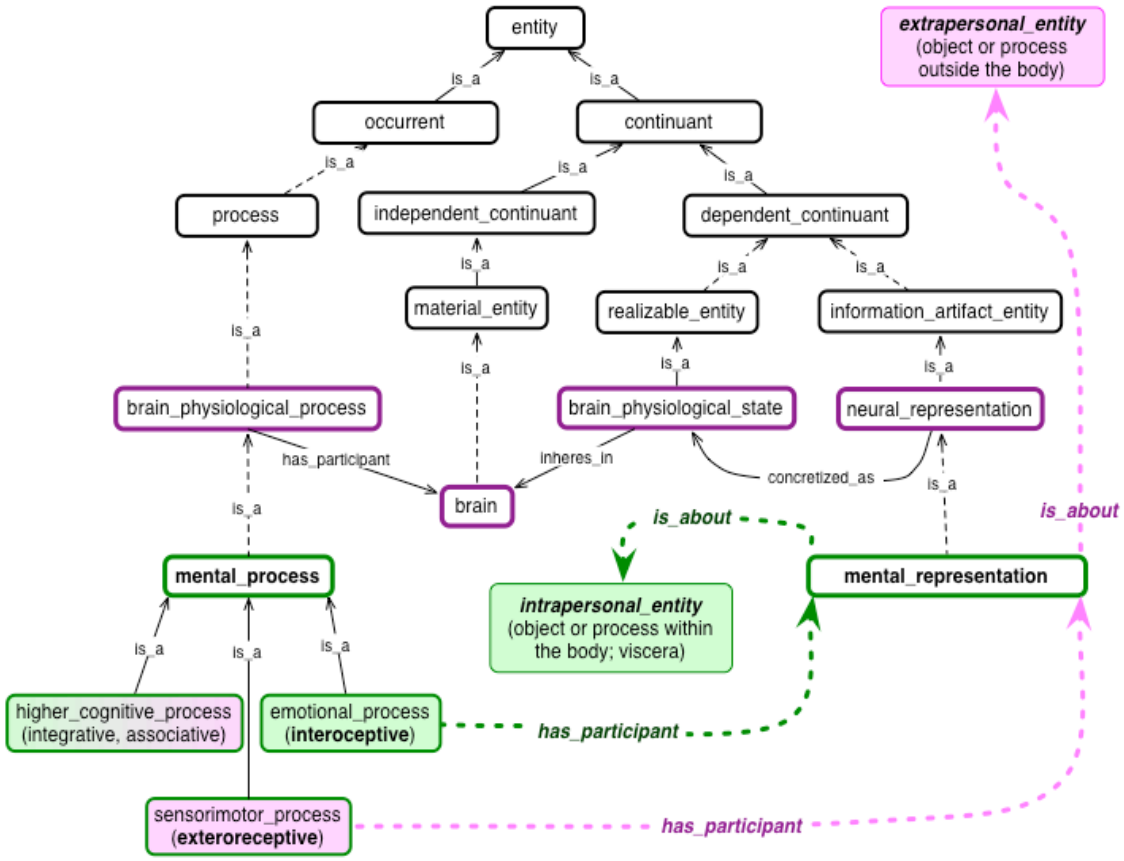

Figure 4. View of proposed mental processing ontology. The term "interoceptive" refers to autonomic systems (see Row 3 in Table 1). The term "exteroceptive" refers to somatic (sensory-motor) information (see Rows 1-2 in Table 1). These regions are interconnected to one another and to other parts of the central nervous system via association cortex. Note that "higher cognitive" areas serve to link together information about the world and about the self.

Figure 4 represents some of the key points discussed above. The subtypes of ***mental processing*** are linked to specific parts of the brain and central nervous sytem. This can help to explain the nature of higher cognitive processes, which are subserved by regions of association cortex, as well as sensory-motor and emotional processes, which are linked, respectively, to sensory-motor and automic systems through other parts of the cortex. Most interesting, some puzzling properties of Mind, such as "aboutness" and subjectivity, can be understood here in a concrete context, by considering how the mind-brain responds to (maps or "represents") the internal (visceral) and external environment.

SUMMARY AND CONCLUSION

In conclusion, there are advantages in defining mental processes as neural processes. First, it avoids the problems associated with view that mind is something non-physical. Second, it helps to explain a variety of psychological conditions and comorbidities. Third, it can support an integrated understanding of mind, brain, and behavior. In this sense, we have already experienced the "Decade of the Mind" (the 1990s): Mind just is the neural activity that makes us who we are.

Finally, it may useful to define a mental process more precisely as a distributed (BFO "aggregate") neural process. Although there is functional specialization within parts of the brain, it is equally clear that each mental process involves actions that are distributed over time and across the brain's neuraxis [17].

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