Epidemiology Special Interest Group

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Disclosures

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The Challenge

How to describe/talk about seizures in a way that is meaningful (and consistent) among

- Tertiary centers (AED selection, diets, devices, surgery)
- Epidemiologist (assess disease burden, risk factors)
- AED trials (consistency of diagnosis & outcomes)
- Resource poor environments (epidem, treatment)

The Tower of Babel

What is required?

- Terms & concepts need to have common meaning

  Controlled Vocabulary

- The terms & concepts need to be organized in a consistent, hierarchical fashion based on the best available evidence

  Classifications, Terminologies, Ontologies

What is a controlled vocabulary?

ISO Standard 1087 (Terminology-Vocabulary)

- Concept: a unit of thought constituted through abstraction on the basis of properties common to a set of objects
- Term: Designation of a defined concept in a special language by a linguistic expression
- Terminology: Set of terms representing the system of concepts of a particular subject field
- Nomenclature: System of terms that is elaborated according to preestablished naming rules

ISO Standard 1087 (Terminology-Vocabulary)

- Dictionary: structured collection of lexical units with linguistic information about each of them

- Vocabulary: Dictionary containing the terminology of a subject field

Examples of Specific Terminologies

- International Classification of Disease (ICD- 9, 10)
- International Classification of Primary Care
- Current Procedural Terminology (CPT)
- Diagnostic & Statistical Manual of Mental Disorders (*definitions & diagnostic criteria)* (DSM 5)
- Systematized Nomenclature of Medicine (SNOMED)

Controlled vocabulary

Rubin et al 2007

- “A CV provides a list of concepts and text descriptions of their meaning and a list of lexical terms corresponding to each concept. Concepts in a CV are often organized in a hierarchy. Thus, CVs provide a collection of terms that researchers can use for indexing resources, such as records in a database. The GO is the most widely used CV serving biomedical researchers.”

Seizure Controlled Vocabulary Resources

- Blume et al Glossary (semiology)

- Nochter (EEG)

What is the relationship of the controlled vocabulary to a diagnostic manual?

- The CV is the dictionary from which the terms used in each component of the DM is derived

- It can be as simple as a list of terms (with definitions) or terms in a hierarchical structure

Diagnostic Manual-ILAE

Overall Plan For the Diagnostic Manual

Overall Goal: To develop a web-based diagnostic manual for seizures and epilepsy that can serve as a resource for clinicians who may not necessarily be epileptologists or even neurologists but who may have occasion to care for patients who present with suspected seizures. This will be updated and modified as evidence and consensus require. The goal is to make the diagnosis of these syndromes and epilepsies as straightforward as possible and to provide clear guidance regarding referral for specialty care.

Please bear in mind that this is the most preliminary stage of the project. We are focused largely on content at this time, and we ask you to forgive and ignore any awkwardness in the format in which materials are presented.

Components of the website when finished:

I. **A controlled vocabulary for seizure semiology:** This is an extension and update of the glossary of ictal semiology (Blume et al, Epilepsia 2001). Currently we have the list of items and their definitions. The ultimate intent is to illustrate each semiological feature with video EEG segments sufficient to demonstrate the concept and its typical range of variation.

II. **A controlled vocabulary for EEG features** relevant to diagnosing epilepsy: Currently we have a list of items. Ultimately, each will be illustrated with EEG tracing segments in at least two montages (longitudinal bipolar and referential) and at two "paper" speeds (15 and 33 mm/sec).

III. **Imitators of seizures:** There are many disorders that are mistaken for seizures. These chapters address the more common and more easily recognized.

IV. **Diagnostic criteria for specific forms of epilepsy, the "chapters":** These are brief, structured guides to enable accurate diagnosis or exclusion of specific epilepsy diagnoses/entities. Please note, we began with only eight syndromes/epilepsies but have added several since. The intention is to continue creating documents for diagnosis of other specific forms of epilepsy. In the first column ("page 1") for each of these "chapters," we present key elements including mandatory features, typical or atypical features, red flags, and exclusionary features. In a second column ("page 2"), we present additional brief commentary.

V. A guide for approaching a patient who presents with paroxysmal events: This will include what information with regard to prior medical and other relevant history, history of the events, evaluations, and other relevant factors is necessary in order make or exclude a particular diagnosis. This is not yet ready to present.

Benign Epilepsy w/Centro-Temporal Spikes (BECTS)

BECTS

Synopsis: Benign epilepsy of childhood with centrotemporal spikes is an age specific epilepsy affecting children most commonly in their early school years. The seizure semiology is brief, hemifacial seizures that may secondarily generalize if they occur nocturnally. This epilepsy occurs in children who are otherwise neurologically and cognitively normal and imaging studies are unremarkable. The EEG shows a normal background with high amplitude centrotemporal sharp waves, which are activated with drowsiness and sleep. Prognosis is excellent with all children remitting by mid to late adolescence.

Edouard Hirsch (France) and Elaine Wirrell (US)

Feature	Page 1	Page 2
Age range affected	3-14 years	Seizures usually resolve by age 13 years, but can occasionally occur up to age 18 yrs (Bouma et al. Neurology 1997)
Evolution from a different earlier onset epilepsy	Rare	5-15% have a history of febrile seizures and a small proportion of children may have a history of early onset benign occipital epilepsy (Panayiotopoulos syndrome) (Panayiotopoulos syndrome. CP Panayiotopoulos. John Libbey , Eastleigh, England. 2002, p 93)
Sex	Both are affected	Slight male preponderance of no diagnostic significance
Antecedent birth & neonatal history	Normal (but not exclusionary)	In rare instances, there may be a history of birth difficulties; however, see development and cognition prior to presentation.
Neurological exam	Normal	
Head size	Normal	
Potential antecedents/ causes	None (but not exclusionary)	In rare instances, there may be a history of other antecedents. These would be considered incidental and not exclude BECTS if the child's profile clearly meets the mandatory electro-clinical criteria without red flags. See development and cognition prior to presentation.
Review of systems	Negative	
Development or cognition prior to presentation	Normal	Red Flag If male with mental retardation need to

Means of organizing terms & concepts into a coherent classification (ontology)

Current classifications

- ILAE C & T- seizures 1981
- ILAE C & T- syndromes 1989
- ILAE both 2010
- ILAE Epidemiology 2010
- ICD-9, 10, (11)
- SNOMED CT
- Others….

ILAE Revised Classification of Epileptic Seizures (1981)

- Partial (focal, local) Seizures
  - Simple: motor, autonomic, psychic, somato or special sensory
  - Complex: at onset, preceded by SPS, automatisms
  - Secondarily generalized tonic-clonic: SPS, CPS, SPS-CPS
- Generalized Seizures
  - Absence: with clonic, atonic, tonic, autonomic, automatic
  - Atypical absence: greater change of tone
  - Myoclonic
  - Clonic
  - Tonic-clonic
  - Atonic

Classification of Epilepsies & Epileptic Syndromes (1989)

- Localization-related
  - *Idiopathic, cryptogenic, symptomatic*
- Generalized
  - *Idiopathic, cryptogenic, symptomatic*
- Undetermined
  - *With both generalized & focal seizures*
  - *Without unequivocal generalized & focal seizures*
- Special Syndromes
  - *Febrile szs, EPC, isolated, specific precipitants*

ILAE Commission… Revision of terminology & concepts of seizures & epilepsy. Epilepsia 2010;51:676-685

SPECIAL REPORT

Revised terminology and concepts for organization of seizures and epilepsies: Report of the ILAE Commission on Classification and Terminology, 2005–2009

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2010 Revision- Syndromes

Table 3. Electroclinical syndromes and other epilepsies

Electroclinical syndromes arranged by age at onset[a]
- Neonatal period
  - Benign familial neonatal epilepsy (BFNE)
  - Early myoclonic encephalopathy (EME)
  - Ohtahara syndrome
- Infancy
  - Epilepsy of infancy with migrating focal seizures
  - West syndrome
  - Myoclonic epilepsy in infancy (MEI)
  - Benign infantile epilepsy
  - Benign familial infantile epilepsy
  - Dravet syndrome
  - Myoclonic encephalopathy in nonprogressive disorders
- Childhood
  - Febrile seizures plus (FS+) (can start in infancy)
  - Panayiotopoulos syndrome
  - Epilepsy with myoclonic atonic (previously astatic) seizures
  - Benign epilepsy with centrotemporal spikes (BECTS)
  - Autosomal-dominant nocturnal frontal lobe epilepsy (ADNFLE)
  - Late onset childhood occipital epilepsy (Gastaut type)
  - Epilepsy with myoclonic absences
  - Lennox-Gastaut syndrome
  - Epileptic encephalopathy with continuous spike-and-wave during sleep (CSWS)[b]
  - Landau-Kleffner syndrome (LKS)
  - Childhood absence epilepsy (CAE)
- Adolescence – Adult
  - Juvenile absence epilepsy (JAE)
  - Juvenile myoclonic epilepsy (JME)
  - Epilepsy with generalized tonic–clonic seizures alone
  - Progressive myoclonus epilepsies (PME)
  - Autosomal dominant epilepsy with auditory features (ADEAF)
  - Other familial temporal lobe epilepsies
- Less specific age relationship
  - Familial focal epilepsy with variable foci (childhood to adult)
  - Reflex epilepsies

2010 Revision- Seizure Classfication

Table 1. Classification of seizures[a]

- Generalized seizures
  - Tonic–clonic (in any combination)
  - Absence
    - Typical
    - Atypical
    - Absence with special features
      - Myoclonic absence
      - Eyelid myoclonia
  - Myoclonic
    - Myoclonic
    - Myoclonic atonic
    - Myoclonic tonic
  - Clonic
  - Tonic
  - Atonic
- Focal seizures
- Unknown
  - Epileptic spasms

[a]Seizure that cannot be clearly diagnosed into one of the preceding categories should be considered unclassified until further information allows their accurate diagnosis. This is not considered a classification category, however.

Different needs for seizure epilepsy ontology

- Clinical care
- Drug, device, other treatment studies
- Epidemiology
- Research
- Communities
  - WHO
  - ILAE
  - CMS

Axes for classification (ontology)

- Clinical
  - Semiology (clinical description)
  - Seizure onset (partial, generalized, both, unknown)
  - Age of onset
  - Age of offset
  - Developmental history
  - Response to medication
  - Family history
  - Natural history (remission, refractory)
- Laboratory
  - EEG
  - MRI
  - Genotype
- Basic science
  - Neurochemistry/pharmacology
  - Cellular electrophysiology
  - Molecular
  - Genetics
  - Systems

Organization of (medical) terminologies & knowledge

- 1603-1830's - London Bills of Mortality
- 1865- Aggregated Statistics (LBM)
- 1860- International Codes of Diseases:
  - Reporting of morbidity & mortality
- 1980's- computers become available
- Multiple terminologies (READ, LOINC, DICOM)
- Need for order

Ontologies

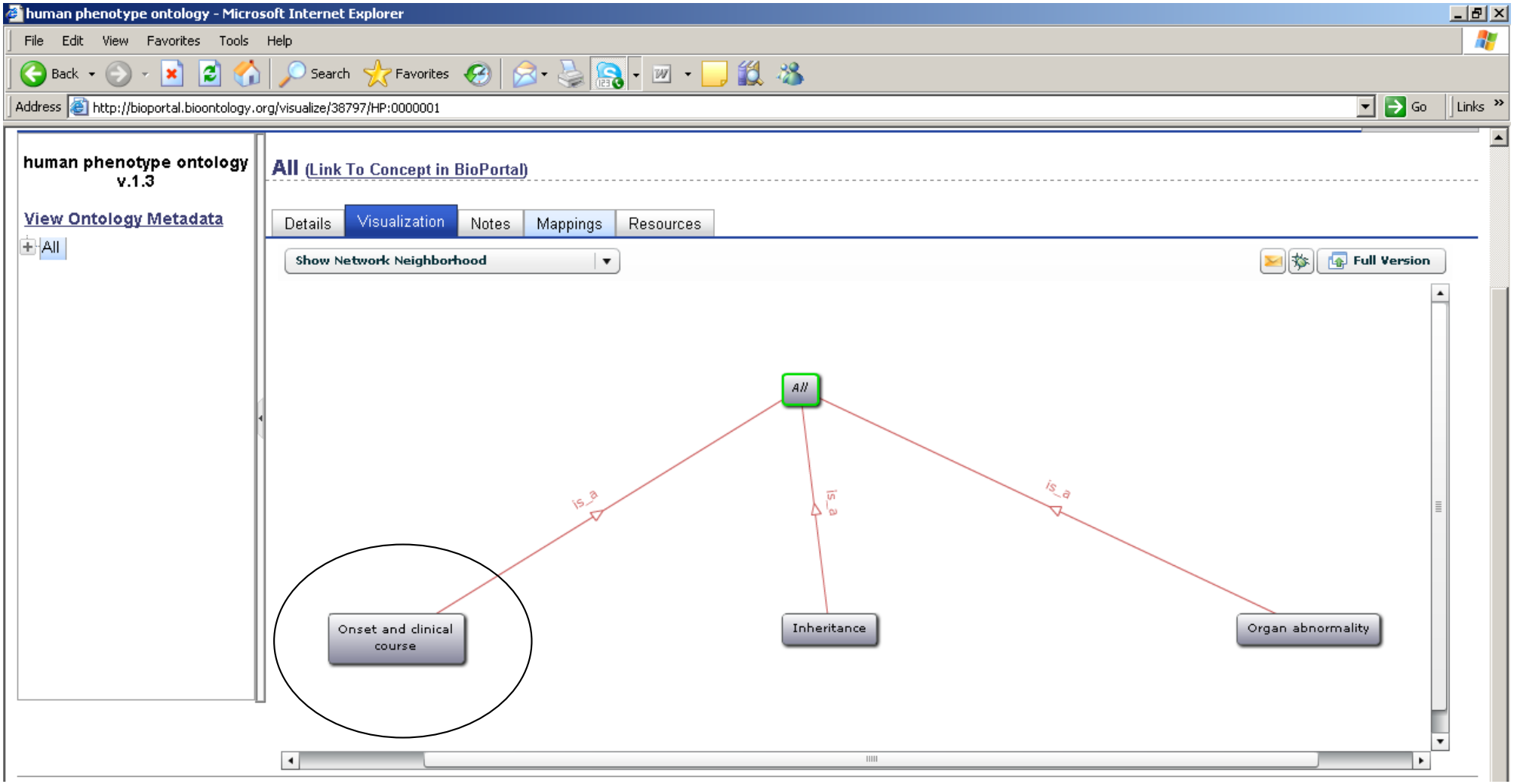
- = formal specification of terms in the domain *(e.g. epilepsy)* and relations among them *(e.g. complex partial is a type of partial seizure which is a type of seizure)*
- Why make one?
  - Share common understanding of information
  - Enable reuse of information
  - Make assumptions explicit
  - Analyze domain knowledge

Ontologies

- 1990's- Knowledge Representation grew out of the principles of Artificial Intelligence

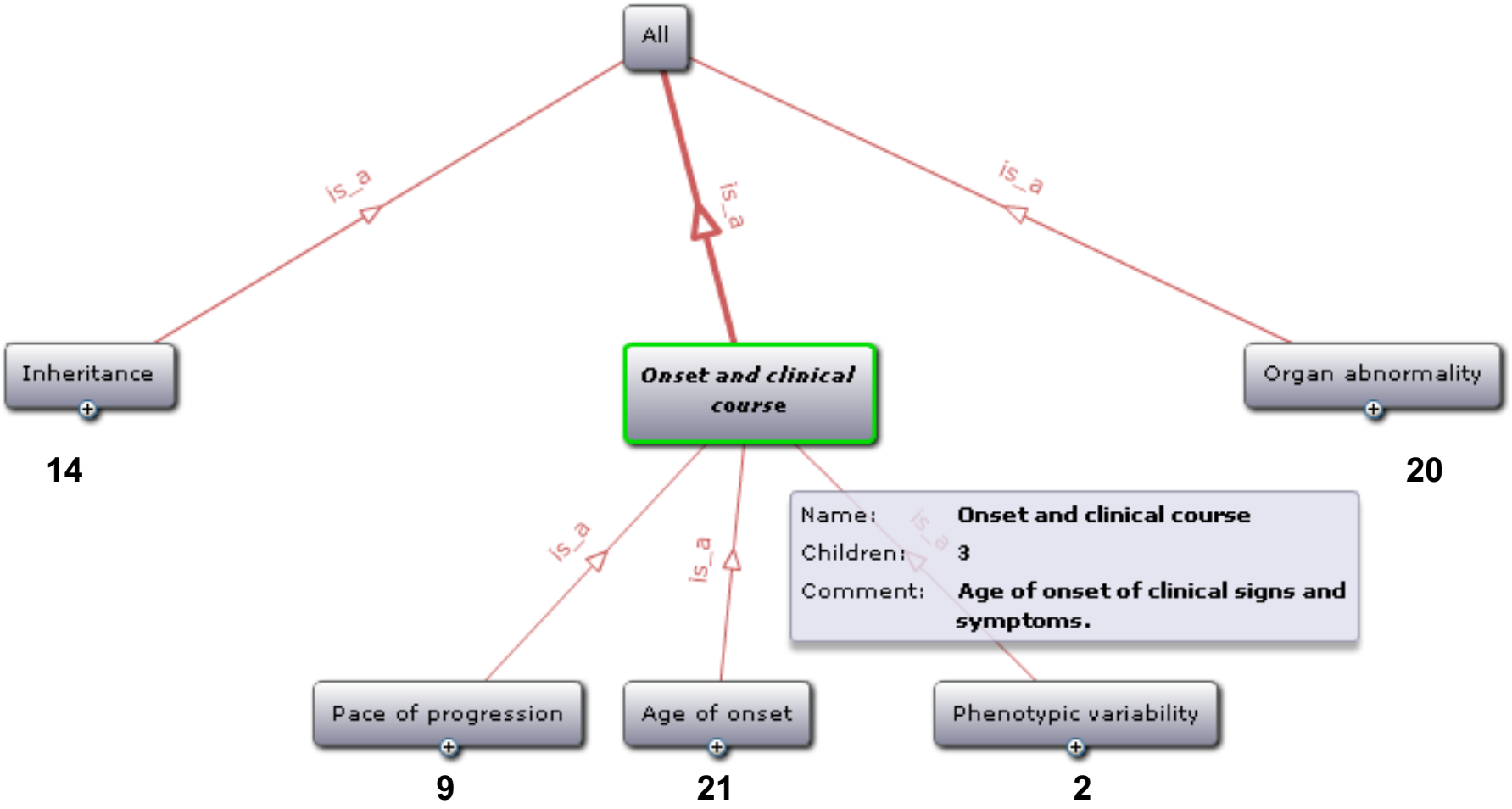
- 2002- Web Ontology Language (OWL)
  - Muliti axial
  - Dynamic information- frequently updated
  - Description logics is self organizing

Human phenotype ontology



http://bioportal.bioontology.org/visualize/38835

Human phenotype ontology



http://bioportal.bioontology.org/visualize/38835

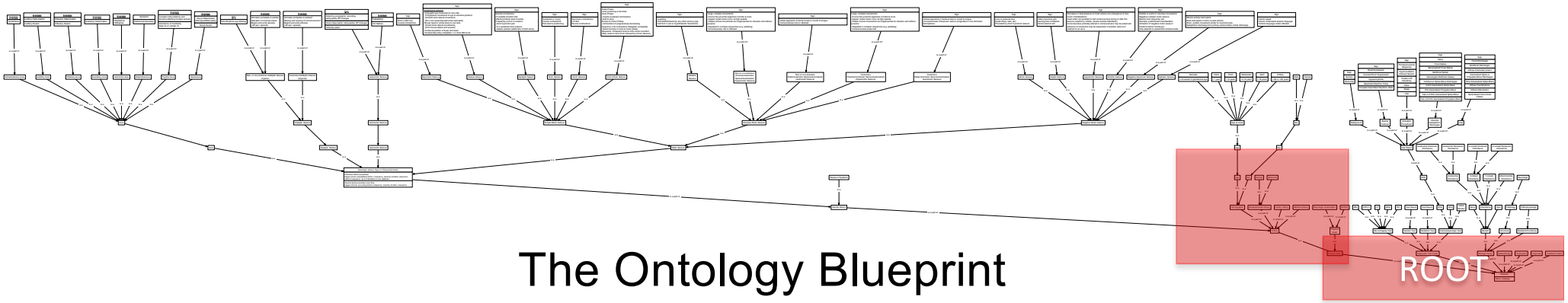
END

A Diagnostic Heuristic Using the Epilepsies Ontology Framework and Decision Table

A Heuristic Decision Table for Human Disease

Robert Yao

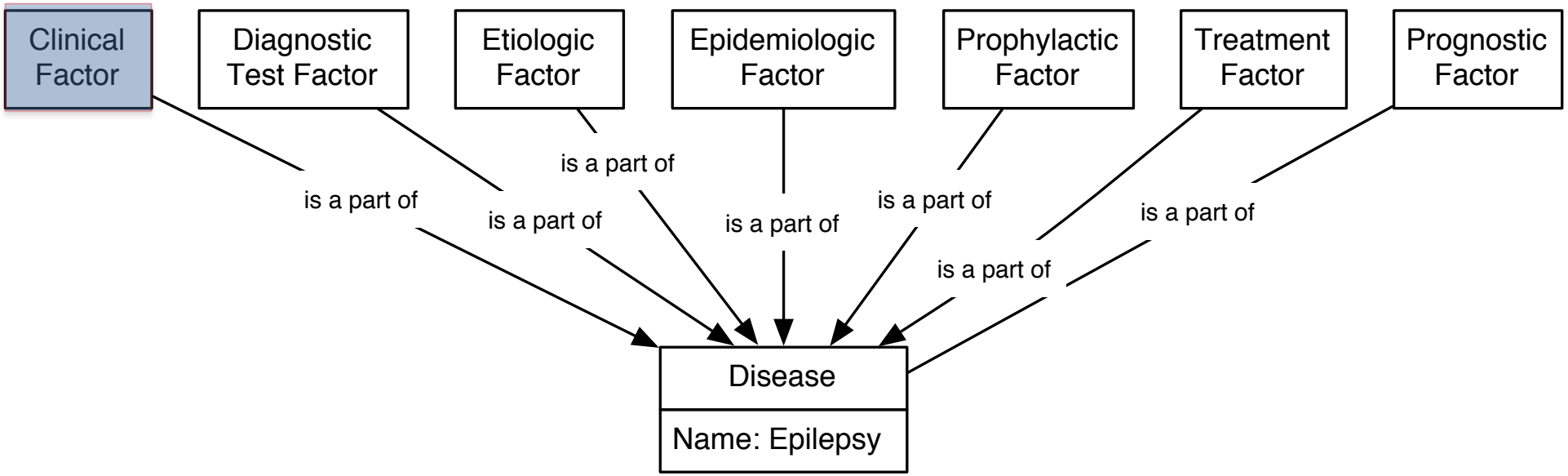
Integration to the Epilepsies Ontology



The Ontology Blueprint

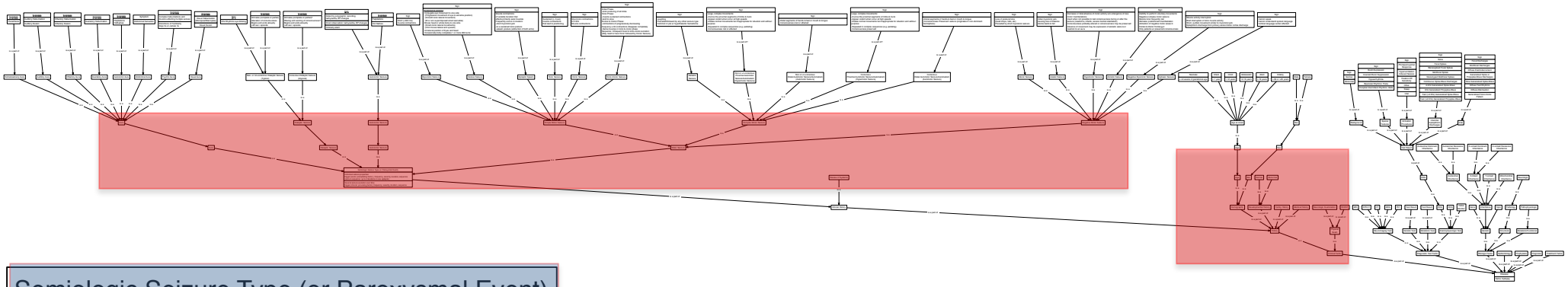
Increased Granularity

What do we do about seizure types?

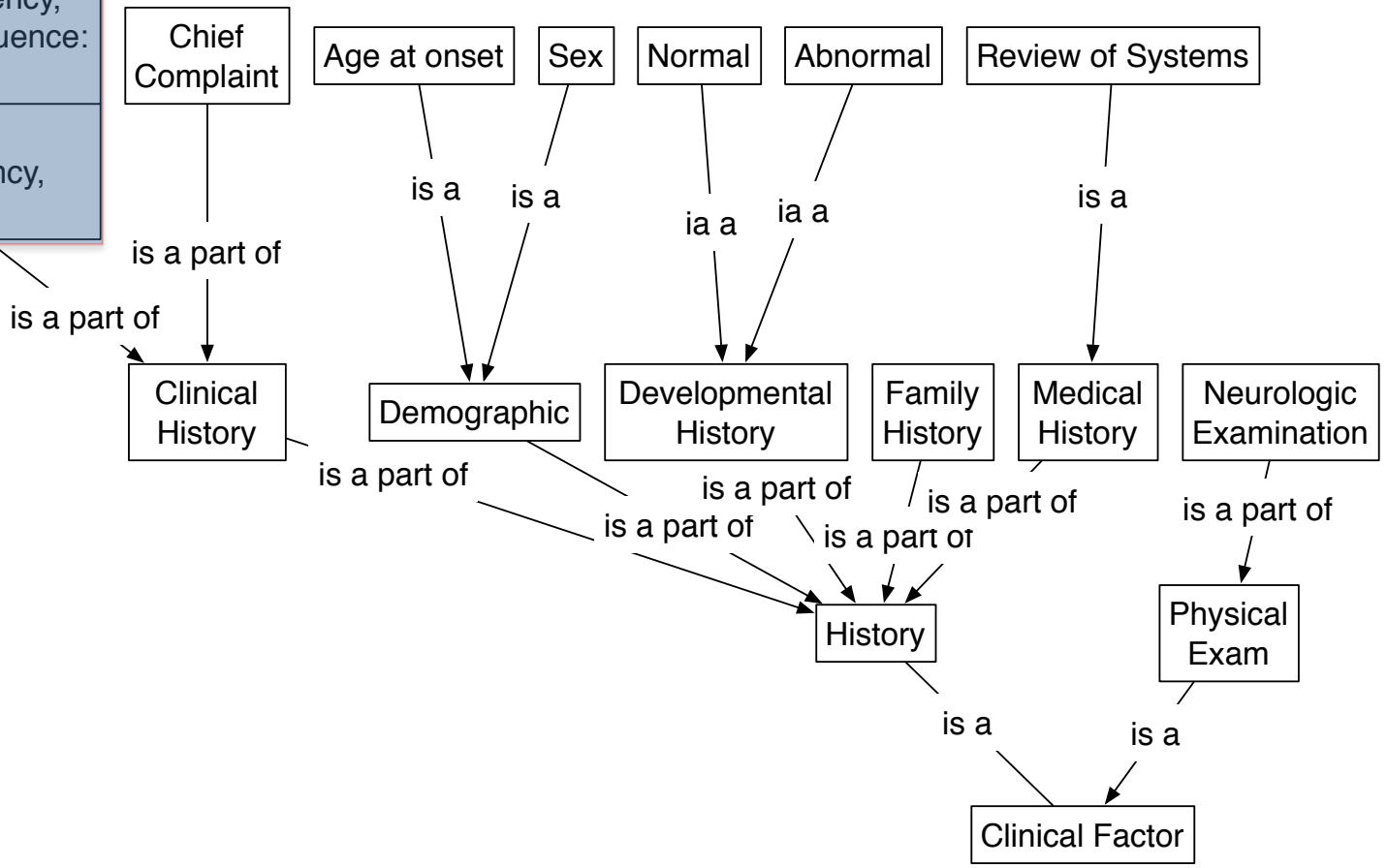


Methods: Aim 1

Clinical

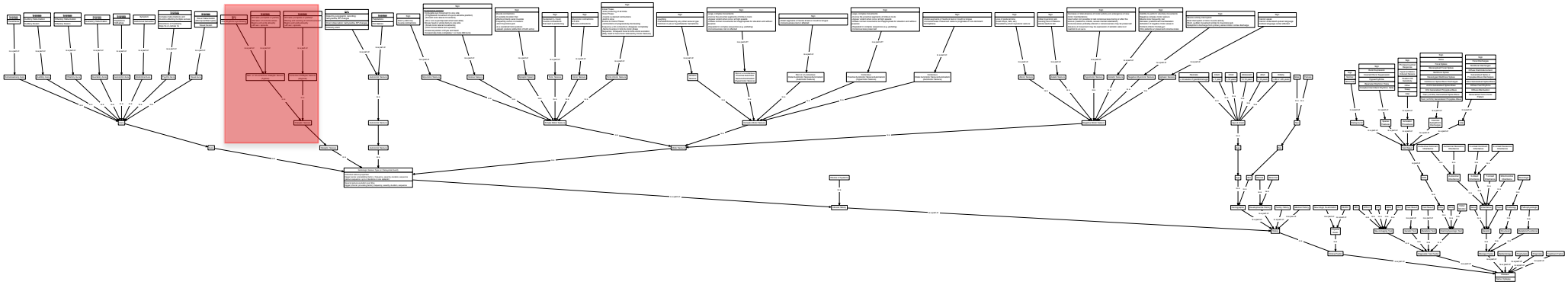


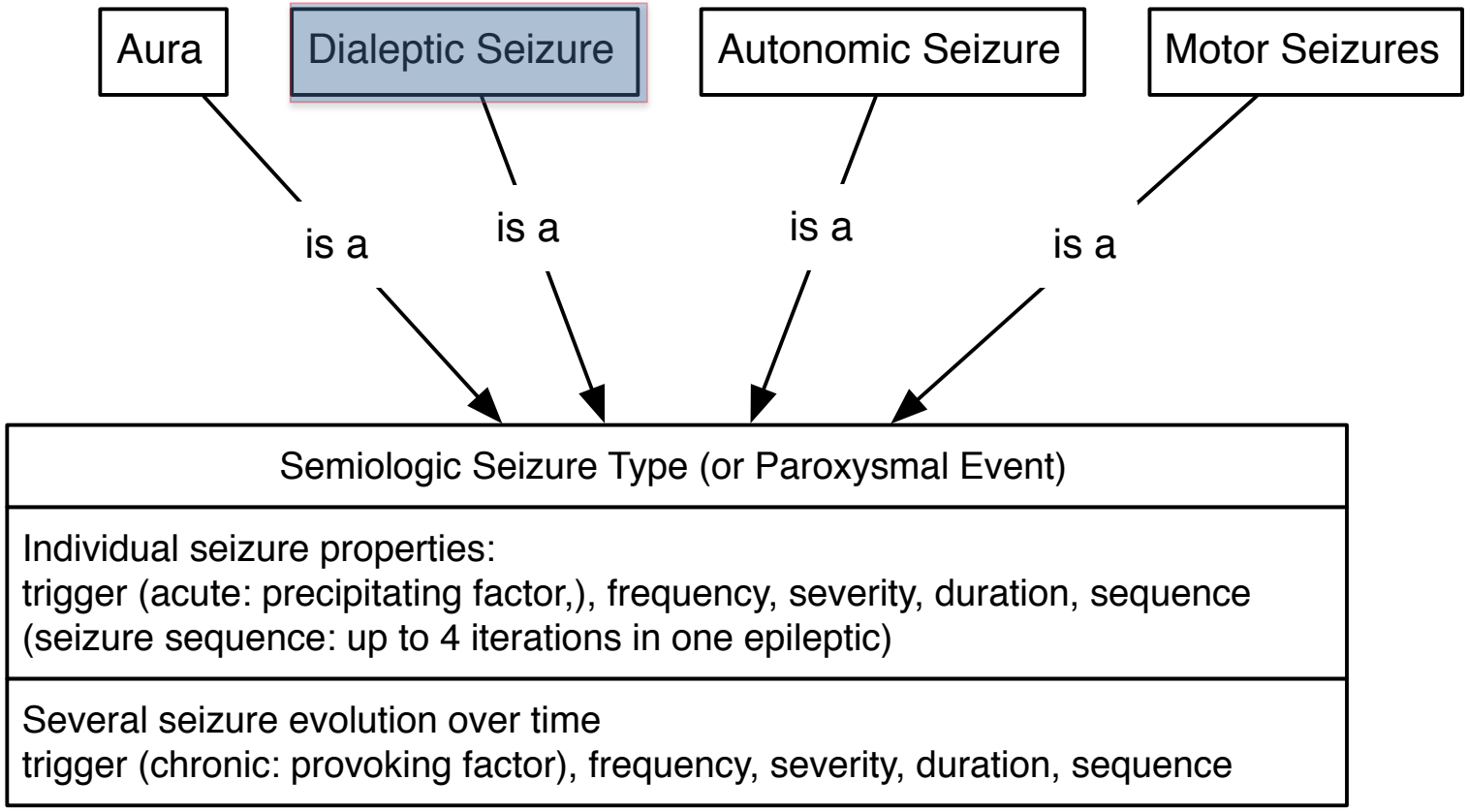
Semiologic Seizure Type (or Paroxysmal Event)
Individual seizure properties: trigger (acute: precipitating factor,), frequency, severity, duration, sequence (seizure sequence: up to 4 iterations in one epileptic)
Several seizure evolution over time trigger (chronic: provoking factor), frequency, severity, duration, sequence



Methods: Aim 1

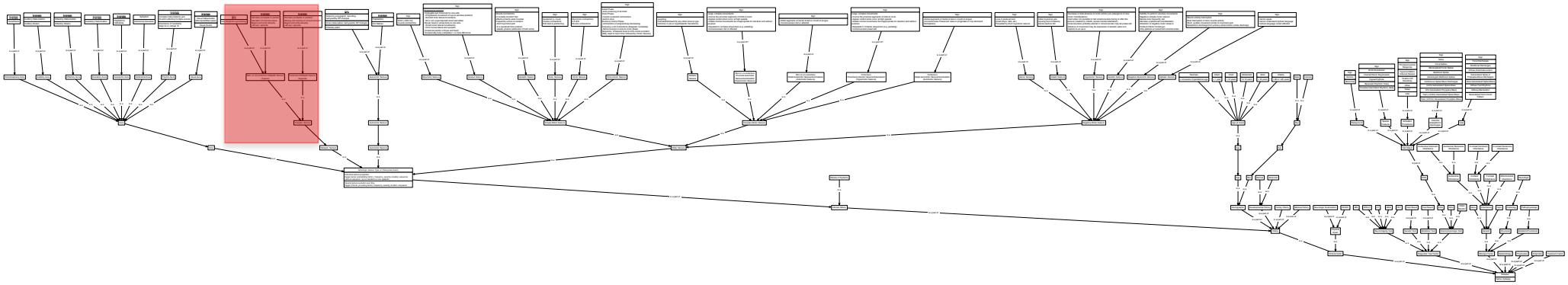
Clinical: Semiology = Seizure Type Observed

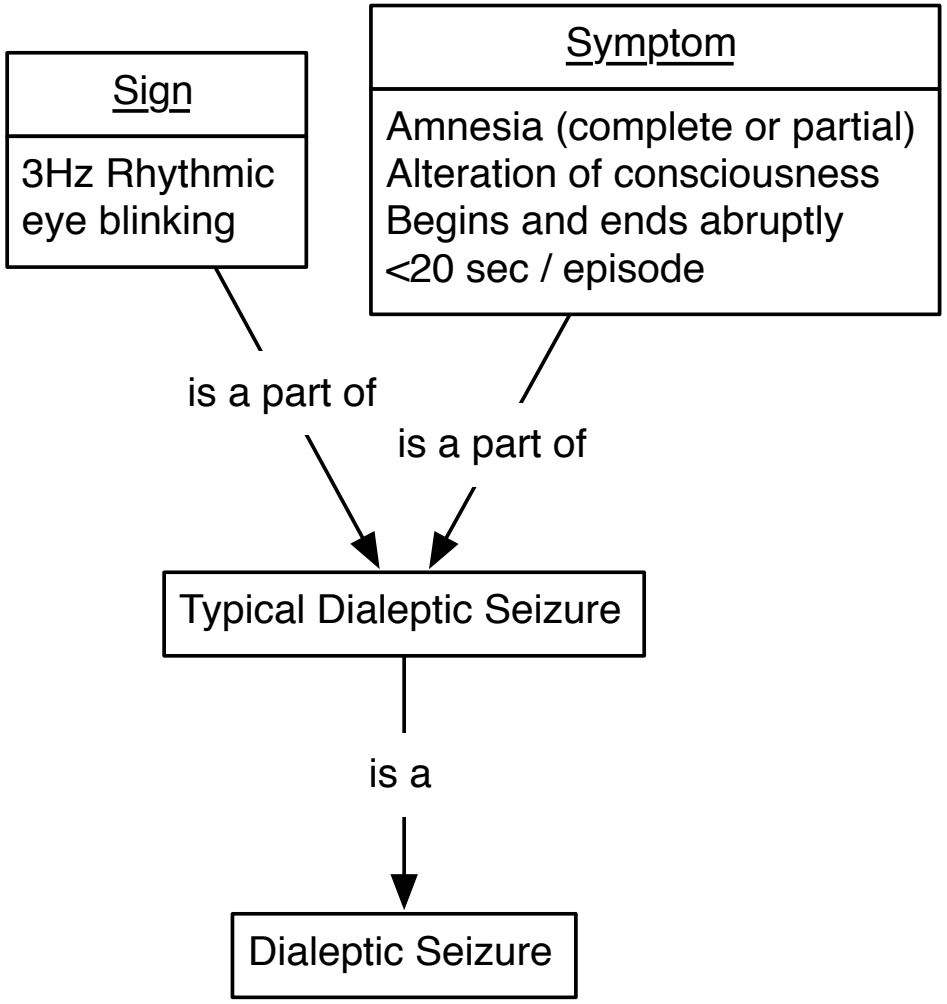




Methods: Aim 1

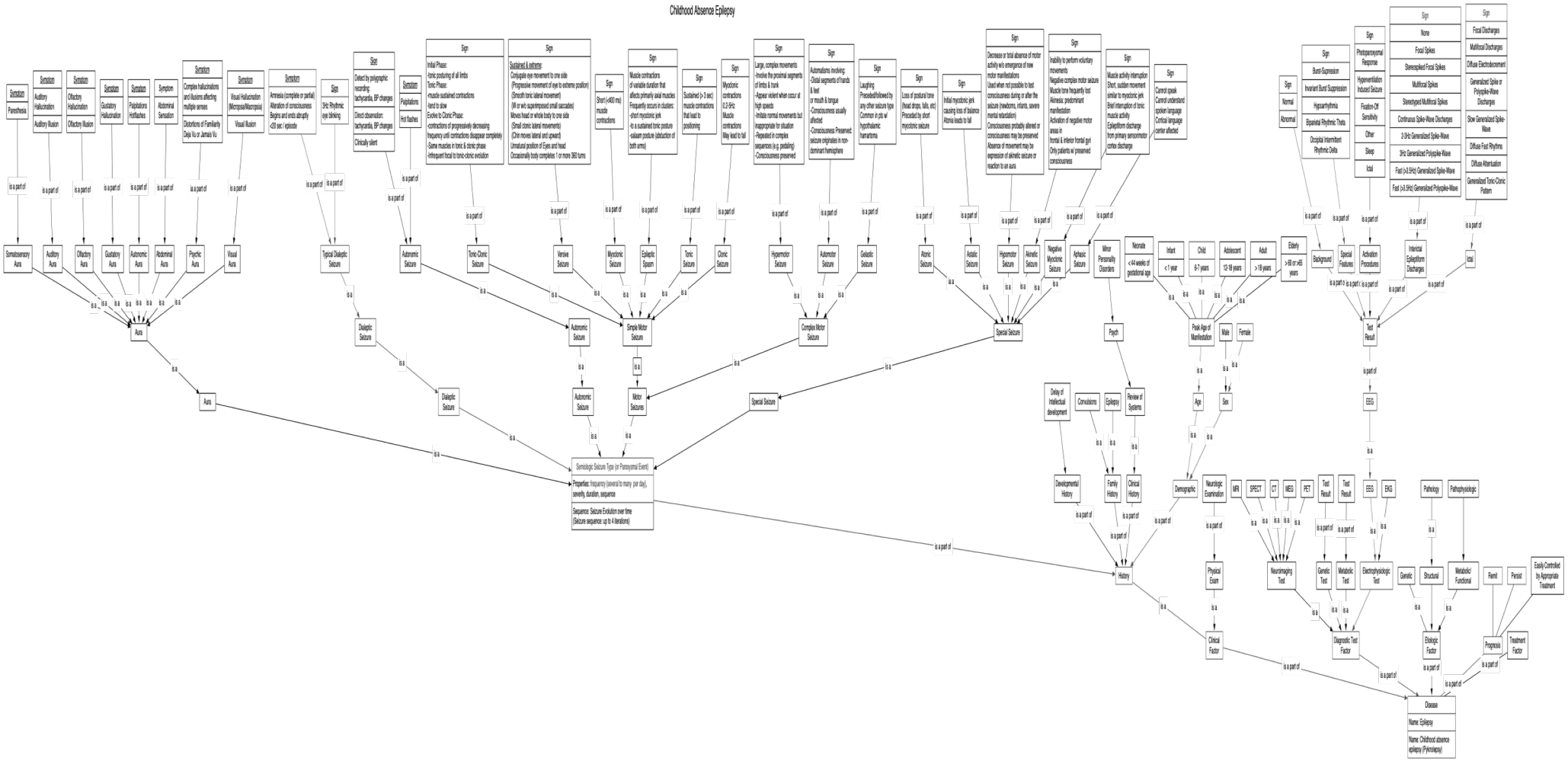
Dialeptic Seizure





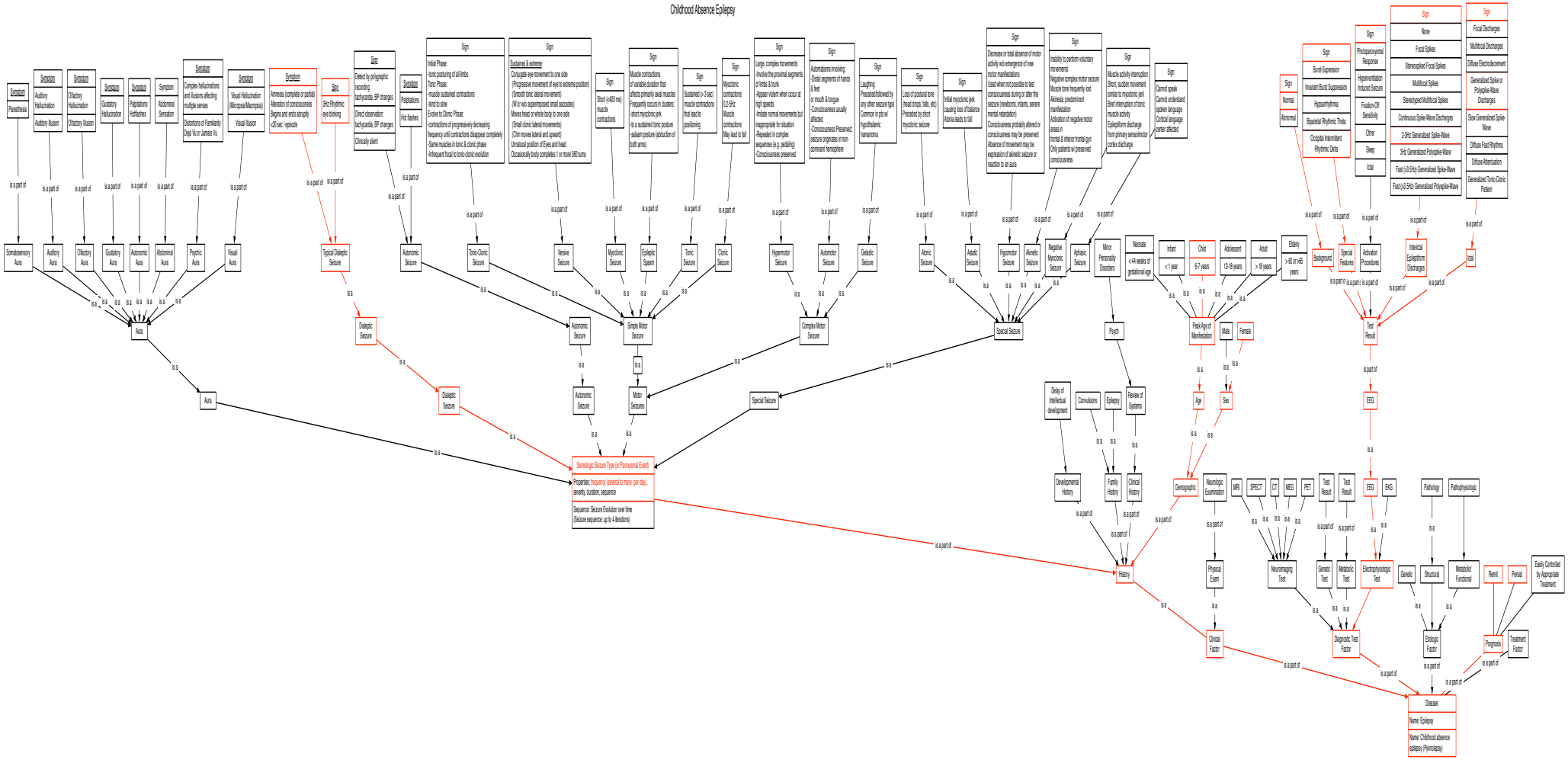
Methods: Aim 1

Epilepsies Ontology



Methods: Aim 1

Instantiating Subspace…



Methods

Childhood Absence Epilepsy