

Data-driven phenomic analysis of epileptic encephalopathies using an ontology-based phenotype database

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Purpose:

- Epileptic encephalopathies are a phenotypically challenging group of epilepsies
- Data-driven **phenomic strategies** to identify phenotypic subgroups
- Application of ontology-based **similarity measures**
- Clustering** of a cohort of epileptic encephalopathy patients

Methods:

- Implementation of validated epilepsy ontology in the **Human Phenotype Ontology (HPO)**¹
- Cartagenia Bench**® platform as phenotype entry matrix
- Analysis of phenotype similarities in 171 epileptic encephalopathy patients
- Assessment of a pairwise **Similarity Index (SI)** between patients
- SI** = Summary measure for loss of Information Content between last common ancestor of 2 phenotypic traits in ontology tree.
- Information Content** = Inverse frequency of a phenotypic trait.

Results

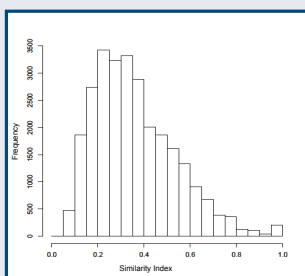


Figure 1: Similarity Index: Distribution of Frequency in all pair-wise comparisons.

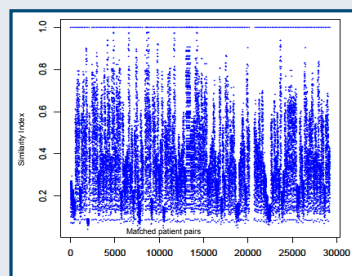


Figure 2: Similarity Index (SI) in pairwise comparisons. Small SI reflects distinct phenotypes, SI=1 equals identical patients.

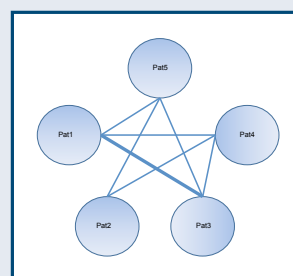


Figure 3: Similarity Network of 5 patients with high SI. Blue lines resemble SI of each patient.

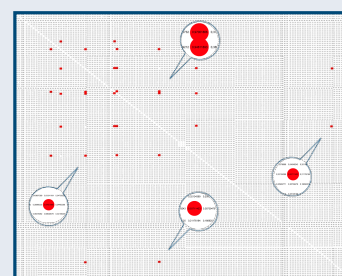


Figure 4: Patient Matrix: red dots mark SI > 0.95 and < 1. Comparisons with high SI values are spread throughout the matrix.

- Similarity Index reveals **normal distribution** (Fig. 1)
- Few pairwise comparisons show high similarity (Fig. 2)
- Comparison with high SI are spread throughout **Patient Matrix** (Fig. 4)
- Ontology-based similarity search reveals cluster of similar patients (Fig. 3)
- Patients with high SI have phenotype of **Idiopathic West Syndrome** with good outcome

Phenotypic Trait		Frequency
Epileptic Spasms		8/8
Seizure onset at 3-6 months		8/8
Seizure offset at 6-12 months		8/8
Hypsarrhythmia		7/8
seizure freedom achieved by	Vigabatrin	3/8
	Dexam.	2/8
	ACTH	2/8
	Clonazepam	1/8
Global developmental delay		3/8
Delayed speech and language development		1/8

Table 1: Phenotypic traits of 8 patients with high SI values

Conclusion:

- Ontology-based analysis of large-scale phenomic data permits subgrouping of patients.
- This clustering provides the basis for omics-style data-driven delineation of epilepsy phenotypes.