The International Neuromodulation Registry: A Graph Database Representation of Patient-Specific Data with Combined Predictive Modeling for Neuromodulation Therapies

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INTRODUCTION

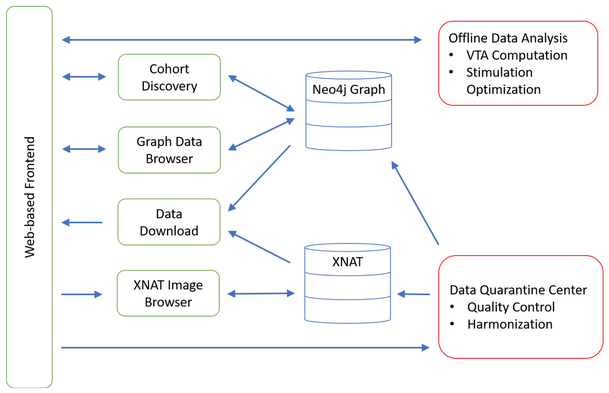
Deep Brain Stimulation (DBS) is a form of neuromodulation therapy, often used in patients with intractable Parkinson's disease, tremor, Tourette's syndrome, chronic pain, epilepsy, and other neurological disorders. However, DBS is a rare treatment and medical centers have relatively few patients qualifying for DBS, meaning that most DBS studies are statistically underpowered and have chronically low n values. Medical centers regularly publish studies on DBS, trying to standardize indications and contraindications for DBS, but these studies frequently contradict each other because sample sizes are too small to represent the population. Here, we present a platform designed to combine disparate datasets from different centers. Using this platform, researchers and clinicians will be able to aggregate patient datasets, transforming DBS studies from being center-based to being population-based.

METHODS

Despite the popularity of relational databases (SQL), we have built this informatics platform on a graph database management system.

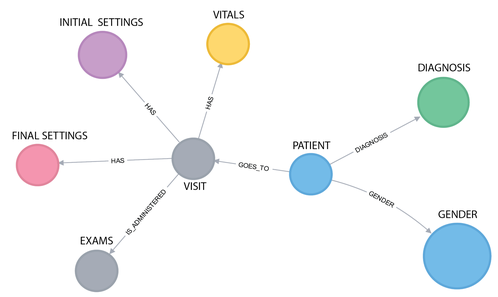
Graph databases are increasing in popularity due to their speed of information retrieval, powerful visualization of complex data relationships, and flexible data models. Our Neo4j DBMS is physically located in the University of Utah Center for High Performance Computing (CHPC) Protected Environment on a virtual machine, giving needs-based flexibility for both memory and storage

Physical Database Schema

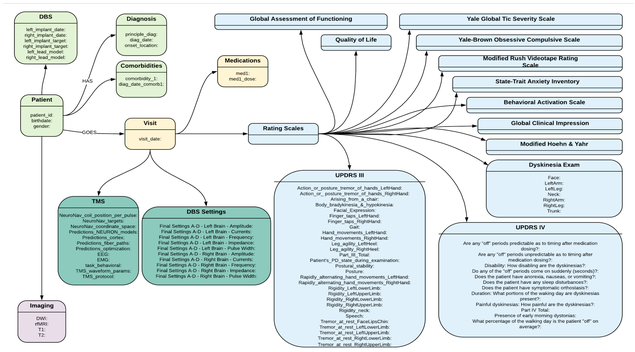


METHODS

Data Model

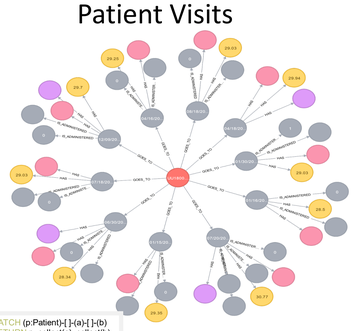


Formal Ontology



RESULTS

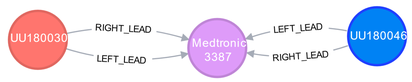
Patient Visits



```
MATCH (p:Patient)-[ ]-(a)-[ ]-(b)
RETURN p, collect(a), collect(b)
LIMIT 1
```

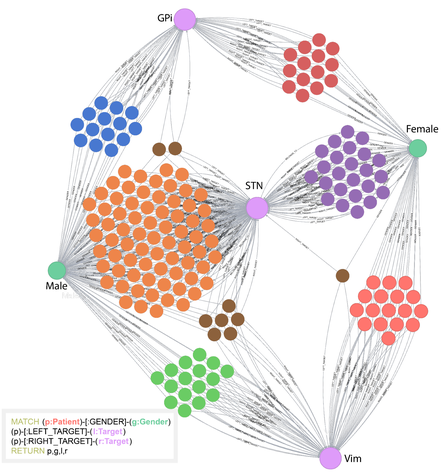
Shortest Path Algorithms

```
MATCH( p1:Patient ),(p2:Patient )
MATCHp=shortestPath(( p1)-[*]-(p2))
RETURNp
```



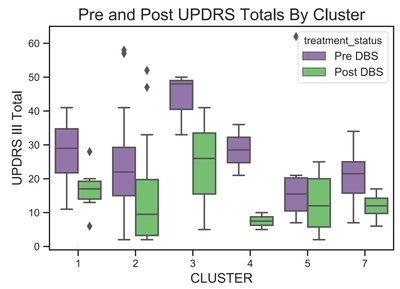

```
MATCH( p1:Patient ),(p2:Patient )
MATCHp=allShortestPaths(( p1)-[*]-(p2))
RETURNp
```

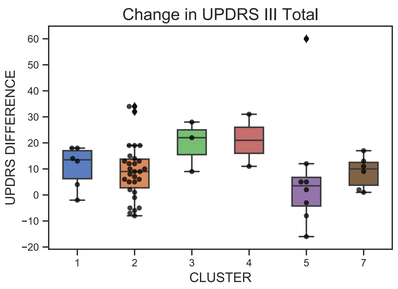
Visual Clustering




```
MATCH (p:Patient)-[:GENDER]-(g:Gender)
(p)-[:LEFT_TARGET]-(:Target)
(p)-[:RIGHT_TARGET]-(:Target)
RETURN p,g,l,r
```

Clustering Analysis





Clustering Results

```
Cluster 1   (GPi & Male)       count: 6
Cluster 2   (STN & Male)       count: 30
Cluster 3   (Vim & Male)       count: 3
Cluster 4   (GPi & Female)     count: 2
Cluster 5   (STN & Female)     count: 8
Cluster 6   (Vim & Female)     count: 0
Cluster 7   (mixed)            count: 6
```

Pre vs. Post UPDRS Totals Analysis

```
Cluster: 1      n = 6      p-value:  0.022*
Cluster: 2      n = 30     p-value:  7.489e-05*
Cluster: 3      n = 3      p-value:  0.072
Cluster: 4      n = 2      p-value:  0.282
Cluster: 5      n = 8      p-value:  0.411
Cluster: 7      n = 6      p-value:  0.018*
```

Change in UPDRS III Totals Between Clusters Analysis

```
One-way ANOVA
=============
F value 0.724
P value 0.608

Clusters 1 & 2     p-value: 0.767
Clusters 1 & 3     p-value: 0.189
Clusters 1 & 4     p-value: 0.232
Clusters 1 & 5     p-value: 0.715
Clusters 1 & 7     p-value: 0.643
Clusters 2 & 3     p-value: 0.136
Clusters 2 & 4     p-value: 0.169
Clusters 2 & 5     p-value: 0.691
Clusters 2 & 7     p-value: 0.905
Clusters 3 & 4     p-value: 0.906
Clusters 3 & 5     p-value: 0.397
Clusters 3 & 7     p-value: 0.077
Clusters 4 & 5     p-value: 0.450
Clusters 4 & 7     p-value: 0.116
Clusters 5 & 7     p-value: 0.863
```

RESULTS

Summary of Patients

Number of Patients	207 (Total)
	Male (138)
	Female (69)
Diagnoses	Parkinson's Disease (158)
	Tremor (91)
	Dystonia (86)
	Chronic Pain (24)
	Epilepsy (11)
	Stroke (2)
Lead Locations	Globus Pallidus Internus (GPi) (35)
	Subthalamic Nucleus (STN) (108)
	Thalamus, Ventral Intermediate Nucleus (Vim) (56)
Lead Models	Medtronic 3387 (215)
	Medtronic 3389 (102)
Avg Age at Surgery	61.6 ± 0.82 years

CONCLUSIONS

This patient registry has been built on a next-generation graph database. Through a formal, but flexible, data model and ontology, this platform is able to harmonize disparate data types and allows for simple visualizations of complex data types.

1. The Neo4j interface readily allows for preliminary discovery as the user can query a subgraph and drag nodes to facilitate clusters and relationships within the data.
2. Neo4j provides native database queries and algorithms to find similarities between patients.
3. Anticipated Use Cases: Cohort discovery, data and imaging download, exploratory analysis

FUTURE DIRECTIONS

1. Build an interface for the Butson lab optimization algorithm (Anderson et al, 2018).
2. Include online analysis methods such as a computational VTA generator.

NEUROMODULATION IMAGING ACCESS DATABASE

neuromod.chpc.utah.edu

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