

BIG DATA ANALYTICS TO CHARACTERIZE TREMOR PREVALENCE AND REGULARITY IN NECK DYSTONIA

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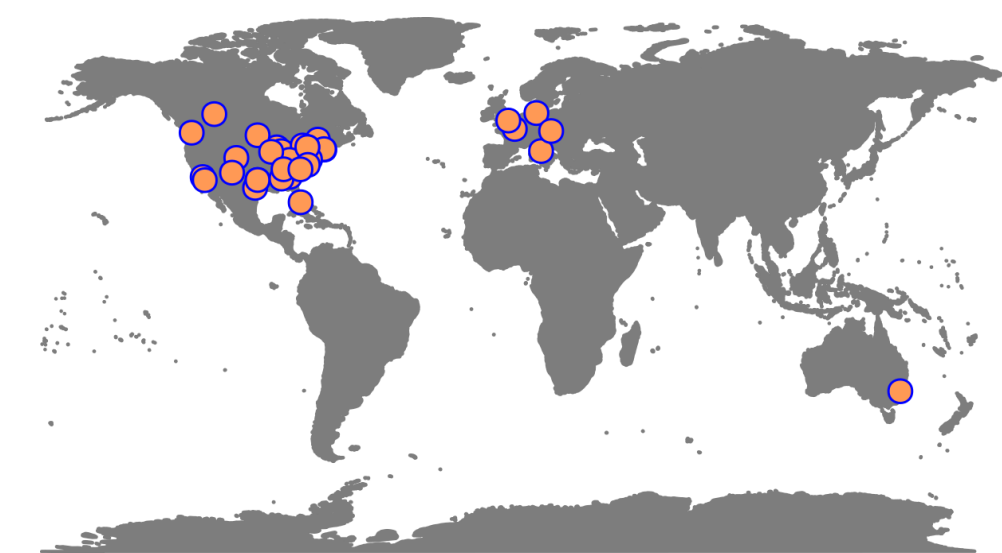
Introduction

- Dystonia is the third most common neurological disorder characterized by abnormal twisting and turning of the body parts and is frequently associated with tremor.
- About three million people worldwide suffer from this devastating neurological disorder.
- The dystonia affecting the neck, also known as torticollis or wryneck, is its most common form affecting about one million people.
- About half of the patients with neck dystonia also have tremor which is frequently underdiagnosed.
- Tremor when present can be coarse, irregular, and jerky, or it can be regular resembling benign essential tremor.
- The biggest clinical challenge is to definitively label tremor as regular or irregular.
- Identifying tremor and whether it is regular, or irregular is critical to determine the care path.
- Failure to identify the tremor and to discriminate between regular or irregular features frequently leads to therapeutic failures, years of poor quality of life, and waste of billions of dollars in revenue.

Aims: We analyzed the **world’s largest cohort of neck dystonia patients** (n=3117) collected from **52 movement disorder centers** **spanned across the Americas, Europe, and Asia**. The *Big Data Analytics* principles were used to evaluate this historically largest dataset, *predicting the features of neck dystonia* that are associated with the presence of tremor. We also computed predictive measures of regular versus irregular tremor type in neck dystonia patients. The ability of predicting co-occurrence of tremor and if it is regular or irregular will facilitate accurate diagnosis and initiate ideal care path.

Data

The world’s largest cohort (3117 neck dystonia subjects) of systemically-evaluated subjects in a prospectively designed, multi-center study (52 centers, three continents)

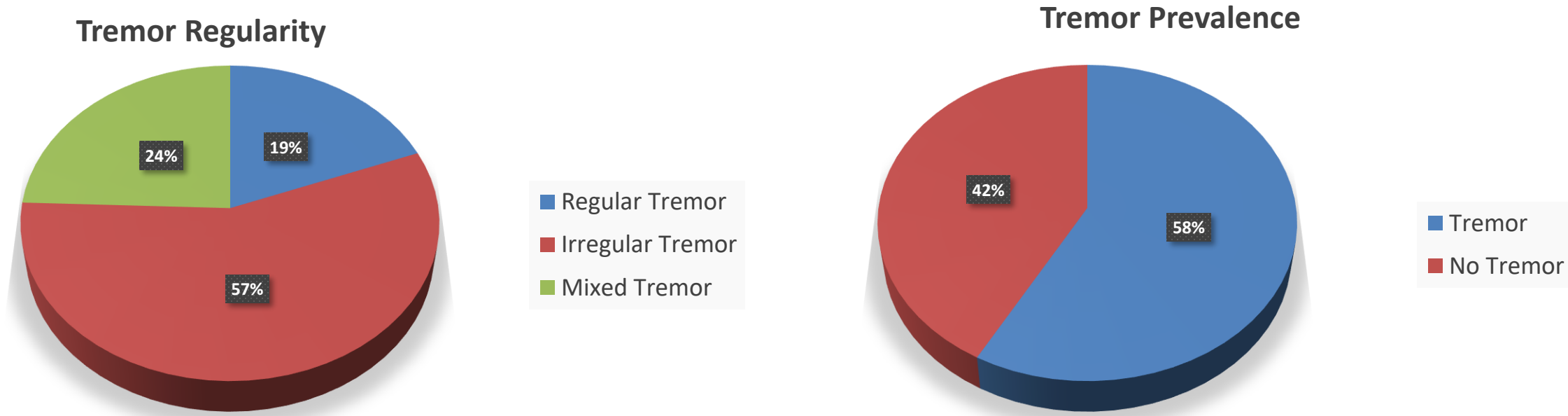


Characteristic	Mean ± SD
Age	59.8 ± 12.4
Age at onset (years)	45.9 ± 14.8
Dystonia duration (years)	13.8 ± 11.9
Dystonia severity (GDRS)	8.3 ± 7.0

Methods

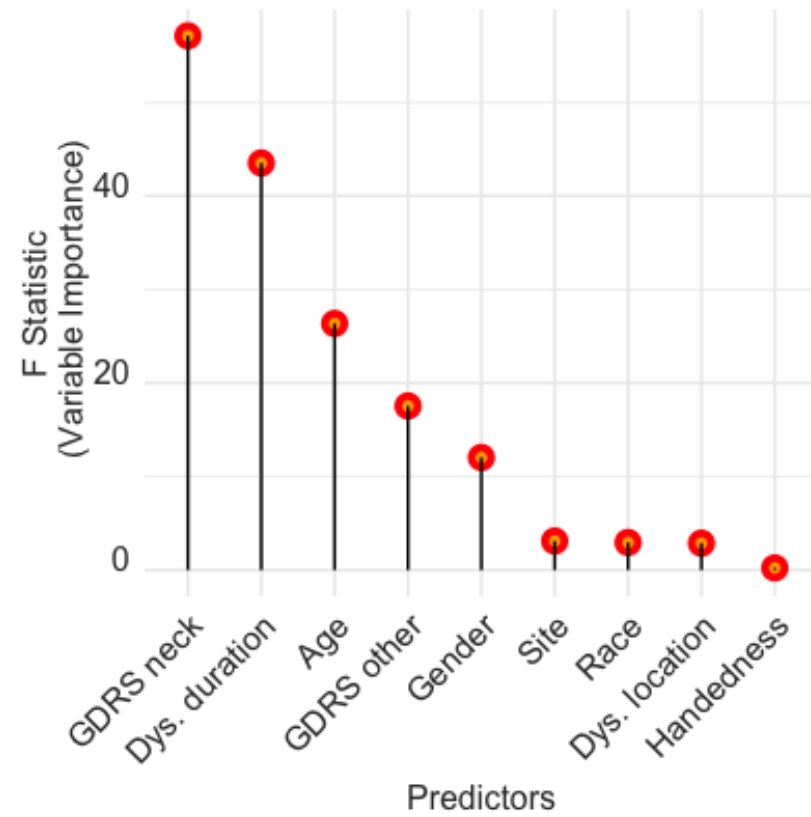
- We used an exhaustive search algorithm based on Akaike information criterion.
- The algorithm selected the most parsimonious generalized linear model out of models with all possible feature combinations.
- A permutation-based random forest feature selection algorithm was utilized to select the most relevant features for tremor prevalence and irregularity based on mean decrease in prediction accuracy.

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Tremor Prevalence

Model: Tremor prevalence ~ Neck dystonia severity + Dystonia duration + Age + severity of dystonia elsewhere + Gender + Site + Race + Dystonia location + Handedness



Feature importance of prevalence predicting parameters. Important predictors of tremor prevalence cause significant decrease in prediction accuracy of a predictive Random Forest model.

Table Binomial multiple logistic regression analyses			
Predictor	Std. Coefficient (95%)	Odds Ratio (95% CI)	P value
GDRS neck	0.318 (0.236-0.401)		<.001
Dystonia duration	0.285 (0.201-0.371)		<.001
Age	0.218 (0.135-0.302)		<.001
GDRS other	-0.218 (-0.322- -0.118)		<.001
Gender (Ref: Female)		0.736 (0.619 - 0.875)	<.001
Site (reference: median site with 52.06% prevalence rate)			
Booth Gardner Parkinson Care Center		2.601 (1.319 - 5.464)	0.008
Houston Methodist Hospital		0.031 (0.001 - 0.158)	<.001
University of Alberta		0.254 (0.083 - 0.645)	0.008
University Of Texas		0.228 (0.083 - 0.567)	0.002
VCU		0.493 (0.243 - 0.971)	0.044
Wake Forest University		0.201 (0.076 - 0.469)	<.001

- ✓ Significant features predicting tremor were determined by Wald tests.
- ✓ More severe forms of neck dystonia, longer disease duration, and patient’s age, in descending order, predicted the presence of neck tremor.
- ✓ The probability of tremor was reduced if the dystonia affected other body parts in addition to the neck.

Conclusion

We identified the most important dystonia characteristics that predict the likelihood of a concurrent tremor in dystonia, and the likelihood of it being irregular, i.e. dystonic tremor.

Tremor Prevalence in Dystonia:

- Severity of neck dystonia and duration of dystonia are the most important predictor of tremor in dystonia.
- Age, dystonia severity outside of the neck and gender also increase the likelihood of concurrent tremor in dystonia but not as substantially as severity of neck dystonia and dystonia duration.

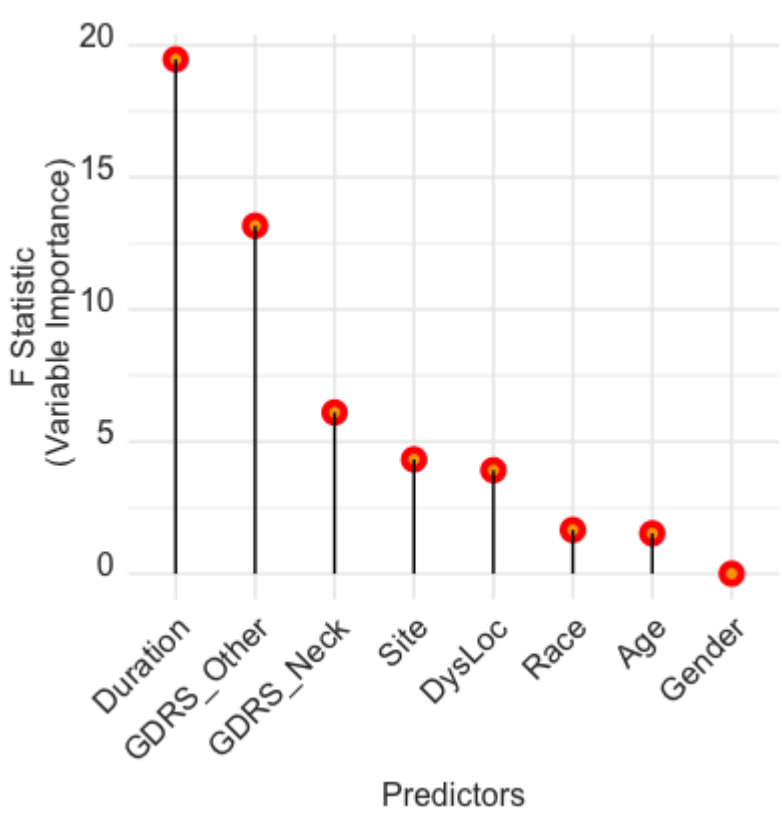
Tremor Irregularity in Dystonia:

- The first feature selection analysis indicated that severity of dystonia affecting the other body parts and the disease duration were most robust indicators for irregular tremor types.
- Increasing severity of dystonia affecting other body parts was associated with lower likelihood of neck tremor while increased age predicted higher likelihood.

Using a large patient cohort and Big Data Analytics, we identified the most relevant clinical traits that can predict concurrent tremor prevalence and irregularity in dystonia

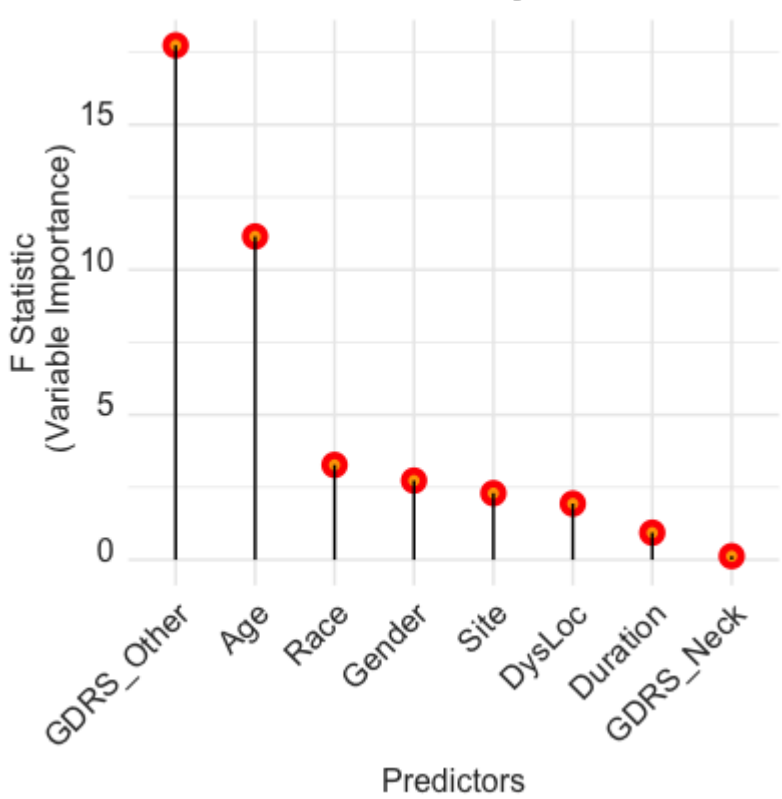
Tremor Irregularity

Model: Tremor irregularity ~ Dystonia duration + severity of dystonia outside of the neck + severity of neck dystonia + Recruitment site + Body part w/concurrent tremor + Race + Age + Gender + Race



Feature importance of irregularity predicting parameters in reference to regular tremor. Important predictors of tremor irregularity cause significant decrease in prediction accuracy of a predictive Random Forest model.

Model: Tremor irregularity ~ Severity of dystonia outside of the neck + Age + Race + Gender + Recruitment site + Body part w/concurrent tremor + Dystonia duration + severity of neck dystonia



Feature importance of irregularity predicting parameters in reference to NO tremor. Important predictors of tremor irregularity cause significant decrease in prediction accuracy of a predictive Random Forest model.

Acknowledgement: This work was supported by grants to the Dystonia Coalition, a consortium of the Rare Diseases Clinical Research Network (RDCRN) that is supported by the Office of Rare Diseases Research (ORDR) at the National Center for Advancing Clinical and Translational Studies (NCATS; U54 TR001456) in collaboration with the National Institute for Neurological Diseases and Stroke (NINDS; U54 NS065701). Aasef Shaikh received a Dystonia Medical Research Foundation (DMRF) Clinical Fellowship, DMRF/Dystonia Coalition Career Development Award, DMRF Brain Network Research Grant, American Academy of Neurology Career Award, George C. Cotzias Memorial Fellowship, and U.S. Department of Veterans Affairs Merit Review Grant. Shaikh has Penni and Stephen Weinberg Research Chair in Brain Health.