

Automated Audio Analysis of Dysarthria in Huntington's disease (Audio-HD)

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- **Luis Sierra**: has declared that there is no conflict of interest.
- **Karen Hildebrand**: has declared that there is no conflict of interest.
- **Clementina Ullman**: has declared that there is no conflict of interest.
- **Magdaline Mwangi**: has declared that there is no conflict of interest.
- **Henry O'Connell**: Chief Executive Officer and Founder of Canary Speech.
- **Samuel Frank**: has declared that there is no conflict of interest.
- **Simon Laganiere**: has declared that there is no conflict of interest.

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Huntington's disease (HD) - Background

- Genetic testing for pathological CAG expansion in HTT
- Slow progressive decline in motor, cognitive and behavioral abilities
 - Pre-motor Manifest  Manifest HD
- Progressive speech/language changes (vast majority of patients)
- Unified Huntington's Disease Rating Scale (UHDRS™) - 124 points
 - Motor Assessment (Item 4): 4 points
 - (0) Normal
 - (1) Unclear, no need to repeat
 - (2) Must repeat to be understood
 - (3) Mostly incomprehensible
 - (4) Anarthria (mute)

Hypotheses:

- Early speech changes are not evident to clinical examination (UHDRS) (Perez et al., 2018)
- Automated analysis of speech output could detect progressive transition from pre-manifest to manifest HD (Romana et al., 2020)
- Speech changes could serve as clinical or research biomarkers (Tovar et al., 2020; Vogel et al., 2012)

Study cohorts:

- Patients with genetically-confirmed Huntington's disease
 - Pre-motor manifest HD
 - Manifest HD
- Healthy Controls

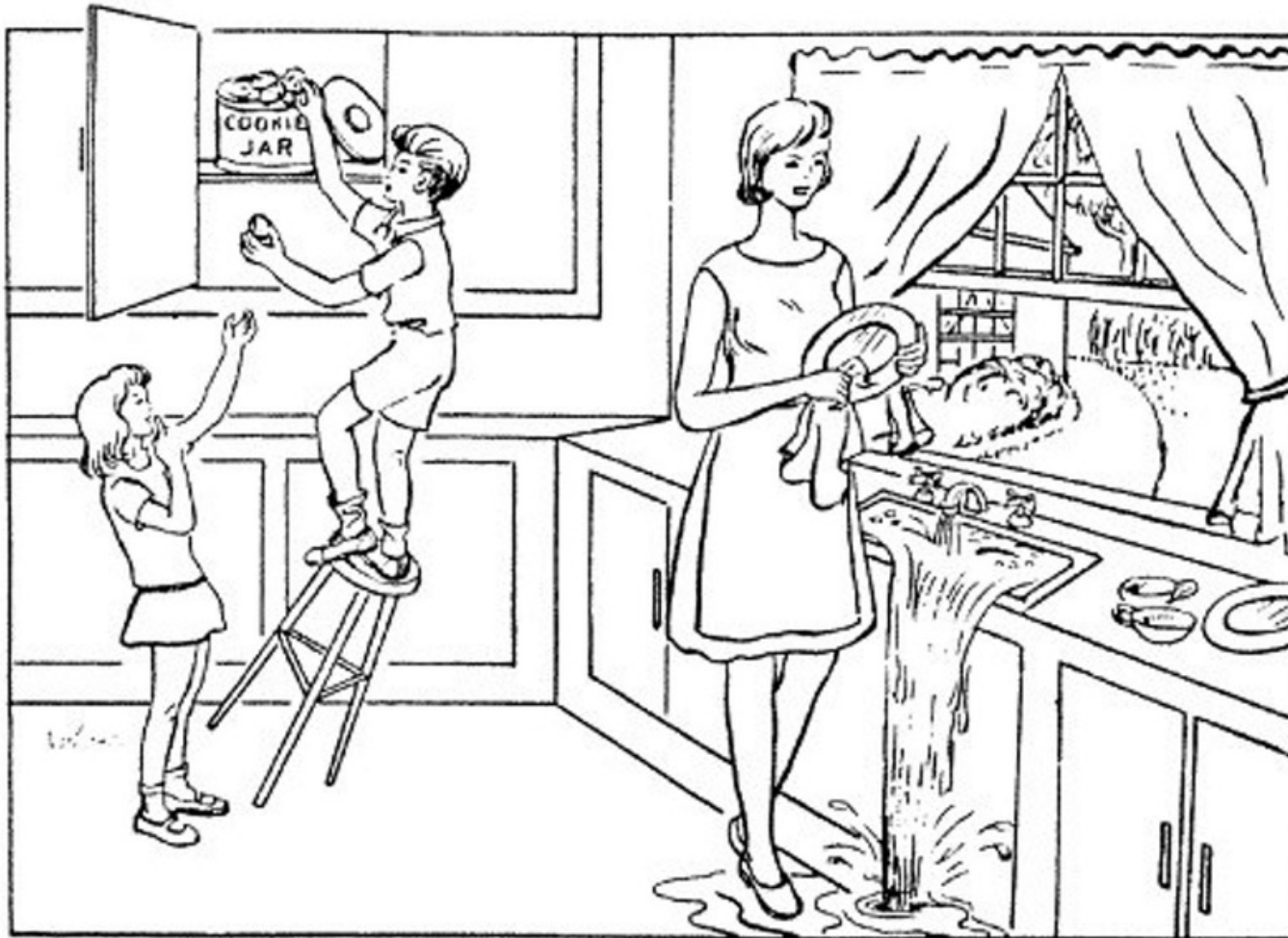
Key Exclusion Criteria:

- Individuals with any other form of dysarthria (acquired, developmental or trauma-related)

- Automated voice application on a tablet with a stand
- Capture different types of speech:
 1. Unconstrained Descriptive Analysis
 2. Constrained Reading
 3. Procedural Narrative: i.e. Tell me how to make a sandwich.
 4. Free Speech: i.e. How are you feeling today?
 5. Single Word Reading

1. Unconstrained Descriptive Analysis

- **Cookie Theft Picture:** Useful in analysis of Syntax in verbal response.



2. Constrained Reading

- **Caterpillar Passage:** targeted to inform the assessment of motor speech disorders.

Do you like amusement parks? Well, I sure do. To amuse myself, I went twice last spring. My most MEMORABLE moment was riding on the Caterpillar, which is a gigantic roller coaster high above the ground. When I saw how high the Caterpillar rose into the bright blue sky I knew it was for me. After waiting in line for thirty minutes, I made it to the front where the man measured my height to see if I was tall enough. I gave the man my coins, asked for change, and jumped on the cart. Tick, tick, tick, the Caterpillar climbed slowly up the tracks. It went SO high I could see the parking lot. Boy was I SCARED! I thought to myself, "There's no turning back now." People were so scared they screamed as we swiftly zoomed fast, fast, and faster along the tracks. As quickly as it started, the Caterpillar came to a stop. Unfortunately, it was time to pack the car and drive home. That night I dreamt of the wild ride on the Caterpillar. Taking a trip to the amusement park and riding on the Caterpillar was my MOST memorable moment ever!

5. Single Word Reading

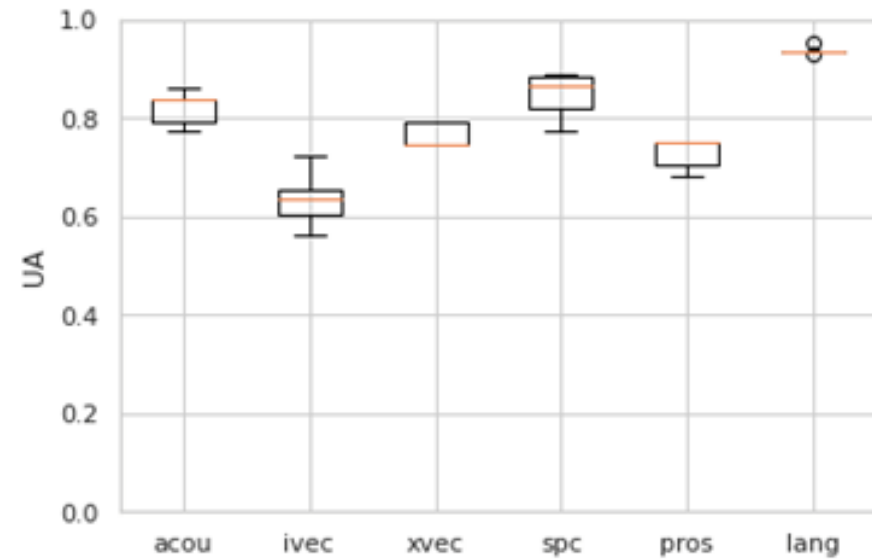
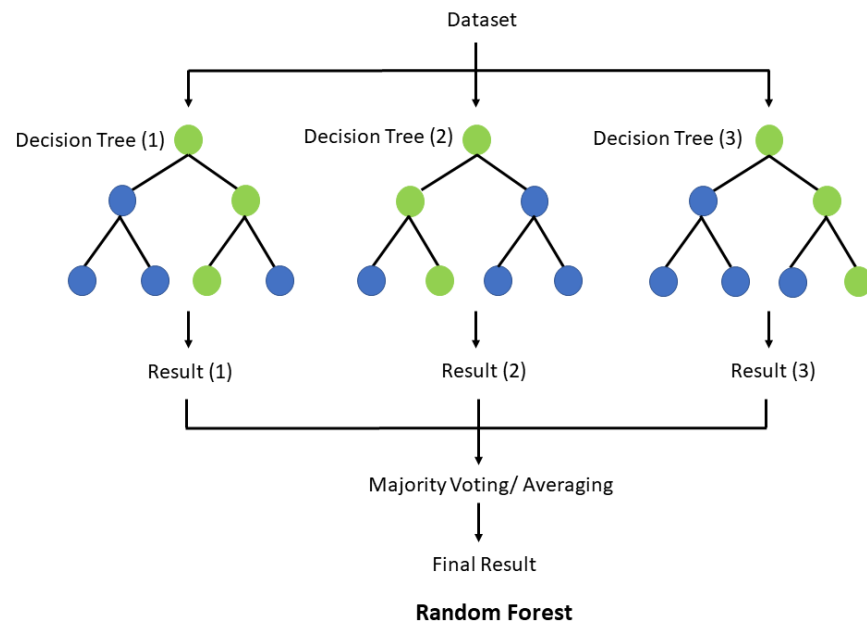
Stroop Color-Word Test

Block 1	Block 2	Block 3
red	■ ■ ■	red
yellow	■ ■ ■	yellow
green	■ ■ ■	green
red	■ ■ ■	red
blue	■ ■ ■	blue
green	■ ■ ■	green
yellow	■ ■ ■	yellow
blue	■ ■ ■	blue
green	■ ■ ■	green
red	■ ■ ■	red
blue	■ ■ ■	blue
yellow	■ ■ ■	yellow

Analysis

Features	Abbreviation	Description
i-vector	ivec	Speech embedding based on GMMs
x-vector	xvec	Speech embedding based on Neural Networks
Language	lang	Prosodic and linguistic features based on spoken words and their timestamps from ASR (Automatic Speech Recognition) result - pause/filler, speech rate, vowel duration, word popularity for free speech, spoken word error rate for read speech, etc.
Speech	spc	Speech signal features such as spectral flux, flatness, jitter, shimmer, phonation time, etc.
Prosody	pros	Prosodic features including f0, energy, speech/silence, pause, breath, etc.
Acoustic statistics	acou	Statistics (mean, std, slope, quantile, kurtosis, skewness,..) of MFCC, PLP, Pitch per frame

Random Forest:



Demographics

Group	(n = 78)	Total Motor Score	CAG Repeat Length	Age	Education Level	Sex (Female)
HD (\pm SD)	46 (23 Pre; 21 Manifest)	16.1 (15.72)	43.1 (3.62)	48.2 (14.0)	15.1 (2.53)	50%
Controls (\pm SD)	32	---	---	42.7 (17.4)	16.3 (2.57)	53%

- ❖ 2 participants were removed from analysis due to inadequate speech samples

Results Summary

Label	Feature	N	Accuracy	Sensitivity	Specificity	AUC
Manifest vs. Others	Lang	76	0.96	0.91	0.98	0.98
Manifest vs. Pre-motor manifest	Lang	44	0.95	0.95	0.95	0.97

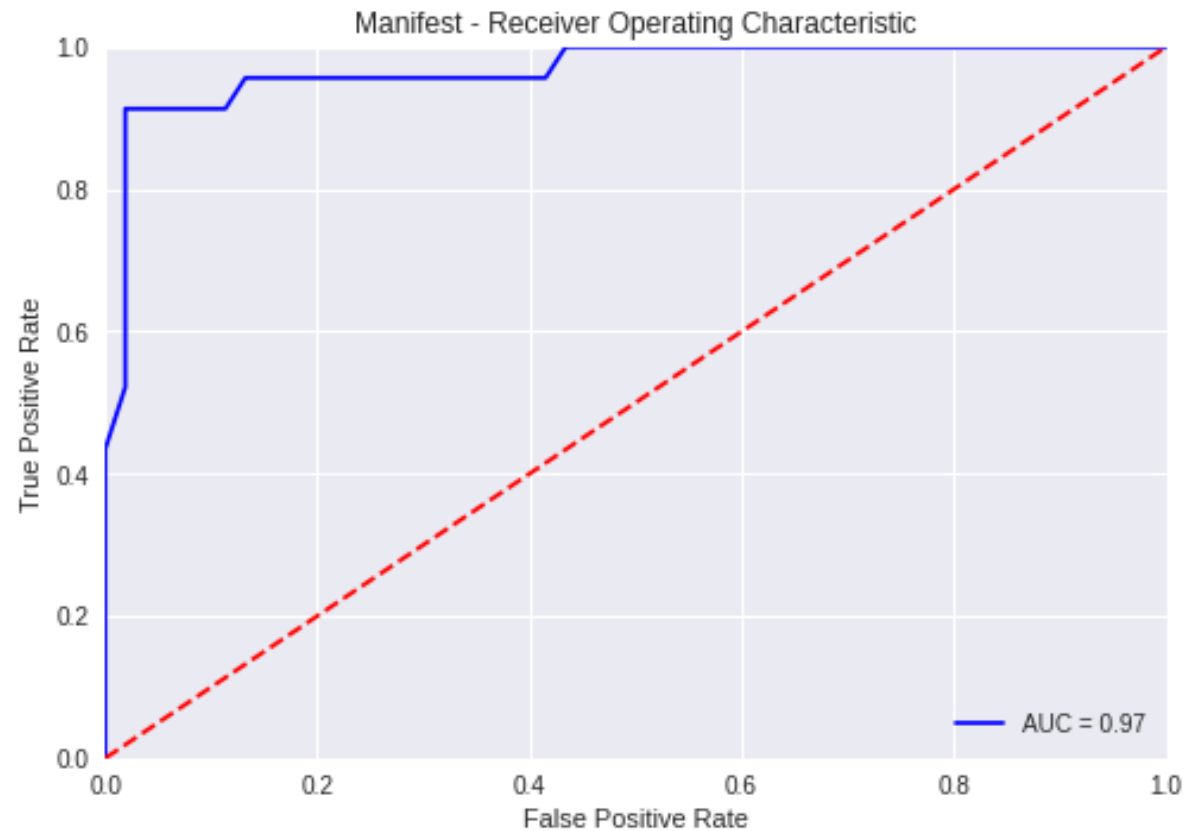
Confusion matrix

Confusion Matrix		Predicted	
		Pre-Motor	Manifest
Actual	Pre-Motor	20	1
	Manifest	1	{22}

Label	Feature	N	Accuracy	Sensitivity	Specificity	AUC
Dysarthria vs. No-Dysarthria	Lang	44	0.82	0.67	0.90	0.85

Conclusions

- 8-minute tablet assessment
- 96% accuracy at distinguishing pre-motor manifest from manifest HD
- High accuracy despite ~41% of manifest HD cohort without clinical dysarthria
- Further training of the model and longitudinal follow up will be critical for determining the overall utility of this approach.



Potential Limitations

- Random Forest analysis can lead to overfitting
- Can be complex and hard to interpret which specific features are most important
- This tool has not yet been validated with other datasets

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