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Voice in Parkinson's Disease: a Machine Learning Study

Francesco Asci, MD

IRCCS Neuromed Institute, Pozzilli (IS), Italy;
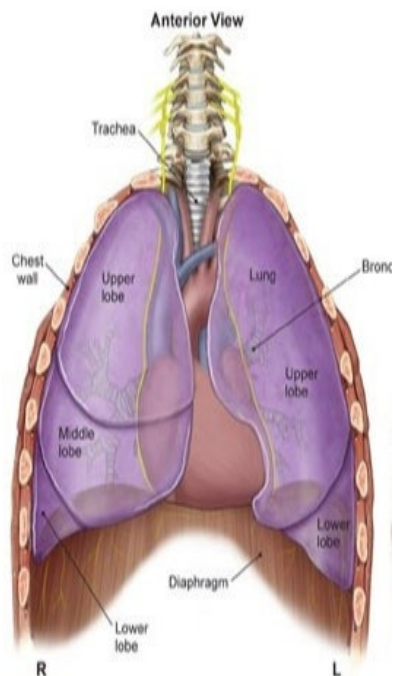Department of Human Neurosciences, Sapienza University of Rome, Italy.

The Human Voice

Human voice originates from the dynamic interaction of the respiratory, phonatory and articulatory systems.
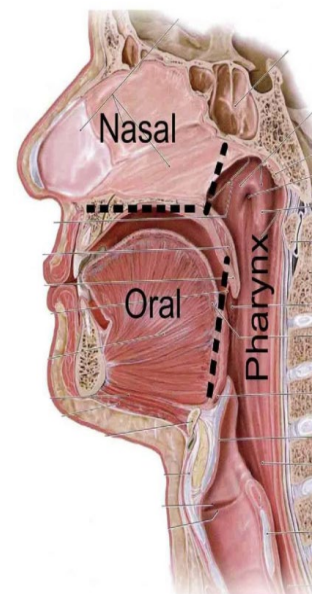The pulmonary air current flows through the vocal folds and resonant structures turning out into the voice sound.
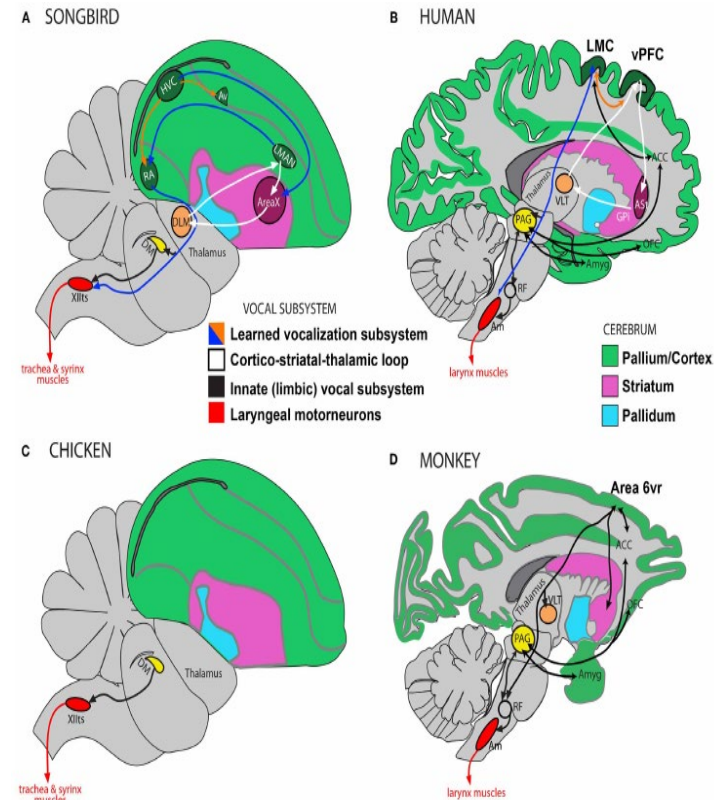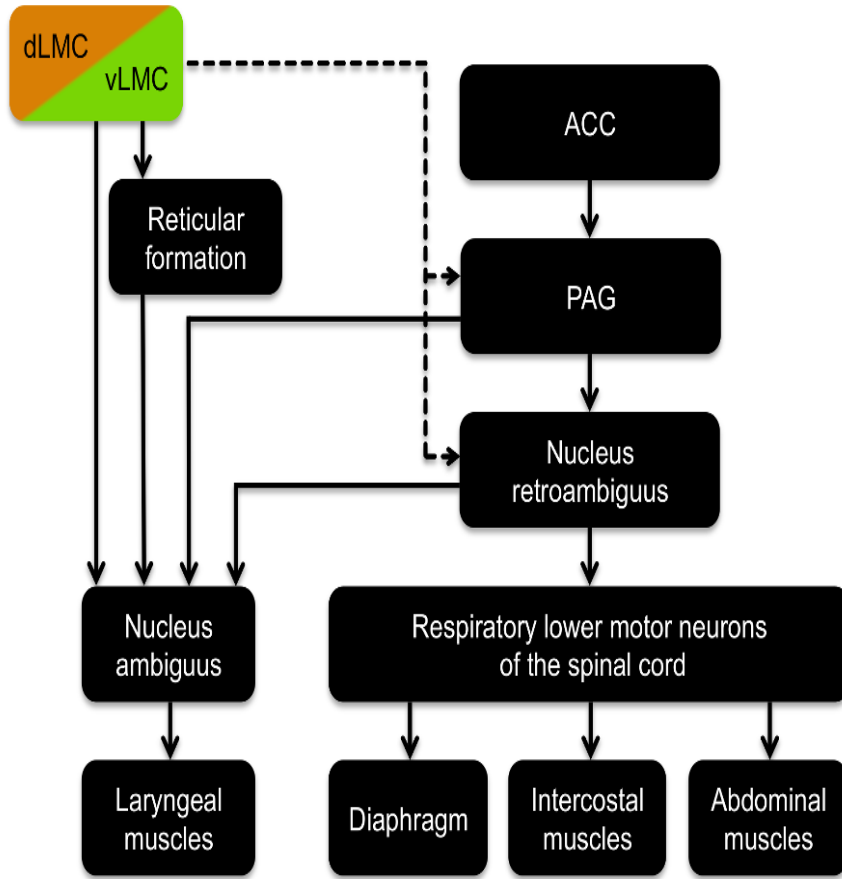
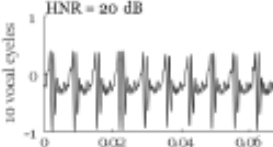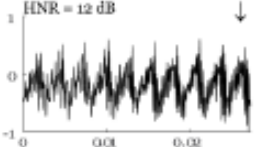**Respiratory System**

Phonatory System
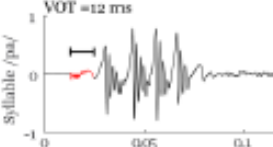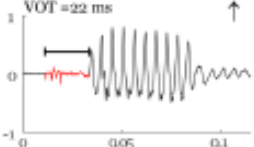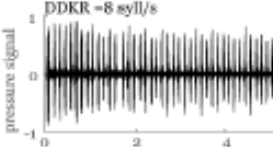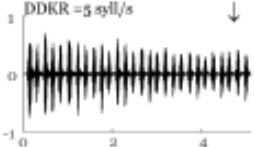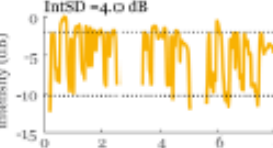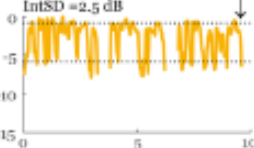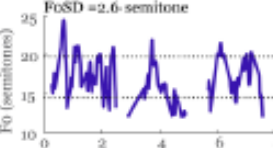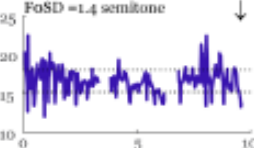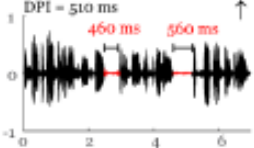
Articulatory System

The **Larynx Motor Cortex (LMC)** is the primary cortical center for vocalization in the human brain

Belyk et al., 2021

Voice in Parkinson's Disease

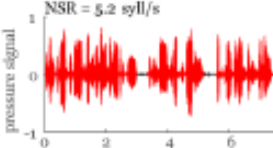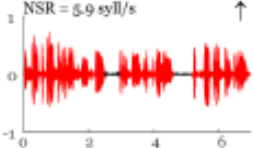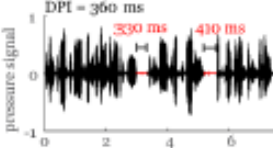| Speech dimension [vocal task]	Acoustic feature definition	Healthy speech example	Hypokinetic dysarthria example	trend
Harsh voice [sustained phonation]	Harmonics-to-noise ratio (HNR), defined as the amplitude of tonal relative to noise components.	HNR = 20 dB	HNR = 12 dB	↓
Imprecise consonants [syllable repetition]	Voice onset time (VOT), defined as the length of the consonant from initial burst to vowel onset.	VOT = 12 ms	VOT = 22 ms	↑
Slow sequential motion rates [syllable repetition]	Diadochokinetic rate (DDKR), defined as the number of syllable vocalizations per second.	DDKR = 8 syll/s	DDKR = 5 syll/s	↓
Monoloudness [reading passage]	Intensity variability (IntSD), defined as the standard deviation of intensity contour after removal of pauses.	IntSD = 4.0 dB	IntSD = 2.5 dB	↓
Monopitch [reading passage]	Pitch variability (FoSD), defined as the standard deviation of pitch contour.	FoSD = 2.6 semitone	FoSD = 1.4 semitone	↓
Articulation rate [reading passage]	Net speech rate (NSR), defined as the total number of syllables divided by the total duration of speech after removal of pauses.	NSR = 5.2 syll/s	NSR = 5.9 syll/s	↑
Prolonged pauses [monologue]	Duration of pause intervals (DPI), defined as the median length of pause intervals.	DPI = 360 ms (330 ms, 410 ms)	DPI = 510 ms (460 ms, 560 ms)	↑

time (seconds)

Rusz et al., 2021

Multidimensional Voice Analysis

➢ **Objective /Quantitative Voice Analysys**

➢ **Voice Cepstral Analysis**

➢ **CPP -** Cepstral Prominence Peak

Normal Voice Signal

Cepstral Peak Prominence 13 dB

Spectrum

Cepstrum
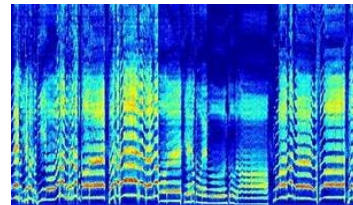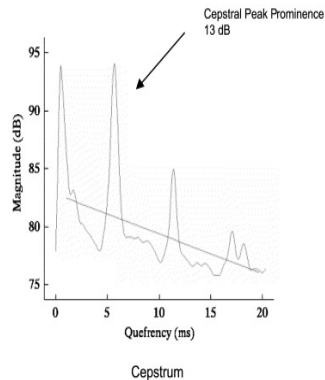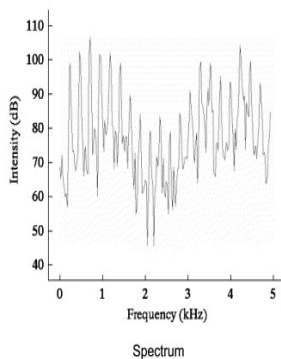
VOICE HANDICAP INDEX

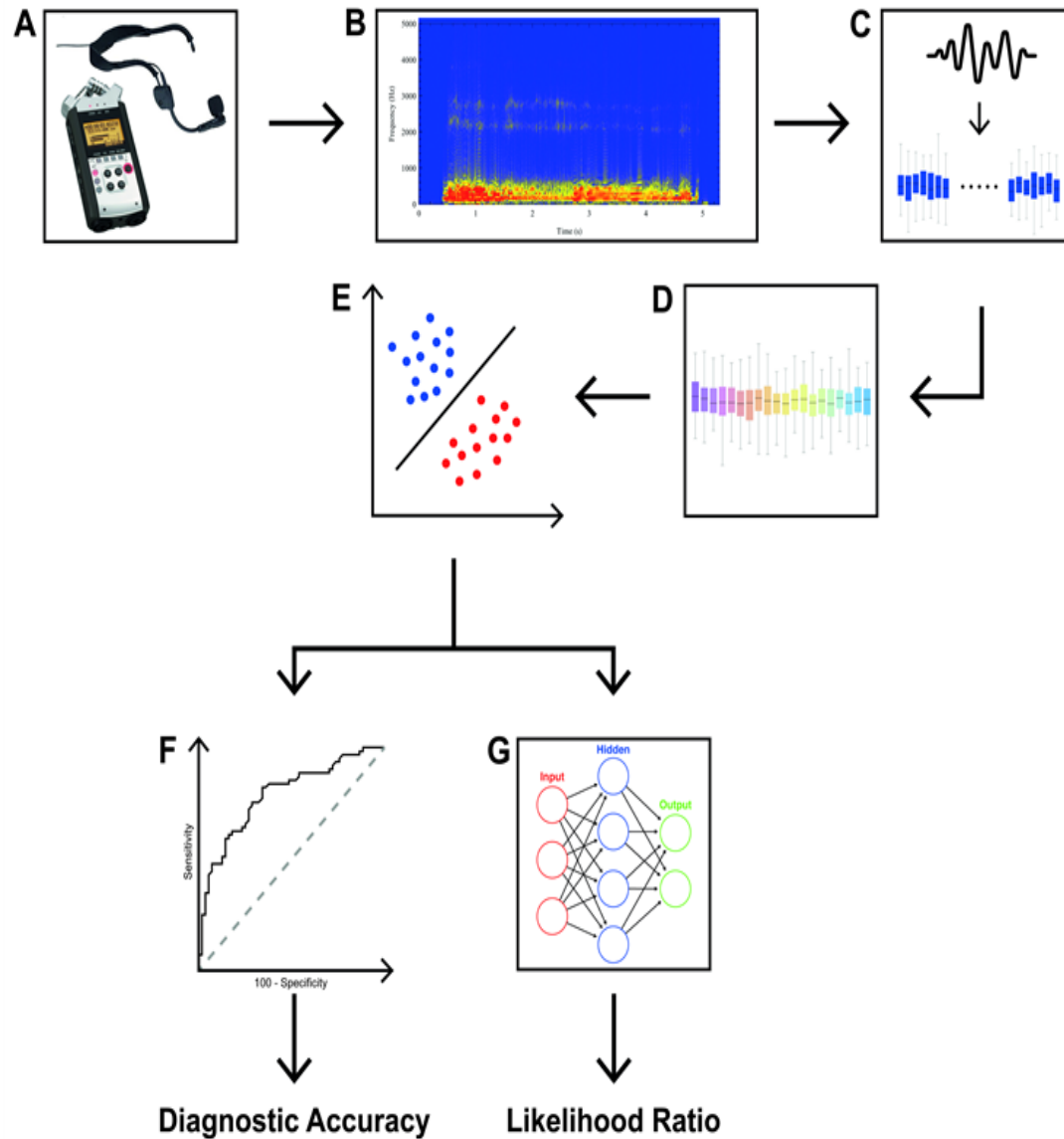| Area fisica	sempre	quasi sempre	qualche volta	quasi mai	mai
Esaurisco l'aria quando parlo					
Il suono della mia voce varia durante la giornata					
La gente mi chiede "Cosa c'è che non va con la sua voce?"					
Mi sembra di dovermi sforzare per produrre la voce					
La chiarezza della mia voce è imprevedibile					
Cerco di cambiare la mia voce per farle avere un suono differente					
Faccio molto sforzo per parlare					
La mia voce è peggiore la sera					
La mia voce viene meno nel mezzo del parlare					

Area funzionale	sempre	quasi sempre	qualche volta	quasi mai	mai
La mia voce è udita con difficoltà dalla gente					
La gente ha difficoltà a capirmi in una stanza rumorosa					
In famiglia hanno difficoltà a udirmi quando chiamo per casa					
Adopero il telefono meno sovente di quanto vorrei					
Tendo ad evitare gruppi di persone a causa della mia voce					
Parlo meno sovente con amici, vicini e parenti a causa della mia voce					
La gente mi chiede di ripetere quando parlo faccia a faccia					
Le mie difficoltà di voce restringono la mia vita personale e sociale					
Mi sento tagliato fuori dalle conversazioni a causa della mia voce					
I miei problemi di voce mi fanno guadagnare meno					

Area emotiva	sempre	quasi sempre	qualche volta	quasi mai	mai
Sono teso a causa della mia voce quando parlo con gli altri					
La gente sembra irritata dalla mia voce					
Trovo che gli altri non comprendano i miei problemi di voce					
Il mio problema di voce mi sconvolge					
Esco di meno per i miei problemi di voce					
La mia voce mi fa sentire handicappato					
Mi scoccio quando la gente mi chiede di ripetere					
Mi sento imbarazzato quando la gente mi chiede di ripetere					
La mia voce mi fa sentire incapace					
Mi vergogno del mio problema di voce					

Hillenbrand et al., 1994, 1996; Heman-Ackah et al., 2002, 2014

Advanced Voice Analysis with Machine Learning

Suppa et al. 2020, 2021, 2022
Asci et al. 2020, 2021 a, b

Laryngeal Dystonia

	Age (years)	Weight (Kg)	Height (cm)	DD (years)	VHI before	VHI after	DCS before	DCS after	MMSE	HAMD	CPPS before	CPPS after
ASD	64.1 ± 13	65.3 ± 11	161.1 ± 16.1	7.7 ± 7.1	56.4 ± 23.2	41 ± 21.8	2.2 ± 0.7	1.2 ± 0.8	29.7 ± 0.7	6.8 ± 4.9	4.2 ± 2.6	5.1 ± 2.6
HS	59 ± 12	70.1 ± 11.3	164.2 ± 9.2	–	–	–	–	–	29.9 ± 0.4	3.4 ± 1.4	7.7 ± 1.4	–
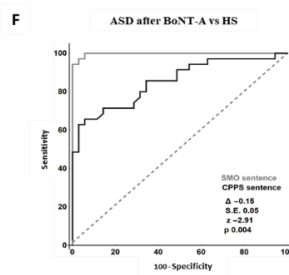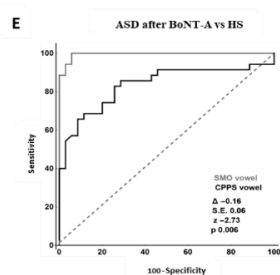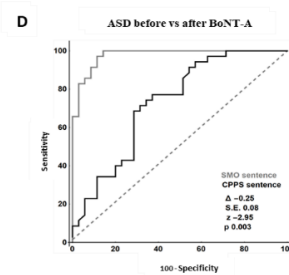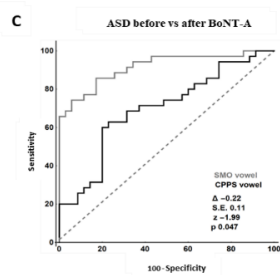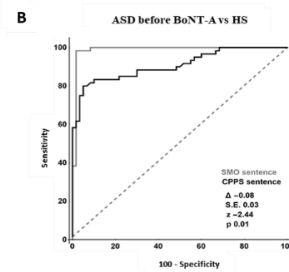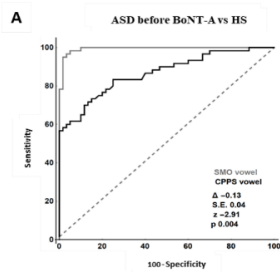
Machine-learning **algorithm** discriminates between:
- **HS** and **ASD**
- ASD patients **before** and **after** **BoNT-A** therapy
- **HS** and ASD patients **after** **BoNT-A** therapy
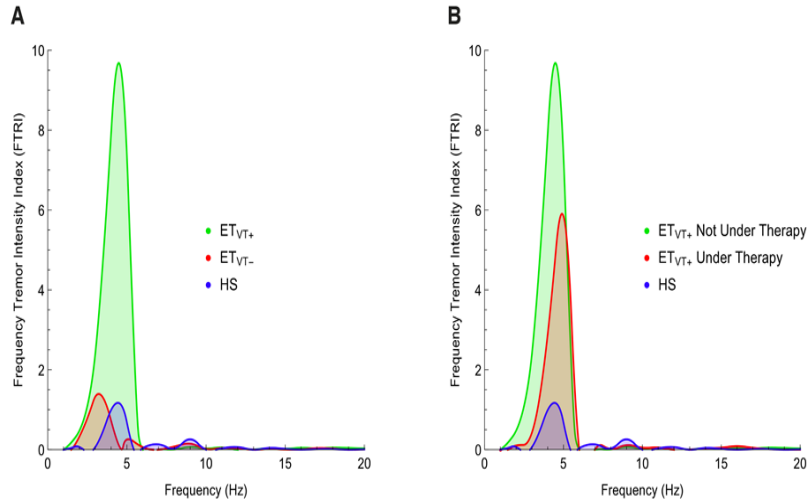
Higher accuracy than **CPPs**

Voice analysis in adductor spasmodic dysphonia: Objective diagnosis and response to botulinum toxin

Antonio Suppa[a,b,1], Francesco Asci[a,1], Giovanni Saggio[c], Luca Marsili[d], Daniele Casali[c], Zakarya Zarezadeh[e], Giovanni Ruoppolo[f], Alfredo Berardelli[a,b,*], Giovanni Costantini[c]

Essential Tremor (ET)

- Machine learning objectively recognizes **ET** patients, with and without an overt **voice tremor**

- Machine-learning objectively evaluates the response to **pharmacological therapies** in ET

- **Future** studies are required to improve performances of machine-learning algorithms in recognizing **neurological disorders** showing voice tremor

Antonio Suppa, MD, PhD,[1,2†] Francesco Asci, MD,[1†] Giovanni Saggio, PhD,[3] Pietro Di Leo, BA,[3] Zakarya Zarezadeh, BA,[3] Gina Ferrazzano, MD, PhD,[1] Giovanni Ruoppolo, MD,[4] Alfredo Berardelli, MD,[1,2*] and Giovanni Costantini, PhD[3]

[1]Department of Human Neurosciences, Sapienza University of Rome, Rome, Italy
[2]IRCCS Neuromed Institute, Pozzilli, Italy
[3]Department of Electronic Engineering, University of Rome Tor Vergata, Rome, Italy
[4]Department of Sense Organs, Otorhinolaryngology Section, Sapienza University of Rome, Rome, Italy
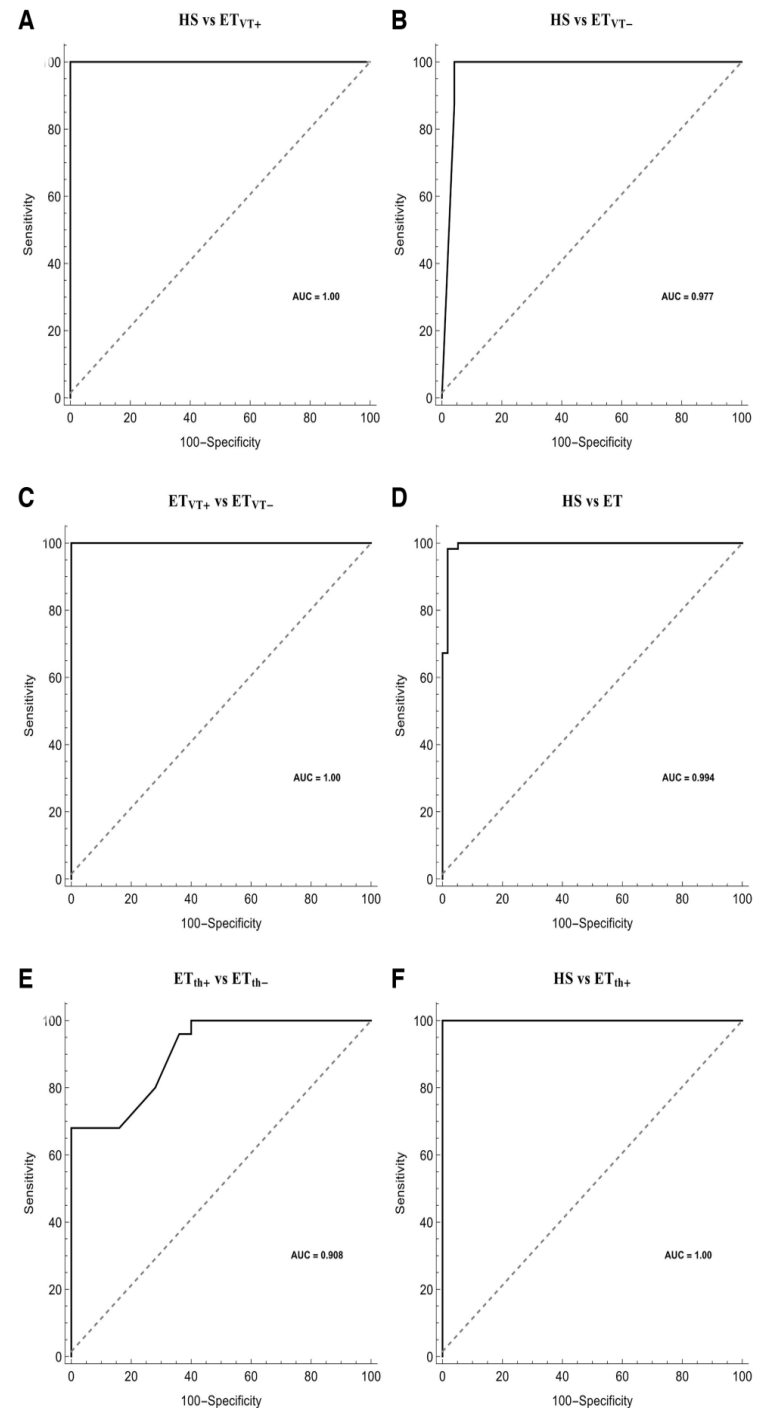
Parkinson's Disease

	Age (years)	Weight (kg)	Height (cm)	DD (years)	MMSE	HAM-D	FAB	H&Y	UPDRS-III OFF	UPDRS-III ON	UPDRS-III-v OFF	UPDRS-III-v ON	VHI OFF	VHI ON
PD (whole group)	68.2 ± 9.2	71.8 ± 11.6	172.1 ± 9.4	5.6 ± 4.7	28.4 ± 2.1	3.5 ± 1.8	16.5 ± 1.4	2.2 ± 0.8	22.3 ± 14.2	–	1.8 ± 1.1	–	16.7 ± 16.9	–
Early-stage PD	64.2 ± 8.6	71.8 ± 10.6	172.9 ± 9.8	2.1 ± 0.9	28.9 ± 1.1	3.2 ± 2.0	16.6 ± 1.0	1.5 ± 0.4	12.1 ± 4.1	–	0.9 ± 0.7	–	7.3 ± 4.9	–
Mid-advanced-stage PD	72.1 ± 8.1	71.9 ± 12.6	171.2 ± 9.0	9.0 ± 4.4	28.0 ± 2.6	3.9 ± 1.6	16.4 ± 1.6	2.8 ± 0.4	32.3 ± 13.5	28.3 ± 13.8	2.7 ± 0.6	2.4 ± 0.5	25.9 ± 19.2	20.0 ± 17.7
HS	70.3 ± 10.3	68.5 ± 10.6	169.0 ± 10.1	–	29.0 ± 0.8	3.3 ± 1.7	16.6 ± 1.1	–	–	–	–	–	–	–

DD, disease duration; MMSE, Mini-Mental State Evaluation; HAM-D, Hamilton Depression Rating Scale; FAB, Frontal Assessment Battery; H&Y, Hoehn and Yahr Scale for assessment stage of PD; HS, healthy subjects; PD, patients with Parkinson's disease; UPDRS-III, Unified Parkinson's Disease Rating Scale part III; UPDRS-III-v, Unified Parkinson's Disease Rating Scale part III, voice impairment subitem; VHI, Voice Handicap Index; OFF, not-under the effect of L-Dopa; ON, under the effect of L-Dopa. Results are expressed as average ± standard deviation.

Cohort definition:
Early-stage: H&Y≤2
Mid-advanced-stage: H&Y>2
OFF-L-Dopa: 12h after the last L-Dopa intake
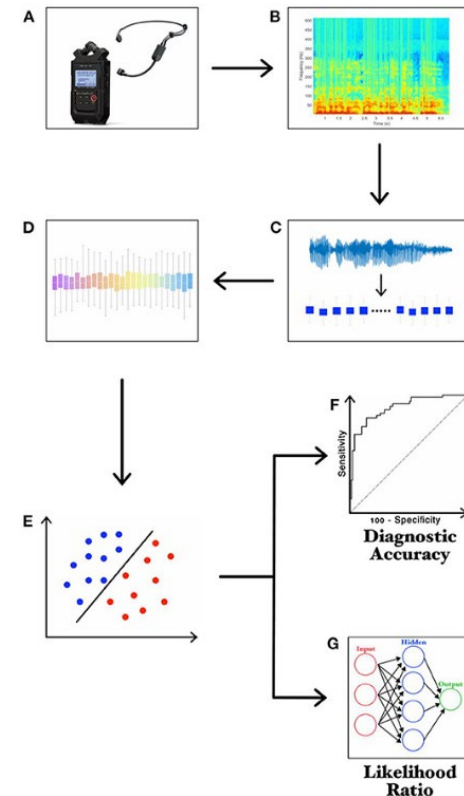ON-L-Dopa: 30-60min following L-Dopa administration

Neurologic evaluation:
H&Y, UPDRS-III, MMSE, HAM-D, FAB
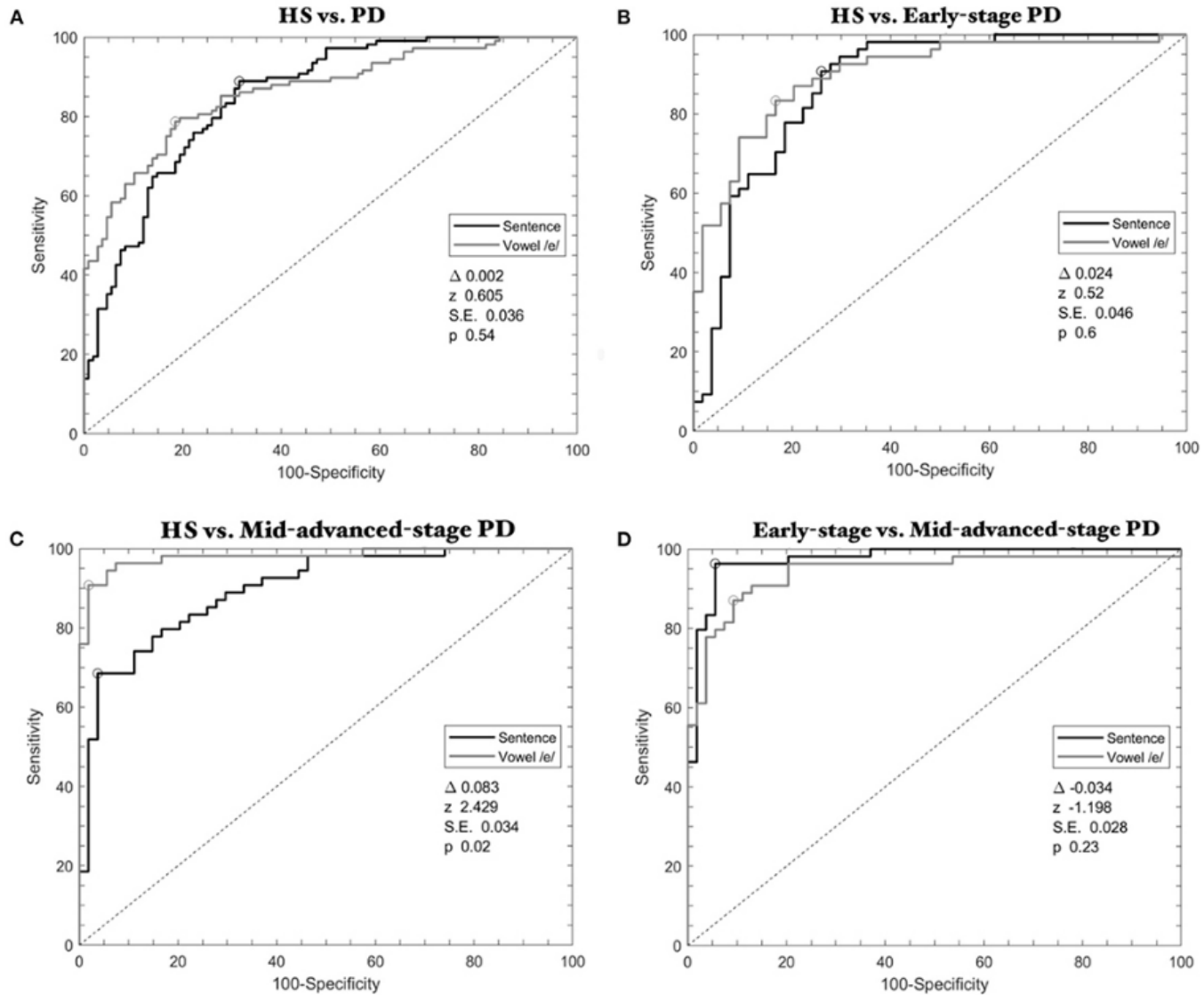
Perceptual voice assessment:
UPDRS-III-v, VHI

Speech tasks:
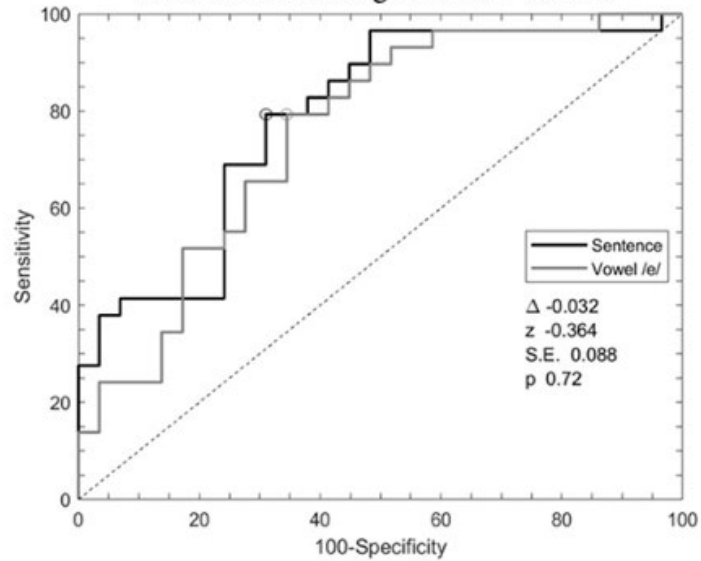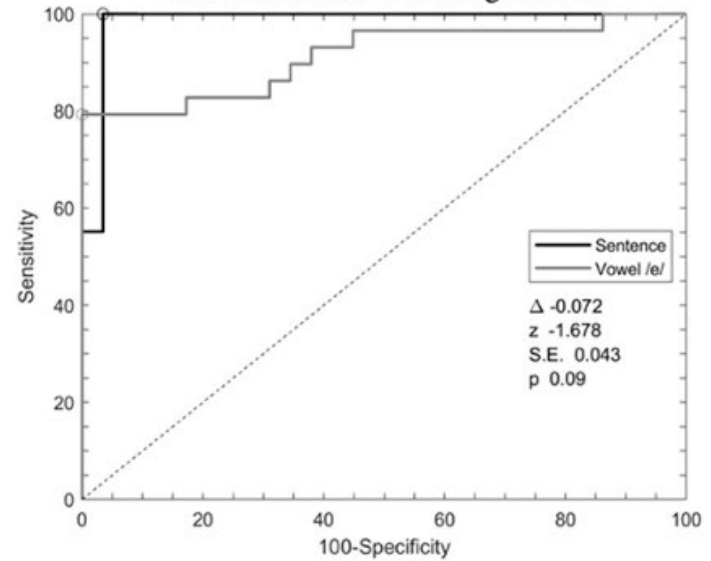sustained emission of a vowel and standard sentence

Results – I

A — HS vs. PD
- Sentence
- Vowel /e/
- Δ 0.002
- z 0.605
- S.E. 0.036
- p 0.54

B — HS vs. Early-stage PD
- Sentence
- Vowel /e/
- Δ 0.024
- z 0.52
- S.E. 0.046
- p 0.6

C — HS vs. Mid-advanced-stage PD
- Sentence
- Vowel /e/
- Δ 0.083
- z 2.429
- S.E. 0.034
- p 0.02

D — Early-stage vs. Mid-advanced-stage PD
- Sentence
- Vowel /e/
- Δ -0.034
- z -1.198
- S.E. 0.028
- p 0.23
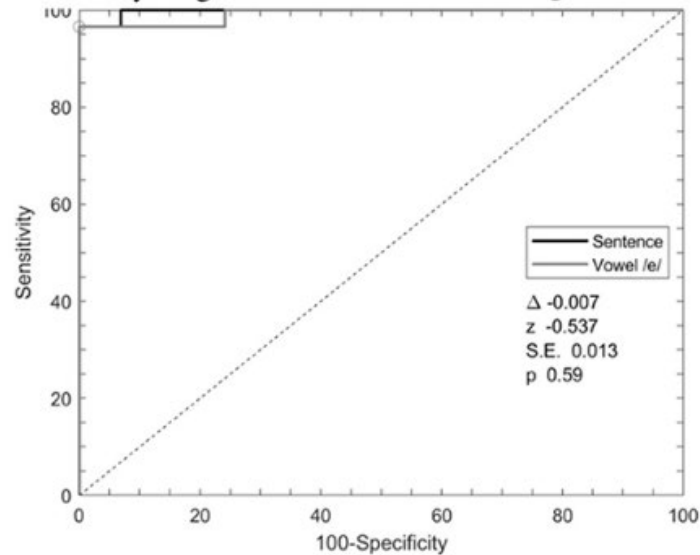
Results – II

Results – III
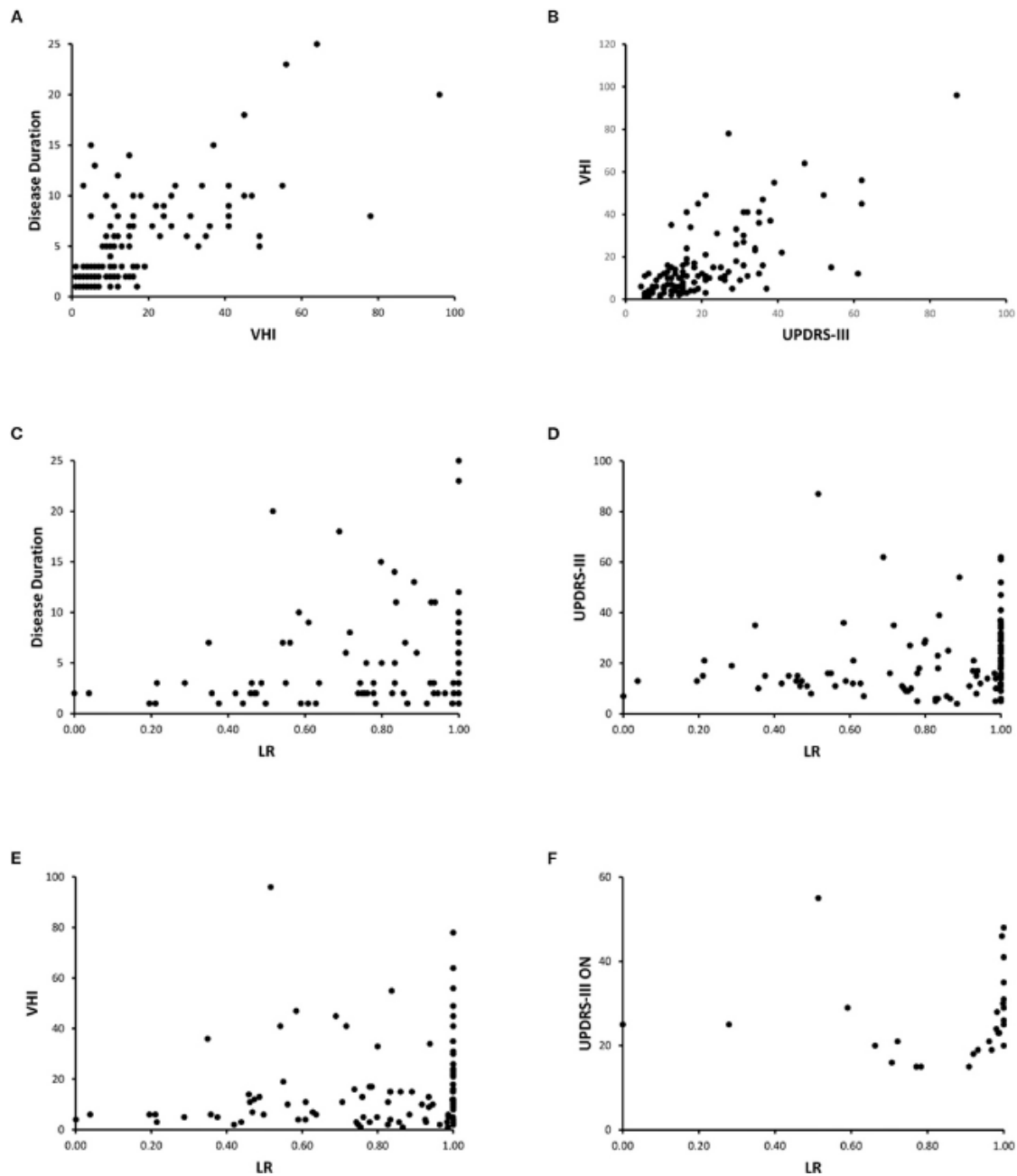
Discussion and Conclusions

- Voice is abnormal in *early-stage* PD

- Voice progressively degrades in *mid-advanced-stage* and can be improved but not restored by L-Dopa

- Machine learning allows tracking disease severity and quantifying the symptomatic effect of L-Dopa on voice parameters

- Hypokinetic dysarthria would represent a potential new biomarker of PD

Voice in Parkinson's Disease: A Machine Learning Study

Antonio Suppa[1,2†], Giovanni Costantini[3†], Francesco Asci[2], Pietro Di Leo[3], Mohammad Sami Al-Wardat[4], Giulia Di Lazzaro[5], Simona Scalise[6], Antonio Pisani[7,8] and Giovanni Saggio[3*]

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[4]Department of Allied Medical Sciences, Aqaba University of Technology, Aqaba, Jordan
[5]Neurology Unit, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy
[6]Department of System Medicine UOSD Parkinson, University of Rome Tor Vergata, Rome, Italy
[7]Department of Brain and Behavioral Sciences, University of Pavia, Pavia, Italy
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