Correlation of Vocal Frequencies with Adrenal and Thyroid Disorders and Parkinson's Disease

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INTRODUCTION

Early diagnosis of hormonal and neurological conditions is challenging. There is a need for simple non-invasive tests to screen and improve the accuracy of current diagnostic models by incorporating additional markers of dysfunction and disease. Signal-based feature analysis of the voice is an emerging non-invasive diagnostic tool.

Voice – a novel diagnostic approach:

Voice signal characteristics have been suggested to be associated with many different pathological conditions, including dyslexia, ADHD, Parkinson's and Alzheimer's, and other neurological disorders. As regulatory systems, endocrine and neurological function are associated multiple pathologic processes such as chronic thyroiditis, autoimmune diseases, adrenal exhaustion, cognitive decline, dementia, and overall motor function. We hypothesize that this process might also involve the anatomic structures associated with voice production. We further hypothesize that with adequate machine learning models, a myriad of conditions can be diagnosed using these methods.

Vocal Signal Feature Analysis

Vocal Signal Feature Analysis (VSFA) uses several measurements that accurately characterize the sound waves generated by the vocal cords. Frequency analysis is a measurement of the rate at which a particular wave repeats. Air which passes through the vocal folds creates a glottal tone. The sound waves and vibrations produce fundamental frequencies. Simultaneously the neuromuscular system vibrates ever so slightly as a person speaks. These "micro-tremors" create subtle changes in the frequencies which are often too small to be detected by the human ear alone. SONIPHI's VSFA is capable of capturing these subtle vibrations in the frequency modulation of the voice. Advanced machine-learning algorithms allow these changes to be characterized into vital informatics which give a clear picture of a person's underlying physical condition.

Furthermore, recent research published in Scientific American (April 2018), indicates that micro-tremors may be a product of mechanical waves propagated by the CNS. Nerve signals are now shown to be mechanical waves and not solely electrical in nature. This new view of the nervous system as a "sonic mechanical system" is the only known explanation of our current understanding of anesthetics and their underlying properties as lipid emulsifiers, which block mechanical wave propagation in the nerve, thus creating a loss of signal in the pathway.

The voice signal hypothetically contains information in the form of Frequency Modulation (FM) that is generated as a result of all nerve propagation in the body occurring in real-time. SONIPHI's advanced algorithms are able to characterize the subtle modulations in the voice, hypothetically caused by these neural signals, as they are composed of mechanical sound waves travelling to and from the brain.

We hypothesize that endocrine and neurological processes may also involve anatomical structures that produce the voice. Furthermore, frequency patterns in the voice can be correlated with different physical conditions. The purpose of the current study was to identify an association between vocal features and thyroid and adrenal dysfunction, as well as Parkinson's disease.

METHODS

Study protocol was approved by an institutional review board (IRB#VF-SO-107), and all patients provided informed consent for participation. Subjects were selected with the following criteria:

Inclusion Criteria:

1. Male or females.
2. No racial restrictions.
3. Between the ages of 17-70.

Exclusion Criteria

1. Individuals with a terminal disease.
2. Individuals unable to complete the conditions of the study.

The study population was divided into 3 groups of patients (37 total) at Clear Center of Health: Parkinson's, hypo or hyper adrenal and thyroid patients. All were diagnosed by Dr. Beth McDougall (owner) at the Clear Center of Health in Mill Valley, California (http://clearcenterofhealth.com). Data collection was conducted by Brandon Muzik (employee). All subjects in the study had their voice recorded to identify matches with voice patterns of the conditions listed above. Each group served as a control for the other groups (i.e., voice recordings for each group that did not have a condition were checked for vocal features corresponding to that condition.)

Patients were asked to speak aloud for 30-45 seconds about any subject (not reading text) into a cellular phone recording device. Their voice was recorded, stored online and analyzed for multiple features of voice intensity and frequency using SONIPHI's clinical (manual) processes. Fast Fourier transform was used in order to extract information from the voice signal. A total of two 30-second separate baseline voice recordings were documented and analyzed for each participant. Analysis was blinded with respect to patient data.

Statistical analysis was conducted using Sensitivity, Specificity, Positive Predictive Value, Negative Predictive Value and Overall Accuracy for each disease type, and calculated from the

corresponding 2 X 2 frequency tables. The corresponding confidence intervals were constructed using the exact binomial distribution.

RESULTS

Table 1 shows demographics for all 32 subjects, 17 subjects had 2 diagnoses, with a total of 47 diagnoses.

Table 1: Demographics (N=32) subjects

Clinical Diagnosis	Number of Subjects[†]
Adrenal	20
Parkinson's	6
Thyroid	19
Control	2

[†]15 subjects had 2 different diagnoses, resulting into a total of 47 diagnoses

Table 2 shows a summary of clinical vs. medical diagnosis for all diagnoses. The hypo adrenal, thyroid diagnosis was the most predominant, with 11 diagnoses and hypo thyroid had 6 diagnoses. None of the subjects in the control groups demonstrated a false positive for any of the conditions that they did not have (not shown).

Table 2: Summary of clinical vs. voice analysis diagnosis - single or multiple diagnoses (N=32)

	Voice Analysis Diagnosis					
Clinical Diagnosis	**Adrenal**	**Adrenal, Thyroid**	**Parkinson's**	**Parkinson's, Adrenal**	**Parkinson's, Thyroid**	**Thyroid**
Adrenal	3	2	0	0	0	0
Adrenal, Thyroid	0	11	0	0	0	2
Parkinson's	0	0	2	1	1	0
Parkinson's, Adrenal	0	0	0	1	1	0
Parkinson's, Thyroid	0	0	0	0	0	0
Thyroid	0	0	0	0	0	6
Control	1	0	0	0	0	0

Overall accuracy of voice analysis for correct clinical diagnosis (single or combined diagnosis): 24/32 = 75% (95% CI: 58-87%).

Figure 3 shows the results for true (+) and false (-) clinical and voice diagnoses. When there was a single diagnosis, there was a direct correlation between both diagnoses. When there was more than one diagnoses, there were 4 false positive voice diagnoses for thyroid, 2 false positive voice diagnoses for the adrenal diagnosis, and 2 false negative voice diagnoses for adrenals.

Table 3: Summary of clinical vs. voice analysis diagnosis for Adrenal, Parkinson's and Thyroid (N=47 individual clinical diagnoses)

N=47		**Voice Analysis Diagnosis**	
	Clinical Diagnosis	-	+
Adrenal	-	27	0
	+	3	17
Parkinson's	-	41	0
	+	0	6
Thyroid	-	28	0
	+	0	19

Table 4 shows the diagnostic evaluation of voice analysis for predicting each clinical diagnosis expressed as sensitivity and specificity for predicting all clinical diagnosis by voice analysis, the positive and negative predictive values and accuracy. In medical diagnosis, test sensitivity is the ability of a test to correctly identify those with the disease (true positive rate), whereas test specificity is the ability of the test to correctly identify those without the disease (true negative rate). As seen, the sensitivity, specificity, positive and negative predictive value (true positive and true negative) and accuracy for the voice analysis for Parkinson's and thyroid were 100%. For the voice analysis of the adrenal diagnosis, the specificity was 100%, sensitivity was 85%, the negative predictive value was 90% and the accuracy was 94%.

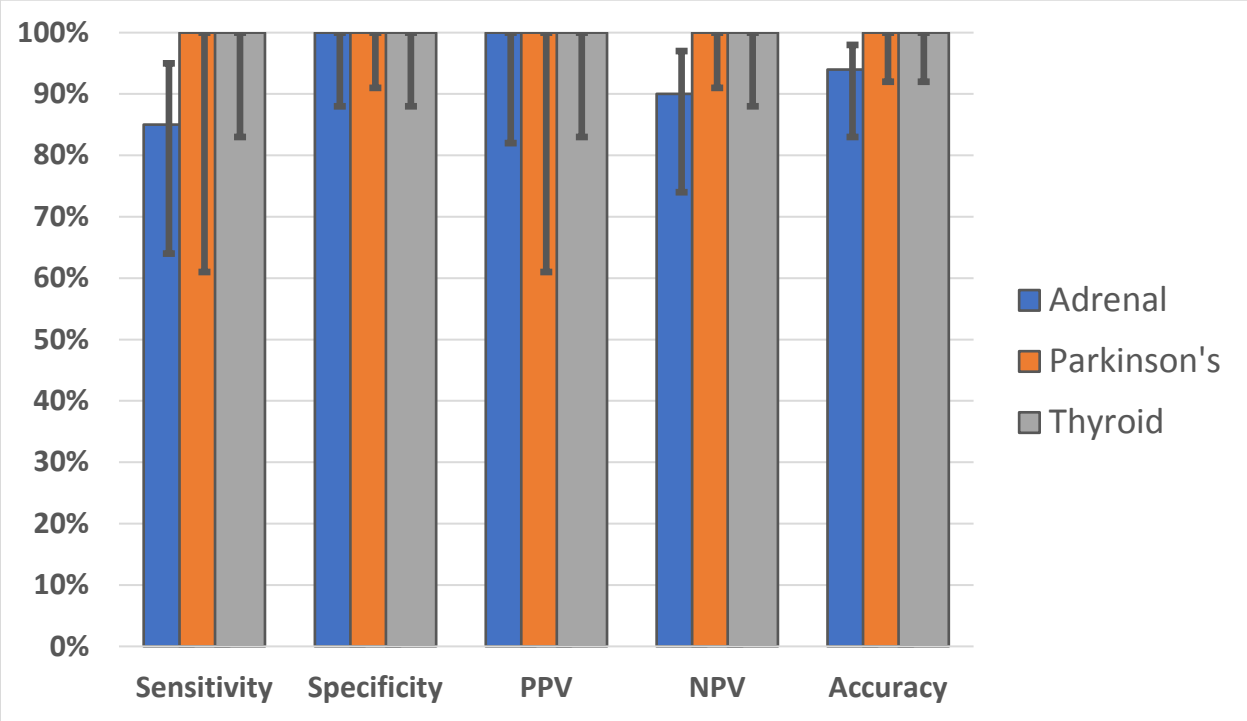
Table 4: Diagnostic evaluating of voice analysis for predicting clinical diagnosis (N=47)

		Value	**95% CI†**
Adrenal	**Sensitivity**	85%	64-95%
	Specificity	100%	88-100%
	Positive Predictive Value	100%	82-100%
	Negative Predictive Value	90%	74-97%
	Accuracy	94%	83-98%
Parkinson's	**Sensitivity**	100%	61-100%
	Specificity	100%	91-100%
	Positive Predictive Value	100%	61-100%
	Negative Predictive Value	100%	91-100%
	Accuracy	100%	92-100%
Thyroid	**Sensitivity**	100%	83-100%
	Specificity	100%	88-100%
	Positive Predictive Value	100%	83-100%
	Negative Predictive Value	100%	88-100%
	Accuracy	100%	92-100%

†95% confidence interval

Figure 1 shows the results for each condition expressed in graphical form.

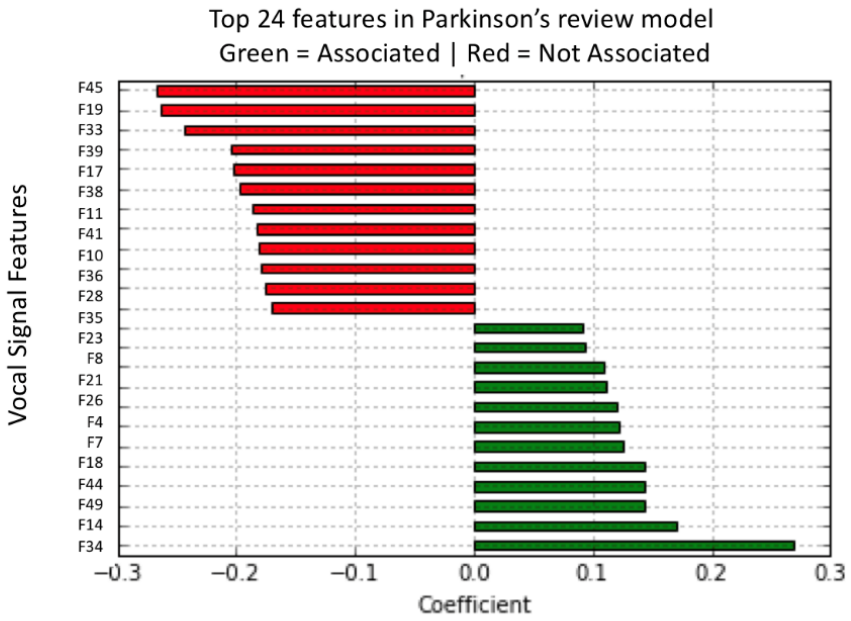
Figure 1: Diagnostic evaluating of voice analysis for predicting clinical diagnosis (N=47) of Adrenal, Parkinson's and Thyroid with 95% confidence intervals (bars); PPV=Positive Predictive Value, NPV=Negative Predictive Value

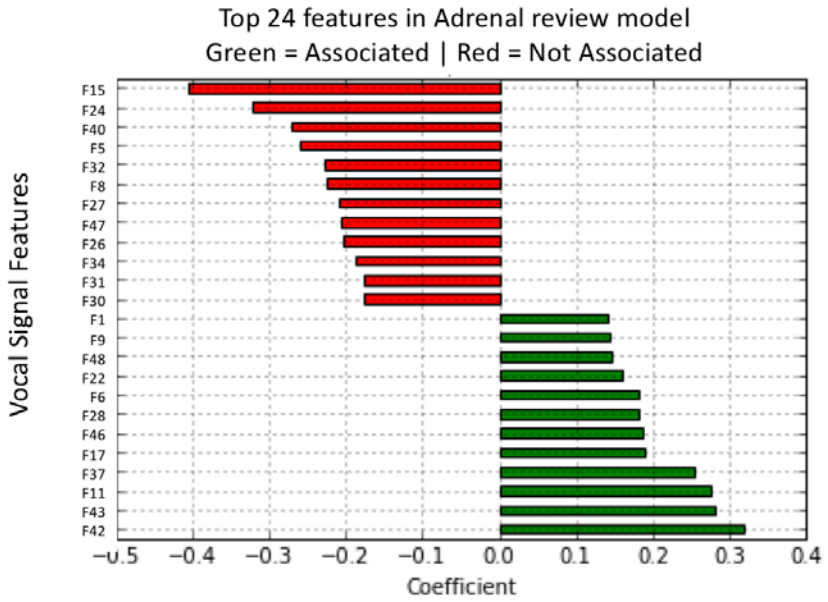


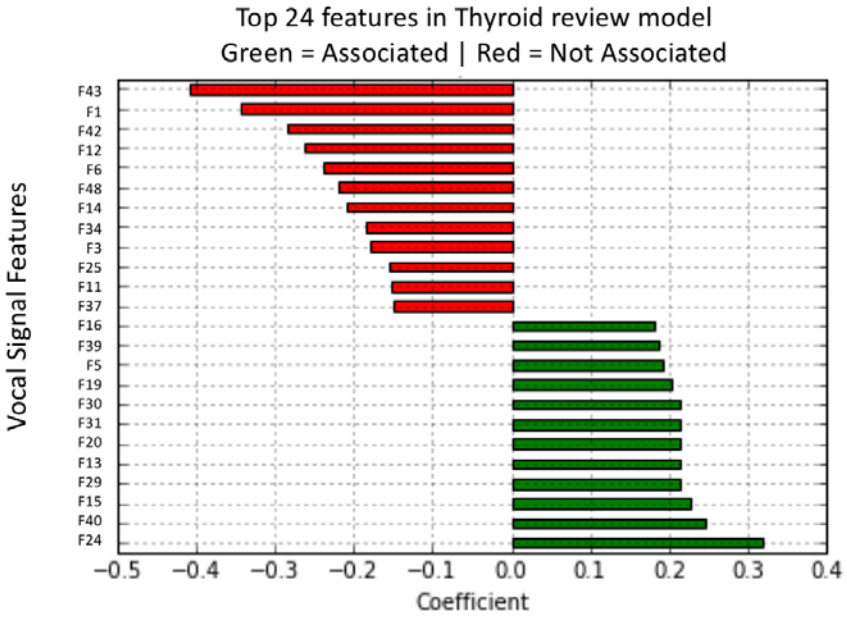
DISCUSSION

These results are striking, with both the Parkinson's and thyroid diagnoses demonstrating 100% sensitivity, specificity, positive and negative predictive value and accuracy, and slightly lower effect for a voice diagnosis for an adrenal diagnosis. Importantly, when there was a single diagnosis, there was a 100% correlation between the voice and clinical diagnosis. When there were 2 diagnoses, the accuracy was slightly lower, but still quite high. A test that is highly sensitive *and* highly specific does both, so it "rarely overlooks a thing that it is looking for" *and* it "rarely mistakes anything else for that thing." Because most medical tests do not have sensitivity and specificity values above 99%, "rarely" does *not* equate to certainty. But for practical reasons, tests with sensitivity and specificity values above 90% have high credibility, albeit usually no certainty, in differential diagnosis. Therefore, the voice analysis test has high credibility for diagnosis of conditions such as Parkinson's, thyroid and adrenal insufficiency and is a beneficial screening tool for assessment of these and potentially other conditions and can serve as a pre-screening device. Further testing is recommended to confirm these findings and extrapolate them to other conditions.

SONIPHI uses a combination of cutting edge analysis techniques to create its correlative databases. In the below example a Linear Regression Machine Learning Algorithm was used to find the possible relationships between continuous variables i.e. vocal features and a known clinical diagnosis. Here, we establish these relationships by fitting a best line, each feature is rated by its coefficient of fit to this line and is rated as either correlative or anti-correlative to the model.




Top 24 features in Adrenal review model
Green = Associated | Red = Not Associated
Vocal Signal Features
F15
F24
F40
F5
F32
F8
F27
F47
F26
F34
F31
F30
F1
F9
F48
F22
F6
F28
F46
F17
F37
F11
F43
F42
−0.5 −0.4 −0.3 −0.2 −0.1 0.0 0.1 0.2 0.3 0.4
Coefficient


Top 24 features in Thyroid review model
Green = Associated | Red = Not Associated
Vocal Signal Features
F43
F1
F42
F12
F6
F48
F14
F34
F3
F25
F11
F37
F16
F39
F5
F19
F30
F31
F20
F13
F29
F15
F40
F24
−0.5 −0.4 −0.3 −0.2 −0.1 0.0 0.1 0.2 0.3 0.4
Coefficient

CONCLUSIONS

This study suggests a strong relationship between voice characteristics and thyroid and adrenal function, and Parkinson's Disease. Voice features analysis holds the potential to assist both individuals and physicians in estimating the pre-test probability of these conditions among patients presenting with symptoms or for individuals as a prescreening test. The applications are particularly interesting for telemedicine, when clinical health care is provided remotely.

SONIPHI is the industry pioneer in the innovative retrieval, delivery, analysis and support of individualized voice data, giving users around the world access to personalized information about their health and well-being, generated from their own voice.