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## Vocal markers of pre-operative anxiety: a pilot study

Gilles Guerrier<sup>1\*</sup>, Laurent Lellouch<sup>2</sup>, Marco Liuni<sup>2</sup>, Andrea Vaglio<sup>2</sup>, Pierre-Raphaël Rothschild<sup>3</sup>, Christophe Baillard<sup>3</sup>, Jean-Julien Aucouturier<sup>2</sup>

<sup>1</sup>Department of Anaesthesia and Intensive Care, Hôpital Cochin, Assistance Publique-Hôpitaux de Paris, Paris, France

<sup>2</sup>Science and Technology of Music and Sound (UMR9912, IRCAM/CNRS/Sorbonne Université), Paris, France

<sup>3</sup>Department of Ophthalmology, Hôpital Cochin, Assistance Publique-Hôpitaux de Paris, Paris, France

\*Corresponding author. E-mail: [gilles.guerrier@aphp.fr](mailto:gilles.guerrier@aphp.fr)

### Introduction

Recent European guidelines in anaesthesia recommend systematic pre-operative anxiety management to prevent its negative peri-operative impact,<sup>1</sup> including impaired memorization of important instructions, and higher incidence of post-operative acute and chronic pain. Usual self-administered questionnaires or scales to assess anxiety in the preoperative setting are time-consuming and rely on the patients' willingness to comply with instructions.<sup>2</sup> Physiological signals such as patients' voice may provide useful information for objective, reliable, and accurate anxiety assessment before surgery. Because of the extensive parasympathetic innervation to the larynx, pharynx, face, and head, stress modifies vocal parameters.<sup>3,4</sup> The effects of acute anxiety on voice are poorly explored in the preoperative context. Our objective was to describe characteristics of patient's vocal parameters related to declared anxiety level in a day-care ophthalmic surgical unit performing cataract surgery.

### Methods

With approval from the Ethics Committee of the French Society of Ophthalmology (IRB 00008855 Société Française d'Ophthalmologie IRB#1), vocal conversations between patients and nurses-assistants were recorded during admission interviews on the day of surgery. The standardized, ca. 5min. interview aims at validating patient identity, address, surgical indication, fasting status, removal of all jewelry, as well as assessing patient anxiety. At the outset of the interview, both patients and nurse-assistants evaluated patient anxiety using a 0-10 visual analogue scale (VAS). Criteria for exclusion were: patients <18yr, under guardianship, non-French speaking patients, communication difficulties, hearing or speaking impairment. All participants gave their written informed consent.

In each recording, we separated patient utterances from the nurse-assistant' utterances by manual inspection using the Audacity software. Was considered as an utterance each moment when the patient spoke alone, framed by words of the nurse-assistant or by periods of silence longer than 2 seconds. We also excluded non-verbal sequences (background noise, coughs, etc.) using an automated criterion. For each patient utterance, we then extracted a number of acoustic features traditionally associated with emotional expressivity and vocal stress<sup>3,4</sup>, including utterance duration; mean, maximum, minimum and standard deviation of fundamental frequency ( $F_0$ ); four standardized measures of pitch perturbation quotient (jitter-~~loe~~, ~~loe\_abs~~, ~~rap~~, ~~ppq5~~), 5 measures of amplitude perturbation quotient (shimmer-~~loe~~, ~~loe\_db~~, ~~apq3~~, ~~apq5~~, ~~apq11~~), and 2 measures of noise-to-harmonic ratio (nhr, hnr). Acoustic features were extracted with the Praat software (see Supplementary material for details).

First, to analyze effects of patient's anxiety on average vocal features, we calculated the average of each utterance's feature, weighted by utterance duration, and tested for main effects using a one-way analysis of variance (ANOVA), using patient's self-reported VAS anxiety as a binary factor ('low' if VAS <5, 'high' otherwise). Second, to analyze the effect of patient anxiety on the temporal evolution of features, we controlled for differences in interview duration by normalizing utterance time location between 0 and 1, and indexed each utterance's feature with their normalized time location. We then used Generalized linear mixed models (GLMMs) to evaluate the contribution of the anxiety factor to the linear regression of each feature's values on normalized time, using random intercepts to account for patient differences. In both procedures, we took  $\alpha=0.05$  as the significance threshold and applied Bonferroni corrections for alternative measures of the same feature ( $F_0$ :  $\alpha_{\text{Bonf}}=0.013$ ; jitter:  $\alpha_{\text{Bonf}}=0.013$ ; shimmer:  $\alpha_{\text{Bonf}}=0.010$ ; nhr:  $\alpha_{\text{Bonf}}=0.025$ ; see Supplementary material for details).

### Results

Between April 1st and June 30th, 2016 the data of 44 patients were collected including 29 female, with a median age of 74 (IQR[69-79]). The median duration of interviews was 6'50" (IQR[5'49"-7'38"]), of which a median 1'55" (IQR[2'47"-1'19"]) were spoken by patients. The median duration of manually-segmented patient utterances was 1.65' (IQR[2.49 - 0.98]). Mean  $F_0$  was 164.7 Hz (SD= 15.8 Hz) for

female patients, and 142.8 Hz (SD=18.5 Hz) for male. Mean anxiety score in patient VAS reports was 3.48 (SD=2.56), and N=11 (25%) patients rated their anxiety level above 5. The correlation between patients' self-report and hetero-evaluation by nursing staff of anxiety level was 91%.

While there was no main effect of anxiety on patient's average measures of  $F_0$  (all p-values>0.44), there was a significant effect of anxiety on how  $F_0$  evolved along with interview time for mean  $F_0$  ( $\chi^2=6.85$ ,  $p=0.008$ ,  $\alpha_{Bonf}=0.013$ ), standard deviation of  $F_0$  ( $\chi^2=8.52$ ,  $p=0.003$ ,  $\alpha_{Bonf}=0.013$ ) and maximum  $F_0$  ( $\chi^2=24.0$ ,  $p<0.001$ ,  $\alpha_{Bonf}=0.013$ )(Figure 1). While the  $F_0$  of low-anxiety patients decreased by an average 3.81% (ca. 1 semitone) along the interview, the  $F_0$  of high-anxiety patients increased by 4.09 % (ca. 1 semitone). None of the other acoustic features (duration, jitter, shimmer, nhr) appeared to be significantly associated with anxiety levels, either on average or relative to time (see Figure 2 in supplementary material).

## Discussion

To date, pre-operative anxiety studies have focused on validating self-questionnaires in different surgical settings rather than identifying reliable objective biomarkers of anxiety. The main finding of our study is that comparison between repeated  $F_0$  measurements may be one acoustic marker for pre-operative anxiety. **Consistent with the literature, this relative  $F_0$  increase in stressed patients compared to less anxious patients may be due to sustained sympathetic nervous system activation<sup>3</sup> balancing the short term vocal fatigue observed over the course of normal conversations.**<sup>4</sup> Contrary to other reports studying anxiety in different stressful contexts, including cognitive workload, social stress, stage fright, and during life-threatening emergencies,<sup>5,6</sup> we found no effect of pre-operative anxiety on voice quality features such as jitter, shimmer or nhr. Reasons for this discrepancy may include low statistical power, linguistic characteristics of the conversations (short utterances in a question-answer mode), top-down control exerted by the patients in front of medical professionals, or lower emotional load due to distant time to surgery. Finally, we found a higher than expected correlation between self-reported anxiety level and hetero-evaluation of patients' anxiety. This suggests that staff's perception might be strongly influenced by patients' reporting, and therefore may lack reliability. In sum, we report a probable association between voice pitch and anxiety among patients awaiting for cataract surgery. This result need to be further evaluated in other surgical contexts on a broader scale and corroborated with other biomarkers involving the vagal tone response to anxiety, including heart rate variations.

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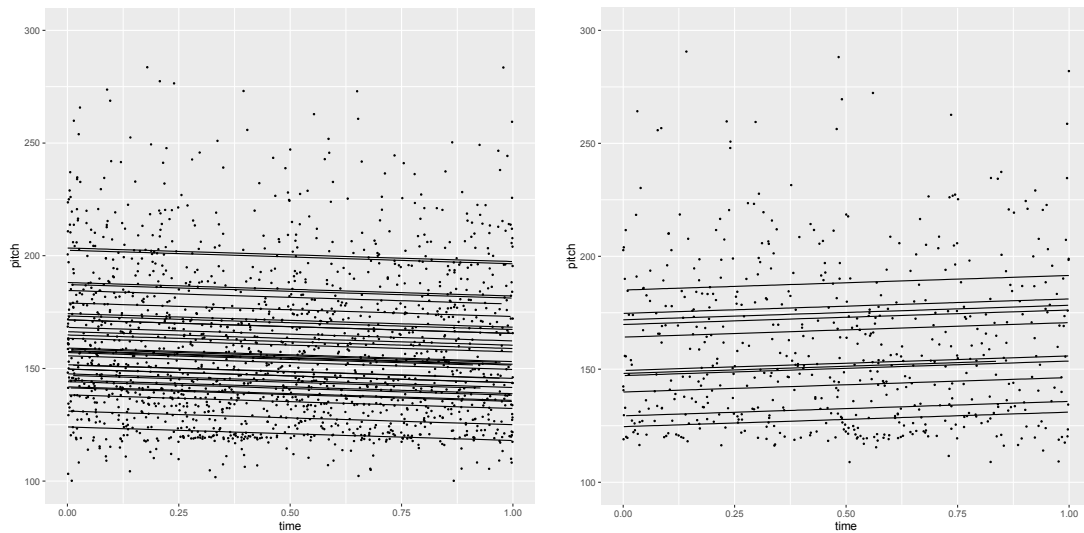
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## Declaration of interest

The authors declare that they have no conflicts of interest.

## Figures

Figure 1. Values and predictions of linear mixed model for the acoustic feature 'pitch' (non-anxious patients ( $AVS<5$ ) on the left and anxious ( $AVS\geq 5$ ) patients on the right).



## Supplementary material

### Definitions

The extracted acoustic features were those frequently used in vocal acoustic analysis and reported to be linked with the expression of emotions. They included:

- duration of patient utterances
- fundamental frequency: mean, standard deviation, minimum and maximum in each utterance
- jitter, reflecting the variations of fundamental period from one cycle to another: local (the average absolute difference between two consecutive periods, divided by the average period), local absolute (the average absolute difference between two consecutive periods), rap (the average for the disturbance, i.e., the average absolute difference of one period and the average of the period with its two neighbors, divided by the average period) and ppq5 (the ratio of disturbance within five periods, i.e., the average absolute difference between a period and the average containing its four nearest neighbor periods, divided by average period)
- shimmer, reflecting local variations of amplitude: local (average absolute difference between the amplitudes of two consecutive periods, divided by the average amplitude), local dB (the average absolute difference of the base 10 logarithm of the difference between two consecutive periods), apq3, apq5 and apq11 (the quotient of amplitude disturbance within 3, 5 or 11 periods, i.e., the average absolute difference between the amplitude of a period and the mean amplitudes of its 2, 4, or 10 neighbors, divided by the average amplitude)
- noise-to-harmonic ratio (nhr), harmonic-to-noise ratio (hnr)

### Acoustic analyses

Acoustic features were extracted with Praat software (version 6.0.40). Patients interviews were imported as long sounds, whose parts were extracted as rectangular windows of duration = 0.1 sec. and relative width = 1. Instantaneous pitch was extracted by cross-correlation (function to Pitch (cc)) with pitch floor = 70 Hz, time step =  $0.75/70 = 0.01$  s, pitch ceiling = 625 Hz and other default parameters.

Jitter was calculated with maximum period factor = 2, and shimmer with maximum amplitude factor = 9.

### **Statistical analyses**

GLMMs analyses were performed to compare three mixed models with random intercept effect of the variable 'patient' :

Full model (M2) :  $\text{feature} \sim \text{time} * \text{anxiety} + (1 | \text{patient})$ ,

Reduced model (M1) :  $\text{feature} \sim \text{time} + \text{anxiety} + (1 | \text{patient})$ ,

Null model (M0) :  $\text{feature} \sim \text{time} + (1 | \text{patient})$ ,

with 'anxiety' corresponding to the binary values of anxiety levels ; 'time' being the median time of each utterance, scaled from 0 to 1 for each patient recording ; and the data from each utterance being weighted by the duration of the utterance in all these three models. Results reported for temporal dynamics of fundamental frequency correspond to the comparison of the full model (M2) with the reduced model (M1). Consistent with ANOVA analyses, the reduced model (M1) did not improve fit compared to the null model (M0), showing the absence of any principal effect of anxiety on features. All reported results in main text use a binary factor for anxiety, cut at the VAS mid-point (VAS < 5: low; VAS  $\geq$  5, high). All results were replicated using correlations with the row 0-10 VAS values.

Figure 2. Boxplots of mean acoustic features vs binary values of anxiety ('N' = not anxious ; 'Y' = anxious).

