Voice Formants in Individuals With Congenital, Isolated, Lifetime Growth Hormone Deficiency

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Summary: Objective. To analyze the voice formants (F1, F2, F3, and F4 in Hz) of seven oral vowels, in Brazilian Portuguese, [a, ɛ, e, i, ɔ, o, and u] in adult individuals with congenital lifetime untreated isolated growth hormone deficiency (IGHD).

Study Design. This is a cross-sectional study.

Methods. Acoustic analysis of isolated vowels was performed in 33 individuals with IGHD, age 44.5 (17.6) years (16 women), and 29 controls, age 51.1 (17.6) years (15 women).

Results. Compared with controls, IGHD men showed higher values of F3 [i, e, and ɛ], $P = 0.006$, $P = 0.022$, and $P = 0.006$, respectively and F4 [i], $P = 0.001$ and lower values of F2 [u], $P = 0.034$; IGHD women presented higher values of F1 [i and e] $P = 0.029$ and $P = 0.036$; F2 [ɔ] $P = 0.006$; F4 [ɔ] $P = 0.031$ and lower values of F2 [i] $P = 0.004$. IGHD abolished most of the gender differences in formant frequencies present in controls.

Conclusions. Congenital, severe IGHD results in higher values of most formant frequencies, suggesting smaller oral and pharyngeal cavities. In addition, it causes a reduction in the effect of gender on the structure of the formants, maintaining a prepubertal acoustic prediction.

Key Words: Growth hormone–Voice–Formant frequencies–Acoustic analysis.

INTRODUCTION

Growth hormone (GH) has fundamental roles on stature and voice, two important factors for self-confidence and social acceptation. The consequences of lack of GH on voice are difficult to study, as isolated GH deficiency (IGHD) is a rare disease occurring in 1 in 3480 to 1 in 10 000 live births.[1] Furthermore, most GH deficient children in the developed world are treated with GH replacement therapy during childhood. We have identified, in Northeastern Brazil (Itabaianinha County, the State of Sergipe), a cohort of individuals with IGHD caused by a homozygous (c.57 + 1 G > A) null mutation in the GH releasing hormone receptor (GHRHR) gene.[2] Most of the adults have never been treated with GH replacement. The untreated individuals have very low serum levels of GH, and of its principal mediator insulin-like growth factor-I, but normal secretion of all the other pituitary hormones.[3] This results in severe short stature, associated with a typical doll-like face, and high-pitched voice.[4] The voice effect seems to be more homogenous than the degree of stature deficit. Although the adult height ranges from 107 to 137 cm in pooled genders,[4] the fundamental voice frequency (f_0) is high, and very similar in both genders, not only in adulthood but also in childhood and senescence.[5,6]

We had previously reported that these IGHD individuals also present marked reduction of cephalic perimeter[7] and a typical pattern of reduction of cephalometric measurements, with marked reduction in both maxillary and mandibular length.[8] In normal subjects, a significant negative association between the formant frequencies and the length of the mandible and maxilla has been reported.[9] Therefore, we hypothesized that the IGHD individuals may have higher formant frequencies.

In this article, we have studied the pattern of vowel formants (F) frequencies in adult IGHD individuals never treated with GH.

SUBJECTS AND METHODS

Subjects were recruited by word of mouth and by an ad placed in the local dwarfs' association building, located in Itabaianinha County. Exclusion criteria were as follows: age <20 years and obvious mental or speech deficiencies. Inclusion criteria were as follows: Portuguese language native speakers, and for IGHD group, being homozygous for the GHRHR c.57 + 1 G > A mutation and having received no previous GH treatment. Inclusion criteria for controls: normal statured individuals living in the same area, with normal genotyped GHRHR alleles. We had previously reported f_0 data and the perceptual-auditory analysis (Grade, Roughness, Breathiness, Asthenia, Strain scale, GRBAS scale) and video laryngostroboscopic assessment[5,6] in subjects from this cohort. This cross-sectional study included 33 IGHD (16 women, 47.3 (16.6) years, 117.5 (5.6) cm and 17 men, 41.8 (18.6) years, 129.4 (5.2) cm); and 29 controls (15 women, 48.8 (13.7) years, 155.2 (6.3) cm and 14 men, 53.6 (21.5) years, 165.3 (9.0) cm).

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F1 (affiliated to the posterior cavity, pharynx), F2 (to the anterior oral cavity), F3 (to the cavities above the vocal folds and around the inferior incisors), and F4 (to the laryngeal tube length)[10] of the seven oral vowels in Brazilian Portuguese [a, ε, e, i, ɔ, o, and u] were measured (Hz) in a quiet room with <40 dB of noise. After training, 3-second sustained vowel emission was studied, using comfortable conversational pitch and loudness levels (SM58 microphone; Shure Inc., Niles, IL) kept at fixed distance of 5 cm from the subject's mouth.[11] Three trials were performed per each vowel. The criteria for trial acceptance/rejection were frequency stability in a range from 0.1 to 3 seconds.[12] Samples were digitally recorded with the by software Sound Forge 10.0 (Professional audio program Sony Creative Software Inc., Madison, WI, USA) in format data (WAV extension), 22 050 Hz sampling frequency, 16-bit and stored for acoustic analysis by software PRAAT (Version 5.3.51)[13], with semiautomatic extraction.

Portuguese vowel inventory internal symmetry was used to compare F1 for vowel height differences and F2 for front-back vowels. Portuguese vowel inventory has an internal symmetry: the central low vowel [a], three unrounded front vowels [i, e, and ε] and three rounded back vowels [u, o, and ɔ], and three pairs, one with two high vowels [i-u], one with two higher-mid vowels [e-o], and the last with two lower-mid vowels [ε-ɔ].[14] The Institutional Review Board of the Federal University of Sergipe approved the protocol, and written informed consent was obtained from all participants.

Statistics

Data are expressed as mean (standard deviation) for variables with distribution normal or median (interquartile range) for variables with nonnormal distribution. MANCOVA for Multivariate analysis of covariance (as it is statistical technique) was used to analyze possible influence of confounder variables in the formant frequencies. The comparison between groups was made by t test for variables with normal distribution and Mann-Whitney test for variables with nonnormal distribution. *Statistical Analysis Package for Social Sciences* (*SPSS*, Version 18.0, IBM., Chicago, IL, USA)[15] was used, and probability values <0.05 were considered.

RESULTS

Table 1 presents the comparison of F1, F2, F3, and F4 (Hz) for the seven oral vowels in pooled genders in IGHD and controls. MANCOVA using F1, F2, F3, and F4 of the seven vowels [a, ε, e, i, ɔ, o, and u] as dependent variables, group and gender as factors, and age as cofactor revealed that F1 differs between IGHD and controls with an effect ($P = 0.026$) of 0.258 (partial eta squared) with an observed power of 0.835 and F3 with an effect ($P = 0.052$) of 0.230 (partial eta squared) with an observed power of 0.763. It was revealed differences between IGHD and controls in F1 [i], with an effect ($P = 0.025$) of 0.085 (partial eta squared) with an observed power of 0.62; F1 [ε] with an effect ($P = 0.012$) of 0.105 (partial eta squared) with an observed power of 0.719; F1 [e] with an effect ($P = 0.033$) of 0.077(partial eta squared) with an observed power of 0.574; F2 [u] with an effect ($P = 0.064$) of 0.059 (partial eta squared) with an observed power of 0.459; F3 [i] with an effect ($P = 0.032$) of 0.078 (partial eta squared) with an observed power of 0.578; F4 [i] with an effect ($P = 0.052$) of 0.065 (partial eta squared) with an observed power of 0.497; and F4 [ɔ] with an effect ($P = 0.041$) of 0.071(partial eta squared) with an observed power of 0.539.

Tables 2 and 3 present the same comparison in women and men, respectively. Female IGHD had higher F1 [i and e] $P = 0.029$ and $P = 0.036$; F2[ɔ] $P = 0.006$; and F4[ɔ] $P = 0.031$; and lower values of F4 [ε] $P = 0.002$ and F2 [i] $P = 0.004$. Male IGHD showed higher values of F3 [i, e, and ε], $P = 0.006$, $P = 0.022$, and $P = 0.006$, respectively and F4 [i], $P = 0.001$ and lower value of F2 [u], $P = 0.034$. Table 4 presents the influence of gender in values of F1, F2, F3, and F4 (Hz) for the seven oral vowels in 31 women and 31 men, separated in IGHD and controls. Male and female IGHD subjects had similar values of formant frequencies, except for F1 [a, ɔ, and ε] $P < 0.0001$, $P = 0.004$, and $P = 0.001$, respectively.

TABLE 1.
Formants Frequencies (Hz) in 33 Individuals With Isolated GH Deficiency (IGHD) and 29 Controls (Gender Pooled)

Formant	Vowel	IGHD	Controls	P
F1	F1 [a]	886 (155)	819 (155)	0.096
	F1 [ɔ]	667 (99)	660 (123)	0.787
	F1 [ε]	**664 (93)**	**612 (101)**	**0.040**
	F1 [o]	483 (77)	500 (121)	0.525
	F1 [e]	**499 (114)**	**447 (79)**	**0.045**
	F1 [u]	475 (117)	439 (107)	0.214
	F1 [i]	**446 (144)**	**379 (97)**	**0.032**
F2	F2 [a]	1568 (205)	1517 (340)	0.480
	F2 [ɔ]	1273 (277)	1309 (398)	0.682
	F2 [ε]	1884 (495)	1983 (314)	0.345
	F2 [o]	1011 (427)	1205 (667)	0.636
	F2 [e]	1986 (596)	2089 (510)	0.471
	F2 [u]	1129 (315)	1338 (553)	0.079
	F2 [i]	2126 (613)	2261 (409)	0.309
F3	F3 [a]	2900 (553)	2809 (349)	0.436
	F3 [ɔ]	2979 (577)	2765 (377)	0.060
	F3 [ε]	2941 (360)	2809 (312)	0.130
	F3 [o]	2777 (419)	2726 (298)	0.578
	F3 [e]	3002 (337)	2882 (267)	0.129
	F3 [u]	2813 (438)	2856 (386)	0.690
	F3 [i]	**3217 (328)**	**3027 (291)**	**0.020**
F4	F4 [a]	3913 (428)	3826 (399)	0.413
	F4 [ɔ]	**3935 (464)**	**3663 (396)**	**0.014**
	F4 [ε]	3882 (370)	3972 (309)	0.304
	F4 [o]	3830 (406)	3667 (231)	0.056
	F4 [e]	3959 (477)	3890 (429)	0.557
	F4 [u]	3912 (408)	3862 (351)	0.613
	F1 [i]	4093 (380)	3913 (392)	0.072

Notes: Data are expressed as mean (standard deviation), except for F2 [o], F3 [ɔ and e], F4 [ɔ] expressed as median (interquartile range). Data with significant differences are indicated in bold.