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DIFFERENTIAL VOICE PARAMETERS
IN HYPOPITUITARY CHILDREN

presented by

Connie Supal

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DIFFERENTIAL VOICE PARAMETERS IN HYPOPITUITARY CHILDREN

By

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ABSTRACT

DIFFERENTIAL VOICE PARAMETERS IN HYPOPITUITARY CHILDREN

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The purpose of this study was to analyze acoustically the voice parameters of a group of hypopituitary children before and after receiving hormonal treatment vs a control group. All subjects were divided into age groups of two-year intervals and ranged in age from 6 to 17 years.

Recordings were obtained from these subjects and choral spectra produced through the use of a PDP 11/40 minicomputer. The spectra were grouped according to hierarchical and multiple scaling algorithms in order to determine quantitatively the relationship between the spectra of hypopituitary children vs the control group. In addition, the glottal frequency of these children was determined by using a Visipitch device and compared by employing the t-test of statistical analysis.

With one exception, the results of the analysis of glottal frequency showed no significant difference between the hypopituitary group vs the control group. The results of the analysis of choral spectra suggested that the acoustical characteristics of the hypopituitary group after treatment approached the acoustical characteristics of the control group.

I wish to dedicate this thesis to my parents who have always given me their love and support throughout every step of my life.

ACKNOWLEDGEMENT

I sincerely wish to express my gratitude to my thesis director, Dr. Oscar I. Tosi, for his ideas, effort, support, and encouragement throughout this project. I also wish to thank the members of the thesis committee, Dr. Leo Deal and Dr. Jerry Higgins, for their review and corrections on the draft on this thesis.

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I. INTRODUCTION

Hypopituitarism is a disorder of the pituitary gland. It is an endocrinological disorder which is one of the major causes of dwarfism in children. This pituitary deficiency manifests itself gradually through the years from birth until about the age of 21, at which time this disorder can usually be diagnosed by the lack of sexual development of the individual. This disorder may lead to a deficiency in growth and other hormones associated with the pituitary gland.

Much of the research in the area of hypopituitarism has only begun in recent years. Clinical diagnosis of this disorder is extremely difficult. One of the major difficulties in diagnosing and treating this disorder is its frequent manifestation concurrently with other hormonal deficiencies. Another problem in diagnosing this disorder is the absence of obvious symptoms until the beginning of adulthood.

Many of the researchers in the area of hypopituitarism have noticed, among other characteristics of this disorder, that the voice may appear high pitched (Horstmann, 1949; Gardiner-Hill, 1937; Martin and Wilkins, 1958). Up to this date, however, no research has been done regarding the acoustic aspects of the voices of hypopituitary individuals.

Lack of growth hormone has been noted to affect all the body's structures. In addition, there may be an imbalance of thyroid and sex hormones which are two of the major determinants of voice characteristics (Tanner and Marshall, 1970; Tosi, 1976). Consequently, it is logically hypothesized that hypopituitary individuals may present differential voice qualities.

Since the spectrum is the physical correlate of voice quality, this study included a spectral analysis of a group of hypopituitary and "normal" children's voices. Also, glottal frequency was analyzed since pitch was the only voice characteristic mentioned by researchers in this field, as previously noted.

An early diagnosis of hypopituitarism is crucial to start proper medical treatment or to avoid unnecessary hormonal injections and painful testing in these children. An acoustical analysis may serve as a complementary diagnostic tool; therefore, research of this possibility could be of great importance to bring more knowledge concerning this hormonal disorder.

Purpose of the Study

The purpose of the present study was to analyze acoustically the voice parameters of hypopituitary subjects before and after receiving various lengths of hormonal treatment, and to compare these characteristics to a group of control subjects. The following questions were

formulated in order to define the scope of this research:

1. Is there a difference in the choral spectra between hypopituitary and control subjects' voices using the TOSI computer program of hierarchical and multiple scaling (Tosi, 1979)?

2. Is there a difference in the choral spectra between hypopituitary subjects' voices before and after receiving hormonal treatment?

3. Is there a difference between the age groups of hypopituitary subjects' choral spectra?

4. Is there a difference between the fundamental frequency of the voices of hypopituitary and control subjects?

5. Is there a difference between the fundamental frequency of the voices of hypopituitary subjects before and after receiving hormonal treatment?

Definition of Terms

Definitions of the major terms employed in this study are as follows:

Hypopituitarism. In this study, hypopituitarism is defined as a disfunction in the pituitary gland as diagnosed by endocrinologists at the Children's Hospital of Michigan Detroit Medical Center.

Choral spectra. Choral spectra as defined by Tosi (1979) are the long-term Fourier transforms of temporal choral speech, as introduced by Tarnoczy (1958). Choral speech is the temporal rearrangement of an individual's

speech (Tosi, 1979). This rearrangement consists of dividing a speech sample into n segments of equal duration and then mixing these n segments into one. The resulting "choral" speech segment has the same duration as each of its n single components. This output would convey to a listener a perception of n persons talking simultaneously (as a "choir"), but, of course, the source is only one person (Figure 1).

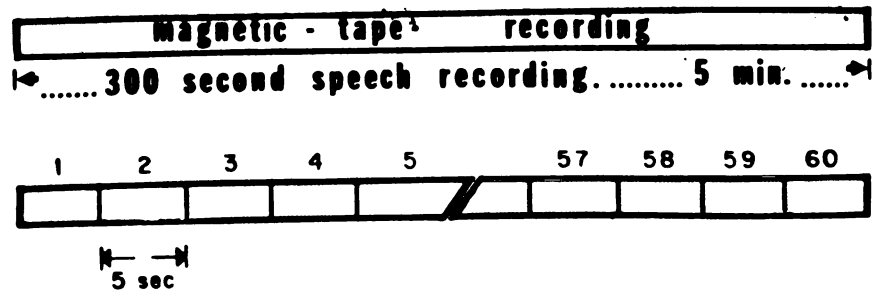
Hierarchical grouping of spectra. Hierarchical grouping of spectra consists of a computer procedure to rank the the similarities or dissimilarities of spectra as defined by Johnson (1967) and Sammon (1969).

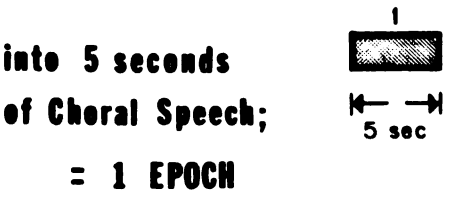
Glottal frequency. It is the fundamental frequency of vibration of the vocal folds. In the present study, glottal frequency of subjects' voices uttering the sound /a/ in isolation was measured by using a Visipitch device (Model 6087, Kay Elemetrics Corporation).

Organization of the Thesis

Chapter I has introduced some general concepts on hypopituitarism and, in particular, the lack of research on the acoustical analysis of the voices of these children. Also mentioned was the great need for research in helping to diagnose this disorder in young children.

Chapter II consists of a review of the literature including classification, physical symptomatology, treatment and psychological factors associated with this disorder.





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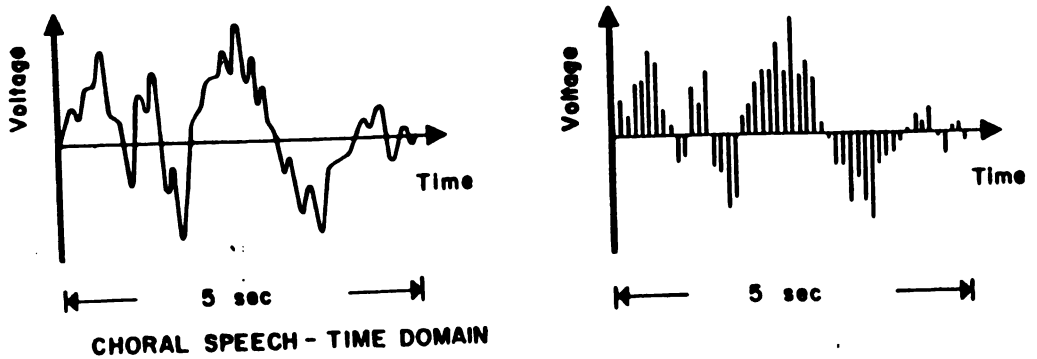

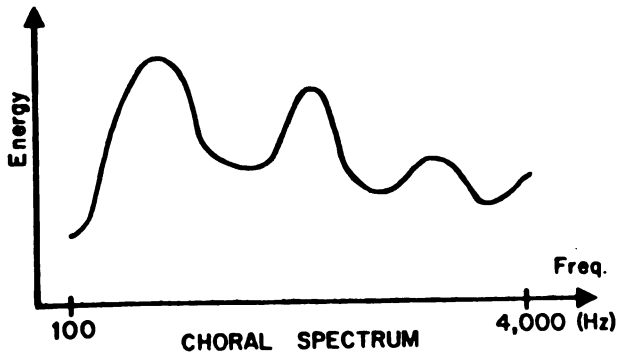

Figure 1. Procedure to obtain choral speech taken from Tosi (1979).

Chapter II consists of a review of the literature including classification, physical symptomatology, treatment and psychological factors associated with this disorder.

Chapter III discusses the selection of the subjects, phonetic materials, the equipment used in the study, and the procedures used to obtain the data.

Chapter IV contains a presentation of the results obtained from hierarchical grouping, Sammon's graph, and glottal frequency analysis including the appropriate charts and tables. A discussion of these results organized in the same manner follows.

Chapter V presents a summary of this study and conclusions which can be drawn from the results. In addition, it contains recommendations for future research.

II. REVIEW OF THE LITERATURE

The phenomenon of dwarfism has been noted throughout history, but it was not until the latter part of the 19th century that the medical community became deeply interested in the problem. Around 1900, Hutchinson and Benda were the first researchers to discover the significance of the pituitary gland in dwarfism. After this time, there appeared more and more reports of dwarfism as a result of pituitary lesions. Erdheim and Levi were among the first to associate this disorder with the pituitary (Hortsmann, 1949). It wasn't until the last two decades, however, that medical experiments began being performed following the discovery of producing pituitary extracts by Evans and Long in 1921 (Hortsmann, 1949).

Classification

Hypopituitarism is an endocrine disorder, specifically of the anterior pituitary gland. This endocrine disorder has been identified as one of the major causes of dwarfism since hypopituitary individuals are noticeably smaller than others of their sex and age (Wilkens, 1958). Some of the causes of dwarfism are bone disease, nutritional and metabolic disorders, circulatory and respiratory disorders, constitutional delayed growth and adolescence, "primordial"

and genetic, and other types. A complete table of the causes of dwarfism taken from Wilkens (1957) is transcribed in Table 1.

Hypopituitarism may be considered to be either idiopathic or organic. Idiopathic usually refers to a biochemical abnormality present from birth, whereas the latter stems from tumors or other gross destructive lesions of the pituitary gland. Organic causes of this disorder are rare.

Human growth hormone (HGH) is only one of the hormones of the pituitary. This hormone, however, has no specific target organ. Instead, almost every organ of the body responds to the action of HGH. Human growth hormone is a single polypetide of 190 amino acids (Roth, Glick, Yalow and Berson, 1963). This hormone is responsible for the transportation of amino acids into cells and allows for the incorporation of these amino acids into protein, an ingredient necessary to maintain all living tissues of the human body. In addition, HGH plays a role in DNA replication, RNA transcription and lipid and carbohydrate metabolism. Humans show physiological responses to growth hormone derived only from other humans or anthropoid sources.

Physical Symptomatology

It is unusual that hypopituitarism reveals itself in a family history of growth delay (Hortsmann, 1949). Children with pituitary deficiency usually have a normal birth size

Table 1. Causes of Dwarfism

I.	Bone Diseases
	A. Chondrodystrophy, Hurler's syndrome, etc.
	B. Rickets, all types
	C. Osteogenesis imperfecta--with multiple factures
	D. Diseases and anomalies of spine
II.	Nutritional or Metabolic Disorders
	A. Celiac disease and cystic fibrosis of pancreas
	B. Chronic renal diseases with acidosis and/or rickets
	C. Hepatic diseases
	D. Nutritional defects and chronic infections
	E. Electrolyte disturbances (hypokalemia, hypercalcemia, etc.)
III.	Circulatory or Respiratory Disorders
	A. Some congenital malformations of the heart
	B. Extensive chronic pulmonary disease--with anoxemia
IV.	Constitutional Delayed Growth and Adolescence
V.	Endocrine Disorders
	A. Hypothyroidism
	B. Hypopituitarism
	C. Sexual precocity with early epiphyseal fusion
VI.	"Primordial" or Genetic Dwarfism
	A. Familial
	B. Spordic (intrauterine dwarfing?)
	C. Syndrome of gonadal aplasia and dwarfism
	D. Autosomal anomalies (mongolism and other trisomies)
VII.	Other Types
	A. Progeria (Gilford-Hutchinson)
	B. Cockayne's syndrome
	C. Dwarfism with severe brain defects

Source: Wilkins (1957).

and experience a normal growth rate for the first 2-4 years of life. As Wilkins (1957) pointed out, this suggests that growth of very young children may not be dependent on the action of growth hormone; but, instead, growth of the individual occurs as a result of the intrinsic qualities of the tissues. Growth does not stop entirely in these children but tends to show a progressive deviation away from the normal growth pattern (Hortsmann, 1949; Wilkins, 1955; Martin and Wilkins, 1958). Physical examination of children with hypopituitarism typically shows that their body proportions are normal for their height but not for their chronological age. Therefore, body build serves of little value when trying to classify this disorder.

In the literature there is usually a distinction made between the terms growth and development. According to Hortsmann (1949), physiologically speaking, growth is an increase in the size of an organ or a system of organs. Growth indicates a quantitative increase, whereas development refers to qualitative changes in tissues or organs towards greater differentiation. The distinction is made between growth and development because in certain pathological conditions the two do not go together.

Hypopituitarism is very difficult to diagnose. One reason for this difficulty is that this disorder gradually progresses from birth to the adult stages of development. It is indistinguishable from other types of dwarfism in

childhood, particularly constitutional growth delay and adolescence (Wilkins, 1957). As was previously mentioned, it is rare that medical experts find obvious signs for the cause of this disorder, such as a tumor or lesion in the pituitary region. In addition, involvement of the pituitary gland can often mask other symptoms which may be suggestive of an organic lesion.

Often times, when there are no obvious explanations for other types of dwarfism, there is a tendency to assign these to a pituitary deficiency (Hortsmann, 1949). Also, differences in the degree of the deficiency of the various pituitary hormones may lead to differences in the clinical picture of these individuals. It is absolutely necessary to diagnose this disorder in childhood in spite of the difficulties involved since it may cause abnormal growth or delayed puberty. Clearly, additional methods are needed to help in the differential diagnosis of this disorder at a time when it may be crucial for effective treatment.

It has been suggested that one major hallmark for hypopituitarism is the retardation of skeletal age. This delay in the osseous development manifests itself by a marked proliferation of the cartilage in the epiphyseal ends of long bones (Hortsmann, 1949; Martin and Wilkins, 1958, Gardiner-Hill, 1937; Seckel, 1960). Often times, other pituitary functions, such as gonadotropic, adrenotropic or thyrotropic deficiencies, may serve as a clue

that there is a pituitary disorder. On other occasions there are no other signs that suggest that this disorder is present, and it may not be until the patient grows older that the lack of gonadotropic activity becomes conspicuous with the failure of the individual to mature sexually. Primary and secondary sex characteristics may completely fail to appear. Some indicators of a pituitary disorder in males are small genital organs; lack of facial, pubic, and axillary hair; and a high pitched voice after the time of normal puberty. In women with this disorder, it may be underdeveloped breasts and the absence or scanty flow of menstruation (Hortsmann, 1949; Wilkins, 1957; Henneman, 1960; Gardiner-Hill, 1937). Also, because of the lack of muscular development which usually occurs in normal children in adolescence, hypopituitary individuals may show muscular weakness and fatigability.

During the pre-adolescent years, it may be impossible to distinguish hypopituitary disorders from other causes of dwarfism. In addition, until about the age of 21, it is difficult to determine whether the deficient pituitary activity is temporary or permanent (Wilkins, 1957). If an individual remains sexually immature well into adult years, he is presumed to be deficient in both GH and gonadotropic hormones of the pituitary. After reaching the adult years, however, individuals with hypopituitarism can usually be divided into groups depending on their pattern of sexual development.

TREATMENT

As was mentioned previously, only human and anthropoid sources of pituitary growth hormone are capable of stimulating growth. The treatment of this disorder varies from individual to individual, depending upon the degree of the deficiency. Growth hormone causes growth in the tissues and increases size without causing excessive osseous or other maturational development. It has been recommended by medical experts (Wilkins, 1957) that intramuscular doses be given from 1 to 5 mg per day. Other experts recommend injections on an interval schedule, such as three times a week instead of every day. The optimal dosage and schedule of treatment have not yet been determined. Often times, growth hormone is also administered with other hormones, depending on the exact nature of the problem. Most physicians disapprove of unnecessary use of hormonal therapy at an early age but realize that delayed adolescence and sexual development may cause serious psychological maladjustments. If the onset of puberty in males has not occurred by the age of 14, it is recommended that intramuscular injections of chorionic gonadotropin, and often times small doses of testosterone, be administered. For females, the problem of hormonal therapy is more serious as follicle stimulating hormone (FSH) has been found to cause cystic changes in the ovaries. At the present time, this drug is only available for research purposes.

Due to the difficulties in diagnosing this disorder, there also seem to be similar difficulties in treating it with the proper drug therapy.

Psychological Factors

It seems obvious that hypopituitarism may cause some psychological problems due to the lack of sexual maturity and growth in these children, particularly in adolescence. The psychological handicaps that may develop depend on the individual's capacity to cope with people's reactions to their small size (Wilkins, 1957). It is not known whether psychological problems are a cause of growth failure or whether it is a consequence of this failure. Little research or reports on this aspect have been produced.

Thus, from the review of the literature it appears that divergent opinions exist regarding the clinical diagnosis of hypopituitarism. The nature of this disorder makes it difficult for medical experts to establish an exact definition of hypopituitarism and, consequently, it is crucial to produce a careful diagnosis in order to rule out other possible causes of abnormal growth and development. As Hortsmann (1957) said, "no other field of medicine demands such a precise diagnosis as hypopituitarism."

III. SUBJECTS, EQUIPMENT, AND PROCEDURES

Subjects

A total of 26 subjects were utilized in this study. These subjects consisted of 11 male and 3 female children diagnosed by a staff physician at the Children's Hospital of Michigan, Detroit Medical Center, as being hypopituitary. The control group consisted of 12 "normal" children matched by age and sex. All subjects were divided into age groups of two-year intervals, ranging in age from 6 to 17 years. They were native to the United States, speaking a midwestern dialect of Standard American English.

The hypopituitary subjects were patients at the above-mentioned medical center. All patients were diagnosed as having idiopathic hypopituitarism except one, who was diagnosed as having an organic etiology. They received hormonal injections as prescribed by their physician according to standard medical procedures, as discussed in "Treatment." The mean time of treatment for the hypopituitary subjects was 30 months.

Phonetic Materials

The phonetic materials used for all recordings consisted of the name and age of each subject, isolated vowels /a/, /e/,

/i/, /o/, /u/, counting from one to ten, and various pre-selected sentences. A complete sample of the phonetic materials used is contained in Appendix A.

Equipment and Procedures

The voices of the hypopituitary subjects before treatment were recorded by the staff at the Children's Hospital of Michigan using standard recording equipment in a normal reverberant room. The recordings obtained prior to receiving hormonal treatment were labelled as "pre-recordings." The recordings of the hypopituitary subjects after receiving hormonal treatment and recordings of the control group were obtained by the author using a portable Sony Cassette tape recorder (Model #110) and a ferrum oxide cassette tape. The recordings obtained after receiving hormonal treatment were labelled as "post-recordings." These recordings were also obtained in a normal reverberant room with no extraneous noises.

Original cassette recordings were played back using the Sony Cassette tape recorder (Model #110) and dubbed onto 1/4" open reel magnetic tapes (Scotch, AV176, Low Noise) using the Ampex tape recorder (Model AG600). Further, these tapes were physically spliced to include only the subjects' voices, editing the voice of the staff person prompting the children during the original recording. In addition, lengthy pauses and extraneous noises which occurred in the pre-

recordings were extracted by segmentation. The final product consisted of 3 one-minute long samples from the voice of each subject/condition (pre, post, control). Each of the subject's sample was separated by a leader tape properly labelled. These tapes will be referred to as master tapes. These master tapes were played back through a Tanberg tape recorder (Model 3300X) and input to an analog-digital (A-D) computer peripheral device in order to be digitalized at a rate of 10,000 readings per second. This rate of sampling was used in order to keep the range of frequencies within 5K Hz (Nyquist, 1928; Tosi, 1979). The digital output from the A-D peripheral was fed into a PDP 11/40 minicomputer (Digital Corporation), and one choral spectra was obtained from each subject's sample through the program labelled CHORAL (Tosi, 1979). A total of 78 spectra were obtained through this procedure.

Each spectra received a file name according to the following protocol: "MH" referring to the initials for the hospital, "B" or "A" referring to before or after treatment recordings, a subject number, and a spectra number. For example, the file name MHB12 refers to Children's Hospital of Michigan, pre-treatment recording, subject number one, and spectra number two. A complete list of these file names is contained in Appendix B. These files were subsequently used for the hierarchical grouping completed in the program labelled TOSI3.

Each spectrum included an X-axis which portrayed frequencies from approximately 60 to 5K Hz with one ordinate every 2.4414 Hz (Dubes, 1979). The vertical axis included energy for each frequency from a range of 0 to 60 dB every 0.5 dB. In other words, each spectrum consisted of approximately 2048 bytes on the horizontal axis and 120 bytes on the vertical axis. Consequently, each spectrum carried a total information of 2.4576×10^5 bytes. Thus, each spectrum could be considered as a 2048-dimensional vector for the purposes of further computer calculations (Figure 2).

The 78 spectra were stored in the RAM (random access memory) disk of the computer to be retrieved for hierarchical grouping and multidimensional scaling. These operations were accomplished by using the software package denominated TOSI3. This package of software starts with hierarchical grouping of spectra as defined by Johnson (1967). Hierarchical grouping consists of comparing all combinations of spectra taking two at a time, point by point, and establishing the average difference of the 2048 ordinates compared. Consequently, each combination of any two spectra yielded a spectra difference number. These numbers are arranged in a square matrix of n x n (n indicates the number of spectra to be compared) columns and rows. The computer searches for the smallest of these numbers in that matrix and collapses (groups) the two spectra for

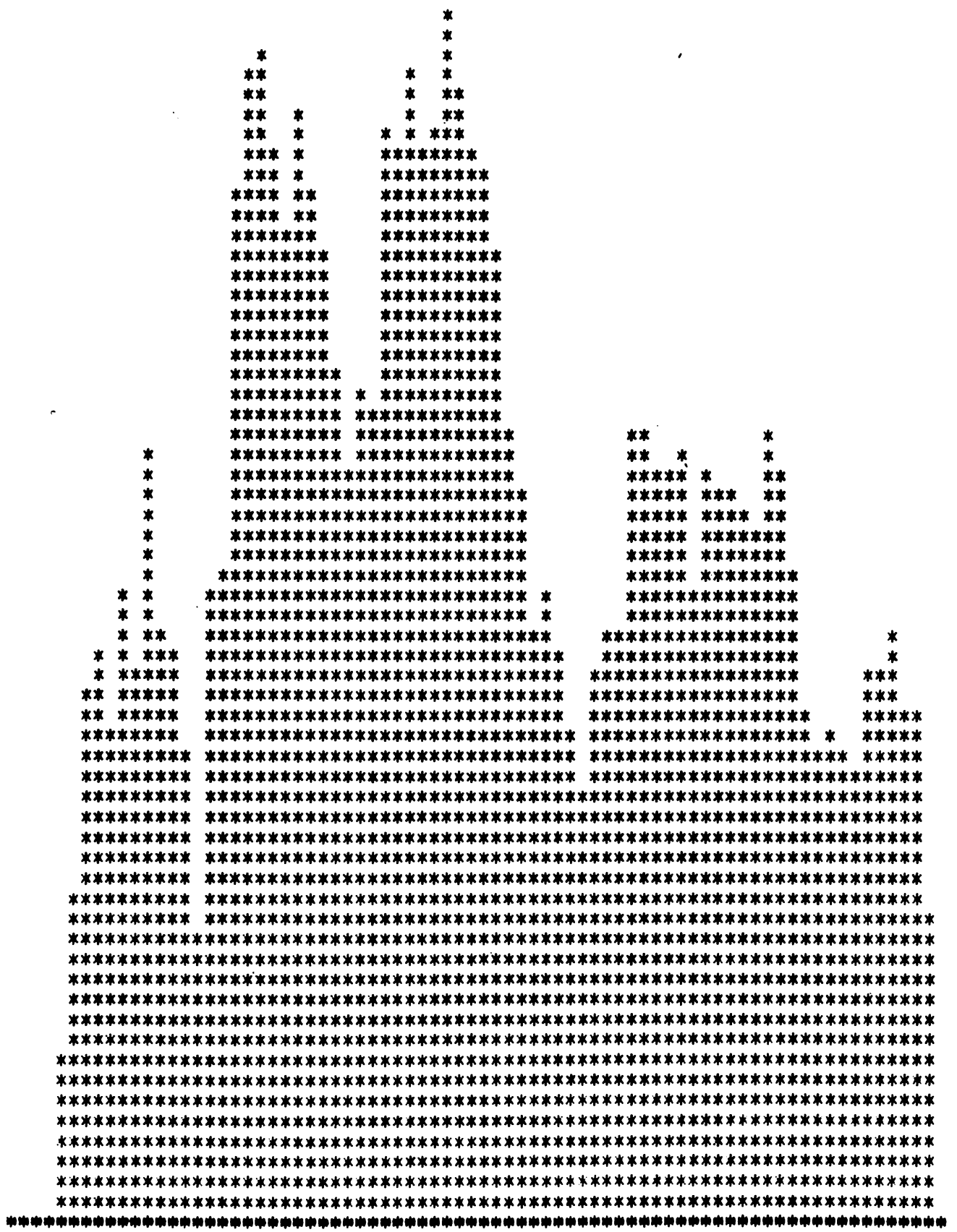

Figure 2. Example of choral spectrum. Horizontal axis is reduced to 76 points in order to accommodate the computer printer and obtain the hard copy.

which the difference is that smallest number. Therefore, a new (n - 1) x (n - 1) matrix is obtained; and the process continues until the matrix is reduced to 1 x 1. These groupings are portrayed in a graph called a dendrogram, (Figure 3). Examination of these dendrograms reveals the closeness or similarities/dissimilarities of a group of spectra. Since in the present case it was known which spectra belonged to which individual, examination of the dendrograms revealed the homogeneity or heterogeneity the voices of each group analyzed. Dendrograms include quantitative information concerning the promptness of grouping of spectra pairs. These quantitative data are labelled "birth" and "lifetime" (Johnson, 1967).

Next in the software package TOSI3 is the multiple scaling and modified Sammon's graph (Sammon, 1969; Tosi, 1979). In the present case, multiple scaling consists of reducing the dimensions of the spectrum vector from 2048 to 2 dimensions. This reduction is essentially calculated by a minimum span tree as introduced by Kruskal (1964) and seen in Figure 4 taken from Tosi (1979). This minimum span tree consists of taking one spectrum and plotting all others by calculating the minimum distances or "stresses" between any two pair of spectra. This plotting is redone several times until the best fitting minimum distance among all spectra is reached. In this process, each spectrum is finally determined by two coordinates,

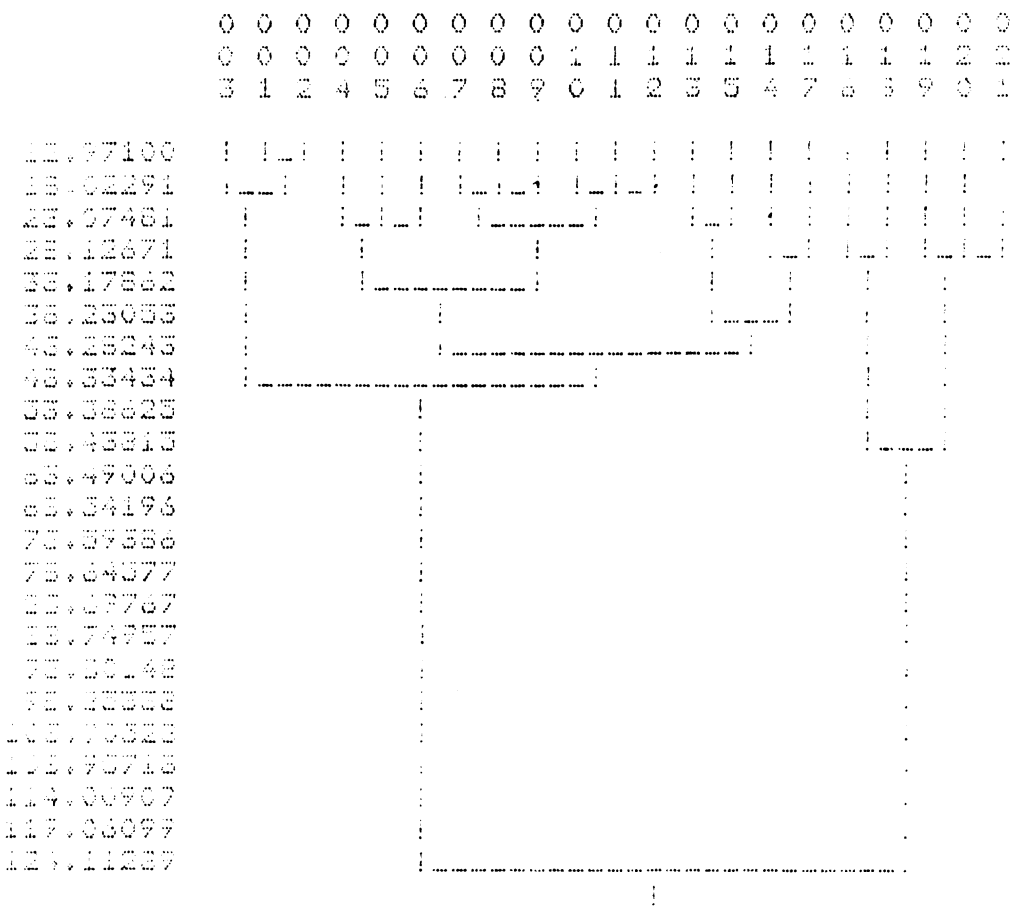

Figure 3. Dendrogram for comparing pre-treatment vs control 12-14 year male group. (Spectra 01-12 correspond to the four hypopituitary subjects, and spectra 13-21 correspond to the three control subjects.)

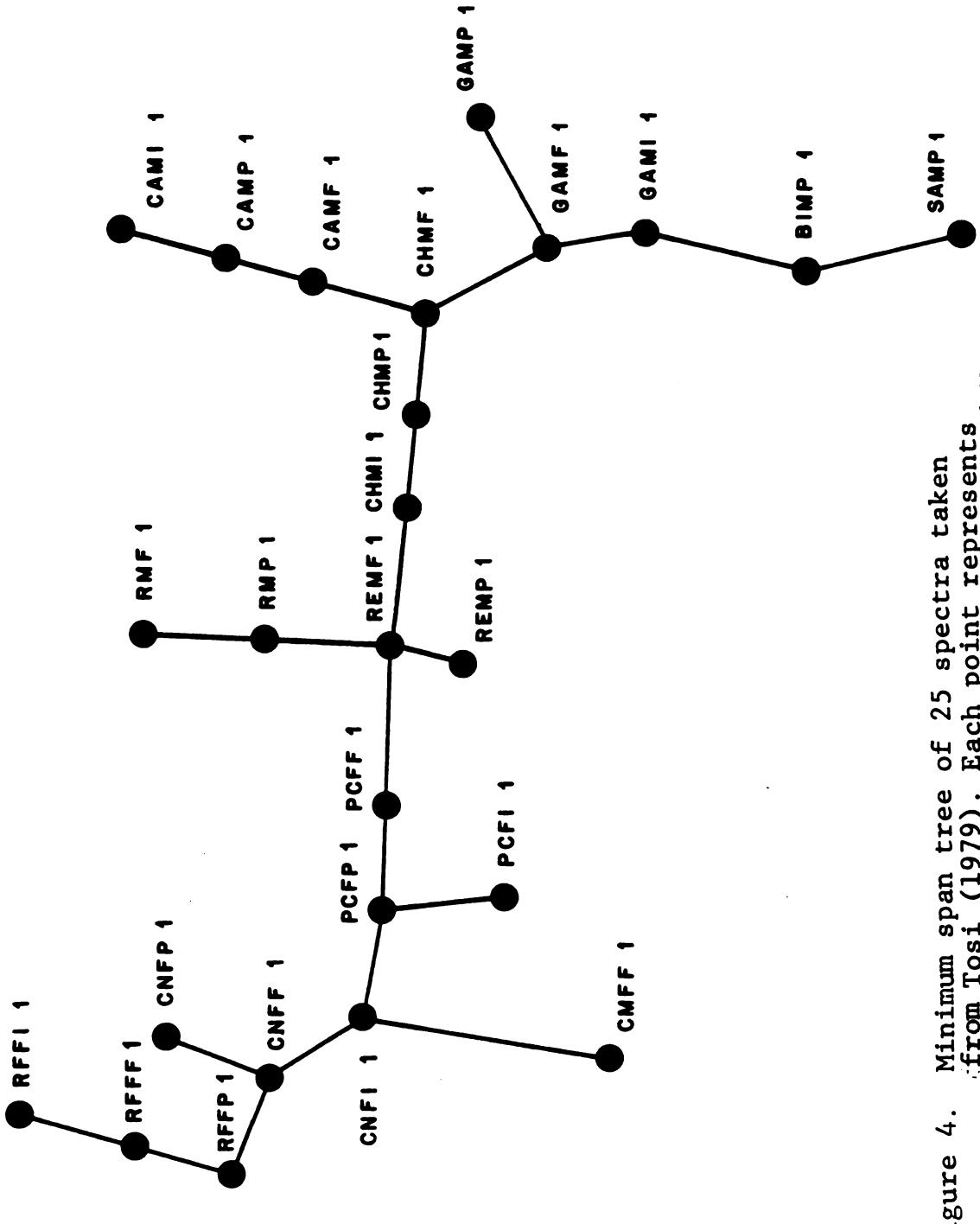

Figure 4. Minimum span tree of 25 spectra taken from Tosi (1979). Each point represents one spectrum in the two dimension, X and Y.

X and Y, which are portrayed in the Sammon's graph. Since each subject is represented by three spectra in the present study, the centroid and radius of dispersion of each subject's group of spectra are computed. The coordinates of the centroids are the average coordinates (X and Y) of the 3 spectra belonging to each subject. The radius of dispersion is the average of the euclidian distances of the centroid to each spectrum of the same individual.

After a hard copy of the Sammon's graph was obtained (Figure 5), the center of mass of the centroids of each group (pre, post, control) was graphically determined. Further, the euclidian distance between these centers of mass (pre vs control and post vs control) was measured. Finally, the following ratios were computed:

1. The ratio of dispersion of hypopituitary subjects pre-treatment over the euclidian distance between center of mass for pre-treatment subjects to the center of mass for the control subjects.

2. The ratio of dispersion of hypopituitary subjects post-treatment over the euclidian distance between the center of mass for post-treatment subjects to the center of mass for control subjects.

3. The quotient of the ratio of (1) divided by the ratio of (2).

The interpretation of the above ratios could be related to the qualitative judgment of the effectiveness of treatment

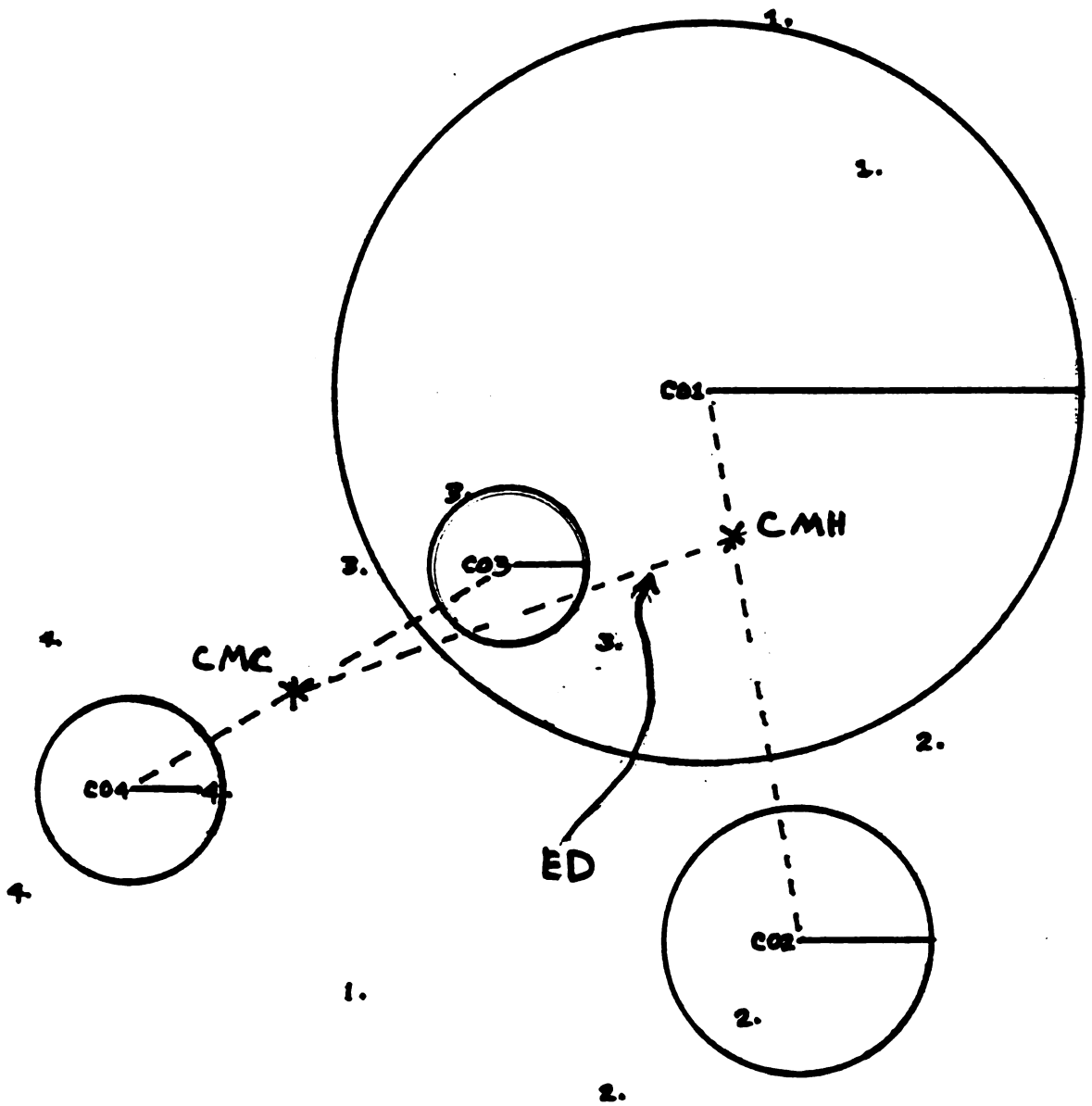

Figure 5. Sammon's graph output. (CMH=center of mass, pre-treatment hypopituitary subjects; CMC=center of mass, control subjects; ED=euclidian distance between center of mass pre and control; CO1 and CO2= centroids of pre-treatment hypopituitary subjects; CO3 and CO4=centroids of control subjects).

in bringing the voices of the hypopituitary subjects closer to the voices of the control subjects. The question now arises as to whether the improvement of the acoustical characteristics (closeness to the control subjects) also implies a general correlated improvement of the individual. Simultaneous measurements yielded by other diagnostic procedures, such as osseous development, along with this acoustical analysis, might answer this question.

To measure the fundamental frequencies of the subjects' voices, recordings of the utterance of the vowel /a/ in isolation were played back through the Ampex tape recorder (Model AG600) connected to the Visipitch (Model 6087, Kay Elemetrics Corp.). A graph of fundamental frequency vs time was portrayed on the CRT of this instrument. The cursor of this instrument was placed at the average vertical position on the graph, and this measurement of fundamental frequency was read from the digital output of the instrument. The time interval on the horizontal axis of the display was set at 2 seconds, considering that in most pre-treatment recordings the duration of the utterance of /a/ was very limited. These recordings are summarized in Table 2.

IV. RESULTS AND DISCUSSION

Since the subjects of this study were divided into sex/age groups for purposes of the analysis of the data, the results are also conveyed in a similar manner. Therefore, spectra belonging to a particular subject/condition (pre, post, control) in a sex/age group were compared with control subjects of the same sex/age group. For example, if an age group contained 3 hypopituitary subjects (3 spectra per subject) in the pre-treatment condition, then they were compared with 3 control subjects (3 spectra per subject) of the same sex and age group. In this example, a total of 18 spectra were compared. The number of spectra compared in each sex/age group/condition ranged from 12 to 21.

Results will be presented according to the following organization: hierarchical grouping, Sammon's diagram output, and glottal frequency measurement.

Results of Hierarchical Groupings

From the examination of dendrograms, the number of spectra that clustered or not were counted, and a ratio was produced by dividing the number that clustered or did not cluster by the total number of spectra in that particular

Table 2. Percentage of Hierarchical Clustering.

		Pre treatment		Post treatment	
Age Group		% cluster	% no cluster	% cluster	% no cluster
6- 8 yr Male	H	100	0	100	0
	N	100	0	100	0
9-11 Male	H	100	0	100	0
	N	100	0	100	0
9-14 yr Female	H	78	22	78	22
	N	100	0	100	0
12-14 yr Male	H	100	0	92	8
	N	78	22	89	11
15-17 yr Male	H	83	17	100	0
	N	100	0	100	0

H=hypopituitary subjects
N=control subjects

sex/age group/condition. These ratios are presented in Table 2. Ratios for perfect clustering ranged from 78 to 100 percent.

Results of Sammon's Output

The data from the Sammon's graph were analyzed according to the methods described in "Procedures." Results from these analyses follow:

1. Dispersion between hypopituitary subjects' spectra. The average dispersion for pre-treatment hypopituitary spectra ranged from 10 to 73 mm, whereas post-treatment spectra ranged from 28 to 62 mm. Normal subjects' average spectra dispersion ranged from 4 to 108 mm. Results are summarized in Tables 3 and 4.

2. Ratios of average dispersion between hypopituitary/condition and euclidian distance between center of mass of the hypopituitary/condition to the center of mass of controls. The ratio of the average dispersion of pre-treatment hypopituitary subjects over the euclidian distance between the center of mass for the control group ranged from 8 to 68 percent. The range of dispersion of post-treatment hypopituitary subjects over the euclidian distance between the center of mass for post-treatment hypopituitary subjects to the center of mass for the control group ranged from 35 to 98 percent.

Table 3. Pre-treatment euclidian distance from Sammon's graph.

Age Group	Subjects Pre-treatment/ control	Dispersion btw. pre-treatment subjects	Average dispersions btw. pre-treatment subjects	Dispersions btw. control subjects	Average dispersions btw. control subjects	Euclidian distance btw. center of mass pre- and control subjects	Ratio of pre-treatment subjects to center of mass pre- and control (1)
6-8 yrs. Male	J.S. B.B. J.M. / D.F. T.L.	C1-C2=50 mm C1-C3=29 C2-C3=47	42 mm	98 mm	49 mm	112 mm	0.38
9-11 yrs. Male	D.S. E.W. / H.Y. B.W.	C1-C2=20 mm	10 mm	73 mm	37 mm	128 mm	0.08
9-14 yrs. Female	D.A. P.P. C.B. / A.R. C.S. L.M.	C1-C2=53 mm C1-C3=82 C2-C3=83	73 mm	C4-C5=44 mm C4-C6=23 C5-C6=46	38 mm	113 mm	0.64
12-14 yrs, Male	C,B, A,G, E,C, E,C, / G,F, J,S, D,L,	C1-C2=51 mm C1-C3=28 C1-C4=26 C2-C3=32 C2-C4=25 C3-C4=18	30 mm	C5-C6= 60 mm C5-C7=161 C6-C7=102	108 mm	44 mm	0,68
15-17 yrs, Male	D,B, L,P. / T,M, M,S,	C1-C2=95 mm	48 mm	C3-C4=74 mm	37 mm	79 mm	0,60

C1, C2,...,C7 are the centroids of the three spectra from each subject in the 2-dimensional Sammon's diagram.

Table 4. Post-treatment euclidian distance from Sammon's graph.

Age Group	Subjects post-treatment/ control	Dispersions btw. post-treatment subjects	Average dispersions btw. post-treatment subjects	Dispersions btw. control subjects	Average dispersions btw. control subjects	Euclidian distance btw. center of mass post- and control subjects	Ratio of post-treatment subjects to center of mass post- and control (2)	Quotient of 1 : 2
6-8 yrs. Male	J.S. B.B. J.M. / D.F. T.L.	C1-C2=61 mm C1-C3=33 C2-C3=91	62 mm	127 mm	64 mm	63 mm	0.97	0.39
9-11 yrs. Male	D.S. E.W. / H.Y. B.W.	C1-C2=63 mm	31 mm	136 mm	68 mm	90 mm	0.35	0.23
9-14 yrs. Female	D.A. P.P. C.B. / A.R. C.S. L.M.	C1-C2= 5 mm C1-C3=48 C2-C3=52	35 mm	C4-C5=13 mm C4-C6=14 C5-C6= 7	11 mm	51 mm	0.69	0.92
12-14 yrs. Male	C.B. A.G. E.C. E.C. / G.F. J.S. D.L.	C1-C2= 6 mm C1-C3=40 C1-C4=38 C2-C3=46 C2-C4=36 C3-C4-63	38 mm	C5-C6= 61 C5-C7=161 C6-C7=103	108 mm	54 mm	0.70	0.97
15-17 yrs. Male	D.B. L.P. / T.M. M.S.	C1-C2=55 mm	28 mm	C3-C4=110 mm	55 mm	28 mm	0.98	0.61

C1, C2,...C7 are the centroids of the three spectra from each subject in the 2-dimensional Sammon's diagram.

3. The quotient of the above two ratios was calculated, and it ranged from 23 to 97 percent. The results for all groups are presented in Tables 3 and 4.

Results of Fundamental Frequency

The fundamental frequencies read on the Visipitch instrument from pre-treatment, post-treatment, and control subjects were divided into the five age groups previously indicated. Through the use of a TRS80 microcomputer (Model III, Radio Shack, Tandy Corp.), several t-tests of statistical analysis were computed with the data arranged in several ways as follows:

1. Pre vs post fundamental frequency analyzed by age group and also by considering the total number of subjects in each condition, i.e., total subjects in the pre-treatment condition vs total subjects in post-treatment condition.

2. Pre vs control fundamental frequency analyzed by age group and also by considering the total number of subjects in each condition.

3. Post vs control fundamental frequency analyzed by age group and also by considering the total number of subjects in each condition.

All the abovementioned t-tests showed no statistically significant differences except in the pre vs post condition, 12-14 year male group. This t-test showed a significant difference at the 0.02 probability level (Tables 6 and 7).

Table 5. Summary of glottal frequency.

Age Group	Hypopit. subjects	F_0 Pre treatment	F_0 Pre average	F_0 Post treatment	F_0 Post average	control subjects	F_0	F_0 Average
6- 8 yrs. Males	J.S.	244		264		D.F.	178	
	B.B.	248	248	230	257	T.L.	258	218
	J.M.	252		276				
9-11 yrs. Males	D.S.	188	226	300	268	H.Y.	254	256
	E.W.	264		236		B.W.	258	
9-14 yrs. Females	D.A.	286		190		A.R.	217	
	P.P.	280	257	248	209	C.S.	232	230
	C.B.	206		190		L.M.	240	
	C.B.	202		140		G.F.	218	
12-14 yrs. Males	A.G.	256	230	202	187	J.S.	184	181
	E.C.	276		238		D.L.	140	
	E.C.	186		170				
15-17 yrs. Males	D.B.	192	188	122	164	T.M.	130	165
	L.P.	184		206		M.S.	200	

Table 6. T-test results of fundamental frequency (by age group).

Condition	6-8 yrs. Male			9-11 yrs. Male			9-14 yrs. Female			12-14 yrs. Male			15-17 yrs. Male		
	$\bar{X}$	S.D.	P	$\bar{X}$	S.D.	p	$\bar{X}$	S.D.	P	$\bar{X}$	S.D.	P	$\bar{X}$	S.D.	P
Pre vs	248	3	0.5	226	38	0.6	257	36	0.4	230	37	0.02	188	4	0.7
post	257	19		268	32		209	27		188	36		164	42	
Pre vs	248	4	0.3	226	54	0.5	257	45	0.3	230	43	0.2	188	7	0.5
control	218	56		256	3		230	12		181	39		165	49	
Post vs	257	24	0.3	268	45	0.7	209	33	0.6	188	42	0.8	164	59	0.9
control	218	57		256	3		230	12		181	39		165	49	

Table 7. T-test results of fundamental frequency (by total subjects).

Condition	Pre-treatment			Post-treatment			Control			P
	N	$\bar{X}$	S.D.	N	$\bar{X}$	S.D.	N	$\bar{X}$	S.D.	
Pre vs post	14	233	37	14	215	49				0..02
Pre vs control	14	233	38				12	209	44	0,70
post vs control				14	215	50	12	209	50	0.30

N=number of subjects

$\bar{X}$=mean

S.D.=standard deviation

P=probability (significance level)

The standard deviation of the mean glottal frequencies from age groups was computed to observe its size and any trend correlated with age and maturation as described by Kent (1976). However, this type of variation was not encountered in the present study. Sizes of standard deviation were large in all groups, as predicted by Murray and Singh (1980).

Discussion of Hierarchical Groupings

Hierarchical grouping is correlated with homogeneity or heterogeneity of subjects' voices. In most sex/age group/conditions a 100 percent grouping was obtained for the hypopituitary and control subjects. One exception was for the 12-14 year male group. In this group, the control subjects clustered only an average of 84 percent, whereas in other age groups, the control subjects clustered 100 percent. This could possibly be explained by considering the instability of the voices at puberty (Tosi, 1976; Tanner, 1970).

For the male hypopituitary subjects in the 12-14 year group, it was observed that pre-treatment subjects clustered 100 percent, whereas the same patients after treatment clustered only 92 percent, thereby approaching the data yielded by the control subjects. This result suggests that the treatment has a possible effect on pubertal development as it relates to voice characteristics.

Another exception to the perfect clustering is found in the only female group studied, in which both pre- and post-treatment hypopituitary subjects yielded the same average figure, 78 percent. Further, by exploring clustering of the individual hypopituitary subjects in this group, it was disclosed that the female who received less treatment (15 months) clustered better (100 percent) than those who received treatment for a longer time (39 and 45 months). These subjects clustered only 67 percent. This may suggest an optimal duration of treatment for female hypopituitary subjects.

Discussion of Sammon's Output

Concerning the Sammon's graph outputs, average dispersion of subjects' spectra is correlated to the homogeneity of the group considered. A comparison of Tables 3 and 4 reveal that the range of the average dispersion for pre-treatment hypopituitary subjects is larger than that of post-treatment hypopituitary subjects.

The quotient of the ratios of the pre- and post-teatment hypopituitary subjects over their distance to the control subjects could be correlated in some way by the degree of improvement of the voice produced by treatment. In all sex and age groups, there was an improvement of the voice characteristics quantified from 23 to 97 percent. The smallest percentage was found in the youngest age groups studied

(6-8 and 9-11 year males; 39 and 23 percent). This result may suggest that treatment produces less effect on hypopituitary subjects before reaching the puberty years. In addition, the 15-17 year male group showed a smaller percentage (61 percent) than the 9-14 year male group, which may suggest an optimal time for treatment.

Discussion of Fundamental Frequency

Although no statistically significant differences were observed through the use of the t-test, contradicting observations of previous authors regarding the high-pitched voices of hypopituitary children, it should be noted that in most cases of this study there was a decrease in the average fundamental frequency after treatment. However, the decrease was not enough to grant a statistically significant difference. The following factors must be considered to properly interpret the lack of statistical significance:

1. Limitations of the number of subjects.
2. Poor pre-recordings.
3. The existence of only one voice sample per individual for the pre- and post-conditions.
4. No consistency in the manner of utterance of the vowel /a/ in isolation during the pre- and post-recordings.

Failure for the standard deviation of the mean fundamental frequency to follow the decreasing rate with age and maturation suggested by Kent (1976) may also be due to the abovementioned factors.

The questions formulated on page 3 can now be answered as follows:

1. Is there a difference in the choral spectra between hypopituitary and control subjects' voices using the TOSI program of hierarchical and multiple scaling (Tosi, 1979)?

In general, the spectra for the hypopituitary and control groups in this study were highly homogeneous, clustering closely.

2. Is there a difference in the choral spectra between hypopituitary subjects' voices before and after receiving hormonal treatment?

In all age groups, the post-treatment hypopituitary spectra came closer to the control group spectra than the pre-treatment spectra.

3. Is there a difference between the age groups of hypopituitary subjects' choral spectra?

Yes, the results between the various age groups differed as shown in Tables 3 and 4. The groups that showed the largest percentage increase were the 9-14 year females and the 12-14 year males (92 and 97 percent). The 15-17 year male group also showed an increase (61 percent); however, it was less than the 12-14 year male group and more than the 6-8 year male group.

4. Is there a difference between the fundamental frequency of the voices of hypopituitary and control subjects?

The t-test of statistical analysis showed no significant difference except for the pre vs post condition, 12-14 year male group.

5. Is there a difference between the fundamental frequency of the voices of hypopituitary subjects before and after receiving hormonal treatment?

Again, the t-test of statistical analysis showed no significant difference except for pre vs post, 12-14 years male group.

V. CONCLUSIONS AND RECOMMENDATIONS

All the acoustical measurements obtained in this study showed an effect of the treatment for these hypopituitary children. The effect was variable in degree, with much less effect concerning the fundamental frequency. The results of this study, therefore, suggest that acoustical analysis of hypopituitary voices can be a valuable and relevant concomitant tool for differential diagnosis.

It would be desirable to perfect the acoustical analyses of hypopituitary children by standardizing the procedures for obtaining the samples including prescribed intervals of time for recordings during the medical treatments of these patients.

Recommendations for future research should include the use of a larger number of subjects with a very well defined medical diagnosis and treatment, and good recordings produced by competent people using the proper standards. A good research design prior to the performance of a formal experiment is highly desirable. However, because of the lack of consistency in the medical aspects of hypopituitarism and the fact that the subjects are patients, experimenters may encounter great difficulty in adhering to a strict research design.

Since the computer algorithms utilized in this study seem to yield relevant information regarding the differences

in voice qualities of these hypopituitary and control children, it is recommended that future research be specifically aimed at standardizing the interpretations of the algorithms discussed in this study. This could be achieved through large amounts of data.

In addition, the construction of a perceptual scale to evaluate hypopituitary patients by qualified listeners (such as a group of experienced speech pathologists) could also be relevant as a screening method for early detection of voice disorders in hypopituitarism.

APPENDICES

APPENDIX A

PHONETIC MATERIALS

1. My name is _____.
2. Today's recording date is _____.
3. My birthdate is _____.
4. I am _____ years old.
5. /a/, /e/, /i/, /o/, /u/
6. My sister has shiny new shoes.
7. Put the puppy in my lap.
8. I like ice cream.
9. I like to chew chewing gum.
10. This is the first of the month.
11. Count from one to ten.
12. This is the end of the recording.

APPENDIX B

MONTHS OF TREATMENT

Subject	Months treatment
J.S.	20
B.B.	23
J.M.	8
D.S.	34
E.W.	30
D.A.	39
P.P.	45
C.B.	62
A.G.	45
E.C.	44
E.C.	21
C.B.	15
D.B.	34
L.P.	9

$\bar{X}$ = 30 mos.

S.D. = 16

APPENDIX C

COMPUTER FILE NAMES

	Hypopituitary			Control	
	Subject	File Name Pre	Post	Subject	File Name
6-8 yrs. Male	J.S.	MHB11	MHA11	D.F.	MHC11
		12	12		12
		13	13		13
	B.B	MHB21	MHA21	T.L.	MHC21
		22	22		22
		23	23		23
	J.M.	MHB31	MHA31		
		32	32		
		33	33		
9-11 yrs. Male	D.S.	MHB41	MHA41	H.Y.	MHC31
		42	42		32
		43	43		33
	E.W.	MHB51	MHA51	B.W.	MHC41
		52	52		42
		53	53		43
9-14 yrs. Female	D.A.	MHB61	MHA61	A.R.	MHC51
		62	62		52
		63	63		53
	P.P.	MHB71	MHA71	C.S.	MHC61
		72	72		62
		73	73		63
	C.B.	MHB81	MHA81	L.M.	MHC71
		82	82		72
		83	83		73
12-14 yrs. Male	C.B.	MHB91	MHA91	G.F.	MHC81
		92	92		82
		93	93		83
	A.G.	MHB101	MHA101	J.S.	MHC91
		102	102		92
		103	103		93
	E.C.	MHB111	MHA111	D.L.	MHC101
		112	112		102
		113	113		103
	E.C.	MHB121	MHA121		
		122	122		
		123	123		

COMPUTER FILE NAMES (CONT.)

	Hypopituitary			Control	
	Subject	File Name Pre	File Name Post	Subject	File Name
15-17 yrs. Male	D.B.	MHB131	MHA131	T.M.	MHC111
		132	132		112
		133	133		113
	L.P.	MHB141	MHA141	M.S.	MHC121
		142	142		122
		143	143		123

MH=Children's Hospital of Michigan
B=pre-treatment recording
A=post-treatment recording
C=control subjects

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