



Immediate Effects of Methylphenidate on Vocal Acoustic Parameters in Children with Attention Deficit Hyperactivity Disorder

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ÖZET:

Dikkat eksikliği hiperaktivite bozukluğu olan çocuklarda akustik parametreler üzerine metilfenidat'ın kısa dönem etkileri

Amaç: Dikkat eksikliği hiperaktivite bozukluğu olan çocuklar, normal çocuklara oranla daha çok ve daha sesli konuşurlar. Bu çocukların seslerini kötü kullanma olasılıkları daha sıktır ve bu durum çocukluk disfonisi için risk oluşturur, ayrıca hiperfonksiyonel ses davranışları iletilmelerini olumsuz etkiler. Dikkat eksikliği hiperaktivite bozukluğu olan çocuklardaki vokal akustik değişkenleri araştıran çalışmalar çok sınırlıdır. Daha da ötesi vokal akustik değişkenler üzerine stimulanların olası etkileri bilinmemektedir. Bu çalışmanın amacı dikkat eksikliği hiperaktivite bozukluğu olan çocuklarda metilfenidat verilmesi sonrasında olası vokal akustik değişiklikleri değerlendirmektir.

Yöntem: Bu çalışmaya DSM IV tanı ölçütlerine göre dikkat eksikliği hiperaktivite bozukluğu tanısı konulan, en az bir yıldır metilfenidat tedavisi alan 22 ergenliğe girmemiş erkek çocuk alınmıştır. Deneklerin ilaçsız dönemde ve metilfenidat sonrası maksimum fonasyon süreleri değerlendirilmiş ve ses örnekleri alınmıştır. Ses örnekleri MXL stereo dijital mikrofon ile yapılmıştır ve çok boyutlu ses programı (MDVP-Multi Dimensional Voice Program) kullanılarak analiz edilmiştir. Akustik parametrelerden s/z oranı, temel frekans, jitter, pitch pertürbasyon oranı, shimmer, amplitüd pertürbasyon oranı ve gürültü-harmoni oranı değerlendirilmeye alınmıştır.

Bulgular: İlaçsız dönemdekine oranla temel frekans, metilfenidat ile anlamlı derecede düşmüştür ($p < 0.001$). Mutlak jitter değerleri metilfenidat ile ilaçsız dönemde karşılaştırıldığında anlamlı düzeyde artmıştır ($p = 0.039$). Metilfenidat ile s/z oranında ve diğer akustik değişkenlerde anlamlı farklılıklar gözlenmemiştir.

Tartışma: Metilfenidat temel frekansını düşürerek konuşmanın rezonansını değiştirmektedir. Metilfenidat motor konuşmayı merkezi olarak baskılayarak sesin ayarlanmasını sağlıyor olabilir.

Anahtar sözcükler: Metilfenidat, dikkat eksikliği hiperaktivite bozukluğu, akustik değişkenler, ses

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ABSTRACT:

Immediate effects of methylphenidate on vocal acoustic parameters in children with attention deficit hyperactivity disorder

Objective: The children with attention deficit hyperactivity disorder are more talkative and aloud than typical children. Children with attention deficit hyperactivity disorder might abuse their voice more often than others and this might be a risk factor for childhood dysphonia, and hyperfunctional vocal behaviors negatively influence their communications. The studies about vocal acoustic variables in children with attention deficit hyperactivity disorder are very limited; moreover possible effects of the stimulants on vocal acoustic variables are unknown. The purpose of the present study was to evaluate possible vocal acoustic changes following methylphenidate administration in children with attention deficit hyperactivity disorder.

Method: The study samples included 22 prepubertal boys that diagnosed to have attention deficit hyperactivity disorder according to the Diagnostic and Statistical Manual of Mental Disorders IV criteria, and have been treated with methylphenidate for at least one year. The voice samples were recorded and analyzed using the Multi Dimensional Voice Program (MDVP) advanced software with MXL stereo medium digital microphone both during baseline (drug free) and after methylphenidate administration. The following acoustic parameters were taken into consideration: s/z ratio, fundamental frequency, jitter, pitch perturbation quotient, shimmer, amplitude perturbation quotient, and noise-to-harmony ratio.

Results: Baseline fundamental frequency decreased significantly following methylphenidate administration ($p < 0.001$). Absolute jitter increased significantly at methylphenidate administration period compare to that of baseline session ($p = 0.039$). There were no statistically significant differences in s/z ratio and the rest of acoustic variables between the baseline and the drug period.

Discussion: We suggested that methylphenidate change the resonance of speech production by lowering the fundamental frequency. Thus, methylphenidate would maintain regularization of loudness by controlling motor speech centrally.

Key words: Methylphenidate, attention deficit hyperactivity disorder, acoustic variables, voice

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INTRODUCTION

Attention-deficit/hyperactivity disorder (ADHD) is one of the most common neurobehavioral disorders in

childhood, and is characterized by developmentally inappropriate levels of inattention, impulsivity, and hyperactivity that are pervasive in several settings. It is estimated that between 3%-5% of children have ADHD.

Boys are more frequently affected than girls in both clinical and community settings (1). The most recent version of the Diagnostic and Statistical Manual of Mental Disorders (DSM IV-TR) divides the symptoms of ADHD into those of inattentiveness and those of hyperactivity and impulsivity. Three types of ADHD have been established according to prominent symptoms in the individual. The types are the predominantly inattentive type, the predominantly hyperactive-impulsive type, and the combined type (2).

Hyperactivity-impulsivity symptoms of ADHD consist of excessive fidgeting and squirming, getting up too fast from seats, running at inappropriate times, playing too loudly, or acting as if on a non-stop motor, blurting out answers before questions completed, difficulty in awaiting turns, and interrupting or intruding others. Some of hyperactivity-impulsivity symptoms are related to speech characteristics. The children with ADHD tend to talk loudly or too fast and to talk incessantly or out of turn, thereby dominating conversations, additionally due to their frequent tantrums and impulsive behaviors they may scream, yell, and shout more often than their peers. Namely, children with ADHD are talkative and aloud. These vocal behaviors in especially children with predominant hyperactivity-impulsivity and combined subtypes may be different than typical children. There are a number of reports addressing speech and language disorders in children with ADHD, but there is so far only one report in the literature about vocal acoustic characteristics of ADHD (3). In that study, Hamdan and colleagues showed that children with ADHD were louder when compared to typical children, and they were also perceived to have significantly more hoarseness, breathiness, and straining in their voice. In addition, there were no significant changes in the acoustic parameters except for the fundamental frequency, which was lower in the ADHD group. Due to these findings, the authors suggest that children with ADHD might abuse their voice more often than others and this might be a risk factor for childhood dysphonia (3).

Psychostimulants are the drugs of first choice for treating ADHD. Carefully designed trials of psychostimulants have found substantial improvement in ADHD core behaviors in 65-75 % of subjects with ADHD (4,5). Methylphenidate (MPH) is the most commonly prescribed psychostimulant (6). Considerable pharmacological and behavioral evidence suggests that use

of MPH produces immediate symptomatic improvement in children with ADHD, and MPH has been found very effective in improving attention span and in decreasing hyperactivity and impulsivity (7,8). However, possible effects of MPH on vocal properties of children with ADHD have not been studied so far. In this study, we hypothesized that MPH would effect acoustic parameters children with ADHD. We also predicted that MPH would reduce vocal loudness due to lowering fundamental frequency.

MATERIALS AND METHODS

Subjects

A total of 22 boys between 7 and 12 years of age were recruited for this study. The subjects were the children with ADHD who have been followed up and been treated at least for one year (range from 1 year to 5 years) in outpatient clinic of the child and adolescent psychiatry at the Gülhane Military Medical Academy. The diagnosis was made according to the criteria from the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) (9) by seeking clinical information from multiple informants including parents, child, and teachers. Measurement tools included standardized rating scales such as the DSM-IV Based Behavior Disorders Screening and Rating Scale. Consecutive children who presented for evaluation to the outpatient clinic of the child and adolescent psychiatry were screened for inclusion in this study. Only children with the combined subtype of ADHD were included to maintain homogeneity of the sample.

Children who met these additional criteria were included into the study: 1- boys aged 7-12 years (prepubertal); 2- at least one year of MPH use and being drug-responsive; 3- no history of specific speech-language impairments and voice-related disorders; 4- no history of other psychiatric disorders (conduct disorder, any anxiety disorder, depressive disorder, learning disorder etc.) except oppositional defiant disorder, and 5- no history of mental retardation, neurological disorders, sensorimotor handicaps, and chronic medical illness (respiratory diseases etc.).

All subjects were native speakers of Turkish. At the time of recording, none of the subjects had cold, allergy, or flu symptoms. The subjects who had taken any

medication except MPH before and at the time of recording were excluded.

The study was approved by the Human Subject Review Committee at the Gülhane Military Medical Academy. The informed consent was obtained from both parents or legal guardian after the standard information about the study provided and nature of the procedures explained to parents or guardian.

Measures

The symptoms and cognitive skills were assessed with the DSM-IV Based Behavior Disorders Screening and Rating Scale and the Raven's Colored Progressive Matrices (RCPM). After assessment for ADHD and satisfaction of inclusionary criteria, language assessments of all children were done by the speech-language pathologist, using the Peabody Picture Vocabulary Test (PPVT) and the Ankara Articulation Test (AAT).

DSM-IV Based Behavior Disorders Screening and Rating Scale. This scale was developed by Turgay (10), and the validity and reliability study in Turkey was performed by Ercan et al. (11). The scale has three subscales to inquire about ADHD, oppositional defiant disorder, and conduct disorder, respectively. These subscales have 41 items which include 9 inattention items, 6 hyperactivity items, 3 impulsivity items, 8 items related to oppositional defiant disorder, and 15 items related to conduct disorder. Parents and teachers rate each item on a 4-point Likert scale from 0 (absent) to 3 (severe).

Raven's Colored Progressive Matrices. The RCPM is a fast, easy-to-administer test and able to obtain a measure related to linguistic, visuoperceptual, and memory cognitive functioning. The test consists of 36 items in the three sets. It is designed for use with young children as well as older people. According to the authors, "the test can be used satisfactorily with people who, for any reason, cannot understand or speak English language" (pg.1) (12).

Peabody Picture Vocabulary Test. The PPVT was designed as a test of receptive vocabulary achievement and verbal ability. In addition, it provides a quick estimate of verbal ability or scholastic aptitude. The PPVT-Turkish version is adopted into Turkish by Jack Katz and Ankara RAM group in 1974 (13). It is an individually administered, norm-referenced test which is available in two forms. Only the Form B is adopted into Turkish. The

Form B contains 3 training items followed by 100 test items arranged in order of increasing difficulty. Each item has four simple, black-and-white illustrations arranged in a multiple-choice format. The subject's task is to select the picture considered to illustrate best the meaning of a stimulus word presented orally by the examiner. The test is designed for persons 2 to 12 years of age. Testing requires only 10 to 15 minutes, because the subject must answer only about 35 to 45 items of suitable difficulty. Administration of the test is different for children below or after 8 years of age. There is no reliability study for the PPVT-Turkish version.

Ankara Articulation Test: Standardization of AAT consisted of 3000 Turkish children between the ages of 2 and 12. The test provides information about a child's articulation ability by sampling spontaneous, cued (both phonetic and semantic) and imitative sound production. Examinees respond to picture plates and verbal cues from the examiner with single-word answers that demonstrate common speech sounds. Test measures articulation of consonant sounds, determine types of misarticulation, and compare individual performance to national, gender-differentiated norms at 75% and 95% comfort levels. There are 47 pictures which enable the examinee to test 53 words in all possible sound combinations in five positions in Turkish (in the beginning, three in the middle, or at the end of a word) (14).

Speech Recording and Analysis Procedures

As part of their voice measurements, prolongations of /s/ and /z/ were obtained and subsequently an s/z ratio was computed for each participant. All participants were asked to take a normal breath and prolong /s/ sound as long as possible and later to prolong /z/ sound at a comfortable pitch and loudness level. Each participant was given three trials to produce both the prolonged /s/ and the prolonged /z/ sounds, with the mean duration taken as the participant's score.

Speech recordings for acoustic analysis were made from the participants in two sessions held before noon: no-medication baseline session and the medication session after MPH administration of 0.5 mg/kg (approximately 60 minutes later), respectively. All participants were seated in a quiet room, and voice

samples were recorded with a high quality dynamic microphone (MXL USB.007 stereo medium digital microphone). The microphone-to-mouth distance was 10cm. and careful positioning minimized aerodynamic noise. No effort was made to control the absolute sound pressure levels of phonation. The participants were instructed to produce a prolonged /a/ sound at a comfortable and habitual levels of pitch and loudness pitch, and attempting to keep the sound as stable as possible for > 6 seconds (or as long as they could manage). The participants were allowed to practice the task several times before the recorded sample /a/ was performed. Three sustained phonations (with each phonation lasting longer than 3 s), were then recorded. The second production was used for acoustic data

analysis. The selected segments were later digitized and analyzed using the Multi Dimensional Voice Program (MDVP) Model 5105 Ver 2.3 of the Computerized Speech Lab Kay Elemetrics (15). The following MDVP acoustic parameters of voice were chosen and analyzed for this study: fundamental frequency (F0), absolute jitter (Jita), jitter percent (Jitt), pitch perturbation quotient (PPQ), shimmer in dB (ShdB), amplitude perturbation quotient (APQ), and noise to harmonic ratio (NHR).

Multi Dimensional Voice Program: Computer-based analysis systems are increasingly available for the clinical assessment of speech and voice functions. These systems have the potential to provide immediate quantitative information to assist clinical assessment and treatment. The MDVP is a computer program, which is developed by

Table 1: Description of the Acoustic Measurements Performed by MDVP

Type	Parameter	Description
Frequency perturbations	F0 (Hz)	Average fundamental frequency for the vocalization. Average fundamental frequency represents the average fundamental frequency for all extracted pitch periods (18). This measure corresponds directly to the vibratory rate of the vocal folds (19) and reflects their biomechanical characteristics (20).
	Jita (ms)	Absolute jitter gives an evaluation of the period-to-period variability of the pitch period. This is the average absolute difference between consecutive periods (20,21).
	Jitt (%)	Jitter percent represents the relative period-to-period (very short-term) variability of the pitch.(Baken and Orliko 2000, Feijoo and Hernández-Espinosa 1990)
	RAP (%)	Relative average perturbation gives the variability of the pitch period with a smoothing factor of 3 periods (20,21).
	PPQ (%)	Pitch period perturbation quotient gives the variability of the pitch period with a smoothing factor of 5 periods (20,21).
	sPPQ (%)	Smoothed PPQ gives the long-term variability of the pitch period with a user-selected number of periods (usually 55) (20,21).
Amplitude perturbations	ShdB (dB)	Shimmer in dB gives the period-to-period variability of the peak-to-peak amplitude within the analyzed voice sample (20,21).
	Shim (%)	Shimmer percent gives the variability of the peak-to-peak amplitude. It represents the relative period-to-period (in short-term) variability of the peak-to-peak amplitude (20,21).
	APQ (%)	Amplitude perturbation quotient gives the variability of the peak-to-peak amplitude with a smoothing factor of 11 periods (20,21).
	sAPQ (%)	Smoothed APQ gives the long-term variability of the peak-to-peak amplitude with a user-selected number of periods (usually 55) (20,21).
Noise	NHR	Noise-to-harmonics ratio is an average ratio of energy of the in-harmonic components in the range 1500–4500 Hz to the harmonic components energy in the range 70–4500 Hz. (22). It is a general evaluation of the noise presence in the analyzed signal (e.g., amplitude and frequency variations, turbulence noise, subharmonic components, and voice breaks). The noise parameters measure the degree of hoarseness caused by air turbulences introduced by the presence of a disorder (17).
	VTI (%)	Voice turbulence index is an average ratio of the spectral in-harmonic high-frequency energy in the range 2800–5800 Hz to the spectral harmonic energy in the range 70–4500 Hz (22).

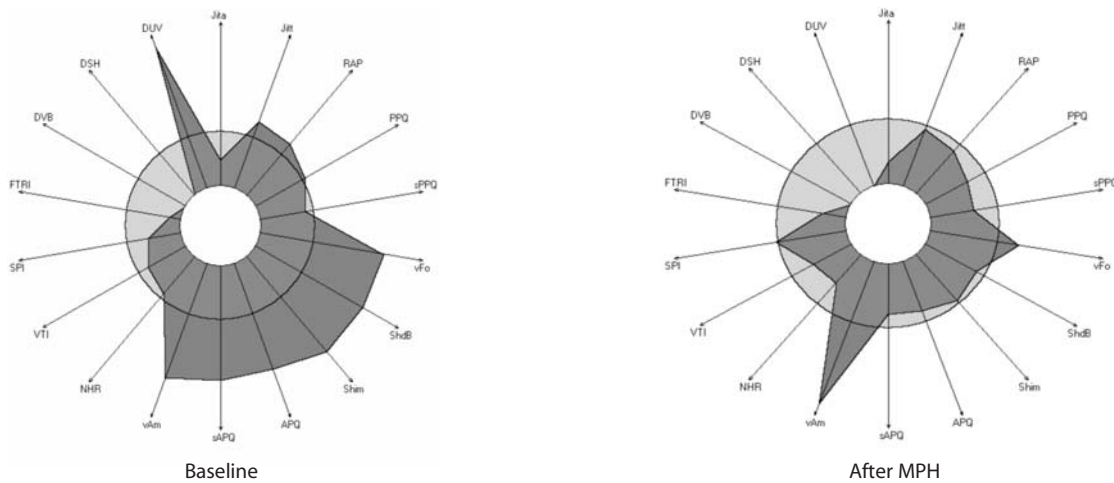


Figure 1: A sample graph of MDVP of a subject during baseline and following MPH administration.

Table 2: Comparison of Acoustic Parameters Between Baseline and Following MPH Administration in Children with ADHD⁶

Variables	Baseline (n=22)	MPH (n=22)	Z	p value
s/z ratio	0.88 (0.63-1.04)	0.89 (0.69-1.08)	0.05	0.96
F0 (Hz)	301.19 (256.72-386.55)	266.17 (202.36-303.71)	4.11	<0.001**
Jita (ms)	42.43 (16.76-195.05)	69.00 (12.96-210.83)	2.07	0.039*
Jitt (%)	1.46 (0.62-5.76)	1.88 (0.37-5.45)	0.89	0.37
PPQ (%)	1.12 (0.37-7.76)	1.98 (0.21-11.45)	1.70	0.09
ShdB (dB)	0.35 (0.19-0.94)	0.51 (0.21-1.87)	1.48	0.14
Shim (%)	3.85 (2.18-9.65)	5.50 (2.26-9.40)	1.51	0.13
APQ (%)	2.70 (0.44-10.14)	2.46 (0.46-16.53)	0.11	0.91
NHR	0.14 (0.10-0.64)	0.15 (0.11-1.00)	1.17	0.24

SData are showed as median (min-max). *p<0.05; **p<0.01; F0: Fundamental frequency, Jita: Absolute jitter, Jitt: Jitter percent, PPQ: Pitch perturbation quotient, ShdB: Shimmer in dB, Shim: Shimmer percent, APQ: Amplitude perturbation quotient, NHR: Noise to harmonic ratio

Kay Elemetrics, is one of the most complete instruments available for the acoustic analysis of voice (15). This system is capable of rapidly calculating a large number of parameters to measure different aspects of the vocal function, facilitating the graphical representation of these parameters. The MDVP appears to have potential for rapid quantitative assessments of voice in both research and clinical applications (16). The MDVP can calculate as many as 33 acoustic parameters from a voice sample. The most important parameters calculated by MDVP are summarized in Table 1 (17,18,19,20,21,22), and a sample graph of MDVP of a subject is shown on Figure I.

Statistical Analysis

All analysis was conducted using SPSS 10.0 and a p value <0.05 was considered significant. Statistical

comparisons between baseline and following MPH measures were performed with Wilcoxon Signed Ranks Test.

RESULTS

The mean age of the subjects was 9.05 ±1.43 (range 7-12) years. The median receptive language age of the subjects was 8.11 (range 6.01-11.08) years with the city norms of the PPVT. The median comfortable expressive age of the subjects 9.11 (range 5.03-9.11) years (in the AAT, 95% comfort is taken into consideration). The median RCPM score was 21 (range 5-30), that reflected intellectually average people according to the manual of the scale. In the DSM-IV Based Behavior Disorders Screening and Rating Scale, the Parent Form, median inattention score was 18 (range 12-22), median

hyperactivity-impulsivity score was 14 (range 12-24), and median oppositional defiant score was 11 (range 5-19).

From the acoustic parameters, baseline fundamental frequency (F0) decreased significantly at MPH administration period ($p < 0.001$). But, absolute jitter (Jita) increased significantly at MPH administration period compared to that of baseline session ($p = 0.039$). There were no statistically significant differences in s/z ratio and the rest of acoustic variables between the baseline and the drug period (Table 2).

DISCUSSION

This clinical trial was designed to investigate the possible effects of MPH on vocal acoustic variables in children with ADHD who are suggested to be more aloud and talkative. We demonstrated that MPH decreased F0, but increased the absolute jitter in children with ADHD. F0 is the indicative of the vocal fold vibratory rate and reflects resonance characteristics. F0 changes in vocal fold tension and subglottal air pressure and its psychological correlate is pitch. In producing loud voice, speakers use F0 to increase the number of glottal closures per time unit, which increases rapid fluctuations in the speech pressure waveform, which, in turn, raises vocal intensity (23). Studies have reported an increase of F0 variation with increased loudness and average F0 of sentences increased with louder speech production (24,25). In our study, F0 showed a significant decrease following MPH administration. In other words, MPH changed the resonance of speech production by lowering the pitch.

Despite the fact that the perceived increase in loudness and straining in children with ADHD indicates and/or makes one to anticipate an increase in F0, Hamdan et al. found the opposite. These authors explained that this might be resulted from the possible increase in mass in the vocal fold secondary to either mucosal swelling or hypertrophy of the vocalis muscle due to hyperfunctional vocal behaviors. However, these authors didn't perform laryngeal endoscopy to show the possible vocal fold changes (3). In our study, unfortunately, vocal acoustic variables of children with ADHD couldn't be compared to those of typical children, because standards and norms for vocal acoustic variables of the healthy Turkish children presently are not available. However, in general, it is

known that for a child, an s/z ratio which is greater than 1.2 is an indication of a laryngeal pathology, and requires further clinical diagnostic management (26). In our study, in both occasions, the ratio was not greater than 1.2. Therefore, no laryngeal pathology was assumed.

Measurement of perturbation refers to the small, rapid, cycle-to-cycle changes of period (jitter) in the fundamental frequency of the voice and amplitude (shimmer) that occur during phonation (19). In our study, MPH didn't change perturbation measures except the absolute jitter. We suggest that the increased absolute jitter was due to the decreased F0 under MPH, because jitter reflects cycle to cycle variation in F0, resulting in a decrease in F0 causes an increase in jitter in return. Absolute jitter and shimmer measures have been shown to be affected by mean F0 and sound pressure level, respectively (27). In contrast, F0 and sound pressure level-adjusted indexes are calculated as a ratio of mean perturbation to mean F0 or amplitude, respectively. Thus, they are normalized to F0 and sound pressure level (28,29). Therefore, in our study jitter percent and pitch perturbation quotient were also chosen, and these variables did not show a significant difference after MPH administration. Perturbation correlates with perceived roughness or hoarseness in the voice (19). However, according to De Krom, the noise to harmonic ratio is the "best predictor of roughness" and abnormal voice in speech production show greater noise levels (30). In our study, MPH didn't affect the noise to harmonic ratio.

One of the core deficits in ADHD is deficient inhibitory control of ongoing motor response, which may be related to underactivity in the brain prefrontal cortex (31,32). It is thus plausible that the same mechanism involving disinhibition of motor control in the neck, abdomen, and limbs may also involve the vocal folds. MPH significantly improves motor planning and inhibition on skeletomotor tasks, in which it decreases response timing variability (33) and improves inhibitory function on the Stop Task (34,35). It is possible that a decreased F0 after MPH administration in children with ADHD may be due to central motor inhibition of MPH. Since in our study, MPH didn't change the value of the s/z ratio, which may suggest that MPH acts more centrally than peripherally on F0 depending on knowledge it has been employed as an indicator of vocal fold function (26).

This clinical trial has some limitations. First, the

parameters of voice are not easily be evaluated fully. Therefore a combination of evaluation techniques, including physiological, acoustical, psychological, and perceptual approaches, are mostly combined for a complete evaluation. During this multifaceted diagnostic approach, the various components should complement and substantiate one another. In this study vocal acoustic parameters were measured, however we didn't perform the perceptual analysis included the following parameters: hoarseness, breathiness, strain, and loudness. Second, the acoustic parameters of ADHD couldn't be compared to those of typical children, because there are no standards and norms for acoustic variables of the healthy Turkish

children. Third, our study was conducted in highly select group of subjects with a narrow age range, and included only boys and the combined subtypes of ADHD. However, all the factors were not possible to get under control.

In conclusion, this clinical trial is the only study that examined the effects of stimulant medication on vocal acoustic parameters in children with ADHD and evaluated a small sample on and off their clinical doses of MPH. We suggest that MPH decreases fundamental frequency in children with ADHD, but our findings should be replicated under blind drug administration and by supporting other vocal analyses.

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