Türkiye Klinikleri Sağlık Bilimleri Dergisi
Turkiye Klinikleri Journal of Health Sciences Turkiye Klinikleri J Health Sci. 2025;10(1):138-44

ORIGINAL RESEARCH ORİJİNAL ARAŞTIRMA
DOI: 10.5336/healthsci.2024-104589

Time Domain Analysis of Frequency Following Response to Speech Stimulus in Turkish-Speaking Children with Typical Hearing: A Descriptive Study

Tipik İşitmeye Sahip Türkçe Konuşan Çocuklarda Konuşma Uyaranına Verilen Frekans Takip Yanıtının Zaman Alan Analizi: Tanımlayıcı Bir Çalışma

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ABSTRACT Objective: The frequency following response is a neurophonic auditory evoked potential that is an important tool for understanding auditory, speech and language processing mechanisms and disorders, as it provides information about the neural representation of speech stimuli. This study aimed to contribute to the literature by analyzing the latency and amplitude values of the V-A-C-D-E-F and O waveforms and the VA complex (slope) which are the time domain components of the frequency following response in Turkish-speaking children with typical hearing. **Material and Methods:** Participants consisted of forty children aged 7-9 years with bilateral typical hearing, bilateral type A tympanograms, ipsilateral-contralateral acoustic reflexes. Participants were evaluated in a soundproof room using an Intelligent Hearing Systems device.The 40 ms /da/ speech stimulus was presented to the right ear via an insert earphone and the responses were recorded from electrodes placed at the centre of the head (Fz:non-inverting/active), the ipsilateral earlobe (inverting/reference) and the contralateral earlobe (ground). **Results:** When the seven characteristic peaks (V-A-C-D-E-F and O), which are the time domain components of the frequency following response, were analyzed; V:6.49, A:7.52, C:18.46, D:22.15, E:30.62, F:39.16 and O:48.06 ms.The mean amplitude measures of the waves were V:0.15, A:-0.17, C:-0.10, D:-0.14, E:-0.22, F:-0.21 and O:-0.16 µV. The mean slope value was 0.31. **Conclusion:** The findings contribute to the literature by providing information on the latency, amplitude and slope values of the frequency following response which can be used in a wide range of areas regarding auditory,speech and language processing disorders in Turkish speaking children with typical hearing.

Keywords: Time domain analysis; frequency following response; speech stimulus

ÖZET Amaç: Frekans takip yanıtı, konuşma uyaranlarının nöral temsili hakkında bilgi sağladığı için işitsel, konuşma ve dil işlemleme mekanizmalarını ve bozukluklarını anlamak için önemli bir araçtır. Bu çalışmada, tipik işitmeye sahip Türkçe konuşan çocuklarda frekans takip yanıtının zaman alanı bileşenleri olan V-A-C-D-E-F ve O dalga formlarının latans ve amplitüd değerleri ile VA kompleksinin (eğim) analizi yapılarak literatüre katkı sağlanması amaçlanmıştır. **Gereç ve Yöntemler:** Katılımcılar, bilateral tipik işitmeye sahip, tip A timpanogramları, ipsilateral-kontralateral akustik refleksleri olan, 7-9 yaşları arasında, tek dilli, anadili Türkçe olan ve sağ elini kullanan 40 çocuktan oluşuyordu. Katılımcılar, ses geçirmez odada, Intelligent Hearing Systems cihazı kullanılarak değerlendirildi. Frekans takip yanıtının zaman alanı analizi için konuşma uyaranı 40 ms /da/, insert kulaklık aracılığıyla sağ kulağa sunuldu ve yanıtlar, başın ortasına (Fz: non-inverting/aktif), ipsilateral kulak memesi inverting/referans) ve kontralateral kulak memesi üzerine yerleştirilen elektrotlardan kaydedildi (ground). **Bulgular:** Frekans takip yanıtının zaman alanı komponentleri olan yedi karakteristik zirvesi (V-A-C-D-E-F ve O) analiz edildiğinde; FFR bileşenlerinin ortalama latans değerleri; V: 6,49, A: 7,52, C:18,46, D: 22,15, E: 30,62, F: 39,16 ve O: 48,06 ms iken ortalama amplitüd değerleri; V: 0,15, A: -0,17, C: -0,10, D: -0,14, E: -0,22, F: -0,21 ve O: -0,16 µV idi. Ortalama VA kompleks (eğim) değeri ise 0,31olarak elde edildi. **Sonuç:** Bulgular, işitsel, konuşma ve dil işlemleme bozukluklarına ilişkin geniş bir alanda kullanılan frekans takip yanıtının tipik işitmeye sahip Türkçe konuşan çocuklardaki latans, amplitüd ve eğim değerleri hakkında fikir vererek literatüre katkıda bulunmuşlardır.

Anahtar Kelimeler: Zaman alan analizi; frekans takip yanıtı; konuşma uyaranı

TO CITE THIS ARTICLE:
Yurdakul Çınar F, Çiprut A. Time domain analysis of frequency following response to speech stimulus in Turkish-speaking children with typical hearing: A descriptive study. Turkiye Klinikleri J Health Sci. 2025;10(1):138-44.

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Peer review under responsibility of Turkiye Klinikleri Journal of Health Sciences.

Received: 26 Jun 2024 ***Received in revised form:*** 26 Oct 2024 ***Accepted:*** 14 Nov 2024 ***Available online:*** 31 Jan 2025

Frequency following response (FFR) is a neurophonic and steady state auditory evoked potential that reflects synchronous neural phase locking to the spectral and temporal components of the auditory signal.[1] FFR reflects auditory neuronal processing responses in auditory subcortical structures from the cochlear nucleus to the inferior colliculus.[2] Although the sources are mainly brainstem and subcortical, recent studies show that FFR can be reliably recorded from the scalp and that there may also be some cortical contributions.[3] Understanding auditory neural processing at the brainstem, subcortical and cortical levels may help to understand processing abnormalities in different populations with speech and language disorders, hearing loss, auditory processing disorders, and learning deficits.[4,5] A variety of complex speech stimuli can be used to evoke the FFR. Although there are many speech stimuli used to evoke FFR, the /da/ syllable seems to be frequently used. Research report that this can be stop consonants have phonetic knowledge and therefore provide robust and reliable traces.[2]

In recent years, speech stimuli evoked FFR is used as a valid and reliable tool to examine brainstem and subcortical coding of speech stimulus.[6,7] The FFR evoked by the speech stimulus /da/ is characterized by seven characteristic peaks, labeled V, A, C, D, E, F and O, when analyzed in the time domain. These peaks represent the time domain component of the FFR.[2] The response to the beginning of the speech stimulus involves a positive peak called as wave V followed by a negative peak called as wave A. Following waves V and A, wave C is transient response, waves D, E, and F are steady-state responses and wave O is the offset response.[1] Investigating FFR with speech stimuli allows the observation of auditory system reaction to speech stimuli, which is not possible with stimuli such as clicks due to the nonlinearity of the auditory system.[1] The potential of FFR to represent speech stimuli and its use in examining spectral and temporal acoustic components that are critical for speech and language development makes FFR an important tool in understanding speech and language development and disorders (speech delay, apraxia, stuttering, phonological disorders, etc.).[4,5,8] Moreover, it may also used in many areas such as examining the auditory system, auditory processing disorders, evaluation of auditory-based cognitive skills, and evaluation of the neural representation of speech sounds processed by different strategies used by hearing aid and cochlear implant users.[8] The FFR, which has a wide range of applications, does not yet have clear normative values like the traditional auditory evoked potential tests (ABR, P300 e.t.c). The FFR, which starts before 10 ms and lasts up to 50 ms, can be influenced by factors that affect speech and language processing strategies. It is therefore very important to carry out large-scale FFR studies. In addition to hearing, speech and language disorders, FFR results from people with different ethnic backgrounds, individual differences and different languages are reported in the literature.[9-11] All these reports are very valuable in providing us with knowledge about FFR that can be used in many areas.

FFR, which provides an idea about the neuroplastic structure of the central auditory system, is an important potential biomarker that can be used in many areas such as monitoring the nature, development and disorders of central auditory, speech and language processing.[7,12] For this reason, examining children with auditory, language and speech processing problems with FFR has an important place in determining early and effective intervention strategies. However, there are few studies analyzing all components of this important biomarker, especially for the pediatric group. Therefore, the FFR findings of children with typical hearing whose native language is Turkish should be examined in detail. In this context, this descriptive study aimed to contributing literature by analyzing the latency and amplitude values of the V, A, C, D, E, F, and O waveforms and the VA complex (slope), which are the time domain components of the FFR in Turkish-speaking children with typical hearing.

MATERIAL AND METHODS

The present study was deemed ethically appropriate by the Ethics Committee of Marmara University Faculty of Medicine. It has been carried out in accordance with the Declaration of Helsinki. Informed consent was obtained from all participants and their parents.

The research was conducted on forty children (20 female and 20 male) in the age range of 7-9 years. The lower age limit for the participant group was set at 7 years old, coinciding with the recommended age for reliable auditory processing assessment.[13] The upper limit was set at 9 years old, preceding the initiation of formal foreign language (English) instruction in public schools. This ensures participants are assessed before potential confounding effects from recent language learning can influence test results. All participants were recruited from public schools where English language acquisition, considered a foreign language in this context, commences in the third grade (approximately 9 years old) of primary school. In addition, the age range was also kept small to minimise the influence of maturation on the test results.

In order to ensure participant homogeneity, participants were composed of monolinguals, native Turkish speakers, and right-handed. The participants had typical bilateral peripheral hearing and normal middle ear function, no history of ear surgery and no history of developmental, genetic, neurological or psychiatric disorders. The participants' peripheral hearing was assessed by conventional audiological evaluation (pure-tone audiometry with the AC 40 Clinical Audiometer, Interacoustics/Denmark) and immittance evaluation (probe tone of 226 Hz with GSI TympStar V.2 Middle-Ear Analyzer, Grason-stadler Inc. Tiger/USA); they had bilateral type A timpanograms, ipsilateral-contralateral acoustic reflexes and normal hearing thresholds between 125 Hz and 8 kHz (≤20 dB HL). Participants whose results of peripheral hearing assessment was within normal limits were considered to have typical hearing.

FREQUENCY FOLLOWING RESPONSE (FFR)

FFR data were collected in a soundproof room while participants were comfortably seated in an examination chair and watching a silent cartoon film. They were asked to remain relaxed and motionless. After cleaning the skin with an exfoliating gel, Ag-AgCl surface electrodes were applied with electrolytic paste to the centre of the head (Fz: non-inverting/active), the ipsilateral earlobe (inverting/reference) and the contralateral earlobe (ground), which were fixed with adhesive tape for ensuring the impedance between the electrodes was less than 5 kΩ. FFR was recorded using Intelligent Hearing System (IHS) smart-evoked potentials (Smart-EPs). The 40 ms/da/stimuli was presented to right ear via an Etymotic Research-3A (ER-3A) insert earphone at a stimulus rate of 11.1 Hz at 80 dB HL with alternating polarity. The total sweeps number was 1024 and the bandpass filter was 100-3000 Hz that was recorded over 60 ms post-stimulus time period. Artifact rejection of ±20-µV was applied to reject epochs that contained myogenic artifacts. The gain factor was 100,000. The initial part of the /da/ stimulus, the response to the onset response corresponding to the explosive consonant /d/, includes a positive peak called as wave V followed by a negative peak called as wave A. The transition from consonant to vowel /a/ begins with negative peak called as wave C (transient response), which is followed by negative peaks as called waves D, E, and F (steady-state responses). FFR is completed by the negative peak trough final response called as wave O (offset response). Time domain analysis of FFR data were performed on the resulting signal profile. Seven specific peaks (V, A, C, D, E, F, and O) were determined. Latencies and amplitudes of FFR components were viewed and marked manually by two audiologists blinded to the study to avoid influencing the findings. If there was a difference in marking, a third blinded audiologist analysed the results and retained the mark that matched two equal analyses.

In addition to latency and amplitude values, VA complex (the slope) was also calculated. This calculation was based on the formula: (amplitude of V-amplitude of A) / (latency of A-latency of V).[14]

DATA ANALYSIS

In sample size calculation of the research, power was calculated by taking at least 80% and a Type-1 error of 5% for each variable. Shapiro-Wilk ($n<50$) and Skewness-Kurtosis test was applied to assess the normality of the data distribution. The "Mann-Whitney U" test was used to compare categorical groups, as the measures were not normally distributed. Statistical analysis was performed using the Statistical Package Program (SPSS for Windows, ver.26, IBM), and the significance level was set at $p<0.05$.

RESULTS

The study analyzed the measurements, obtained from the FFR investigation using 40 ms /da/ speech stimulus of forty typically hearing children. The mean age of the participants was 8.1 years (minimum of 7.2 years and maximum of 8.11 years).

The test was carried out without difficulties, and collection lasted roughly 20 min. Seven characteristic peaks of the FFR as V, A, C, D, E, F, and O, were obtained from all participants (Figure 1).

Table 1 indicates the descriptive latency values of the FFR components as well as the slope value. Descriptive amplitude measurements of V, A, C, D, E, F, and O waves are also presented in Table 2.

In addition, when latency and amplitude values of FFR components are analyzed according to gender; there were no statistically significant differences between the genders (p>0.05) (Table 3).

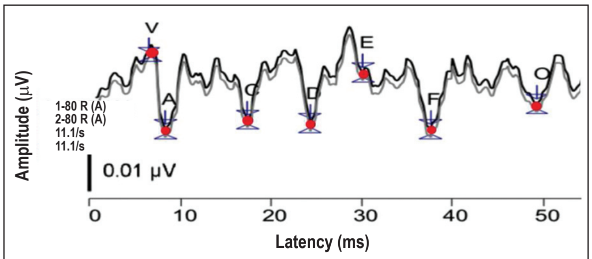

FIGURE 1: Waveform model of the FFR with 40 ms/da/ speech stimulus eliciting seven characteristic response peaks highlighted V, A, C, D, E, F, and O (black and red point).

TABLE 1: Descriptive latency values of the time domain FFR.

Latency (ms)	Minimum	X̄±SD	Maximum
V	6.14	6.49±0.26	6.96
A	7.25	7.52±0.31	8.10
C	16.20	18.46±0.39	19.01
D	21.90	22.15±0.32	23.75
E	29.80	30.62±0.54	33.60
F	38.60	39.16±0.30	40.85
O	47.90	48.06±0.65	48.60
Slope VA (µV/ms)	0.29	0.31±0.09	0.33

SD: Standard deviation.

TABLE 2: Descriptive amplitude values of the time domain FFR.

Amplitude (µV)	Minimum	X̄±SD	Maximum
V	0.09	0.15±0.08	0.28
A	-0.23	-0.17±0.06	-0.10
C	-0.32	-0.10±0.11	-0.07
D	-0.28	-0.14±0.13	-0.04
E	-0.24	-0.22±0.05	-0.12
F	-0.34	-0.21±0.07	-0.11
O	-0.35	-0.16±0.09	-0.06

SD: Standard deviation.

DISCUSSION

This descriptive study aimed to characterize time domain analysis of FFR to speech stimulus in Turkish speaking pediatric population without hearing complaints. This aim is also valuable in terms of presenting the first data on latencies and amplitudes of FFR test for Turkish speaking children, which does not have clear norm values like traditional auditory evoked potential tests (ABR, P300 e.t.c) and can be affected by many factors. FFR test, which reflects the response generated at the brainstem, subcortical and cortical levels to speech stimuli; it can be used as a potential biomarker for many conditions including auditory processing disorders, learning disorders, dyslexia, hearing loss, language disorders and phonological disorders.[4,5] It can also be used to monitor the effectiveness of the device and speech and language development in people using hearing aids or cochlear implants.[1,2] This non-invasive test can be applied to very large areas and can be performed comfortably in a short time. In our study it took about 20 minutes for the pediatric group. Many studies have reported that FFR variability in the test and retest and good intra- and intra-subject reproducibility.[14,15] Since the present study was a cross-sectional study, re-test was not performed, but inter-subject reproducibility was confirmed. We obtained all the components of time domain FFR, which represents the spectral and temporal processing of speech stimuli at the brainstem and subcortical levels; waves V and A were the onset response to the speech stimulus /da/, and wave C was the transient response which corresponds to the plosive consonant /d/ and the consonant-to-vowel transition /a/, waves D, E, F were the steady state responses, and

TABLE 3: Comparison of latencies and amplitudes (means±standard deviations) of time domain FFR in male and female participants.

FFR Components	Female (n=20) Latency (ms)	Male (n=20) Latency (ms)	*p value*	Female (n=20) Amplitude (µV)	Male (n=20) Amplitude (µV)	*p value*
V	6.47±0.24	6.51±0.21	0.64	0.014±0.06	0.13±0.08	0.56
A	7.51±0.31	7.53±0.29	0.84	-0.16±0.07	-0.15±0.08	0.06*
C	18.52±0.26	18.49±0.32	0.14	-0.11±0.10	-0.12±0.09	0.07*
D	22.30±0.24	22.55±0.19	0.28	-0.14±0.08	-0.13±0.07	0.48
E	30.23±0.42	30.36±0.36	0.09*	-0.24±0.07	-0.19±0.11	0.36
F	39.20±0.52	39.18±0.54	0.62	-0.18±0.07	-0.16±0.010	0.64
O	48.10±0.21	48.36±0.1	0.89	-0.16±0.08	-0.18±0.07	0.61

Mann-Whitney U test, *p<0.05

wave O was the offset response. When the values we obtained were compared with the FFR values obtained from typically hearing children in the literature, it was observed that they were mathematically similar.[14,16] While analysing FFR data, some researchers prefer to exclude labelling the wave C component due to a perceived lack of representativeness. However, the wave C, which is the transient response, is important to represent because it is a particularly emphasized component in representing auditory processing, speech processing, and experience-driven neuroplasticity.[7]

In the present study the existence of this component was demonstrated with 100% latency and amplitude values. Comprehensive representation of all FFR components is crucial for elucidating atypical conditions. Establishing normative data is essential for identifying these deviations. When compared to normative values, prolonged latencies and reduced amplitudes may be associated with abnormal speech coding, slow neural transmission and/or neural asynchrony in the central auditory system at brainstem and subcortical levels.[17,18] Furthermore, comparing FFR data obtained before and after intervention and auditory/speech rehabilitation provides valuable insights into the trajectory of auditory/speech processing.[2] For example, a reduction in prolonged latencies and an increase in reduced amplitudes of FFR components can indicate positive treatment outcomes. This information can be used to guide ongoing treatment decisions and optimize individual auditory therapy/rehabilitation plans. FFR test, which is a method that can be used to objectively evaluate auditory, speech and language processing skills in all age groups, from neonates to the geriatric population, allows both the evaluation of the maturation of these skills and the evaluation of auditory, speech and language processing skills of children who unable to cooperate with subjective tests.[19,20]

In this regard, studies aimed at establishing FFR norms are warranted. The present study, which presents FFR data obtained from typically developing, homogeneous participants, may inspire normalization studies and contribute to the examination of the maturation effect. This descriptive study also provides a comparison opportunity for the colleagues who will use FFR in children in their studies.

Furthermore, the presentation of such study data from different parts of the world will provide insight into the processing of speech stimuli at the brainstem, subcortical and cortical levels of individuals with different languages, different ethnic origins, different climatic conditions and different socio-cultural structures. Collecting data on a national basis and creating study protocols that can be evaluated on an international basis can provide insight into our understanding of the foundations of speech and language development. Our results were obtained from monolingual, Turkish-speaking, right-handed and typically developing children aged 7-9 years. In this respect, present study was one of the first studies reporting the results of FFR applied to Turkish-speaking children. Sanfins and colleagues reported their study in which they performed FFR with a 40 ms /da/ stimulus in monolingual, Italian speaking, right-handed Italian children aged 9-14 years.[14] In the results of Sanfins et al., they reported that there were differences in latencies and amplitudes compared to adults, as expected from the literature.[14] They also reported gender differences for the latency of wave O. Although we cannot make comparisons due to the different age ranges and protocol differences, national reports are important to provide insight. There were no significant differences between the genders in our results.

While some studies found no difference between the genders, others reported only a few prolongations of latency of FFR components.[21,22] This issue, which is inconclusive, should be investigated by increasing the number of participants. The present study, in which we report data from the FFR test, which is a potential biomarker for investigating auditory, speech and language processing skills in typically developing children, is very important in terms of providing ideas for researchers in these fields. Moving forward, we aim to expand our participant pool and conduct a normalization study utilizing FFR data collected from children and adolescents, additionally investigating the maturational effect on spectral and temporal processing of speech stimulus at brainstem, subcortical and cortical levels.

CONCLUSION

This study is one of the first studies examining the time domain analysis of the FFR in typically developing monolingual Turkish-speaking children. The results of the study are important in terms of their potential to serve as a reference level for studies using FFR in children and to contribute to research on auditory, language and speech processing using FFR test.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

***Idea/Concept:** Fatma Yurdakul Çınar, Ayça Çiprut; **Design:** Fatma Yurdakul Çınar; **Control/Supervision:** Fatma Yurdakul Çınar; **Data Collection and/or Processing:** Fatma Yurdakul Çınar; **Analysis and/or Interpretation:** Fatma Yurdakul Çınar, Ayça Çiprut; **Literature Review:** Fatma Yurdakul Çınar, Ayça Çiprut; **Writing the Article:** Fatma Yurdakul Çınar; **Critical Review:** Ayça Çiprut; **References and Fundings:** Ayça Çiprut; **Materials:** Fatma Yurdakul Çınar, Ayça Çiprut.*

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