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*Original Research Article*

# Comparison of the Effect of Three Strategies in Individuals with Sloping Sensorineural Hearing Loss

**Reuben Jebaraj P[1], Manjula P[2]**

[1]Junior Research Fellow, Department of Audiology, [2]Professor of Audiology,
All India Institute of Speech & Hearing, Manasagangothri, Mysuru- 570006, India

Corresponding Author: Reuben Jebaraj P

## ABSTRACT

**Background:** Advances in hearing aid technology especially for the individuals with sloping sensorineural hearing loss have improved drastically. However, research pertaining to use of such technology and its outcomes has been limited.
**Aim:** To compare the performance of older adults with sloping SNHL with three amplification strategies.
**Method:** Aided warble tone thresholds, speech identification scores using recorded high frequency Kannada word lists and SNR-50 were measured. These measures were obtained in three aided conditions, i.e., conventional frequency amplification (CFA), frequency compression amplification (FCA) and amplification up to 1.7fe (1.7feA).
**Results:** The FCA was better than CFA as well as 1.7feA at 0.5 kHz. However, at 4 kHz CFA was better than FCA as well as 1.7 feA. Further, the speech identification scores in all the three fitting strategies resulted in similar performance using high frequency words. It was also revealed that the FCA was better than CFA and 1.7 feA though these outcomes were not significantly different. The SNR-50 measures with FCA showed little benefit in comparison with the other two strategies which were similar in the older adults with cochlear dead regions.
Friedman's test results indicated that using a CFA, FCA and 1.7feA strategies there was a significant difference between all the three strategies in the frequencies 0.5 kHz and 4 kHz. Wilcoxon signed ranks test between these three strategies on the aided thresholds revealed that there was a significant difference between each strategy. At 500 Hz FCA was better when compared to CFA and 1.7 feA. But at 4000 Hz CFA was better than FCA and 1.7 feA. In SNR-50 measures results revealed CFA strategy was better when compared to FCA strategy.
**Conclusion** Similar benefit with all the three aided conditions was noted using the three fitting strategies on aided thresholds and speech identification in quiet. Improved performance was evident for the SNR-50 measure when using conventional frequency and amplification up to 1.7feA when compared to the FCA.

***Keywords:*** Conventional frequency amplification, Frequency Compression amplification, Amplification up to 1.7fe, Speech Identification scores, SNR-50, sloping SNHL

## INTRODUCTION

Hearing loss involves two factors, [1] viz., reduced audibility of the incoming signals and a distortion issue that affects auditory performance in terms of signal-to-noise ratio (SNR). The audibility issue is best addressed by providing the person with a hearing aid. Fitting of hearing aid for such individuals should focus on providing audibility of the speech signal in the frequency region of hearing loss. However, this goal of providing audibility with regular hearing aid can be difficult to achieve in cases of high frequency hearing losses. Kuk, Keenan [2] have stated four reasons that make the fitting of hearing aids for individuals with high frequency hearing loss difficult. They are the presence of dead regions in the cochlea, insufficient gain/output capability of the hearing aid, limited frequency bandwidth, and higher chances of acoustic feedback before the desired gain can be reached.

The second issue is the perception of high frequency speech cues that gets altered in listeners with severe high frequency loss who do not have sufficient residual hearing to receive these cues, even with high-gain hearing aids. Persons with too severe high frequency hearing loss do not benefit from amplification of frequencies above 3 kHz, frequency-lowering is often used to provide information about those components. [3] The frequency lowering strategies are aimed at improving audibility of essential speech cues and, thus, are expected to improve speech intelligibility while maintaining speech quality. However, these strategies can also introduce non-linear distortion. [4-6] The typical audiological evaluation does not address the distortion component of hearing loss. McDermott [7] demonstrated that using frequency compression reduces the spacing between harmonics, modifies spectral peak levels, and alters spectral shape for phonemes within the hearing aid's dynamic range. These cues are important for phoneme perception and the benefits of frequency compression must be considered in the light of distortions produced as a result of such strategies.

The people with hearing loss primarily experience, at least when the hearing loss is mild or moderate, [8] difficulty in understanding speech in noisy situations. [9,10] The most common complaint in adults with hearing loss is that they can hear what is said but cannot understand what is said, especially in a noisy situation. [11] Everyday listening environments usually contain background noise. [12] Noise affects both audibility and availability of speech cues important for speech perception in individuals with hearing loss. Frequency compression improves audibility and availability of high frequency phonemes [13] at the expense of spectral alterations. It is possible there could be an interaction between noise and frequency compression. Further, individuals with sloping high frequency hearing loss are reported to have cochlear dead regions. Moore, Huss [14] have suggested that high frequency hearing loss and a steeply sloping audiogram may be associated with a cochlear dead region, but this is not always the case. It is likely that high frequency amplification may play a limited role in improving, and may even impair speech perception in patients with high frequency cochlear dead regions. [15-21] Fitting of hearing aids in such individuals have been studied by Moore and colleagues on speech recognition by listeners with severe-profound high frequency hearing loss and extensive high frequency dead regions (DR). [20,19] They concluded that, for subjects with this type of impairment, amplification could be useful for frequencies up to about 1.7 times the lower edge frequency (fe) of the DR.

Further, fitting of hearing aid in older adults is a challenge. Pichora-Fuller, Schneider [22] showed that younger and older adults with good hearing differ with respect to their ability to recognize both low- and high- context words in a background babble. Typically, the SNR required by older adults for recognition of low-context words is about 2-7 dB greater than those required by younger adults. In addition to changes in hearing with aging there could also be possible effect on the auditory processing of words. [23]

Latest improvements in electronic circuits and digital technology have evolved the hearing aids to accommodate better processing strategies that theoretically can enhance the experience of the users. But research pertaining to the effects of various amplification strategies on the same individual has always been limited. Hence, the present study was initiated to know the effects of these processing strategies in participants having sloping high frequency hearing loss.

## METHODS

This study was designed to evaluate the influence of three amplification strategies on speech recognition, in individuals with sloping SNHL, without hearing aid experience. The three strategies that were evaluated include conventional frequency amplification (CFA), frequency compression amplification (FCA) and amplification 1.7 times edge frequency (*f*e) (1.7 feA)

**Participants:** A total of 46 ears of participants in the age range from 16 to 65 years participated in the study. All the participants recruited for the study were registered clients of All India Institute of speech and hearing (AIISH), Mysore. The participants were native speakers of Kannada language (a Dravidian language of Karnataka state in South India) with a minimum education of 8th standard. All the participants who fulfilled the selection criteria were recruited after obtaining the written informed consent. The ethical guidelines of the All India Institute of Speech and Hearing, [24] India were followed.

***Selection Criteria***

All the clients having post-lingually acquired sloping sensorineural hearing loss (with an ABG <10 dB) in the test ear were recruited in the study. In the present study, sloping configuration of hearing loss, operationally defined as an audiogram with a difference between the highest and the lowest thresholds of at least 40 dB.

***Test room and Instrumentations***

The entire testing process was carried out in an air conditioned, sound treated double room suite. [25] A calibrated double channel clinical audiometer with TDH 39 earphone was used to acquire the air-conduction thresholds, SRT, and SIS and Radio ear B-71 bone vibrator to acquire the bone-conduction thresholds. The aided performance was measured with the loud speaker Martin Audio C-15 (1m distance at $0^o$ Azimuth) of the audiometer. A calibrated middle ear analyzer was used to ensure normal status of the middle ear. TEN(HL) CD [26] to administer Threshold Equalizing Noise (Hearing level) test to confirm the presence or absence of cochlear dead region. A personal computer was used to route the speech stimuli and the TEN test through the auxiliary input of the audiometer. A digital B.T.E hearing aid with the feature for non-linear frequency compression was used as the test hearing aid, and HiPro to connect the hearing aid to the computer for programming were used. The speech identification test consisting of words from high frequency Kannada speech identification test developed by Yathiraj and Mascarenhas [27] was used as test material.

**Procedure:**

Routine audiological evaluations were carried out to ensure that the participant met selection criteria. After ensuring the sloping sensorineural hearing loss, the participants were administered the TEN (HL) test for the identification of dead regions in the cochlea. [28] The TEN (HL) CD was played through a computer and the stimuli were presented through TDH-39 earphones via auxiliary input of the clinical audiometer. The TEN(HL) test was administered as described by Moore, Glasberg, [26] in which masked thresholds were measured using a 2 dB final step-size. The edge frequency (fe), that is, the frequency from which a cochlear dead region starts, was noted down for all participants.

Each of the test ears of the participant was fitted with the test hearing aid coupled to the test ear using a custom ear mould. The hearing aid was programmed based on the audiometric thresholds and the NAL-Nonlinear (NAL-NL1) prescriptive procedure. Optimization of hearing aid settings was done after the initial fit, by ensuring the audibility of the Ling's six sounds. Finally, the fitting status was saved into the hearing aid (as Program 1, i.e., P1 with CFA). The non-linear frequency compression in the default setting recommended by the software was enabled and saved in the Program 2 (P2 with FCA). In the third program (P3 with 1.7feA), the high frequency limit for amplification was set at 1.7 times edge frequency. For example, the upper limit of amplification was set at 3400 Hz if the edge frequency (fe) of cochlear dead region was at 2000 Hz. The settings of P1, P2 and P3 were stored in the database of the computer. The data were collected from each test ear when the hearing aid was in each of the three programs, P1, P2 and P3. That is, only the program that was being tested was enabled during the testing condition and other programs were disabled. Aided thresholds for warble tones, Speech Identification Scores and Signal to noise ratio-50 measures for high frequency word lists were obtained using three hearing aid fitting strategies, viz., CFA in P1, FCA in P2 and 1.7feA and P3. Thus, aided thresholds for warble tones (at 0.5, 1, 2, 4 and 6 kHz), Speech Identification Scores (SIS) and signal–to-noise ratio-50 (SNR-50), were obtained in each of the three aided conditions for each test ear.

The sound field aided thresholds were obtained for warble tones at 0.5, 1, 2, 4, and 6 kHz in each of the three amplification conditions for each test ear. The SIS was measured using recorded high frequency Kannada speech identification test, [27] presented at 40 dB HL. The responses were audio recorded and later scored by the main investigator in each of the aided test condition for each test ear of the participant. The SIS was scored as the number of words correctly identified out of 25 words in the list. For measurement of SNR-50, the speech was presented at a constant level of 40 dB HL. The level of speech noise was varied in order to obtain the SNR (in dB) at which 50 % of the words were identified correctly. This was considered as the speech reception threshold in noise or SNR-50. [29] The SNR-50 was measured in a sound field condition using the recorded Kannada high frequency word list. This procedure was repeated in each of the three aided test conditions, viz., CFA, FCA, and 1.7feA. The data on aided thresholds for five warble tone frequencies, SIS for high frequency word list, and SNR-50 for each test ear were subjected to statistical analyses.

## RESULTS

The performance data of the 46 test ears of the participants were analyzed using Statistical Package for the Social Sciences soft ware (SPSS for Windows, version 17.0). Table 1 provides the mean, median and standard deviation (SD) of the aided thresholds, SIS for high frequency wordlist and SNR-50 measures in the three aided conditions. Further, comparison of the three fitting strategies in terms of aided warble tone thresholds, SIS, and SNR-50 was also done.

**Table. 1. Mean, Median, and standard deviation (SD) of aided thresholds, SIS for HF Words and SNR-50 measures in three aided conditions (CFA, FCA & 1.7feA) for 46 test ears of participants.**

| Test Conditions | Aided Conditions | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | CFA | | | | FCA | | | 1.7 Fe | | |
| | Frequencies | Mean | Median | SD | Mean | Median | SD | Mean | Median | SD |
| Aided thresholds | 0.5 kHz | 34.78 | 31.25 | 13.62 | 32.93 | 29.73 | 12.18 | 35.65 | 31.11 | 13.92 |
| | 1 kHz | 34.56 | 33.18 | 12.10 | 33.80 | 33.05 | 11.50 | 33.36 | 33.33 | 14.26 |
| | 2 kHz | 43.15 | 40.58 | 11.89 | 42.71 | 41.11 | 11.95 | 47.39 | 45.62 | 15.04 |
| | 4 kHz | 47.39 | 46.53 | 14.82 | 48.91 | 48.50 | 14.97 | 52.50 | 52.89 | 20.86 |
| | 6 kHz | 60.10 | 57.08 | 16.41 | 57.06 | 53.61 | 15.83 | 50.54 | 50.00 | 17.16 |
| SIS (Max.=25) | | 19.58 | 21.70 | 4.65 | 20.04 | 21.41 | 4.13 | 19.23 | 21.12 | 4.51 |
| SNR-50 | | 3.13 | 5.45 | 7.52 | 4.86 | 6.14 | 6.01 | 4.47 | 5.82 | 6.02 |

*Note:* CFA=Conventional Frequency amplification, FCA=amplification with frequency compression, & 1.7feA= amplification up to 1.7 times edge frequency.

The Table 1 shows that the mean and median of the aided thresholds were poorer for high frequencies than for low frequencies, in each of the three amplification strategies. Table 1 also depicts that the mean and median of SIS for high frequency words was comparable with the three amplification strategies. It must be noted here that though the strategies did not improve the speech identification in quiet, there was no reduction in the performance. The mean, median and standard deviation of SNR-50 in the participants with three amplification strategies are also depicted in Table 1. The SNR-50 values did not show any pattern with reference to the three amplification strategies.

The mean, median and standard deviation values when compared in the three aided conditions at 0.5 kHz revealed that the aided thresholds were lower in frequency compression condition compared to the other two aided conditions as shown in Table 1. At 1 kHz, the aided thresholds were comparable for conventional frequency, frequency compression, and amplification up to 1.7 fe as shown in Table 1. At 2 kHz, the aided thresholds were lowest for conventional frequency followed by frequency compression and amplification up to 1.7 fe. Similar findings were noted for 4 kHz where the best threshold value (lowest) was obtained for conventional frequency and worst (highest) threshold value was obtained for amplification up to 1.7 fe aided condition. On the other hand, the aided thresholds at 6 kHz were better for amplification up to 1.7 fe condition followed by frequency compression and then by conventional frequency aided condition.

The mean, median and standard deviation for the *speech identification scores* with the three amplification strategies are depicted in Table 1. From the table it can be noted that the median value was identical across all the three aided conditions. However, a slightly better mean value was obtained for frequency compression condition when compared to conventional frequency and amplification upto 1.7 fe.

The mean, median and standard deviation using SNR-50 measures in the participants when tested with the Conventional frequency amplification, frequency compression and amplification upto 1.7fe conditions are depicted in Table 1. It can be noted that the median values (Median=5.45) were similar for conventional frequency amplification and the amplification upto 1.7fe condition (Median=5.82). Further, it can be noted that the median value (Median=6.14) is higher for frequency compression condition when compared to the other two conditions tested. It must be noted here that a higher value of SNR-50 reflects a poorer performance and a lower value of SNR-50 reflects a better performance.

In order to know whether the performance was significantly different between the three amplification strategies, non-parametric test of significance was administered. Prior to this, the data collected from the test ears of participants of the current study were subjected to Shapiro-Wilk's test of normality to check the normality of distribution. The test revealed that the collected data did not follow normal distribution for majority of the parameters studied ($p<0.05$). Hence, a non-parametric test, i.e., Friedman's test was administered.

### *1. Comparison of aided warble tone measurements for the three amplification strategies:*

**Table 2. Significant difference ($\chi^2$ and p value) between the three aided conditions for aided thresholds, speech identification scores for high frequency words (SIS) and SNR-50, on Friedman's test.**

| Aided Measures | Test Conditions | $\chi^2$ | p value |
|---|---|---|---|
| CFA Vs. FCA Vs. 1.7*fe*A | 0.5 kHz | 9.75 | 0.008** |
| | 1 kHz | 0.42 | 0.80 |
| | 2 kHz | 3.23 | 0.19 |
| | 4 kHz | 17.26 | 0.000*** |
| | 6 kHz | 5.56 | 0.062 |
| | SIS | 4.26 | 0.11 |
| | SNR-50 | 12.79 | 0.002** |

*Note*: CFA = Conventional frequency amplification, FCA = Amplification with frequency compression, & 1.7feA = Amplification up to 1.7 times edge frequency; **=p<0.01; *** = p < 0.001.

The non-parametric Friedman's test of differences among repeated measures was administered to know if the difference between the amplification strategies was significant. It was noted that there was a significant difference between the amplification strategies on certain performance measures (Table 2). In order to know the amplification condition that brought about the significant difference, Wilcoxon Signed Rank test was administered, whenever indicated.

From Table 2, it can be noted that the amplification strategies brought about a significant difference in the aided thresholds at 0.05 kHz and 4 kHz and SNR-50. The SIS did not show any significant difference between aided conditions. To know if the aided warble tone thresholds differed with different amplification strategies, Friedman's test was administered (Table 2) which revealed that the amplification strategies did bring about significant change at frequencies 0.05 kHz (p<0.05) and 4 kHz (p<0.001) as given in Table 2.

**Table 3. Significant difference (|z| *and p values) between the three aided conditions for aided thresholds at 0.5 k and 4 kHz.***

| *Frequency at which aided thresholds was sig. different* | Sig diff. | CFA Vs. FCA | CFA Vs. 1.7feA | FCA Vs. 1.7feA |
|---|---|---|---|---|
| 0.5 kHz | Z | -2.63 | -1.58 | -2.74 |
| | *p* | 0.009** | 0.114 | 0.006** |
| 4 kHz | *Z* | *-2.15* | *-2.48* | *-2.06* |
| | *p* | *0.031** | *0.013** | *0.039** |

*Note:* CFA=Conventional frequency amplification, FCA=Amplification with frequency compression, 1.7feA= Amplification up to 1.7 times edge frequency; * = p < 0.05, ** = p<0.01.

Wilcoxon's signed rank test (Table 3) revealed a significant difference between CFA & FCA conditions (p< .01 level) and also between FCA and 1.7feA at 0.5 kHz (p< .01). CFA was better than 1.7fe similarly FCA was better than 1.7fe. However, there was no significant difference between CFA and 1.7feA as can be seen in Table 3.Further, the result revealed a significant difference between 'CFA and 1.7feA', between 'CFA and FCA', as well as between 'FCA and 1.7feA' at .05 level of significance for the 4 kHz warble tone threshold. CFA was better than FCA which in turn was better than 1.7fe.

***2. Comparison of SIS Scores for the three amplification strategies:***

In order to know if the SIS differed with different amplification strategies, Friedman's test was administered (Table 2) which revealed that the amplification strategies did not bring about a significant change in SIS performance (p>0.05) with the three amplification strategies.

***3. Comparison of SNR-50 for the three amplification strategies:***

To know if the SNR-50 differed with different amplification strategies, Friedman's test was administered (Table 2) which revealed that the amplification strategies did bring about significant change in SNR-50 (p<0.01) between aided conditions. In order to know which strategy brought about a significant improvement in noise, Wilcoxon's signed rank test was performed (Table 4).

**Table 4: Significant difference (|z| and p values) between three amplification strategies in SNR-50.**

| | | CFA vs. 1.7feA | CFA vs. FCA | FCA vs. 1.7feA |
|---|---|---|---|---|
| *SNR-50* | \|z\| | -1.83 | -3.18 | -.697 |
| | p | 0.067 | 0.001*** | 0.486 |

*Note:* CFA=Conventional frequency amplification, FCA= Amplification with frequency compression, & 1.7feA= amplification up to 1.7 times edge frequency; *** = p < 0.001

The results revealed a significant difference in performance between the CFA and FCA; with CFA being better than FCA at p < .001 level of significance. However, no significant difference was obtained between the, CFA and 1.7feA, and FCA and 1.7feA as can be seen in Table 4.

## DISCUSSION

The purpose of the current study was to investigate the influence of three hearing aid fitting strategies (conventional frequency amplification - CFA, frequency compression amplification - FCA, &

amplification up to 1.7 fe – 1.7feA) on aided thresholds, speech identification scores as well as SNR-50 measures in individuals with sloping sensorineural hearing loss. The results are discussed in terms of effect three hearing aid fitting strategies on aided warble tone thresholds, aided speech identification scores for high frequency words, and aided SNR-50 measures.

***Effect of amplification strategies on warble tone thresholds.***

The aided warble tone threshold measurements using conventional frequency amplification, FCA as well as 1.7feA condition indicate that the participants had better thresholds in the low frequencies as compared to high frequencies. The aided thresholds for frequencies upto 4 kHz was found to be better in conventional frequency amplification. But aided threshold at 6 kHz was better for frequency compression amplification as well as 1.7fe. Therefore better performance at low frequencies could be attributed to audibility factors and poorer hearing thresholds at high frequencies in combination with bandwidth limitation for high frequencies in conventional frequency amplification resulted in poor aided threshold at 6 kHz. Similar findings by McCreery, Alexander [30] in listeners who use conventional frequency amplification often have reduced access to high frequency sounds due to the degree of hearing impairment, the limited bandwidth of the hearing-aid receiver (<5000–6000 Hz) or a combination of both factors.

***Effect of amplification strategies on aided speech identification scores.***

In the present study speech identification measurements involving the CFA, FCA and 1.7feA revealed that the SIS were comparable across all the three strategies. However, a slightly higher mean value was obtained for frequency compression strategy (FCA) compared to the other two strategies. Findings of the present study were in agreement to those reported by Ellis and Munro. [31] were in their subjects showed that frequency compression provides additional benefits in speech recognition than that conferred by conventional amplification strategies. In literature, the bandwidth of amplification is one factor that has been shown to influence both sound quality and speech recognition. [32,33] In a speech perception study done by Hornsby and Ricketts [34] demonstrated that adults with hearing loss experience improvement in speech understanding as high-frequency audibility increased. High-frequency amplification in individuals with steeply sloping high-frequency losses, either had a beneficial effect on, or did not significantly degrade, speech understanding. Further they reported importance of extended high-frequency amplification for listeners with a wide range of high-frequency hearing losses, when seeking to maximize intelligibility. Audibility has been repeatedly shown to be a key factor in speech recognition. Non-Linear Frequency Compression (NLFC) is reported to improve audibility for high-frequency sounds and speech recognition in quiet. [35] This was observed in a study on children with moderate hearing loss tested with high-frequency consonant identification test. It has been reported that NLFC improves audibility and speech recognition in quiet for adults and children with severe to profound high-frequency hearing loss, though this improvements in speech recognition in the presence of noise was not evident. [13,36] While NFC can improve audibility, it also inherently introduces spectral distortions, which lead to changes in harmonic spacing, spectral peaks, and spectral shape. [7] Thus, it can be construed that speech identification scores get better in the aided condition provided the aided condition improves the audibility of hearing even at all frequencies especially in the high frequencies. However, in the present study there was no significant difference in performance across strategies that were assessed but a higher mean for FCA reveal that this strategy gave a better performance.

***Effect of amplification strategies on SNR-50.***

The findings of SNR-50 measurements using CFA, FCA and 1.7 feA indicate that there was a significant difference between 'CFA and FCA'; with the latter being poorer than the former. The results of the present study are in discordance with studies which claim similar performance in participants with CFA and FCA for speech recognition in noise. [2,37,38] Since, results revealed using FCA participants in the present study performed poorly. This study in agreement with the findings of the McDermott (7) who reported that frequency lowering actually degraded speech recognition in noise.

A consequence of frequency compression is that it may make audible high-frequency noise that would have otherwise been inaudible with conventional amplification, which could impair speech understanding. [35] Distortion of cues primarily due to hearing loss, amplification and more so formant frequency relationship being lost due to non-linear frequency compression. The findings of the present study are in agreement with a study by Simpson, Hersbach. (39) They found that when testing speech in the presence of noise, the frequency compression scheme provided only limited benefit to listeners who had steeply sloping hearing losses.

The SNR-50 measurements while using 1.7feA showed almost similar performance as that of CFA in the present study. Baer, Moore (20) reported that persons with hearing loss with dead regions in the high frequencies were unable to use amplified high frequency speech information than persons with hearing loss without cochlear dead regions. In their study for subjects without dead regions performance generally improved with increasing cut-off frequency up to 7.5 kHz in noise than in quiet. However, in their study on most subjects with dead regions, performance improved with cut-off frequency only up to 1.5 to 2 times the edge frequency of the dead region, but hardly changed with further increases. In the present study even we found similar performance between the CFA and 1.7feA in our participants when tested in the presence of noise, this may be due to presence of dead regions in our subjects.

Conclusions

The three test conditions (aided warble tone thresholds, SIS, and SNR-50 measures) tested with CFA, FCA and 1.7 feA and their performance were compared within the same group of participants. The mean aided threshold at 6 kHz was highest for CFA followed by FCA however these thresholds were least in 1.7feA. This suggests better hearing through1.7feA followed with FCA and least hearing by CFA. A small improvement in mean aided threshold value at 6 kHz was noted for 1.7feA compared to CFA and FCA. For speech identification in quiet, the mean SIS was slightly higher in FCA compared to the performance with other two strategies. There was no difference in SIS with CFA and 1.7feA strategies. Further, speech perception in noise was found to be best in CFA condition followed by 1.7feA and poorest in FCA conditions.

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***Conflict of Interest:*** Authors declare no conflict of interest.

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