

Original Article

Long-Term Effects of Hearing Aid Use on Auditory Spectral Discrimination and Temporal Envelope Sensitivity and Speech Perception in Noise

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BACKGROUND: The aims of this study were to evaluate the long-term effects of hearing-aid use on auditory spectral discrimination, temporal envelope sensitivity, and speech perception ability and to determine whether hearing performance changes with the duration of hearing-aid use.

METHODS: The study included 13 elderly participants (64.15 ± 9.87 years) who had used hearing-aids for 12 months in everyday life. We compared the auditory performance without hearing-aids at the time of pre-fitting with the auditory performance with hearing-aids at 1 month and 12 months after fitting. Three different psychoacoustic measurements were made at their most comfortable levels to exclude the effect of amplification: (1) spectral-ripple discrimination, (2) temporal modulation detection, and (3) speech recognition in white noise.

RESULTS: Repeated-measures analysis of variance demonstrated that the duration of hearing-aid use significantly affected spectral-ripple discrimination thresholds and 100 Hz temporal modulation detection threshold ($P < .05$). Post hoc tests revealed that the improvements in spectral discrimination in the early post-fitting stage (1 month) did not seem to increase over the period of hearing-aid use, whereas the temporal envelope sensitivity improved continuously over time (up to 12 months).

CONCLUSION: These results imply that hearing-aid users adapt to hearing-aid processing for spectral discrimination immediately, whereas they need time to adapt to hearing-aid processing for temporal envelope sensitivity. Alternatively, long-term hearing-aid use could induce positive plastic changes exclusively in terms of temporal envelope sensitivity.

KEYWORDS: Auditory spectral resolution, auditory temporal resolution, hearing aid, hearing loss, signal-to-noise ratio, speech perception

INTRODUCTION

Hearing aids (HAs) can partially restore the auditory threshold of listeners with hearing impairments by the amplification of sound, which is essential for improving their speech identification. However, amplification alone is insufficient to normalize the speech perception abilities of these listeners. Though amplification can effectively compensate for the loss of sensitivity, supra-threshold distortion may require more advanced signal processing to improve hearing, especially in the presence of background noise or reverberations.¹⁻³ Hearing aids are unable to “correct” hearing loss because the complex nature of the deteriorated auditory system and the deficit in supra-threshold auditory processing are not (or less) remediated by HAs.⁴ On average, the use of HAs reduces the hearing handicap for speech perception in a quiet environment by 70%.⁵ Supra-threshold distortion for listeners with hearing impairment is fundamentally associated with auditory spectral discrimination and temporal envelope sensitivity,^{4,6,7} which involve the auditory system from the cochlea hair cells to the auditory cortex.^{8,9} Previous studies have demonstrated that speech perception in hearing-impaired listeners relies on the perception of auditory spectral discrimination,¹⁰ the temporal envelope,^{11,12} the temporal fine structure,¹³ and the spectrotemporal modulation sensitivity.^{7,14}

Another factor is that the personal traits of listeners affect their ability to adapt to frequency-dependent amplitude-compressed sound. Hearing aids' signal processing introduces substantial changes to the acoustic signals and therefore HA users may need time to adapt to the changes in the acoustic signals conferred by HAs.^{15,16} However, despite proper fitting and a sufficient adaptation period, some HA users are still unsatisfied with their ability to perceive speech, especially in situations in which listening is difficult.¹⁷ In these cases, HA users might be told by their clinician or audiologist that their hearing performance will improve over time. Many studies have demonstrated a change in speech perception after HA fitting, but the results vary. Several studies with non-linear HAs have reported evidence of acclimatization in terms of speech perception,^{18–20} whereas others have not.^{2,21} Moreover, the effect varied across HA users. Several authors focused on the changes in intensity discrimination^{22,23} or the tolerance of loudness²⁴ over time after HA fitting. However, previous studies have not considered the improvements in auditory spectral discrimination and temporal envelope sensitivity conferred by HAs over the period of HA use. Because spectral discrimination and temporal envelope sensitivity in hearing play key roles in speech perception,²⁵ investigating changes in these factors over time should help us to understand the potential acclimatization in speech processing conferred by HAs and are expected to provide clues to the technical development of HAs.

Therefore, we designed a long-term follow-up study to evaluate the changes in 3 psychoacoustic performance measures (spectral discrimination, temporal envelope sensitivity, and speech perception in noise) from before to after HA use.

METHODS

Participants

The study included 13 elderly participants (64.15 ± 9.87 years; 4 men, 8 women) who had used HAs for 12 months in everyday life as the first-time users. Among these subjects, 4 used unilateral HAs and 9 used bilateral HAs. The participants had just been fitted with HAs for the first time and underwent more than 2 additional fittings within 1 month when starting to use their HAs. Participants with chronic otitis media, retrocochlear lesions, endolymphatic hydrops, or hearing loss with a conductive or surgically correctable component were excluded. We also excluded participants with cognitive dysfunction or a history of cerebral accident. The hearing thresholds at various frequencies without the HAs at the time of pre-fitting are presented in Table 1. The pure-tone averages (0.5 kHz, 1 kHz, 2 kHz, and 3 kHz) of the individual participants without HAs at the time of pre-fitting and without and with HAs at 1 month and 12 months after fitting are presented in Table 2. The pure-tone averages for the unaided condition (without HA) did not differ among the 3 time points (pre-fitting, and 1 and 12 months after fitting) and those for the aided condition (with HA) did not differ between the time points at 1 and 12 months ($P > .05$). The details of the types and number of channels for HAs are presented in Table 1. We compared the auditory performance without HAs at the time of pre-fitting with the auditory performance with HAs at 1 month and 12 months after fitting. All the participants used their HAs with the setting “digital noise reduction on” and in the adaptive directional microphone mode. All HAs were fitted with NAL-NL2, and it was confirmed that the output levels of the HAs were in the target range via Audioscan Verifit 2 real-ear measurement system (Etymotic Design, Inc., Dorchester, Ontario, USA). Ethical committee approval

was received from the Nowon Eulji Medical Center (No. 2016-01-012). Written informed consent was obtained from all participants who participated in this study.

Procedure

Three different psychoacoustic measurements were made with and without HAs: (1) spectral ripple discrimination (SRD), (2) temporal modulation detection (TMD), and (3) speech recognition threshold (SRT) in noise. The SRD test evaluated spectral discrimination by measuring the ability of the participants to discriminate a reversal in the phase of a ripple shape. Temporal modulation detection was used to evaluate the listener's sensitivity to the temporal envelope by discriminating modulated noise from steady noise. Detailed procedures of each test are presented in Supplementary Procedure.

All testing was conducted in a sound-attenuating booth (Acoustic systems, Austin, Tex, USA). The stimuli were presented with a customized MATLAB program, with a sampling frequency of 44 100 Hz. The stimuli were routed through an audiometer (Madsen Astera 2; GN Otometrics, Taastrup, Denmark) and presented by a loudspeaker located 1 m in front of the individuals. To evaluate the benefits of HAs on hearing performance, apart from the increased output sound pressure level, we measured the most comfortable level (MCL) for each participant at all 3 time points (pre-fitting [without HA] and at 1 and 12 months after fitting [with HA]) and tested them for the pre-fitting condition (without HAs) and the post-fitting conditions (with HAs) at each measured MCL. Detailed MCLs at all 3 time points are presented in Table 3. For the unilateral HA users, the ear on the contralateral side was plugged, and the bilateral HA users were tested while wearing both HAs. The order of the 3 tests was randomized within and across participants. A Korean version of the International Outcome Inventory for Hearing Aids (K-IOI-HA) was used at each time point after fitting to evaluate the effects of and satisfaction with the HAs. We compared the 3 different test results for the pre-fitting performance without HAs and the performance with HAs at 1 month and 12 months after fitting, and compared K-IOI-HA at 1 month, 6 months, and 12 months after fitting.

Analysis

PASW Statistics 18 software (SPSS Inc.; Chicago, IL, USA) was used for all statistical analyses. Repeated-measures analysis of variance (ANOVA) was used to compare the 3 different test results and the K-IOI-HA results for the pre-fitting measurements and those made at 1 month and 12 months after fitting. An independent samples *t*-test or the Mann–Whitney *U* test was used to compare age and pure-tone averages between the 2 groups. The χ^2 test was used to compare the sex distribution. The correlations between the change in SRT in noise (between pre-fitting and post-fitting measurements) and the change in the SRD threshold or TMD threshold were also analyzed with Pearson's correlation or Spearman's rank correlation.

RESULTS

Changes in SRD, Speech Perception in Noise, and TMD

Figure 1A shows the SRD thresholds in ripples/octave for all participants as a function of time from fitting. Repeated-measures ANOVA demonstrated that time significantly affected SRD ($F(2:24) = 4.919$; $P = .016$). The post hoc test using Bonferroni correction revealed that the SRD threshold was higher (i.e. better spectral discrimination) with HAs at 1 month and 12 months after fitting than without HAs before

Table 1. Age, Sex, Hearing Thresholds at the Time of Pre-fitting, Hearing-Aid Type and Number of Channels

Participants No.	Aided Side	Sex	Age	Hearing Thresholds (dB HL)																Hearing-Aid Type	No. of Channels
				Right (kHz)								Left (kHz)									
				0.25	0.5	1	2	3	4	8	PTA	0.25	0.5	1	2	3	4	8	PTA		
1	R	F	80	50	65	65	75	65	65	75	75	67.5	50	60	65	60	60	65	65	61.3	4
2	B	F	81	25	40	55	65	70	70	70	70	57.5	20	30	55	65	65	70	65	53.8	7
3	B	F	55	25	70	55	45	50	50	50	75	55.0	15	60	50	45	50	50	55	51.3	6
4	R	M	69	35	35	50	40	45	70	100	42.5	70	70	100	95	110	110	105	95.0	6	6
5	B	F	50	20	10	65	105	115	115	105	73.8	15	10	60	115	120	115	105	76.3	6	6
6	B	F	52	50	50	60	50	45	40	30	51.3	50	60	65	55	45	45	40	56.3	8	8
7	R	F	67	55	70	80	50	50	55	65	62.5	35	40	35	15	20	25	70	27.5	6	6
8	L	M	60	65	75	80	90	95	100	110	85.0	70	60	70	90	90	105	110	77.5	8	8
9	B	F	64	15	20	35	50	70	70	70	43.8	15	20	35	50	60	75	70	41.3	14	14
10	B	F	68	50	40	35	35	55	55	75	41.3	70	65	55	45	50	55	80	53.8	6	6
11	B	M	59	40	45	70	75	80	100	105	67.5	15	25	40	70	75	90	100	52.5	10	10
12	B	F	57	45	45	55	60	60	65	60	55.0	45	55	60	60	65	65	65	60.0	10	10
13	B	M	72	25	35	55	90	80	70	100	65.0	25	30	65	75	65	70	90	58.8	8	8
Average			64.15								59.05								58.88		
SD			9.87								12.90								16.86		

PTA, pure tone average; R, right; L, left; B, both; CIC, complete in the canal; BTE, behind the ear; RIC, receiver in the canal; SD, standard deviation.

Table 2. The Pure-Tone Averages (0.5, 1, 2, and 3 kHz) of the Individual Participants Without Hearing Aids at the Time of Pre-fitting and Without and With Hearing Aids at 1 Month and 12 Months after Fitting

No.	Aided Side	Sex	Age	Pure-Tone Average (dB HL)									
				Right					Left				
				Unaided (Pre-fitting)	Unaided (1 M)	Aided (1 M)	Unaided (12 M)	Aided (12 M)	Unaided (Pre-fitting)	Unaided (1 M)	Aided (1 M)	Unaided (12 M)	Aided (12 M)
1	R	F	80	67.5	67.5	45.0	67.5	32.5	61.3	61.3	ND	62.5	ND
2	B	F	81	57.5	56.3	45.0	57.5	50.0	53.8	56.3	46.3	56.3	51.3
3	B	F	55	55.0	55.0	40.0	58.8	42.5	51.3	47.5	42.5	48.8	36.3
4	R	M	69	42.5	43.8	33.8	43.8	35.0	95.0	93.8	ND	95.0	ND
5	B	F	50	73.8	78.8	30.0	73.8	45.0	76.3	55.0	32.5	76.3	37.5
6	B	F	52	51.3	57.5	38.8	57.5	27.5	56.3	51.3	36.3	53.8	31.3
7	R	F	67	62.5	66.3	50.0	65.0	46.3	27.5	23.8	ND	23.8	ND
8	L	M	60	85.0	85.0	ND	85.0	ND	77.5	77.5	47.5	77.5	46.3
9	B	F	64	43.8	43.8	30.0	43.8	28.8	41.3	41.3	27.5	41.3	23.8
10	B	F	68	41.3	41.3	36.3	41.3	25.0	53.8	53.8	38.8	53.8	30.0
11	B	M	59	67.5	67.5	52.5	67.5	37.5	52.5	40.0	52.5	51.3	32.5
12	B	F	57	55.0	55.0	47.5	62.5	47.5	60.0	60.0	48.8	61.3	45.0
13	B	M	72	65.0	65.0	37.5	65.0	41.3	58.8	58.8	45.0	58.8	41.3
Average			64.15	59.05	60.22	40.53	60.69	38.24	58.88	55.42	41.77	58.50	37.53
SD			9.87	12.90	13.23	7.50	12.47	8.45	16.86	17.19	7.87	17.63	8.48

SD, standard deviation, R, right; L, left; B, both; ND, not done.

Table 3. Psychoacoustic Data of the Individual Participants at the Time of Pre-fitting and Without and With Hearing Aids at 1 Month and 12 Months after Fitting

No.	Most Comfortable Level (Sound Field, dB HL)				Spectral Ripple Discrimination				Speech Perception Threshold in Noise				Temporal Modulation Detection 10 Hz				Temporal Modulation Detection 100 Hz			
	Unaided (Pre-fitting)	Aided (1 M)	Aided (12 M)		Unaided (Pre-fitting)	Aided (1 M)	Aided (12 M)		Unaided (Pre-fitting)	Aided (1 M)	Aided (12 M)		Unaided (Pre-fitting)	Aided (1 M)	Aided (12 M)		Unaided (Pre-fitting)	Aided (1 M)	Aided (12 M)	
1	75	60	60	0.22	0.51	0.18	0.18	0.18	-1.89	-1.89	-5.11	-5.11	-21.87	-23.07	-25.00	-25.00	-11.93	-12.93	-17.80	-17.80
2	70	60	65	0.17	0.47	0.25	0.25	0.25	3.44	-1.44	4.33	4.33	-19.60	-19.73	-20.27	-20.27	-0.13	-2.13	-12.60	-12.60
3	75	70	60	0.22	0.22	0.22	0.90	0.90	0.89	-2.78	-0.89	-0.89	-26.47	-25.73	-26.80	-26.80	-11.80	-13.27	-17.33	-17.33
4	70	60	55	0.42	1.02	1.07	1.07	1.07	-0.22	-3.11	-1.00	-1.00	-18.47	-17.47	-18.40	-18.40	-4.27	-12.73	-13.87	-13.87
5	80	70	65	0.26	0.49	0.21	0.21	0.21	-3.33	-5.11	-4.55	-4.55	-24.93	-19.07	-25.07	-25.07	-12.53	-12.20	-19.53	-19.53
6	65	60	50	2.10	2.80	2.61	2.61	2.61	-2.34	-2.55	-4.22	-4.22	-30.33	-26.00	-26.73	-26.73	-18.80	-18.13	-16.93	-16.93
7	80	70	75	0.42	1.31	0.82	0.82	0.82	-0.89	-2.89	-2.22	-2.22	-17.73	-13.53	-23.40	-23.40	-0.93	-0.73	-3.73	-3.73
8	85	65	70	1.65	1.52	2.12	2.12	2.12	8.11	7.89	3.00	3.00	-16.73	-18.93	-19.27	-19.27	-0.53	-2.80	-7.40	-7.40
9	65	70	70	1.60	1.61	1.48	1.48	1.48	6.33	1.22	3.89	3.89	-23.73	-19.60	-23.13	-23.13	-16.73	-10.93	-13.40	-13.40
10	75	70	70	0.15	0.15	1.15	1.15	1.15	-1.45	0.22	-0.55	-0.55	-8.60	-21.93	-21.53	-21.53	-13.20	-5.20	-11.13	-11.13
11	80	75	65	2.24	2.60	2.15	2.15	2.15	-3.89	-1.11	-3.44	-3.44	-21.27	-26.27	-27.33	-27.33	-12.60	-12.07	-12.80	-12.80
12	85	80	60	0.22	0.22	0.22	0.22	0.22	4.67	3.33	6.00	6.00	-24.80	-22.20	-27.40	-27.40	-15.70	-17.80	-13.60	-13.60
13	75	70	70	1.07	1.34	1.49	1.49	1.49	4.00	3.78	1.56	1.56	-23.80	-20.60	-24.47	-24.47	-4.47	-8.67	-13.60	-13.60
Average	75.38	67.69	64.23	0.83	1.10	1.13	1.13	1.13	1.03	-0.34	-0.25	-0.25	-21.41	-21.09	-23.75	-23.75	-9.51	-9.97	-13.36	-13.36
SD	6.60	6.33	7.03	0.80	0.88	0.81	0.81	0.81	3.88	3.57	3.70	3.70	5.41	3.67	3.09	3.09	6.55	5.69	4.29	4.29

SD, standard deviation.

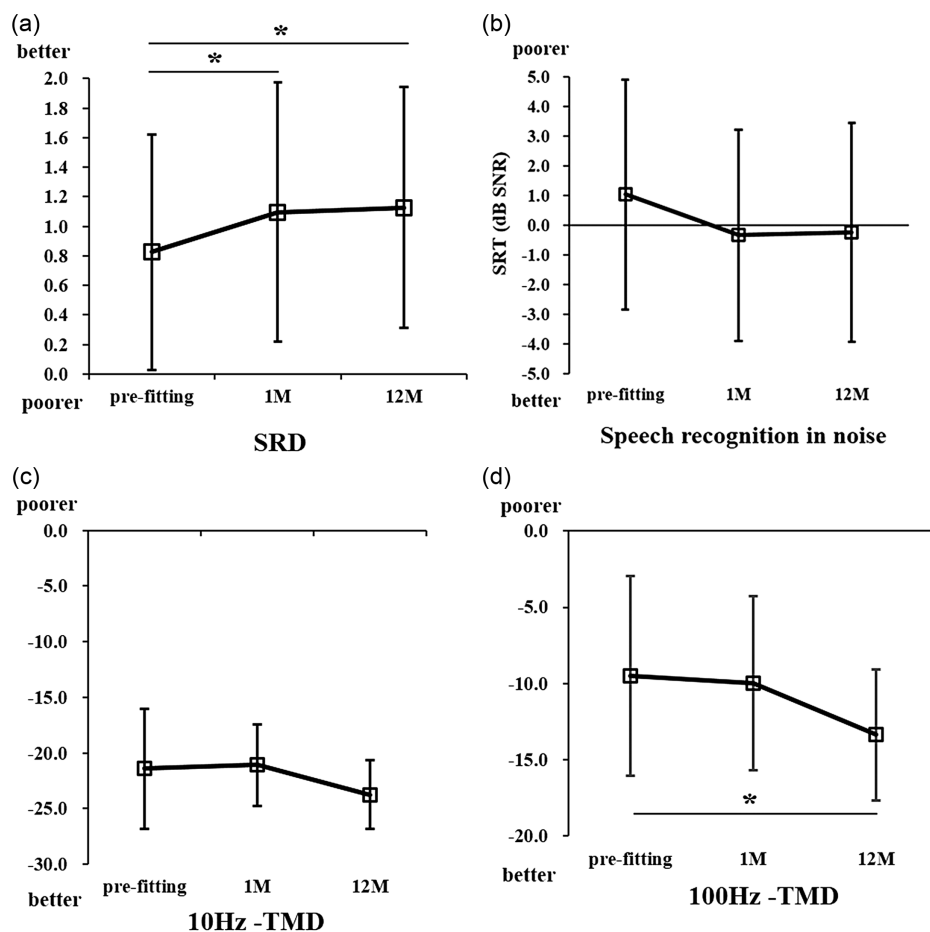


Figure 1. Changes in the spectral-ripple discrimination (SRD) threshold, the speech reception threshold (SRT) in noise, and the temporal modulation detection (TMD) threshold for all participants. (A) SRD threshold was higher (better spectral discrimination) with hearing aids (HAs) at all individual time points after fitting than without HAs before fitting ($P < .05$), but there were no significant differences in SRD among the time points after fitting. (B) SRD at 10 Hz did not change over time. (C) TMD at 10 Hz did not change over time. (D) TMD at 100 Hz was significantly lower (better temporal envelope sensitivity) only at 12 months after fitting when compared with before fitting ($P < .05$).

fitting ($P = .023$ and $P = .032$, respectively). However, there were no significant differences in SRD between at 1 month and 12 months after fitting (Figure 1A).

No significant time-dependent changes were found in SRT (dB SNR) or TMD at 10 Hz ($P > .05$; Figure 1B, C).

Figure 1D shows the 100 Hz TMD thresholds in dB for all participants as a function of time from fitting. Repeated-measures ANOVA demonstrated that time significantly affected 100 Hz TMD ($F(2;24) = 6.22$;

$P = .007$). A post hoc test using Bonferroni correction revealed significantly lower TMD thresholds (i.e., better temporal envelope sensitivity) with HA only at 12 months than without HAs before fitting ($P = .048$). Detailed data at all 3 time points are presented in Table 3.

Changes in K-IOI-HA Scores

The mean K-IOI-HAs were 23.77 ± 4.28 at 1 month after fitting, 24.85 ± 4.28 at 6 months after fitting, and 24.15 ± 4.90 at 12 months after fitting. Repeated-measures ANOVA showed no significant time-dependent changes in K-IOI-HAs ($F(2;24) = 0.592$; $P > .05$).

Table 4. Correlations Analyses of the Changes in the Spectral-Ripple Discrimination Threshold and Temporal Modulation Detection Threshold Versus the Changes in the Speech Recognition Thresholds from Before Fitting to after Fitting

	Δ Speech Recognition Thresholds	
	1 Month After Fitting	12 Months After Fitting
Δ Spectral-ripple thresholds	r	-0.024
	P	.938
Δ Temporal modulation detection thresholds (10 Hz)	r	-0.551
	P	.051
Δ Temporal modulation detection thresholds (100 Hz)	r	0.170
	P	.579

Correlation Analyses

In 13 HA users, there were no significant correlations between the changes in SRD, 10 Hz TMD or 100 Hz TMD, and the changes in SRT before fitting and after fitting at any time point ($P > .05$, Table 4).

DISCUSSION

We assumed that unaided sound presented at the MCL in the sound field would similarly affect the amplification afforded by HAs. In this study, unaided MCL was significantly higher than aided MCLs at 1 month and 12 months after fitting, but there was no difference between aided MCLs at 1 month and 12 months after fitting. Therefore, we anticipated that a comparison of the pre-fitted performance without HA and the post-fitted performance with HA at each MCL would demonstrate the additional benefit from HA amplification comes from the frequency-shaping of the gain, which better accommodates individual hearing loss and which is not present during adjustments of the unaided MCL.

This prospective study revealed the main effect of duration of HA use on SRD and 100 Hz TMD. The profile plots for SRD showed an improvement with HAs at 1 month after fitting compared with before fitting. These results might imply that HA users adapt early to HAs processing of spectral discrimination or gain the benefits of HAs in terms of auditory spectral discrimination, as revealed in the days soon after the initial fitting. However, these benefits did not seem to increase over duration of HA use given that no significant differences between 1 month and 12 months were demonstrated by the post hoc tests.

In the TMD test, the ability to detect the amplitude modulation of a sound is believed to measure the detection of change in the envelope of the sound in the time domain. The plots of the changes in 100 Hz TMD revealed a gradual improvement over time and ultimately showed a significant difference at 12 months after fitting compared with before fitting. This result implies that sensitivity at the 100 Hz temporal envelope is enhanced as the HA users adapt to the HA processing. In contrast, 10 Hz TMD hardly changed over time. Because HAs apply some dynamic-range compression, it is possible that the time-varying gain affects the output modulation depth at 10 Hz but is too slow to affect the 100 Hz fluctuations. Over time, the listeners adapted to the HA processing and were able to utilize the increased audibility more effectively. Alternatively, the enhancement of temporal envelopes detection at 100 Hz could be attributed to the plasticity of the central auditory system. Reduced spectral discrimination is attributed primarily to the loss of sharp tuning of the basilar membrane or the broadening of peripheral auditory filters.⁸ However, temporal coding is processed by the phase locking of the auditory neuron to the temporal modulation of the sound,²⁶ and the auditory cortex plays a key role in the temporal processing of sound.¹⁰

There is conflicting evidence concerning the existence of functional improvement over duration of HA use. Several studies have shown an improvement in performance over time, whereas other studies have shown no change. Gatehouse¹⁵ compared the changes in speech perception in noise over a 12-week period after HA fitting in monaurally fitted ears, using the unfitted ears as the controls. Aided and unaided speech perception and the benefit remained stable in the unfitted ears. However, in fitted ears, there was a significant increase in the benefit over time, from 4 weeks to 12 weeks after fitting. Munro and Lutman²⁷ also demonstrated an improvement in the benefit score for

speech perception over time in fitted ears but no change in unfitted ears. These findings were only detected at the highest presentation level (69 dB SPL) because this level of aided speech was “new” to the participants with hearing impairment. However, in another study in a similar setting, there was no evidence of auditory acclimatization in HA users. No improvement over time (from baseline to 12 weeks) was detected in the fitted ears of new HA users relative to that in the unfitted ears of the same users or to that in the fitted ears of experienced users.²¹ Another study demonstrated that syllable recognition in noise improved more and over longer periods in participants using wide-dynamic-range compression HAs than in those using linear amplification HAs (4.6% improvement over the first 8 weeks vs. 2.2% over the first 4 weeks).²⁰ In the present study, although the follow-up period was 12 months, which is much longer than in previous HA studies, we found no evidence of acclimatization in terms of speech perception that could be attributed to the HAs. Several studies have reported the progressive influence of the HA on intensity discrimination over time after fitting, particularly at loud intensity levels and high frequencies.^{22,23} The long-term use of HAs also affected the tolerance of loudness, so that fitted ears showed greater tolerance of loudness than did unfitted ears.²⁴

There are several limitations in the present study. First, the sample size was quite small due to the difficulty in recruiting participants. Second, the unaided MCL was not matched to the equivalent output signal level after amplification with an HA. Moreover, simple loud presentation of the unaided MCL with adjustments may not fully cover the frequency shaping of the gain conferred by HA.

CONCLUSION

Hearing aids were found to be beneficial in terms of auditory spectral discrimination and 100 Hz temporal envelope sensitivity, for up to 12 months after fitting relative to the unaided performance before fitting. The improvements in spectral discrimination in the early post-fitting stage (1 month) did not seem to increase over the period of HA use, whereas the temporal envelope sensitivity improved continuously over time (up to 12 months post-fitting). These results imply that HA users adapt to HA processing for spectral discrimination immediately, whereas they need time to adapt to HA processing for temporal envelope sensitivity. Alternatively, long-term HA use could induce positive plastic changes or functional acclimatization exclusively in terms of temporal envelope sensitivity.

Ethics Committee Approval: Ethical committee approval was received from the Nowon Eulji Medical Center (No. 2016-01-012).

Informed Consent: Written informed consent was obtained from all participants who participated in this study.

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Author Contributions: Concept – H.J.S.; Design – H.J.S.; Supervision – H.J.S., J.H.W.; Resources – D.H.K., J.H.W.; Materials – D.H.K., J.H.W.; Data Collection and/or Processing – E.S.L., H.S.O.; Analysis and/or Interpretation – Y.A., E.S.L., H.S.O.; Literature Search – E.S.L., H.S.O.; Writing Manuscript – Y.A., H.J.S.; Critical Review – H.J.S., J.H.W.

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Conflict of Interest: The authors have no conflicts of interest to declare.

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