No change in the acoustic reflex threshold and auditory brainstem response following short-term acoustic stimulation in normal hearing adults

Hannah Brotherton[a]

Manchester Centre for Audiology and Deafness, University of Manchester, Manchester Academic Health Science Centre, Manchester, M13 9PL, United Kingdom

Christopher J Plack[b]

Manchester Centre for Audiology and Deafness, University of Manchester, Manchester Academic Health Science Centre, Manchester, M13 9PL, United Kingdom

Roland Schaette

Ear Institute, University College London, London, WC1X 8EE, United Kingdom

Kevin J Munro[c]

Manchester Centre for Audiology and Deafness, University of Manchester, Manchester Academic Health Science Centre, Manchester, M13 9PL, United Kingdom

Running title: Auditory brainstem activity following auditory stimulation

[a] Current Address: Department of Communication Sciences & Disorders, University of South Florida, 4202 E. Fowler Avenue, PCD1017, Tampa, Florida. Electronic mail: Hannah.brotherton@usf.edu

[b] Also at Department of Psychology, Lancaster University, Lancaster, LA1 4YF, United Kingdom

[c] Also at Central Manchester University Hospitals NHS Foundation Trust, Manchester Academic Health Science Centre, Manchester, M13 9WL, United Kingdom

ABSTRACT

Unilateral auditory deprivation or stimulation can induce changes in loudness and modify the sound level required to elicit the acoustic reflex. This has been explained in terms of a change in neural response, or gain, for a given sound level. However, it is unclear if these changes are driven by the asymmetry in auditory input or if they will also occur following bilateral changes in auditory input. The present study used a cross-over trial of unilateral and bilateral amplification to investigate changes in the acoustic reflex thresholds (ARTs) and the auditory brainstem response (ABR) in normal hearing listeners. Each treatment lasted 7 days and there was a 7-day washout period between the treatments. There was no significant change in the ART or ABR with either treatment. This null finding may have occurred because the amplification was insufficient to induce experience-related changes to the ABR and ART. Based on the null findings from the present study, and evidence of a change in ART in previous unilateral hearing aid use in normal hearing listeners, the threshold to trigger adaptive changes appears to be around 5 days of amplification with real ear insertion gain greater than 13-17 dB.

I. INTRODUCTION

The auditory system has the ability to compensate for fluctuations in the acoustic environment (Kappel *et al.*, 2011). One proposed mechanism is that the mean firing rate is maintained through changes in neural sensitivity or gain, which acts to optimise neural firing (Schaette and Kempter, 2006). It is hypothesized that the neural gain is modified by homeostatic plasticity (Turrigiano, 1999). This homeostatic neural gain mechanism can be likened to an internal volume control: the neural response increases to compensate for a reduction in auditory input and decreases to compensate for an increase in sensory stimulation (Turrigiano, 1998), without a change in threshold.

Previous studies that have characterised the neural gain mechanism have used physiological outcome measures, such as the acoustic reflex threshold (ART: Munro and Blount, 2009; Maslin *et al*., 2013; Munro and Merrett, 2013; Munro *et al*., 2014) and the auditory brainstem response (ABR: Decker and Howe, 1981; Schaette and McAlpine, 2011; Gu *et al*., 2012), as well as perceptual measures, such as loudness (Formby *et al.*, 2003; 2007). So far, changes in the ART and ABR have only been investigated following a unilateral change in auditory input.

Studies using the ART have shown that the pattern of change between the two ears differs following a unilateral change in auditory input. After 5 days of unilateral hearing aid use (15-20 dB real ear insertion gain (REIG) at high frequencies), Munro and Merrett (2013) reported a 2-3 dB increase in the sound level required to elicit an acoustic reflex in the treatment ear and a 1 dB decrease in the control ear. The change in ART is consistent with a decrease and increase in neural gain in the treatment and control ear, respectively. An ear-specific change in ART has also been reported following 7 days of short-term unilateral auditory deprivation

(30 dB attenuation at 2-4 kHz): a decrease in the sound level required to elicit an acoustic reflex in the treatment ear and an increase in the control ear (Munro and Blount, 2009; Maslin *et al.*, 2013; Munro *et al.*, 2014). This change in ART in opposite directions may reflect an attempt of the auditory system to balance the asymmetry in auditory input. For example, a complimentary binaural effect has been reported by Darrow *et al.* (2006) following unilateral lesioning of the lateral superior olive in adult mice. The authors reported an increase in the amplitude of wave I of the ABR on the affected side and a reduction on the unaffected side.

An alternative interpretation for the deprivation-induced change in ART is that a change in hearing thresholds has occurred. An improvement in hearing thresholds could result in a lower sound level required to elicit the acoustic reflex without a change in sensation level (i.e., level above hearing threshold). However, this interpretation is unlikely to explain the change in ART following acoustic deprivation, as previous unilateral earplug deprivation studies in normal hearing listeners did not report an improvement in hearing thresholds (Munro and Blount, 2009; Munro *et al.*, 2014). Furthermore, no improvement in hearing thresholds were reported in adult animals following unilateral earplug use (Whiting *et al.*, 2009).

The ABR is another physiological measure that has been used to investigate the change in neural gain in normal hearing listeners. For example, Decker and Howe (1981) recorded the ABR in normal hearing listeners after 10, 20 and 30 hours of unilateral earplug use, but no significant change in amplitude was observed. However, there is evidence from the tinnitus literature (Schaette and McAlpine, 2011; Gu *et al.*, 2012) suggesting that the ABR could provide a useful measure of change in neural gain. The ABR revealed a smaller peak-to-trough amplitude of wave I compared to a non-tinnitus control group with a matched mean audiogram. In contrast, the amplitude of wave V has been shown to be unaffected (Schaette and McAlpine, 2011) or even enhanced (Gu *et al.*, 2012) in the tinnitus group.

Changes in loudness have been investigated following both unilateral and bilateral changes in auditory input (Formby *et al.*, 2003; 2007; Munro and Merrett, 2013; Munro *et al.*, 2014). Following 5 days of unilateral amplification (15-20 dB real ear gain at 2-4 kHz), participants required a 3-5 dB increase in sound level to match pre-treatment loudness (Munro and Merrett, 2013). In a subsequent study using a unilateral earplug (25-35 dB attenuation at 2-4 kHz) for 7 days, participants required a decrease in the sound level of 5 dB to match pre-treatment loudness (Munro *et al.*, 2014). In both of these unilateral studies, the pattern of change was similar in the treatment and control ear. Combining the ART and loudness data across studies, the findings suggest that there could be two distinct neural gain mechanisms operating at different levels in the auditory system (Munro *et al*. 2014): the neural gain mechanism underlying the changes in loudness could be operating above the level of the SOC, which is the highest auditory structure in the acoustic reflex arc.

A similar pattern of change in loudness has also been reported following bilateral auditory deprivation and stimulation (Formby *et al.*, 2003; 2007). Following 2 weeks of bilateral earplug use, the sound level required to match pre-treatment loudness judgments decreased (Formby *et al*., 2003). Conversely, an increase in sound level was required to match pre-treatment loudness judgments following use of bilateral noise generators (Formby *et al.*, 2003). Therefore, until there is a study investigating the effect of a bilateral treatment on the ART, it is unclear if the change in neural gain is due to an asymmetry between ears, or if the change in neural gain occurs in both ears. However, the change in loudness could simply be due to a change in the participant’s behavioural response criterion in reaction to increased acoustic stimulation. This is supported by evidence of a reduction in loudness discomfort levels in noisy factory workers (Niemeyer, 1971).

The aim of the present study was to investigate changes in ART and ABR following augmented unilateral and bilateral auditory input (use of low gain hearing aids) in normal hearing adults. Participants were asked to wear unilateral and bilateral hearing aids, in a balanced design, for 7 days, with a one-week wash-out period between treatments. It was hypothesized that if the asymmetry in auditory input drives the change in neural gain, there would be an increase in sound level required to elicit an acoustic reflex in the treatment ear following unilateral but not bilateral hearing aid use. Similarly, it was hypothesized that the amplitude of ABR would decrease following unilateral but not bilateral hearing aid use.

II. METHODS

A. Participants

Twenty-nine volunteers (25 female and four males; median 23 years; range 19-44 years) participated in the study. For the ABR measurements, the sample size was based on previous findings by Schaette and McAlpine (2011) and Gu *et al*. (2012), which had sample sizes ranging from 15 to 21. For the ART measurements, a power analysis revealed that 13 participants were required for a power of 80%, assuming a within-subject difference of 4 dB (s.d. ± 6) on a two-tailed paired samples t-test at 5% significance level. We recruited a total of 29 participants, to allow for attrition or a smaller than expected effect size. All participants were screened for normal hearing sensitivity [<20 dB hearing level (HL) from 0.25 to 8 kHz and no asymmetry >10 dB at any frequency] and normal middle-ear function on tympanometry (middle ear pressure +50 to -50 daPa, middle ear compliance 0.3-1.5 cm^3). Participants with tinnitus and hyperacusis were not included in this study. Pure-tone audiometry was performed before and after hearing aid use. For the unilateral hearing aid condition, the difference in mean pure tone thresholds in the treatment and control ear at 2 and 4 kHz (the frequency range of amplification provided by the hearing aids) was ≤1 dB (±5). For the bilateral hearing aid condition, the difference in mean pure tone thresholds in the left and right treatment ear was ≤1 dB (±6). Therefore, pure tone thresholds were stable throughout the course of the study. Uncomfortable loudness levels (ULLs; used when setting the maximum output of hearing aids) were determined in each ear following the procedure recommended by the British Society of Audiology (British Society of Audiology, 2011). The study received ethics approval from The University of Manchester (ref: ethics/15191).

B. Hearing aids

The participants were fitted with Starkey Propel 4, non-occluding receiver-in-the-canal (RIC) hearing aids. These are 12-channel wide dynamic range compression devices. Participants were asked to wear the hearing aid(s) for 7 days, with a 7 day wash-out period separating the two treatments. The duration of the study was based on the length of time used in previous auditory stimulation studies that have investigated changes in ART and/or loudness in normal hearing listeners (Formby *et al.*, 2003; Formby *et al.*, 2007; Munro and Merrett, 2013). The wash-out period between treatments was justified by the findings of Formby *et al*. (2003): a one week period between treatments was sufficient for loudness to return to pre-treatment levels.

The order of treatments was randomly allocated to each participant. The investigator was blinded to the order of treatments. This was achieved by asking each participant to choose two sealed envelopes: one envelope provided instructions for the order of treatments (unilateral or bilateral first) and the second envelope stated which ear (right or left) was to be used in the unilateral hearing aid condition. Participants were also asked to remove the hearing aids immediately before entering the test session room in order to maintain blinding.

The amount of amplification provided by the hearing aids was measured using a real-ear probe-tube microphone. A calibrated probe-tube microphone was inserted into the ear canal and the response to a 65 dB sound pressure level (SPL) pink noise signal was measured before and after inserting the hearing aid (with the power switched on). The reference microphone was disabled during the aided measurements to reduce errors due to amplified sound leakage from the non-occluded ear canal. The level of amplification provided by the hearing aids was based on the study of Munro and Merrett (2013) that found that unilateral amplification with a REIG of 15-20 dB (2-4 kHz) was acceptable to normal hearing listeners. The compression ratio in this frequency region was 1.4:1 and the threshold knee point was 30 dB SPL (attack and release time of 12 and 182 ms, respectively). In the present study, participants were given an opportunity to experience wearing both hearing aids (up to 1 hour) before data collection commenced. It was during this period that the initial amplification was reported to be uncomfortable in the bilateral condition, presumably due to binaural summation of loudness. Therefore, fine tuning was carried out until the participants deemed the level of amplification comfortable. Compared to Munro and Merrett (2013), approximately 2-3 dB less amplification (identical for the unilateral and bilateral condition) was provided in order for the participants to tolerate the hearing aids (Fig. 1). This was verified using real-ear probe-tube microphone measurements with the same hearing aid settings as previously used in this study. The maximum output of the hearing aid (real-ear saturation response; RESR) was measured with the hearing aid in place and turned on. An input signal of a pure tone sweep, presented at 85 dB SPL (the highest available on the real ear measurement system) was used to operate the hearing aid at, or close to, saturation. The

RESR value was compared to the participant’s ULL to ensure the RESR did not exceed the ULL values. In no participant did the RESR exceed the ULL. REIG was measured after each 7-day period, using the real-ear probe-tube microphone measurements, to verify that the REIG of the hearing aids had not changed. The mean difference (and standard deviation) between day 0 and 7 (at 2, 3 and 4 kHz) was around 2 dB (±2 dB) for both the unilateral and bilateral conditions and was not statistically significant. The mean difference in REIG between ears for the bilateral hearing aid condition was <1 for all frequencies except at 8 kHz, where the difference was 3 dB.

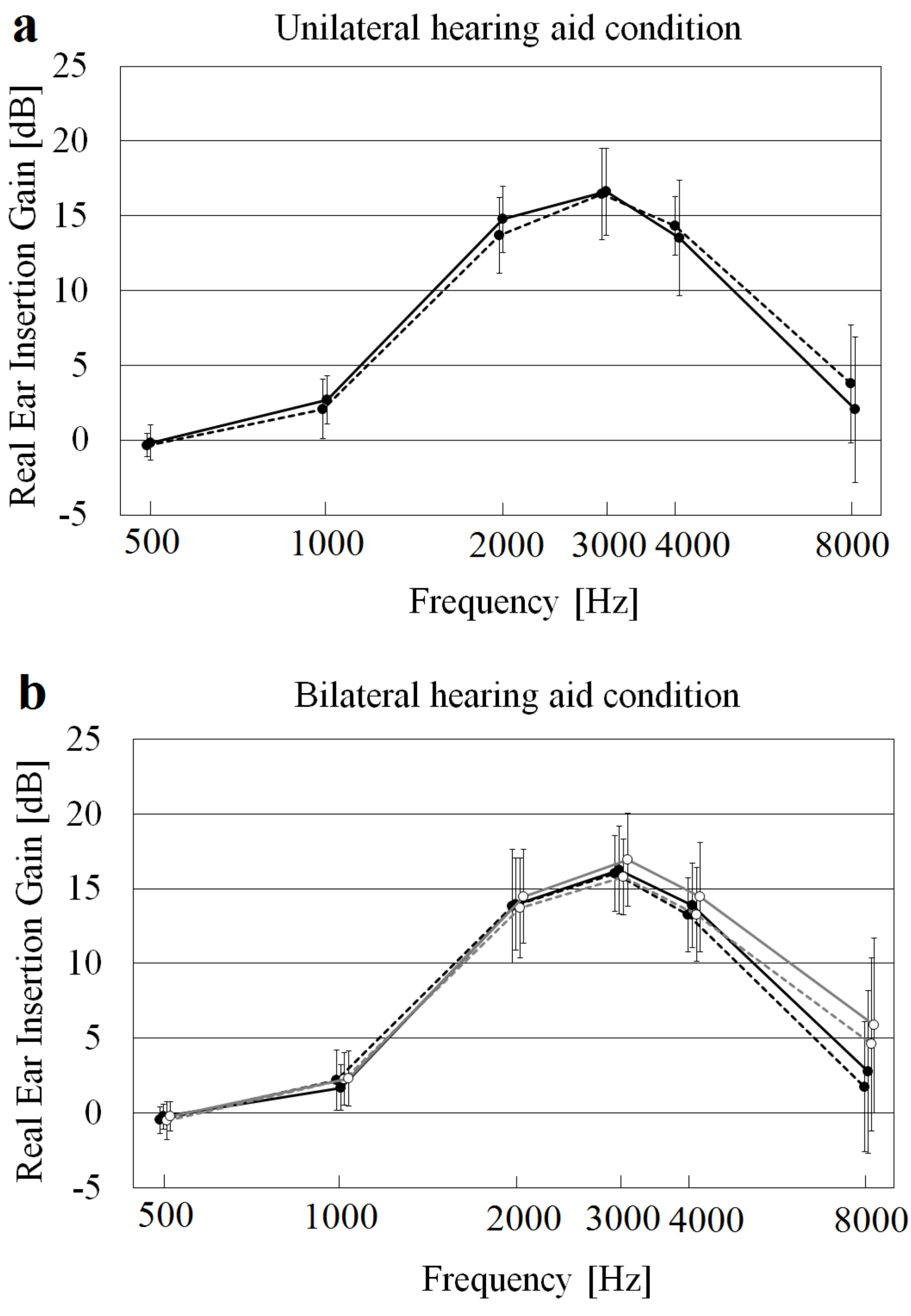


FIG. 1. Mean frequency-dependent real-ear insertion gain provided by the hearing instruments pre- (dashed lines) and post-treatment (solid lines) for the a) unilateral hearing aid condition in the treatment (filled circles) and b) bilateral hearing aid condition in the right

(black lines with filled circles) and left treatment ear (grey lines with open circles). Error bars show ±1 standard error (n = 29).

All participants were trained to insert the hearing aids in each ear. Participants were asked to wear the hearing aids throughout the waking day, removing them before bedtime and reinserting the following morning. Participants were also asked to remove the hearing aids before showering and reinsert immediately afterwards. Hearing aid log books were provided to each participant to motivate and encourage participants to wear the hearing aids for the instructed length of time. Mean daily use was 16 hours based on self-report. Participants were asked to report the time, in hours, of insertion and removal using a log book. However, some participants failed to report exact times of usage. Therefore the average daily use of 16 hours reported in this present study is an estimate of the average daily hearing aid use. A more detailed measurement of daily use could not be retrieved from the automatic software data logging of each device that was inspected at the end of the study. The data logging was not active (or recorded) during the study. The mean sound exposure that was recorded by the data logging software revealed an average value of 54 dB SPL (± 4). A detailed case history of noise exposure before hearing aid use and the type of acoustic environments participants were exposed to during the study were not recorded.

C. Acoustic reflex thresholds

Tympanometry was performed prior to measuring the ART and the equivalent ear canal volume (ECV) was recorded. ART measurements were made immediately before and after each 7 day test condition. ART measurements were always completed at the start of each test session. Ipsilateral ARTs were measured using the GSI Tympstar middle ear analyser with a

226 Hz probe tone. Ipsilateral measurements involved presenting the eliciting stimulus and measuring the reflex in the same ear. The stimulus used to elicit a reflex was a broadband noise. The frequency specificity of the treatment was not an aim of the present study. ARTs were included in the present study to confirm if any change in neural gain had occurred following unilateral and bilateral hearing aid use. BBN comprises the frequency range where the hearing aid had the maximum effect and has shown to produce large, clear changes in ARTs following short term changes in auditory input (Brotherton *et al.*, 2016). The stimulus was of fixed duration (1 second) and presented at an initial level of 60 dB HL. The sound level was increased in 5 dB steps until the reflex was detected (reduction in compliance of >0.02 cm^3). Increasing the stimulus by a further 5 dB confirmed the reflex growth. The stimulus was decreased by 10 dB and increased in 2 dB steps to determine the ART. The stimulus was presented two additional times at the apparent ART to confirm repeatability and then increased by a further 2 dB to confirm reflex growth. If a change in compliance was not seen at the maximum stimulus eliciting level of 95 dB HL, 5 dB was added onto the maximum value and taken as the ART, as done in previous ART studies (Munro and Blount, 2009; Munro *et al.*, 2014). Otoscopy was performed before tympanometry and ART measurements. ART measurements were obtained prior to any hearing aid use on day 0. ART measurements were not obtained after participants had worn the hearing aids for 1 hour and following any adjustments in REIG. No participants were removed from the analysis due to evidence of hearing aid use. The data included in the present study were taken from participants that did not show any evidence of pressure marks or cerumen impaction that may have occurred as a result of hearing aid use.

D. Equivalent ear-canal volume

The equivalent ECV provided an estimate of the volume of air trapped between the probe tip and the tympanic membrane (Fowler and Shanks, 2002) . It is known that, for a given input, a smaller ECV would result in a higher sound level intensity, eliciting a reflex at a lower level compared to a larger ECV. Because apparent changes in ARTs could simply reflect a difference in ear canal insertion depth of the oto-admittance probe (i.e. a deep insertion depth after hearing aid use could result in a lower dial reading using the same sound level prior to hearing aid use), we recorded the equivalent ECV registered by the oto-admittance system. For the unilateral hearing aid condition, the difference in mean ECV was around 0.05 ml (± 0.14) and 0.02 ml (± 0.16) in the treatment and control ear, respectively. For the bilateral hearing aid condition, the difference in mean ECV was around 0.01 ml (± 0.11) and 0.05 ml (± 0.13) in the left and right treatment ear, respectively. Therefore, the ECV was stable throughout the course of the study.

E. Auditory brainstem response

ABR measurements were recorded immediately before and after 7 days of treatment. ABR measurements were made prior to any hearing aid use on day 0. ABR measurements were not obtained after participants had worn the hearing aids for 1 hour following any adjustments in REIG. ABR measurements were obtained using the NeuroScan System (STIM and SCAN). Disposable silver/silver chloride electrodes were placed in an array that consisted of a three-channel montage: vertex, ipsilateral and contralateral mastoids (positive), high forehead (ground) and the nape of the neck (negative). Electrode impedances were maintained at <3kΩ. Stimuli consisted of a 0.1-ms alternating rectangular clicks, presented monaurally (in a balanced design) via ER-3A insert earphones at 80 dB re normal hearing level (nHL; ca 110 dB peSPL) at a rate of 11.1 clicks/s. On-line analysis consisted of an artefact rejection ratio of ±20 µV and digital filtering from 30 to 3000 Hz. Off-line analysis was completed using Scan v4.5 (Neuroscan^{TM}) and consisted of referencing to the ipsilateral mastoid. The positive electrode remained as the vertex. An epoch window extending from 10 ms before and 15 ms after each click presentation was extracted. Artefact rejection ratio was applied at ±50 μV and digital filtering from 150 to 1500 Hz, using a slope of 24 dB/Oct. Signals were averaged (8000 sweeps) and a linear detrend was applied to the data. The peak-to-trough amplitude of waves I, III and V were initially identified using an automated detection algorithm for the maximum peak to the following minimum trough within a time window of 1-3, 3-5 and 5-8 ms for wave I, III and V, respectively. The windows for each wave was established based on the grand average waveform. The waveforms were also checked visually to ensure that the waves fell within the time window. The I-V amplitude ratio was also calculated. The peak data from 6 participants (a random 20% of the collected data) were verified by a second investigator. These values reflect a time window that has not been corrected for the time delay (around 1 ms) introduced by the 256 mm of ER-3A earphone tubing.

III. STATISTICAL ANALYSIS

The data were inspected before analysis to confirm that it was appropriate to use parametric statistics. For both the ART and ABR data, the raw data were analyzed using a three-way (time [2] X condition [2] X order [2]) mixed ANOVA with time (day 0 and 7) and condition (unilateral and bilateral hearing aid treatments) as within-subject factors, and order (unilateral/bilateral hearing aid first) as the between-subject factor (see Table I). The data from the treatment ear for the unilateral condition and the left treatment ear from the bilateral condition were included in the analysis (the same findings were obtained if the right ear of the bilateral condition was used). The degrees of freedom were modified using the Greenhouse-Geisser correction when there was a statistically significant deviation from sphericity on Mauchly's test (Kinnea and Gray, 2009). The ABR analyses were corrected for multiple comparisons (0.05/3) using Bonferroni correction. All analyses were performed using SPSS version 22.

IV. RESULTS

A. Acoustic reflex threshold

The mean ARTs before and after 7 days of unilateral augmented stimulation are shown in Fig. 2. There was negligible difference between the two ears at baseline. There was a 2 dB difference between the ears after 7 days of treatment. For the unilateral condition, this was primarily due to a reduction in ART in the control ear. For the bilateral condition, the ART increases in both ears but by a slightly larger amount in the left ear. The ANOVA revealed no significant treatment effect or interactions (see Table I).

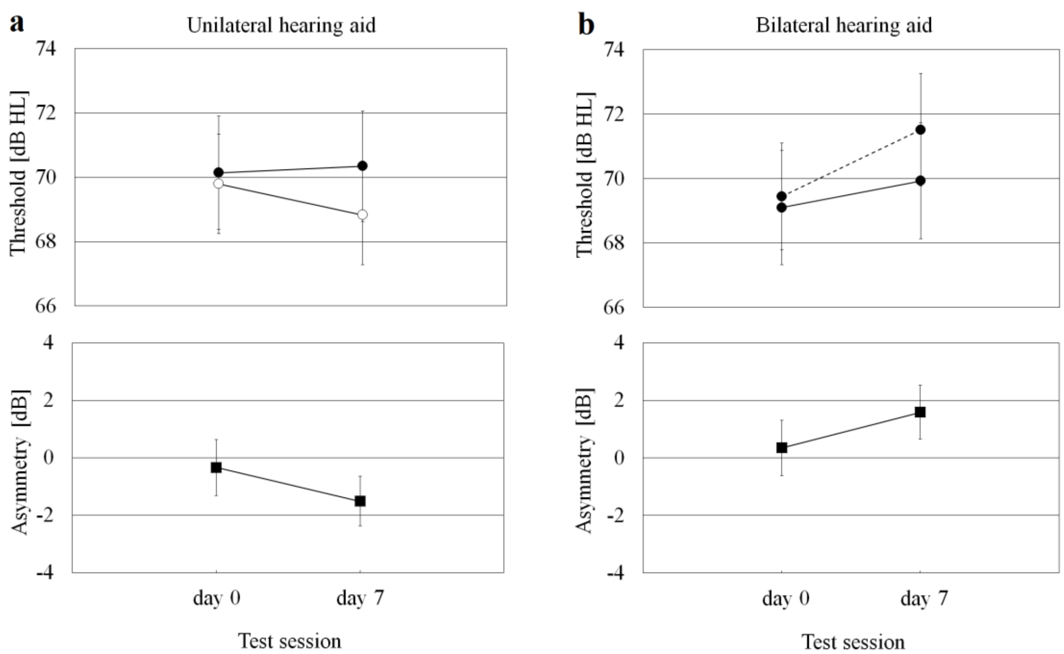


FIG. 2. Mean ART results following a) unilateral hearing aid use and b) bilateral hearing aid

use. Top panel: Mean ART for treatment ear (filled circles) and control ear (open circles) for the unilateral hearing aid condition. Mean ART for the right (filled circles, solid line) and left treatment ear (filled circles, dotted line) for the bilateral hearing aid condition. Bottom panel: Difference between the control minus the treatment ear for the unilateral hearing aid condition. Difference between the left treatment ear minus the right treatment ear for the bilateral hearing aid condition. Error bars show ± standard error of the mean (*n* = 29).

TABLE I. Summary of a mixed model analysis of variance on the acoustic reflex data with time (day 0 and 7) and treatment (unilateral and bilateral hearing aid condition) as within-subject factors, and order (unilateral hearing aid condition first and bilateral hearing aid condition first) as the between-subject factor (*n* = 29)

Factor	df	*F*	*p*
Between subject factor			
Order	1, 27	0.432	0.517
Within subject factors			
Time	1, 27	3.645	0.067
Time*order	1, 27	0.002	0.961
Treatment	1, 27	0.145	0.706
Treatment*order	1, 27	0.145	0.706
Time*treatment	1, 27	1.973	0.172
Time*treatment*order	1, 27	1.472	0.236

B. Auditory brainstem response

The grand average ABR waveform, is shown in Figure 3. The mean peak-to-trough amplitudes of wave I, III and V after unilateral hearing aid use are shown in Figure 4. The changes in the mean peak-to-trough amplitude of wave I, III and V were negligible. In the treatment ear, wave I increased by 14 nV, wave III decreased by 14 nV and wave V increased by 6 nV. For the control ear, wave I decreased by 15 nV, wave III decreased by 24 nV and wave V decreased by 24 nV. The I-V amplitude ratio decreased by 8 nV.

The mean peak-to-trough amplitude of wave I, III and V after bilateral hearing aid use are shown in Figure 5. The changes in the mean peak-to-trough amplitude of wave I, III and V were negligible: For the right ear, wave I decreased by 13 nV, wave III decreased by 12 nV and wave V decreased by 8 nV. For the left ear, wave I decreased by 20 nV, wave III decreased by 4 nV and wave V decreased by 12 nV. The I-V amplitude ratio decreased by < 1 nV.

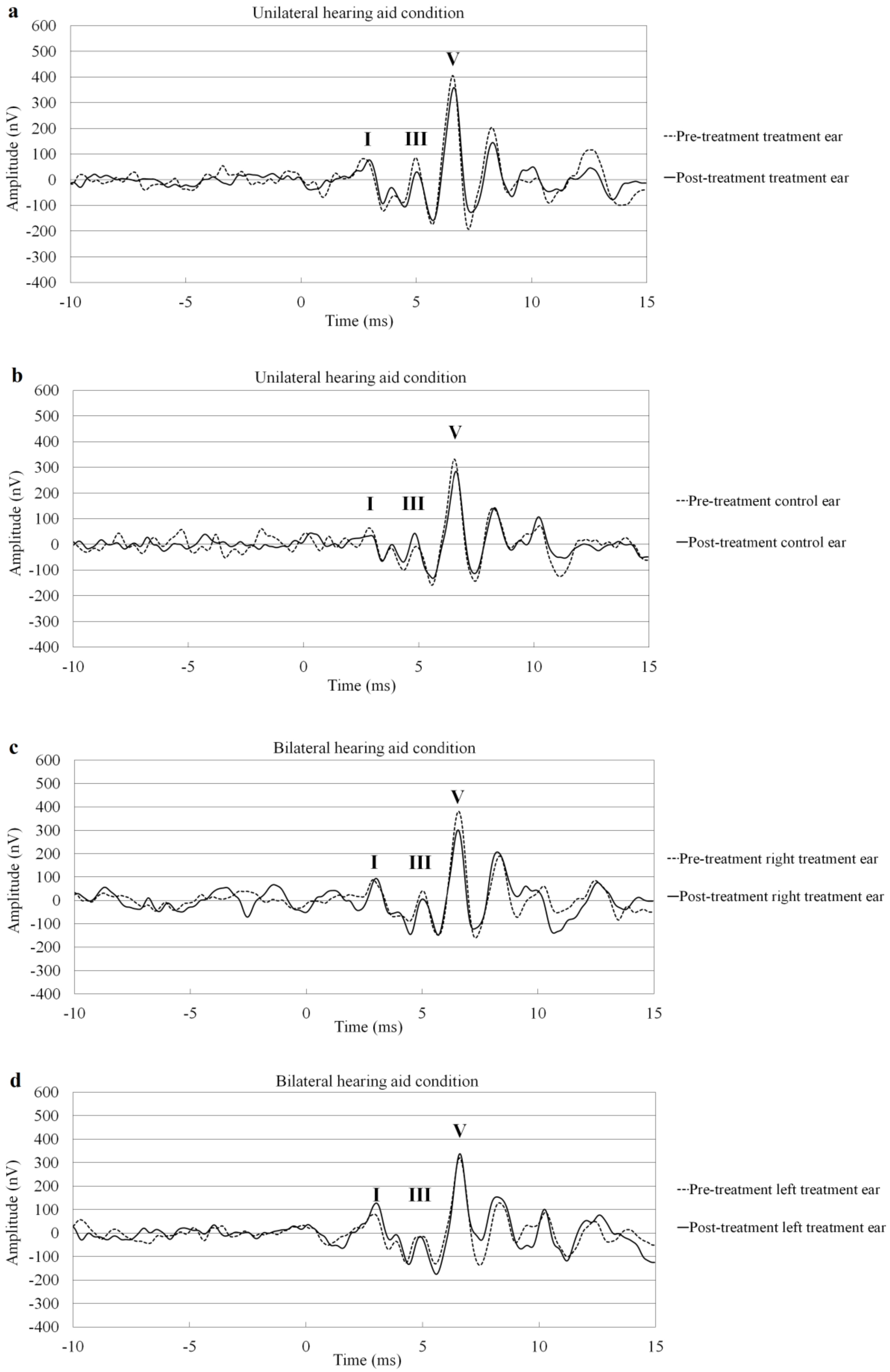
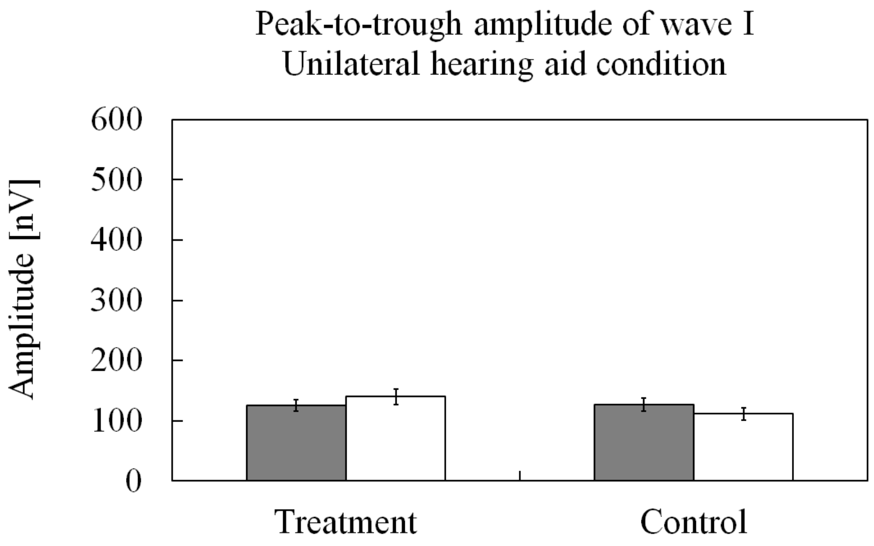
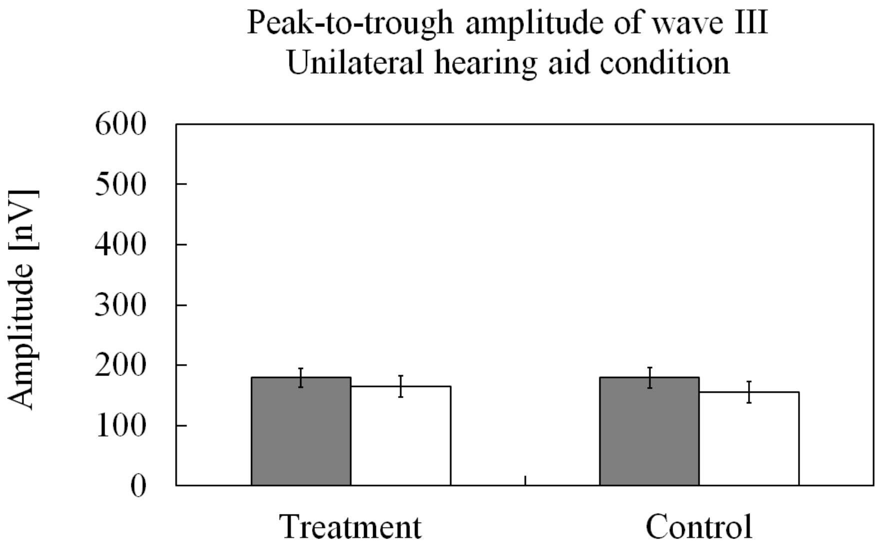

a
Unilateral hearing aid condition
Amplitude (nV)
Time (ms)
I
III
V
Pre-treatment treatment ear
Post-treatment treatment ear
b
Unilateral hearing aid condition
Amplitude (nV)
Time (ms)
I
III
V
Pre-treatment control ear
Post-treatment control ear
c
Bilateral hearing aid condition
Amplitude (nV)
Time (ms)
I
III
V
Pre-treatment right treatment ear
Post-treatment right treatment ear
d
Bilateral hearing aid condition
Amplitude (nV)
Time (ms)
I
III
V
Pre-treatment left treatment ear
Post-treatment left treatment ear

FIG. 3. Grand average ABR waveforms for the a) treatment and b) control ears in the unilateral hearing aid condition, and the c) right and d) left treatment ears in the bilateral hearing aid conditions (n = 29).


Peak-to-trough amplitude of wave I
Unilateral hearing aid condition
Amplitude [nV]
600
500
400
300
200
100
0
Treatment
Control


Peak-to-trough amplitude of wave III
Unilateral hearing aid condition
Amplitude [nV]
600
500
400
300
200
100
0
Treatment
Control

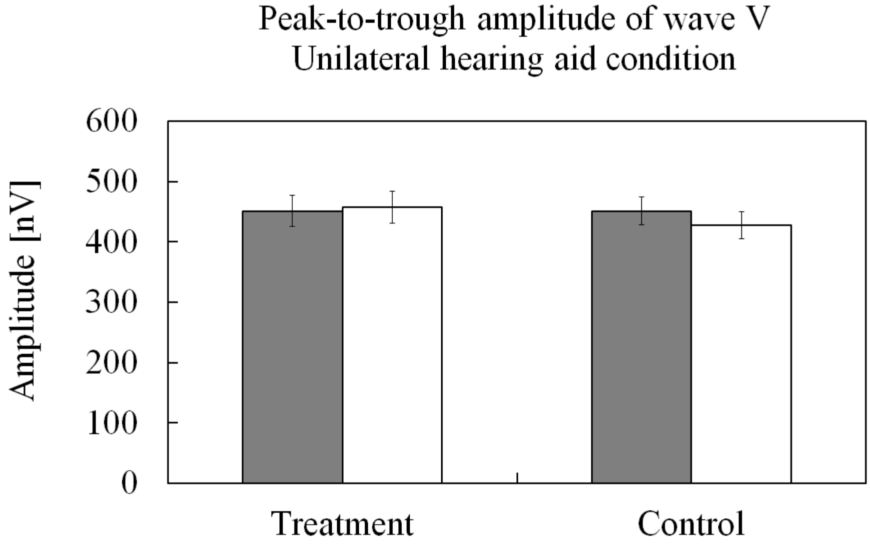
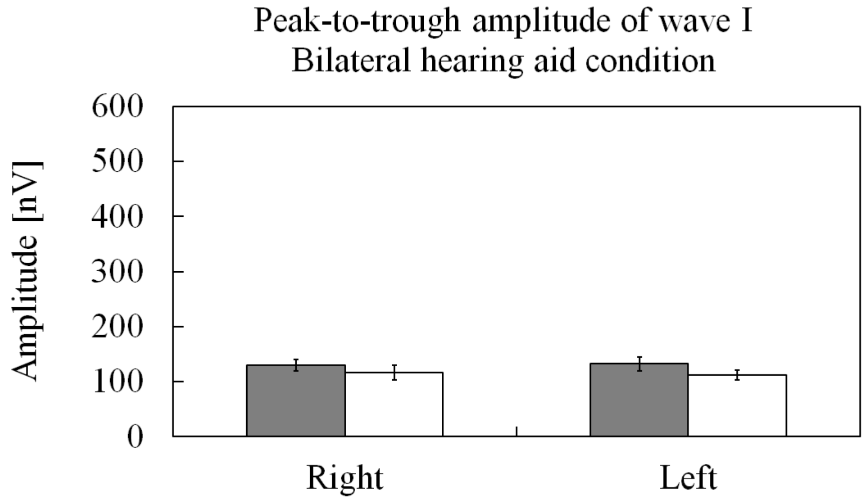
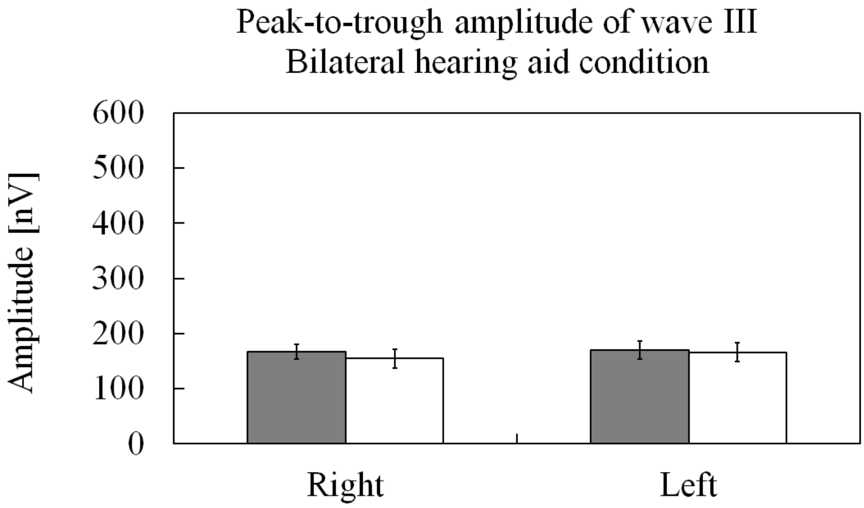

Peak-to-trough amplitude of wave V
Unilateral hearing aid condition
Amplitude [nV]
600
500
400
300
200
100
0
Treatment
Control

FIG. 4. Mean peak-to-trough ABR data of wave I, III and V for the treatment and control ear before (grey columns) and after (white columns) 7 days of unilateral hearing aid use. Error bars show ± standard error (n = 29).


Peak-to-trough amplitude of wave I
Bilateral hearing aid condition
Amplitude [nV]
600
500
400
300
200
100
0
Right
Left


Peak-to-trough amplitude of wave III
Bilateral hearing aid condition
Amplitude [nV]
600
500
400
300
200
100
0
Right
Left

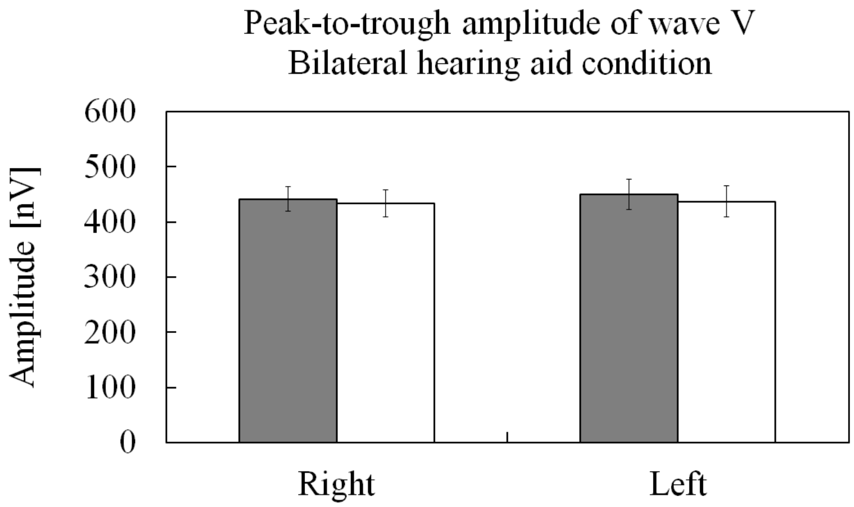

Peak-to-trough amplitude of wave V
Bilateral hearing aid condition
Amplitude [nV]
600
500
400
300
200
100
0
Right
Left

FIG. 5. Mean peak-to-trough ABR data of wave I, III and V for the right and left treatment ear before (grey columns) and after (white columns) 7 days of bilateral hearing aid use. Error bars show ± standard error (n = 29).

The raw ABR data were analyzed using a separate three-way (time [2] X condition [2] X order [2]) mixed ANOVA for wave I, III, V and the I-V amplitude ratio (See Table III). The only significant finding was an interaction between time and order for wave V, which survive Bonferroni correction. This means that the change in wave V after 7 days of hearing aid use was different depending on the order of treatments. i.e. if the initial condition was unilateral, there was a greater reduction in the mean peak-to-trough amplitude of wave V in both conditions, compared to when the initial condition was bilateral (Fig. 6). The next step was to determine the source of the interaction. A two-factor (time [2] X treatment [2]) repeated-measures ANOVA was carried out for the two orders of treatment (Table III). When the treatments were completed in the order of unilateral followed by bilateral there were no significant findings. When the treatments were completed in the order of bilateral followed by unilateral there were no significant findings.

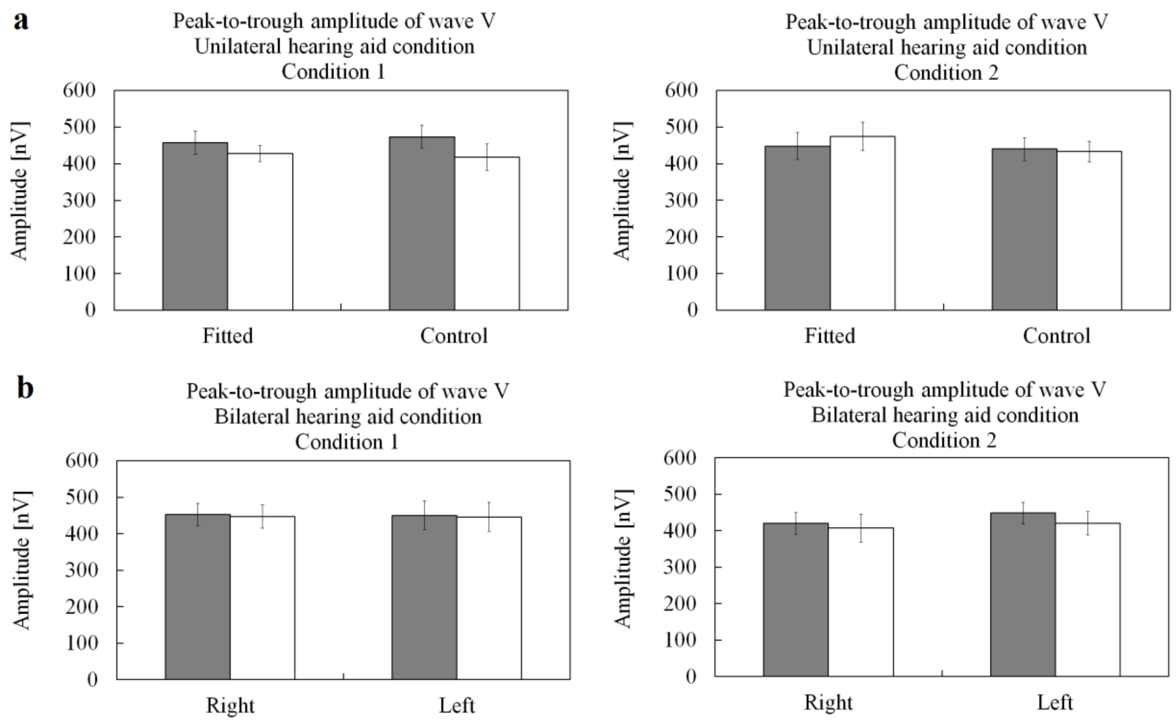


FIG. 6. Mean peak-to-trough ABR data of wave V for the unilateral and bilateral hearing conditions ordered according to a) when the unilateral hearing aid condition was completed first (*n* = 10) or second (*n* = 19) and when b) the bilateral hearing aid condition was completed first (*n* = 19) or second (*n* = 10). Error bars show ± standard error.

TABLE II. Summary of a mixed model analysis of variance on the auditory brainstem response data of waves I, III, V and I-V amplitude ratio with time (day 0 and 7) and treatment (unilateral and bilateral hearing aid condition) as within-subject factors, and order (unilateral hearing aid condition first and bilateral hearing aid condition first) as the between-subject factor (*n* = 29).

Factor	df	*F*	*p*
Wave I			
Between subject factor			

Order	1, 27	0.005	0.945
Within subject factors			
Time	1, 27	0.636	0.432
Time*order	1, 27	2.395	0.133
Treatment	1, 27	0.868	0.360
Treatment*order	1, 27	0.020	0.888
Time*treatment	1, 27	2.693	0.112
Time*treatment*order	1, 27	0.005	0.946
Wave III			
Between subject factor			
Order	1, 27	0.066	0.799
Within subject factors			
Time	1, 27	1.807	0.190
Time*order	1, 27	1.481	0.234
Treatment	1, 27	0.058	0.812
Treatment*order	1, 27	0.014	0.906
Time*treatment	1, 27	1.205	0.282
Time*treatment*order	1, 27	2.168	0.152
Wave V			
Between subject factor			
Order	1, 27	0.092	0.764
Within subject factors			
Time	1, 27	1.611	0.215
Time*order	1, 27	8.113	0.008

Treatment	1, 27	0.226	0.638
Treatment*order	1, 27	0.009	0.925
Time*treatment	1, 27	0.746	0.395
Time*treatment*order	1, 27	0.339	0.339
I-V			
Between subject factor			
Order	1, 27	0.585	0.451
Within subject factors			
Time	1, 27	0.202	.657
Time*order	1, 27	0.075	0.787
Treatment	1, 27	0.131	0.720
Treatment*order	1, 27	0.002	0.966
Time*treatment	1, 27	0.624	0.436
Time*treatment*order	1, 27	1.998	0.169

TABLE III. Summary of a repeated-measures analysis of variance on the auditory brainstem response data of wave V when the orders of treatment was completed as unilateral first/bilateral second (n = 10) and bilateral first/unilateral second (n =19).

Factor	df	*F*	*p*
Unilateral first/bilateral second			
Time	1, 9	1.398	0.267
Treatment	1, 9	1.141	0.313
Time*Treatment	1, 9	0.201	0.664
Bilateral first/unilateral second			
Time	1, 9	0.843	0.371
Treatment	1, 9	0.207	0.654
Time*Treatment	1, 9	3.776	0.068

V. DISCUSSION

This study set out to determine if the change in neural gain acts in response to an asymmetry in auditory input, by comparing the change in the ART and ABR after 7 days of unilateral and bilateral hearing aid use.

A. Acoustic reflex threshold

There was no significant change in ART after 7 days of unilateral or bilateral hearing aid use. However, there was a trend of increase ARTs in the treatment ear and a decrease in the control ear after unilateral hearing aid use, and an increase in ARTs in both ears (albeit larger in the left treatment ear) after bilateral hearing aid use. No significant changes in ART to a BBN stimulus were found after 7 days of low-gain amplification. It is possible that the amplification did not sufficiently modify the sensory environment to induce a change in neural gain that could be detected using ARTs. Although we attempted to prescribe the same REIG as Munro and Merrett (2013; 15-20 dB at 2-4 kHz) this was not tolerated by normal hearing listeners in the bilateral condition because of binaural summation: amplified sound perceived as louder with two hearing aids relative to one hearing aid (Reynolds and Stevens, 1960). The REIG was adjusted to 13-17 dB to avoid loudness discomfort. The level was fixed for both the unilateral and bilateral hearing aid treatments so that any effect would be due to the hearing aid condition. Considering binaural summation may have occurred during the bilateral hearing aid condition, any binaural summation of loudness was insufficient to induce a change in neural gain. Furthermore, in the present study, the duration of hearing aid use was longer (7 days) compared to Munro and Merrett (2013; 5 days). Other aspects regarding the design of the present study were similar to previous studies. The duration of hearing aid use on a daily basis is comparable to that of Munro and Merrett (2013). In both studies, the participants were asked to wear the hearing aids continuously, except for bedtime. The sample population in both studies was young adults who were students in higher education.

The present findings suggest we did not reach the amplification threshold required to trigger adaptive changes that could be detected using the ART. This threshold must lie above the 13-17 dB level of amplification provided in the present study. Table IV summarises the attenuation/amplification level, days of treatment, and the amount of change in ART from previous studies using normal hearing listeners.

The earplug studies used a 7 day treatment period with high frequency attenuation in excess of 30 dB. This resulted in a reduction in ART of around 5-7 dB. The single hearing aid study used a 5 day treatment period with high frequency amplification of around 15-20 dB. Thus, the change in auditory input was less than for the earplug studies and it is notable that the increase in ART was smaller at around 3 dB. Therefore, since the present study did not show a significant change in ART, it is likely that the minimum amplification is 15-20 dB for a minimum of 5 days.

TABLE IV. A summary of the attenuation/amplification level values, days of treatment and the amount of change in ART from recent studies in normal hearing listeners.

Auditory deprivation: unilateral earplug use			
Study	**Attenuation**	**Days of treatment**	**Mean change in ART**
Munro and Blount (2009)	0.5-1 kHz: ≥22 dB 2-4 kHz: 36 dB	7 days	Treatment ear: 5-7 dB decrease Control ear: 1-3 dB increase
Maslin *et al.* (2013)	0.25 kHz: <10 dB 3-4 kHz: >30 dB	7 days	Treatment ear: 3-7 dB decrease Control ear: 2 dB increase
Munro *et al.* (2014)	0.5-1 kHz: ≤16 dB 2-4 kHz: ≥25 dB	7 days	Treatment ear: 1-6 dB decrease Control ear: 2 dB increase
Increased auditory stimulation: unilateral hearing aid use			
Study	**Amplification**	**Days of treatment**	**Mean change in ART**
Munro and Merrett (2013)	0.5-1 kHz: 0 dB 2-4 kHz:15-20 dB	5 days	Treatment ear: 3 dB increase Control ear: 1 dB decrease

B. Auditory brainstem response

The present study was unable to demonstrate a change in the peak-to-trough amplitude of wave I, III, V and the I-V amplitude ratio following unilateral or bilateral hearing aid use. This finding is consistent with the lack of change in ART.

One unexpected finding was the interaction of time and order when analysing the wave V data. If the participants had already completed the unilateral treatment, there was a reduction in mean amplitude that was not present if they had no previous treatment. There was little difference in REIG between the two groups. The group that commenced with the unilateral treatment had 14-17 dB REIG and the group that commenced with bilateral treatment had 13-16 dB REIG. It is possible that this marginal difference in amplification between groups could have caused this effect: the group with marginally more amplification showed an effect.

The present study should also be replicated with a greater level of amplification, and larger sample size, to investigate the effect of unilateral and bilateral sound treatments on the ABR. This could be achieved by providing a narrower frequency band of amplification to avoid binaural summation causing loudness discomfort. An alternative design would be to use unilateral and bilateral earplugs. It may be helpful for future studies to include measures of noise exposure, case history reports of noise exposure before hearing aid use, noise exposure reports during hearing aid use and subjective measurements of the type of acoustic environments participants were exposed to during the study. The data logging of the hearing aids did reveal an average exposure of 54 dB SPL during hearing aid use. However, this reading was taken at the end of the study and did not allow an insight into the average noise exposure during unilateral versus bilateral hearing aid use. Different acoustic environments could have directly impacted hearing aid output and therefore the stimulation received. There was minimal risk to the participant's hearing from wearing the low-level gain hearing aids. Extensive efforts were made to ensure that the maximum output was at, or below, uncomfortable loudness levels. The REIG was verified using the probe-microphone measurements before and after hearing aid use to ensure the hearing aid insertion gain remained the same. According to The Noise at Work Regulations (1989), the maximum permitted sound exposure for daily exposure (8 hours) is 90 dB(A). When adopting a 3 dB exchange rate for calculating noise exposure, for a doubling of exposure time 16 hours is permitted for a sound exposure level not exceeding 87 dB(A). The average noise exposure during the present study was 54 dB SPL. If replication of this study occurs with a greater level of amplification, the investigator should use subjective and objective hearing aid verification to ensure that the level of amplification does not exceed 15-20 dB, ensuring that the maximum output of the hearing aid does not exceed the recommended maximum noise exposure levels for 16 hours/day

VI. CONCLUSION

This study was unable to demonstrate a change in neural gain using ART despite previous studies using unilateral augmented stimulation. The most parsimonious explanation for the current finding is that the level of augmented stimulation was insufficient to change the neural gain. The findings suggest that the minimum level of amplification used in future studies should be greater than 13-17 dB, for a period of at least 7 days. There was no change in the peak-to-trough amplitude of wave I, III and V following unilateral or bilateral auditory stimulation. It remains unclear if the ABR will show evidence of a change in neural gain following bilateral hearing aid use with greater augmented stimulation. A minimum threshold of 15-20 dB for a minimum of 5 days may have some clinical relevance when fitting hearings aids for the treatment of tinnitus and/or hyperacusis.

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