Cortical auditory evoked potentials (CAEPs) in response to multi-tone (MT) stimuli in hearing-impaired adults.

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Abstract

Objective: To determine if one-octave multi-tone (MT) stimuli increase the amplitude of cortical auditory evoked potentials (CAEPs) in individuals with a hearing loss when compared to standard pure-tone (PT) stimuli and narrow-bands noise (NBN).

Method: CAEPs were obtained from 16 hearing impaired (HI) adults in response to PT and MT auditory stimuli centered around 0.5, 1, 2 and 4 kHz and NBN centered around 1 and 2 kHz. Hearing impairment ranged from a mild to a moderate hearing loss in both ears. The auditory stimuli were monaurally delivered through insert ear-phones at 10 and 20dB above threshold. The root mean square (RMS) amplitude of the CAEP and the detectability of the responses using Hotelling's T^2 were calculated and analyzed.

Results: CAEP amplitudes elicited with MT stimuli were in average 29% larger than PT stimuli for frequencies centered around 1, 2 and 4 kHz. No significant difference was found for responses to 0.5 kHz stimuli. Significantly higher objective detection scores were found for MT as compared to PT. For the 1 and 2 kHz stimuli, the CAEP amplitudes to NBN were not significantly different to those evoked by PT but a significant difference was found between MT stimuli and both NBN and PT. The mean detection sensitivity of MT for the four frequencies was 80% at 10 dB SL and 95% at 20dB SL, and was comparable with detection sensitivities observed in normal-hearing subjects.

Conclusion: Using MT stimuli when testing CAEPs in adults with hearing impairment showed larger amplitudes and a higher objective detection sensitivity compared to using traditional PT stimuli for frequencies centered around 1, 2 and 4 kHz. These findings suggest that MT stimuli are a clinically useful tool to increase the efficiency of frequency-specific CAEP testing in adults with hearing impairment.

Introduction

In many clinical settings, cortical auditory evoked potential (CAEP) testing is increasingly being used for hearing threshold estimation (Lightfoot and Kennedy 2006; Van Dun et al. 2014) as well as hearing aid fitting evaluation (Van Dun et al. 2012). Often, CAEP testing is used in populations where accurate behavioral responses cannot be elicited such as in infants, children, and populations with a disability, as well as cases of pseudohypacusis, as the test can be conducted on awake participants. Studies have shown that CAEPs are present on average at 5 to 10dB above behavioral threshold for normal-hearing and hearing-impaired subjects (Van Dun et al. 2014; Picton 2011; Tsui et al. 2002).

For the CAEP test to be a viable option for widespread use in clinics there is a need to reduce testing time for threshold estimation. To achieve this, a key challenge is to maximize the amplitude of the CAEP and increase detection sensitivity. Several studies suggest that changing the stimulus parameters affects the amplitude of cortical responses. CAEPs are sensitive to factors such as stimulus level (Picton et al. 1970), rise-time, (Onishi and Davis 1968) duration (Alain et al. 1997), the length of the stimulus onset asynchrony (SOA) (Bardy, Van Dun, Dillon, and Cowan 2014), the mode of presentation (Bardy, Van Dun, Dillon, and McMahon 2014; Butler 1968), background noise (Billings et al. 2009), and the spectral contents of the stimulus (Jacobson et al. 1992). Previous EEG and MEG studies have shown that cortical responses can be enhanced by using spectrally rich stimuli in comparison to pure-tone stimuli at equal intensity (Jenkins III et al. 2010; Seither-Preisler et al. 2003; Shahin et al. 2005; Soeta and Nakagawa 2006). One recent study in normal-hearing adults showed that the spectrally complex sound positively influences the amplitude of the cortical response. Bardy et al. (in press) used multi-tone stimuli (MT) with four sinusoidal components uniformly distributed on a logarithmic frequency scale in the octave around the center frequency. Results from the study showed on average 32 % RMS amplitude increase in response to the novel stimuli for the frequencies 1, 2 and 4 kHz compared to sinusoidal pure-tone (PT).

It has been shown that hearing-impaired subjects have wider critical bandwidths than normal (Florentine et al. 1980; Margolis and Goldberg 1980). Consequently, hearing-impaired subjects integrate sound energy over a wider frequency range than normal-hearing subjects for the detection of complex signals (Higgins and Turner 1990). This is mainly due to the loss of the active mechanism in the cochlea which affect frequency selectivity. Moreover, some past literature has suggested that cortical responses in the hearing-impaired population can differ from those in normal hearers. Research has shown that degree of hearing loss influences the latency and amplitude of the cortical response in adults with a sensorineural hearing loss (Oates et al. 2002; Korczak et al. 2005; Mathew et al. 2015). Changes in latency and amplitude were seen when subjects were presented with speech sounds. Greater changes in latency were seen in the later evoked-related-potential compared to the earlier N1.

Considering these results, it is crucial to validate whether new MT stimuli, recently successfully trialed with normal-hearing subjects (Bardy et al. in press), have the potential to increase CAEP amplitudes in adults with hearing impairment as well. The first aim of this study is to investigate the effect of the auditory stimuli spectral characteristics on the amplitude of the cortical responses of hearing-impaired (HI) adults tested with complex MT stimuli, PT and narrow-bands noise (NBN). The second aim of this study is to investigate the detection sensitivity of CAEPs when presented 10 dB and 20 dB above threshold and to compare the results obtained for HI to the results for normal-hearing (NH) subjects.

Methods

Subjects

Sixteen hearing-impaired subjects (ranging from 54 to 82 years of age) were recruited for the study (9 males, 7 females). Behavioral thresholds for audiometric frequencies can be found in Table 1. Written consent was obtained from participants and the study was approved and conducted under the ethical oversight of the Australian Hearing Human Research Ethics Committee. Participants received a small monetary compensation for taking part in the study.

Table 1.

Stimuli	Threshold (dB SPL)	RET 0 dB HL (dB SPL)	PT- PT_{500} (dB)	MT – PT_{500} (dB)	MT - PT (dB)
PT_{500} 0.25 kHz	36.7 ± 12.7	14			
PT_{500} 0.5 kHz	33.7 ± 14.6	5.5			
PT_{500} 1 kHz	34.0 ± 17.7	0			
PT_{500} 2 kHz	46.6 ± 13.9	3.0			
PT_{500} 4 kHz	48.0 ± 14.3	5.5			
PT_{500} 8 kHz	50.0 ± 13.1	0			
PT 0.5 kHz	36.8 ± 12.1		3.1 ± 4.9		
PT 1 kHz	37.0 ± 15.9		3.0 ± 9.3		
PT 2 kHz	47.9 ± 14.0		1.3 ± 3.3		
PT 4 kHz	49.1 ± 14.0		1.2 ± 2.1		
MT 0.5 kHz	40.4 ± 13.4			6.7 ± 5.5	3.6 ± 5.3
MT 1 kHz	37.0 ± 15.0			3.0 ± 10.5	0.0 ± 4.5
MT 2 kHz	49.8 ± 13.9			3.1 ± 4.9	1.9 ± 5.3
MT 4 kHz	55.1 ± 12.8			7.2 ± 6.5	6.0 ± 5.7
NBN 1 kHz	38.7 ± 13.0				
NBN 2 kHz	47.3 ± 14.0				

Table 1. Behavioral mean thresholds and standard deviations across 16 subjects for six 500-ms pure-tones (PT_{500}) (0.25 – 8 kHz), and eight 50-ms auditory stimuli used for the recording of CAEPs. The threshold for each stimuli corresponds to the average across the right and left ear. The eight stimuli consisted of four PTs with frequencies 0.5, 1, 2 and 4 kHz, four one-octave MT stimuli with the same center frequencies and two one-octave narrow bands of noise (NBN) centered around 1 and 2 kHz. The reference equivalent threshold (RET, i.e. 0 dB HL) using insert earphones according to ISO (Standardization 1994) is provided in the third column. Lastly, the mean threshold differences and standard deviations between 50 and 500 ms PTs, between 50 ms MTs and 500 ms PTs, and between 50 ms MTs and 50 ms PTs are provided in the last three columns.

Auditory stimuli

Four sinusoidal pure-tone (PT), four one-octave multi-tone (MT) stimuli at 0.5, 1, 2 and 4 kHz and two one-octave narrow-bands of noise (NBN) centered around 1 and 2 kHz were generated in MATLAB (Mathworks). All stimuli were 50 ms in duration with 10 ms rise-fall times to minimize spectral splatter. To create the MT stimuli, a series of inharmonically related sinusoids equal in amplitude with zero phase delay at stimulus onset were added together. The individual sinusoids were uniformly distributed around the center frequency on a logarithmic frequency scale. The spectral characteristics for each stimulus are summarized in Table 2. In addition, six sinusoidal 500 ms PT stimuli at 0.25, 0.5, 1, 2, 4 and 8 kHz were generated for behavioral testing.

Table 2.

Center Freq. (kHz)	**Frequency of Each Sinsoidal Component**			
0.5	0.353	0.445	0.561	0.707
1	0.707	0.890	1.122	1.414
2	1.414	1.781	2.244	2.828
4	2.828	3.563	4.489	5.656

Table 2. Frequency content of multi-tone stimuli (in kHz).

Transducer and Calibration

All stimuli during the experiment were presented through ER-3A insert earphone (Etymotic Research). The calibration for both PT and MT stimuli was conducted using 4000 ms continuous stimuli. All stimuli were acoustically calibrated at 70 dB SPL according to the ISO standard 389-2 (ISO 1994) in an HA-2 2-cc coupler (IEC 60318-5), incorporating a 1-in 4144 microphone, a 1-to-1/2-in DB0375 adaptor, and a 4230 sound level meter (all Brüel & Kjær).

Automatic threshold estimation

Participants were tested with automatic computerized audiometry using an adaptive staircase procedure based on work conducted by Convery et al. (2014). The presentation level at the start was 70 dB SPL with adaptive step size 10 – 5 – 2 dB changing respectively after 1 – 2 and 4 reversals. The average of the last four reversals was taken as the participant’s threshold (which is referred to as 0 dB SL). Duration between stimulus presentations was randomized and ranged from 1000 to 4600 ms. Only the responses of the subject which occurred within a 1.5-second time window commencing from the onset of the stimulus were recorded.

First, participants were tested with six 500ms PT stimuli ranging from 0.25-8 kHz in both the right and left ear. Second, the researcher randomly selected one ear to test twelve 50 ms stimuli (including two additional stimuli not reported in this study).

Electrophysiological recording of CAEPs

Sequence generation and presentation

Using the obtained behavioral thresholds, sound sequences were generated for electrophysiological recording. While the results often stimulus conditions are reported in this study, twelve auditory stimuli (including two additional stimuli not reported in this study) were randomly presented at two sensation levels (10 and 20 dB SL) in a single sequence, making the total number of conditions 24. The stimulus onset asynchrony (SOA), which represents the time interval between the onset of two successive stimuli, was jittered uniformly between 1000 and 3000 ms. Each condition was presented 60 times which resulted in a testing time of 48 min. The stimuli were presented monaurally according to the ear selected (9 left ears and 7 right ears).

Data acquisition

Active electrodes were placed at Cz and FCz while the reference electrode was placed on the contralateral mastoid to the ear being tested and the ground electrode was placed on FPz. NuPrep EEG abrasive skin prepping gel was used to prepare the participant’s skin prior to applying electrodes. Water-soluble electrode paste was used to ensure a good connection between the electrodes and skin to achieve impedances of less than 5 kOhm across all electrode sites. Testing was conducted in an audiometric booth adhering to ANSI standard S.3.1-1999.

During testing, subjects were seated comfortably in a dimmed, sound attenuated booth. Subjects watched a muted close-captioned DVD of their choice and were instructed to ignore the stimulus being presented in their ear.

Data analysis

Waveforms from both FCz and Cz electrodes were analysed in reference to the mastoid at the contralateral ear. Amplification gain was uniform across all electrodes at 2010 with a sampling rate of 1000 Hz and bandpass filter of 0.01-30 Hz. EEGLAB (Delorme and Makeig 2003) was used to process the EEG files. Data consisted of 100 ms pre- and 600 ms post-stimulus onset (700ms per epoch) with baseline correction and exclusion of epochs in excess of ±75 µV.

Response amplitude

For each condition, the response amplitude of the cortical response was expressed as the root mean square (RMS) of the grand averages of the epoched waveforms within a window of 250 ms beginning 30 ms after stimulus onset. The amplitude data were log-transformed prior to statistical analysis to stabilize the variance across conditions (Zacharias et al. 2011).

Residual Noise amplitude

To estimate the residual noise amplitude present in the average waveform, the variance across epochs was firstly calculated for each sample point of the waveform from onset to 600 ms post-stimulus onset. The mean variance across the waveform corresponds to the EEG noise power (in μV^2). The residual noise amplitude in the average waveform (in µV) was then estimated by dividing the square root of the EEG noise power by the square root of the number of epochs.

Measure of response detection

Objective measures of CAEP response presence were calculated using the Hotelling's T^2 statistic, applied on the recorded epochs in a time range covering from 51 to 347 ms after onset for each testing condition. In this time range, the epochs were reduced to 9 equidistant (i.e 33 ms wide) averaged voltage levels also called bins. The bin width and number of bins were chosen based on earlier data (Golding et al. 2009). Response detection was based on the p-value obtained from a one-sample Hotelling's T^2 test on the bin-averaged data. For every testing condition, using a sequential test strategy, the p-value was calculated after the collection of 9 epochs and subsequently, every additional two epochs. As the average SOA was 2 s, the p-value versus testing time could be presented for every subject. First, a measure of response detectability strength was calculated by converting the p-values into z-scores (assuming a normative z-distribution) and by cumulative summation of the z-score values. Second, detection sensitivities measures were calculated. For the detection sensitivity measure, the multiple testing in such sequential p-value estimation increases the probability of response falsely detected (i.e. false positive rate). Therefore, a correction of the significance level p was calculated using non-trial epochs. During the recording, a minimum of 780 non-trial epochs per subject was collected using portion of EEG signal selected randomly between 1 and 1.3 s after any stimulus onset (only if the SOA was higher than 2 s). Using 455 sets of 52 non-trial epochs per subject, we found that the p-value criteria had to be lowered to 0.006 to keep the false detection rate at 5%.

Statistical analysis

Statistical analysis was conducted using a repeated measures analysis of variance (ANOVA) on log-transformed RMS amplitudes and the measures of response detection using Statistica 7.1 (StatSoft, Inc.). Greenhouse–Geisser corrections for sphericity were applied, as indicated by the cited ε value. Post-hoc comparisons were calculated using Tukey's test (Keselman 1998; Park et al. 2009).

Results

Behavioral thresholds

The means and standard deviations of the behavioral thresholds are depicted in Table 1. It shows higher thresholds for the 50ms PTs when compared to the 500 ms PT stimuli (on average by 2.1 dB). Moreover, it indicates that thresholds for the MTs are generally higher than for the PTs (on average by 2.9 dB).

Fig. 1

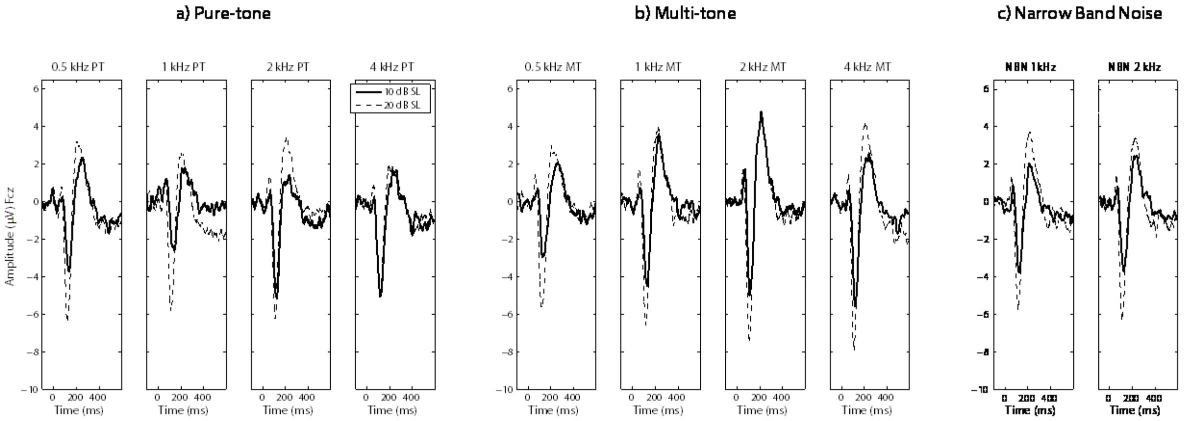

Fig. 1: Grand mean CAEP waveforms for the pure-tone (PT), multi-tone (MT) and narrow-band noise stimuli at 10 and 20 dB SL.

Figure 1 displays the CAEP waveforms elicited by the different auditory stimuli. The response morphology typically shows a robust P1, N1, P2 response with amplitudes that vary as a function of the signal type and presentation level.

Fig. 2

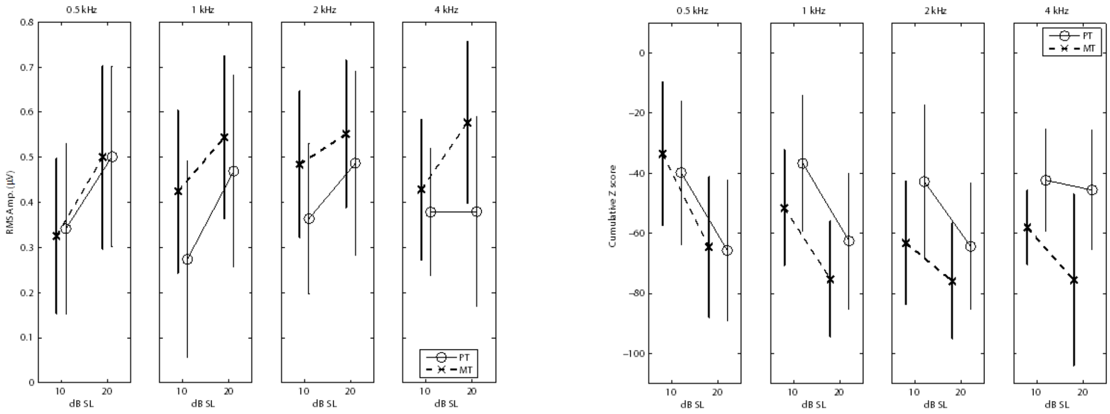

Fig. 2: RMS amplitudes (left) and cumulative z-scores (right) of the CAEPs recorded for PTs (solid line) and MTs (dashed line) with frequencies 0.5, 1, 2 and 4 kHz. Error bars are depicting standard deviations.

RMS amplitudes and objective detection (cumulative z-scores)

Figure 2 summarizes the RMS amplitudes and cumulative z-score values across 16 subjects for the PT and MT stimuli with frequencies 0.5, 1, 2 and 4 kHz at intensities 10 and 20 SL averaged across channels (i.e. FCz and Cz). A 4-way 2 x 2 x 4 x 2 analysis of variance (ANOVA) was performed on both CAEP RMS amplitudes and cumulative z-scores, with EEG channel (FCz-M versus Cz-M), stimulus (PT versus MT), frequency (0.5, 1, 2 and 4 kHz) and sensation level (10 versus 20 dB SL) as repeated-measures variables. Relative to PTs, the MTs showed a significant increase in RMS amplitudes (F(1,15) = 53.87; p = 0.000002; ε = 1) and significantly more negative cumulative z-scores (F(1,15) = 33.19; p = 0.00004; ε = 1), which is associated with better detection of the CAEP. An interaction between stimulus and frequency was present (RMS amplitude: F(3,45) = 5.63; p = 0.006; ε = 0.73; z-score: F(3,45) = 5.65; p = 0.003; ε = 1) and a Tukey post-hoc analysis revealed no significant RMS amplitude differences for the

500 Hz between the MTs and PTs (RMS amplitude: $p=0.99$; z-score: $p=0.99$) while significant differences were found for the other frequencies (i.e. 1, 2 and 4 kHz) ($p < 0.05$). Table 3 shows the RMS amplitude ratio MT/PT for the two levels of each frequency tested. Averaged across the 1, 2 and 4 kHz stimuli, MT stimuli elicited CAEP responses which were in average 29% larger in amplitude compared to PT stimuli. There was a significant main effect of channel with larger RMS amplitudes ($F(1,15) = 85.46$; $p < 0.000001$; $\varepsilon = 1$) and lower cumulative z-scores ($F(1,15) = 27.28$; $p = 0.00001$; $\varepsilon = 1$) for FCz-M (mean RMS: 0.49 µV; 95% confidence interval 0.41 – 0.57 µV; mean cumulative z-scores: -56; 95% confidence interval -62 -49) versus Cz-M channels (mean RMS: 0.38 µV; 95% confidence interval 0.41 – 0.57 µV; mean cumulative z-scores: -47; 95% confidence interval -55 -38). A main effect of level was observed, with higher sensation levels showing significantly larger RMS amplitudes ($F(1,15) = 57.17$; $p = 0.000002$; $\varepsilon = 1$) and more negative cumulative z-scores ($F(1,15) = 43.08$; $p < 0.00001$; $\varepsilon = 1$).

RMS amplitude for NBN, MT and PT at frequencies 1 and 2 kHz

In order to investigate the effect of the spectral complexity of the auditory stimulus on the cortical response amplitude, the CAEP RMS amplitudes elicited by one-octave NBN, one-octave MT and PT stimuli were compared in a 2 x 3 x 2 x 2 repeated-measures ANOVA with channel, stimulus, frequency and level. Fig. 3 shows RMS CAEP amplitudes as a function of stimulus, for the two frequencies (1000 and 2000 Hz) and the stimulus level (10, 20 dB SL). A main stimulus effect was found ($F(2,30) = 15.70$; $p = 0.00009$; $\varepsilon = 0.91$). Tukey pairwise comparisons revealed no significant difference between PT and NBN ($p = 0.49$) but a significant difference between MT stimuli and both NBN and PT ($p < 0.001$).

Fig. 3

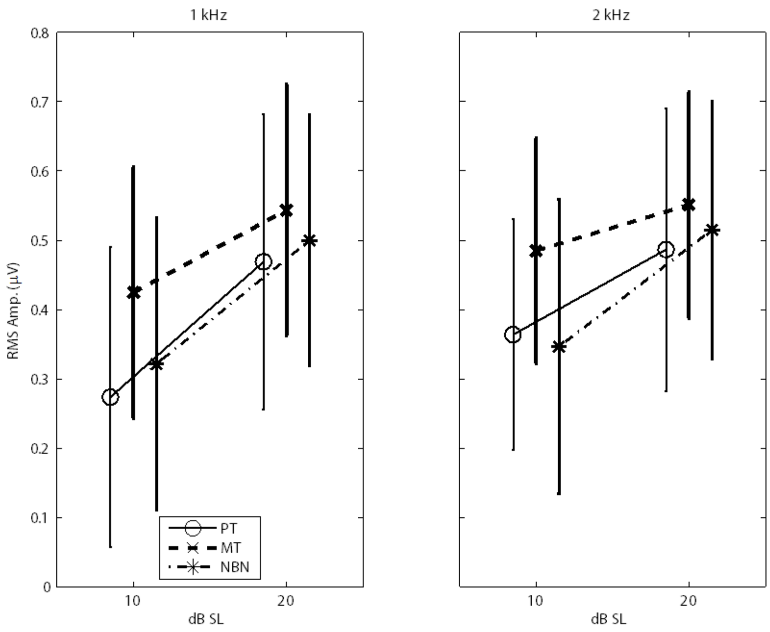

Fig. 3. CAEP RMS amplitudes, collapsed over electrode positions FCz and Cz, for 1 and 2 kHz PT, MT and NBN stimuli for two sensation levels 10 dB, 20 dB. Vertical lines represent standard deviations between participants.

Group difference analysis (Normal-hearing versus Hearing-impaired)

RMS amplitudes and objective detection (cumulative z-scores)

To investigate the effect of hearing loss on the CAEP, we combined data of the present study with data collected previously and reported in Bardy et al. (in press) in which CAEPs were recorded in normal-hearing adults using the same auditory stimuli and recording protocol. Two separate 5-way 2 x 2 x 4 x 2 x 2 ANOVA were performed on the RMS amplitude and the cumulative z-scores. The between-groups variable was hearing loss status (normal-hearing versus hearing-impaired) while the repeated-measures variables were EEG channel (Fz-M versus Cz-M), stimulus (PT versus MT), frequency (0.5, 1, 2 and 4 kHz) and sensation level

(10 versus 20 dB SL) (see Fig. 4). No significant main effect of group was observed for either the RMS amplitude (F(1,14) = 0.0007; p = 0.98; ε = 1) or the cumulative z-scores (F(1,14) = 3.43; p = 0.08; ε = 1).As expected a main effect of stimulus was observed (RMS amplitude: (F(1,14) = 56.50; p = 0.000003; ε = 1); cumulative z-scores: (F(1,14) = 43.66; p = 0.00001; ε = 1) and the interaction Group x Stimulus was not significant (F(1,14) = 1.32; p = 0.27; ε = 1) which supports the fact that the MT have the potential to increase CAEP detection in both NH and HI subjects.

Fig. 4

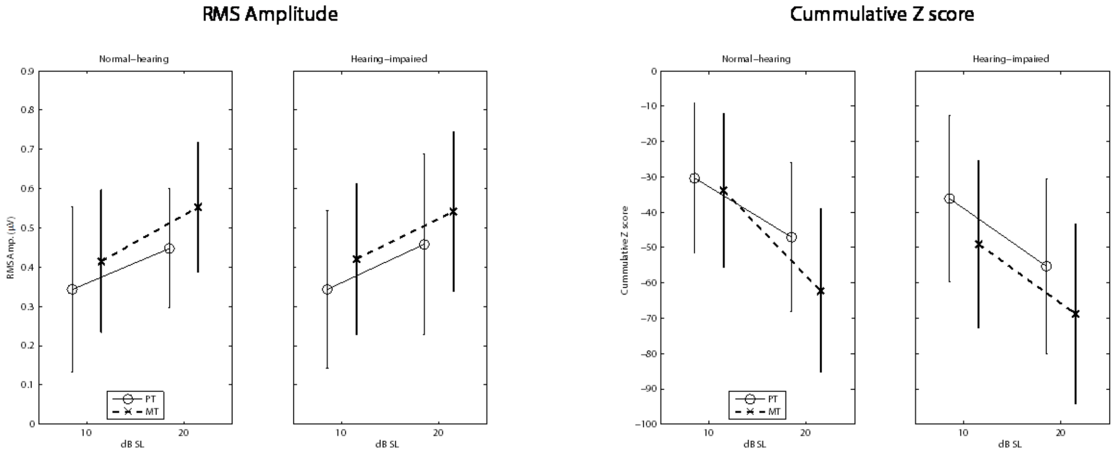

Fig. 4: RMS amplitude (left) and Cummulative z-score (right) for CAEPs recorded for PTs (solid line) and MTs (dashed line) for NH and HI subjects at 10 and 20 dB SL. Each point represent the average value across the four frequencies 0.5, 1, 2 and 4 kHz and the channels FCz and Cz. Error bars are depicting standard deviations.

Figure 5 displays the percentage of hearing-impaired and normal-hearing subjects for whom a CAEP was detected at channel FCz-M as a function of sensation level, stimulus frequency and stimulus type (i.e. PT versus MT). Table 3 shows that after 52 epochs recorded at 10 dB SL, the sensitivity is 68% for normal-hearing subjects and 80% for hearing-impaired subjects using MT. Taking in consideration the interaction between frequency and stimulus type, the mean sensitivity at 10 dB SL increases when combining the MT frequencies 1, 2 and 4 kHz and PT frequency 500 Hz. A present cortical response is then detected for 78% of NH subjects and 84% of hearing-impaired subjects. Of interest, the mean residual noise amplitude in the average waveform after 52 epochs was 2.01 μV in HI and 2.04 μV in NH subjects with a standard deviation of 0.31μV and 0.36 μV. It corresponds to a noise amplitude per epoch of 14.50 μV in HI and 14.73 in NH subjects with a standard deviation of 2.25 μV and 2.64μV. The residual noise amplitude results were obtained using a EEG signal filtered between 0.01 and 30 Hz.

Fig. 5

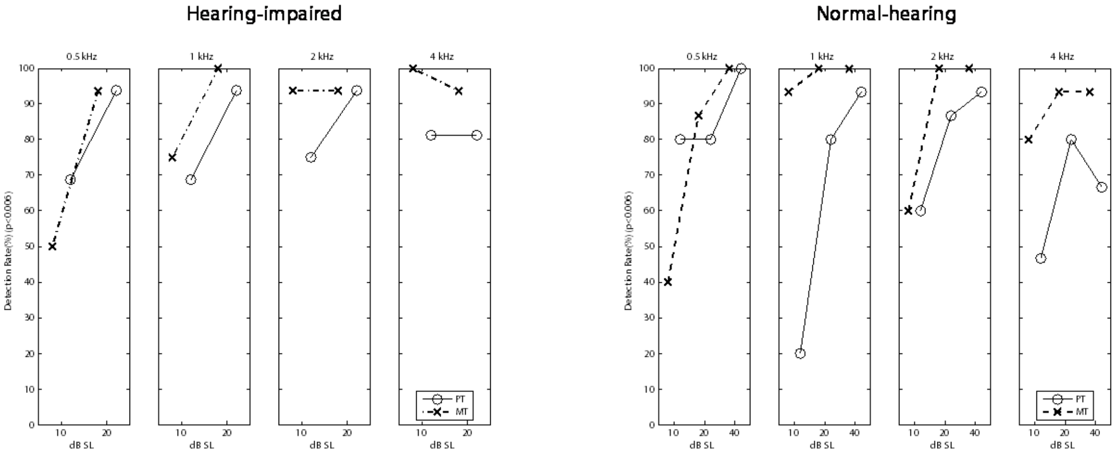

Fig. 5: Percentage of subjects for whom a CAEP was detected at FCz (using an objective detection criterion of $p < 0.006$) for PT and MT stimuli, at 10 and 20 dB SL for hearing-impaired (left) and at 10, 20 and 40 dB SL normal-hearing subjects (right), for frequencies 0.5, 1, 2 and 4 kHz after 52 epochs which corresponds to 104 s recording time per condition.

Discussion

In this study, CAEPs were recorded in 16 hearing-impaired participants using four pure-tone (PT) with frequencies 0.5, 1, 2, 4 kHz, four one-octave multi-tone (MT) stimuli with the same center frequency and two one-octave narrow-bands noise (NBN) centered around 1 and 2 kHz. All stimuli were presented at 10 and 20 dB above threshold. The results showed larger CAEP amplitudes for MTs when compared to PTs for frequencies 1, 2 and 4 kHz in hearing-impaired subjects. The amplitude increase of the CAEP was associated with a significantly better objective CAEP detection using the Hotelling's T^2 statistic. These findings are in agreement with previous results in normal-hearing subjects (Bardy et al. in press). For the 1 and 2 kHz stimuli, no significant amplitude difference was found between the PT and the NBN, suggesting that the spectral complexity more than the bandwidth of the auditory stimuli affects the CAEP amplitude. Bardy et al. (in press) discusses possible physiological explanations of the CAEP amplitude increase, not repeated in this discussion. However, no studies have investigated the effect of multi-tone stimuli compared to PTs on the CAEP amplitude in populations with a hearing loss.

Behavioral Threshold

The automatic computerized audiometry revealed elevated mean behavioral thresholds for the short PT (i.e. 50 ms) compared to the long PT (i.e. 500 ms) stimuli. This is in agreement with previous research, where shorter stimuli are associated with both higher thresholds (Olsen and Carhart 1966) and reduced loudness (Epstein and Florentine 2006). Moreover, the data showed that the mean behavioral thresholds for three out of four MTs were higher compared to the PT stimuli of the same duration. It is well recognized that the spectral bandwidth of complex sounds such as the MT, where components are located in multiple critical bands, plays an important role in determining loudness and threshold. As Zwicker et al. (1957) showed, increasing bandwidth while keeping the overall SPL constant causes loudness to increase at medium and high levels, but to decrease at low input levels. At medium and high input levels, the loudness increases in the original narrow region is lower than the increase in loudness caused by having more than one frequency region contributing to loudness. At low input levels, such as near threshold, the very steep growth of loudness with input level means that the reverse is true: the loudness decreases in the original narrow region is greater than the increase in loudness caused by having multiple frequency regions contribute to loudness. For the same reason, hearing thresholds should be greater for the MT stimulus than for the PT stimulus, even though the MT stimulus is louder at higher input levels. These effects are all well modelled by the Moore et al. (1997) loudness model. However, it is unlikely that the cortical response amplitude growth observed for the MTs compared to the PTs is caused by the difference in loudness growth between the two stimuli alone. If this was the case, similar cortical amplitude growth should be observed between the CAEPs recorded in response to NBN and MT stimuli, as they share the same bandwidth.

Difference between normal-hearing (NH) and hearing-impaired (HI) group

According to (Higgins and Turner 1990), the integration of complex sounds that are wider than the critical bandwidth of the auditory filter occurs over a broader frequency range for hearing-impaired subjects when compared to normal-hearing subjects (i.e. summing the intensities of more widely separated frequency components). However, the absence of interaction between subject and stimulus indicates that the broader-than-normal critical bandwidths of auditory filters normally observed for the hearing-impaired subjects does not change the stimulus effect (i.e. larger CAEPs using MTs versus PTs). Considering that the subjects tested in this study were presenting a mild-to-moderate degree of hearing loss, further research would need to investigate if a difference can be observed for more severe degrees of hearing loss. Moreover, in combination with data recorded with an identical protocol in Bardy et al. (in press), the present results show the trend for the responses to be more easily detected (p = 0.08) for hearing-impaired, as compared to the normal-hearing subjects in response to frequency-specific stimuli presented at 10 and 20 dB SL. Considering the age group difference between the HI (mean 66 years 6 months; SD 14 years 6 months) and the NH (mean 31 years; SD 6 years 10 months) group, Goodin et al. (1978) reported a decrease of the CAEP amplitude with age. Therefore, it is unlikely that the age group difference is the reason for the trend toward better detection of the CAEP for the HI group. In Contrast, this might reflect the CAEP amplitude growth curve difference between the two groups which has been reported by (Morita et al. 2003). More specifically, Morita et al. (2003) showed that hearing-impaired subjects have steeper CAEP amplitude growth curves than normal-hearing subjects, which was also associated with larger CAEP amplitudes for stimuli presented at low sensation levels. In both groups, the mean detection sensitivity collapsed over four frequencies was higher than 68% and 95% at 10 and 20 dB SL respectively after 52 epochs recorded (104 s) using MTs.

CAEPs detection sensitivity

The good detection sensitivity of CAEPs at low sensation levels in this study might reflect several strategies employed to enhance the cortical amplitude and decrease the adaptation of the cortical response. First, the cortical amplitude enhancement using MTs is relevant, as any 10% amplitude increase could decrease testing time up to 21 %, assuming that the signal-to-noise ratio (SNR) as a voltage ratio is proportional to the square root of the number of sweeps. Second, strategies used in this study such as multi-stimuli randomization, multi-level randomization and SOA randomization between 1 and 3 s makes the sound sequence to be less predictable. Even though this study does not control for presentation randomization, which was not found to significantly affect response amplitude in Lightfoot and Kennedy (2006), all these factors have the potential to reduce the adaptation of the cortical response and therefore be beneficial for CAEP detection for hearing threshold estimation.

Further sensitivity improvement at low sensation levels could potentially be achieved by the number of epochs, which was fixed to 52 epochs in the present study, might need to be increases in order to reach lower residual noise values necessary to detect low amplitude CAEP responses.

Clinical significance

The present study showed an advantage using MT over PT stimuli for frequencies 1, 2 and 4 kHz in hearing-impaired subjects. It also demonstrated an increased sensitivity of CAEP detection when testing 10 or 20 dB above threshold. As MT stimuli evoke enhanced responses in a normal-hearing population as well (Bardy et al. in press), a significant potential exists to use the newly designed MT stimuli for hearing threshold estimation in both populations. Due to the narrow-band characteristics of the MT stimuli, a possible limitation of using these stimuli compared to PT stimuli can be the underestimation of hearing thresholds at the center frequency in case of steeply-sloping or notched audiometric configurations (Walker et al. 1984).

Further research.

The current study showed that CAEP detection sensitivities increased significantly when using more complex tones, which is beneficial for clinical practice. However, not all cortical responses were detected at levels above behavioral threshold when one would expect to. This behavior has been confirmed in other studies using objective detection of CAEPs (Hoth 1993; Tsui et al. 2002; Van Dun et al. 2014), albeit with significantly different stimulus parameters and detection paradigms. As this research was conducted using a fixed set of parameters and off-line processing, there is an urgent need to implement intelligent online processing schemes able to adapt parameters during testing depending on the recorded response. This area will be the scope of future research.

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References

Alain C, L Woods D, Covarrubias D. (1997) Activation of duration-sensitive auditory cortical fields in humans. Electroencephalogr. Clin. Neurophysiol. 104: 531-539.

Bardy F, Van Dun B, Dillon H, Cowan R. (2014) Least-squares (LS) deconvolution of a series of overlapping cortical auditory evoked potentials: a simulation and experimental study. J. Neural Eng. 11: 046016.

Bardy F, Van Dun B, Dillon H, McMahon CM. (2014) Deconvolution of overlapping cortical auditory evoked potentials (CAEPs) recorded using short stimulus onset-asynchrony (SOA) ranges. Clin. Neurophysiol. 125: 814-826.

Bardy F, Van Dun B, Dillon H. (in press) "Bigger is better: Increasing cortical response amplitude via stimulus spectral complexity". Ear Hear.

Billings CJ, Tremblay KL, Stecker GC, Tolin WM. (2009) Human evoked cortical activity to signal-to-noise ratio and absolute signal level. Hear. Res. 254: 15-24.

Butler RA. (1968) Effect of changes in stimulus frequency and intensity on habituation of the human vertex potential. J. Acoust. Soc. Am. 44: 945-950.

Commission IE. (2006) Simulators of human head and ear - Part 5: 2 cm3 coupler for the measurement of hearing aids and earphones coupled to the ear by means of ear inserts*IEC 60318-5*, IEC, Geneva.

Convery E, Keidser G, Seeto M, Freeston K, Zhou D, Dillon H. (2014) Identification of Conductive Hearing Loss Using Air Conduction Tests Alone: Reliability and Validity of an Automatic Test Battery. Ear Hear. 35: e1-e8.

Delorme A, Makeig S. (2003) EEGLAB: an open source toolbox for analysis of single-trial EEG dynamics including independent component analysis. J. Neurosci. Methods 134: 9-21.

Epstein M, Florentine M. (2006) Loudness of brief tones measured by magnitude estimation and loudness matching. J. Acoust. Soc. Am. 119: 1943-1945.

Florentine M, Buus S, Scharf B, Zwicker E. (1980) Frequency selectivity in normally-hearing and hearing-impaired observers. J. Speech Lang. Hear. Res. 23: 646-669.

Golding M, Dillon H, Seymour J, Carter L. (2009) The detection of adult cortical auditory evoked potentials (CAEPs) using an automated statistic and visual detection. Int. J. Audiol. 48: 833-42.

Goodin DS, Squires KC, Henderson BH, Starr A. (1978) Age-related variations in evoked potentials to auditory stimuli in normal human subjects. Electroencephalogr. Clin. Neurophysiol. 44: 447-458.

Higgins MB, Turner CW. (1990) Summation bandwidths at threshold in normal and hearing-impaired listeners. The Journal of the Acoustical Society of America 88: 2625-2630.

Hoth S. (1993) Computer-aided hearing threshold determination from cortical auditory evoked potentials. Scand. Audiol. 22: 165-177.

Jacobson GPP, Lombardi DMMA, Gibbens NDMA, Ahmad BKM, Newman CWP. (1992) The effects of stimulus frequency and recording site on the amplitude and latency of multichannel cortical auditory evoked potential (CAEP) component N1. Ear Hear. 13: 300-306.

Jenkins III J, Idsardi WJ, Poeppel D. (2010) The analysis of simple and complex auditory signals in human auditory cortex: magnetoencephalographic evidence from M100 modulation. Ear Hear. 31: 515-526.

Keselman H. (1998) Testing treatment effects in repeated measures designs: An update for psychophysiological researchers. Psychophysiol. 35: 470-478.

Korczak PA, Kurtzberg D, Stapells DR. (2005) Effects of sensorineural hearing loss and personal hearing aids on cortical event-related potential and behavioral measures of speech-sound processing. Ear Hear. 26: 165-185.

Lightfoot G, Kennedy V. (2006) Cortical Electric Response Audiometry Hearing Threshold Estimation: Accuracy, Speed, and the Effects of Stimulus Presentation Features. Ear Hear. 27: 443-456.

Margolis RH, Goldberg SM. (1980) Auditory frequency selectivity in normal and presbycusic subjects. J. Speech Lang. Hear. Res. 23: 603-613.

Mathew AK, Purdy SC, Welch D, Pontoppidan NH, Rønne FM. (2015) Electrophysiological and behavioural processing of complex acoustic cues. Clin. Neurophysiol.

Moore BC, Glasberg BR, Baer T. (1997) A model for the prediction of thresholds, loudness, and partial loudness. Journal of the Audio Engineering Society 45: 224-240.

Morita T, Naito Y, Nagamine T, Fujiki N, Shibasaki H, Ito J. (2003) Enhanced activation of the auditory cortex in patients with inner-ear hearing impairment: a magnetoencephalographic study. Clin. Neurophysiol. 114: 851-859.

Oates PA, Kurtzberg D, Stapells DR. (2002) Effects of sensorineural hearing loss on cortical event-related potential and behavioral measures of speech-sound processing. Ear Hear. 23: 399-415.

Olsen WO, Carhart R. (1966) Integration of acoustic power at threshold by normal hearers. The Journal of the Acoustical Society of America 40: 591-599.

Onishi S, Davis S. (1968) Effects of duration and rise time of tone bursts on evoked V potentials. J. Acoust. Soc. Am. 44: 582-590.

Organization IS. (1994) Reference zero for the calibration of audiometric equipment. Part 2: Reference equivalent threshold sound pressure levels for pure tones and insert earphones*Acoustics*, International Organization for Standardization Geneva, Geneva.

Park E, Cho M, Ki C. (2009) Correct use of repeated-measures analysis of variance. Korean J Lab Med 29: 1–9.

Picton T, Goodman W, Bryce D. (1970) Amplitude of evoked responses to tones of high intensity. Acta Otolaryngol. (Stockh.) 70: 77-82.

Picton T. (2011) Late auditory evoked potentials: Changing the things which are. In: *Human auditory evoked potentials*. Stach BA, ed. Plural Pub Incorporated, San Diego, USA.

Seither-Preisler A, Krumbholz K, Lütkenhöner B. (2003) Sensitivity of the neuromagnetic N100m deflection to spectral bandwidth: a function of the auditory periphery? Audiology and Neurotology 8: 322-337.

Shahin A, Roberts LE, Pantev C, Trainor LJ, Ross B. (2005) Modulation of P2 auditory-evoked responses by the spectral complexity of musical sounds. Neuroreport 16: 1781-1785.

Soeta Y, Nakagawa S. (2006) Complex tone processing and critical band in the human auditory cortex. Hear. Res. 222: 125-132.

Tsui B, Wong LL, Wong EC. (2002) Accuracy of cortical evoked response audiometry in the identification of non-organic hearing loss: Exactitud de la audiometría por respuestas corticales evocadas en la identificación de hipoacusia no orgánica. Int. J. Audiol. 41: 330-333.

Van Dun B, Carter L, Dillon H. (2012) Sensitivity of cortical auditory evoked potential detection for hearing-impaired infants in response to short speech sounds. Audiol. Res. 2: e13, 65-76.

Van Dun B, Dillon H, Seeto M. (2014) Estimating Hearing Thresholds in Hearing-Impaired Adults through Objective Detection of Cortical Auditory Evoked Potentials. J. Am. Acad. Audiol.

Walker G, Dillon H, Byme D. (1984) Sound field audiometry: Recommended stimuli and procedures. Ear Hear. 5: 13-21.

Zacharias N, Sielużycki C, Kordecki W, König R, Heil P. (2011) The M100 component of evoked magnetic fields differs by scaling factors: Implications for signal averaging. Psychophysiol. 48: 1069-1082.

Zwicker E, Flottorp G, Stevens SS. (1957) Critical band width in loudness summation. The Journal of the Acoustical Society of America 29: 548-557.