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#### Clinical Neurophysiology xxx (2015) xxx-xxx



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journal homepage: www.elsevier.com/locate/clinph

# Electrophysiological and behavioural processing of complex acoustic cues

Abin Kuruvilla Mathew<sup>a,\*</sup>, Suzanne C. Purdy<sup>a</sup>, David Welch<sup>b</sup>, Niels H. Pontoppidan<sup>c</sup>, Filip Marchman Rønne<sup>c</sup>

<sup>a</sup> Discipline of Speech Science, School of Psychology, University of Auckland, Auckland, New Zealand
<sup>b</sup> Section of Audiology, University of Auckland, Auckland, New Zealand
<sup>c</sup> Eriksholm Research Centre, Denmark

#### ARTICLE INFO

Article history: Accepted 1 April 2015 Available online xxxx

Keywords: Cortical evoked potentials Acoustic change complex Complex tones Pitch Temporal fine structure Hearing loss

#### HIGHLIGHTS

- Cortical auditory evoked responses are sensitive to the encoding complex acoustic cues important for pitch perception.
- Combined approach using behavioural and electrophysiological tests are useful to measure pitch processing in individuals with normal hearing and sensorineural hearing loss.
- Individuals with sensorineural hearing loss have reduced sensitivity to complex acoustic cues compared to controls.

#### ABSTRACT

*Objectives*: To examine behavioural and neural processing of pitch cues in adults with normal hearing (NH) and adults with sensorineural hearing loss (SNHL).

*Methods*: All participants completed a test of behavioural sensitivity to pitch cues using the TFS1 test (Moore and Sek, 2009a). Cortical potentials (N1, P2 and acoustic change complex) were recorded in response to frequency shifted (deltaF) tone complexes in an 'ABA' pattern.

*Results:* The SNHL group performed more poorly than the NH group for the TFS1 test. P2 was more reflective of pitch differences between the complexes than N1. The presence of acoustic change complex in response to the TFS transitions in the ABA stimulus varied with deltaF. Acoustic change complex amplitudes were reduced for the group with SNHL compared to controls.

*Conclusion:* Behavioural performance and cortical responses reflect pitch processing depending on the salience of pitch cues.

*Significance:* These data support the use of cortical potentials and behavioural sensitivity tests to measure processing of complex acoustic cues in people with hearing loss. This approach has potential for evaluation of benefit from auditory training and hearing instrument digital signal processing strategies.

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#### 1. Introduction

E-mail address: amat527@aucklanduni.ac.nz (A.K. Mathew).

The impact of sensorineural hearing loss (SNHL) is particularly noticeable while listening to speech in noisy backgrounds (Festen and Plomp, 1990; Gordon-Salant, 1985). Even when amplification is provided, a persistent complaint of hearing aid users is difficulty understanding speech in noise (Kochkin, 2007). A listener's ability to extract cues for pitch perception is an important factor for successful communication in background noise. The main acoustic cues contributing to the streaming of signals in noise are the

#### http://dx.doi.org/10.1016/j.clinph.2015.04.002

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Abbreviations: CAEPs, cortical auditory evoked potentials; Cz, central zero; Fz, frontal zero; SNR, signal to noise ratio; ENV, envelope; TFS, temporal fine structure; NH, normal hearing; SNHL, sensorineural hearing loss; TEN, threshold equalising noise; ANOVA, analysis of variance.

<sup>\*</sup> Corresponding author at: Discipline of Speech Science, School of Psychology 721.321, Tamaki Campus, The University of Auckland, Private Bag 92019, Auckland 1142, New Zealand.

slowly varying temporal envelope (ENV) and the rapidly varying temporal fine structure (TFS) (Moore, 2014). While ENV cues are primarily important for speech perception in quiet, TFS cues are important for speech perception in noise, sound localisation, music perception, and pitch perception (Moore, 2008). Recent studies using psychophysical measures have shown that listeners with SNHL have reduced ability to benefit from TFS information while the perception of ENV information is well preserved (Hopkins et al., 2008; Lorenzi et al., 2006, 2009; Moore et al., 2006b). It is thought that this lack of TFS sensitivity might account for poor speech understanding in noise and music perception in individuals with SNHL. Although most studies report group differences in the ability to make use of TFS cues between people with normal hearing (NH) and those with SNHL, performance varies greatly within each group, despite similar audiometric configurations (Hopkins et al., 2008: Hopkins and Moore, 2010: Strelcvk and Dau, 2009).

The processing of pitch-related acoustic cues can be investigated using objective cortical auditory evoked potentials (CAEPs) that reflect differential neural encoding of stimulus acoustic cues. CAEPs elicited using brief stimuli (clicks, tone bursts) consist of three peaks (P1-N1-P2) that occur within 300 ms (ms) after stimulus onset (Martin et al., 2008). N1 is a transient response evoked by short-term envelope change (Onishi and Davis, 1968). P2 is sensitive to attention and stimulus parameters such as intensity and pitch (Crowley and Colrain, 2004), as well as musical experience (Seppänen et al., 2012). CAEPs elicited using complex long-duration stimuli with acoustic changes within the stimulus have multiple N1-P2 complexes evoked by the stimulus onset, the acoustic change, and the stimulus offset (Digeser et al., 2009; Martin et al., 2008; Ostroff et al., 1998; Sharma et al., 2000). Cortical responses encoding the change in an ongoing stimulus have been described as the acoustic change complex (Martin and Boothroyd, 1999). Acoustic change complexes have been recorded in response to both speech and non-speech sounds (Martin and Boothroyd, 1999; Ostroff et al., 1998), as well as to acoustic changes within a speech sound such as formant frequency transition within a vowel (Martin and Boothroyd, 2000). The acoustic change complex shows distinct neural patterns in response to changing speech syllables in adults using hearing aids and cochlear implants (Friesen and Tremblay, 2006; Tremblay et al., 2006). The acoustic change complex was used in the current study to show differential neural encoding of complex acoustic cues important for pitch processing. Establishing a link between electrophysiological and behavioural TFS measures may help future research determine optimal hearing aid settings for robust speech perception in noise. Moreover, it would be useful to determine pitch-related enhancements in cortical responses corresponding to specific stimulus acoustic cues.

Sensitivity to changes in pitch cues has been extensively studied using complex tones (Hopkins and Moore, 2007; Moore and Moore, 2003; Schouten et al., 1962). Complex tones resemble the sounds of vowels in normal speech and sounds produced by many musical instruments. Pitch extraction of a complex tone primarily depends on the harmonic resolvability and this in turn depends on the number in the harmonic sequence, *N*, rather than the absolute FO (Houtsma and Smurzynski, 1990; Plack et al., 2005). Pitch discrimination is usually good when filtered complex tones contain only low-numbered harmonics, which may be resolved at the level of the cochlea, i.e. N < 8, due to access to both place (spectral) and TFS (temporal) cues. Complexes with only high-numbered harmonics (partially resolved), with N between 8 and 12 harmonics produce a weaker pitch percept which might be conveyed solely based on TFS information (Bernstein and Oxenham, 2003; Moore et al., 2006a). Hence, pitch perception depends on the salience of pitch cues. Most cochlear implants have only a small number of channels and thus TFS cues important for pitch perception are typically not successfully encoded by these instruments (Wilson and Dorman, 2008). On the other hand, although hearing aids restore audibility (ENV cues) and convey TFS cues, SNHL listeners cannot utilise TFS cues for pitch and music perception (Chasin and Russo, 2004). The current study aimed to increase understanding of behavioural pitch discrimination abilities in NH adults and adults with either mild or high frequency SNHL, using low- and high-numbered harmonic complex tones. Behavioural results were compared to the neural encoding of pitch cues measured using the acoustic change complex. This combined approach using behavioural and electrophysiological measures will help determine stimulus acoustic cues dominant for pitch processing at the level of cortex.

#### 2. Materials and methods

#### 2.1. Participants

Ten young adults with NH aged 21-36 years (mean: 29 years, SD 4.6) and 9 adults with either mild or high frequency SNHL aged 20-55 years (mean: 37 years, SD 11.8) were recruited. Although there is a considerable variation in the age of participants, age effects on CAEPs are commonly reported when results are compared between young adults and people aged 60+ (Harris et al., 2009; Kim et al., 2012; Tremblay et al., 2004). Picton et al. (1984) who studied CAEPs across a broad age range from 20 to 79 years found no age effects for P1, N1, and P2 latencies and amplitudes. All NH adults were right handed, English speakers, with normal Type A tympanograms with present acoustic reflexes. Audiometric thresholds of the listeners with SNHL are shown in Table 1. All participants in the SNHL group were right handed, English speakers and had air-bone gaps of less than 15 dB and normal tympanograms. Audiograms for the NH and SNHL participants are shown in Fig. 1. Written informed consent was obtained from all participants before testing. The study was approved by the University of Auckland Human Participants Ethics Committee.

#### 2.2. Stimulus conditions

Processing of pitch differences were tested for two stimulus conditions with strong (N6) and weak pitch salience (N12). Stimuli consisted of bandpass filtered harmonic and frequency shifted (deltaF) complex tones. Pitch processing was separately investigated using both spectral excitation and TFS cues (N6 condition) and TFS cues alone (N12 condition). Here *N* is used to refer to the harmonic number corresponding to the centre of the bandpass filter through which all tones were passed. Spectrograms of the stimuli are shown in Fig. 2. Values of the fundamental frequency (F0) and number of components in the passbands were 200 Hz and 3 for the N6 stimulus condition and 100 Hz and 5 for the N12 stimulus condition, respectively. The filter centre frequency

Audiometric thresholds measured for the right ear for each SNHL participant.

| Listener | Frequency (kHz) |     |    |    |    |    |  |  |
|----------|-----------------|-----|----|----|----|----|--|--|
|          | 0.25            | 0.5 | 1  | 2  | 4  | 8  |  |  |
| SNHL1    | 15              | 10  | 10 | 35 | 55 | 65 |  |  |
| SNHL2    | 5               | 5   | 10 | 10 | 30 | 35 |  |  |
| SNHL3    | 10              | 15  | 15 | 20 | 60 | 80 |  |  |
| SNHL4    | 10              | 15  | 10 | 25 | 35 | 45 |  |  |
| SNHL5    | 15              | 15  | 15 | 15 | 35 | 30 |  |  |
| SNHL6    | 20              | 30  | 10 | 10 | 5  | 5  |  |  |
| SNHL7    | 10              | 15  | 5  | 25 | 25 | 25 |  |  |
| SNHL8    | 10              | 10  | 30 | 10 | 5  | 5  |  |  |
| SNHL9    | 30              | 30  | 35 | 45 | 35 | 55 |  |  |



**Fig. 1.** Audiogram for the right ears of the 10 NH and nine SNHL participants. The thin and thick black lines represent the individual and mean audiograms of the SNHL participants. The thick white line and associated light-grey shaded area represent the mean audiometric thresholds and range for the NH participants, respectively. The dashed grey line indicates the audiometric inclusion criteria used in the present study.

was 1200 Hz for all stimuli. The lowest harmonic component within the passbands for the two conditions tested here was 1000 Hz. These stimulus parameters resulted in tone complexes with resolved (N6) and mostly unresolved (N12) components.

#### 2.3. Behavioural sensitivity to pitch cues

Pitch discrimination was assessed behaviourally using the TFS1 test downloaded from http://hearing.psychol.cam.ac.uk (Moore and Sek, 2009a). This test involves discrimination of a harmonic complex tone (A) from an inharmonic complex tone (B) in which the harmonics are shifted upwards by the same amount in Hz, deltaF. The TFS1 test was a two-interval forced-choice task with feedback. Each interval contained four bursts of sound in either AAAA or ABAB sequences. On each trial, two consecutive intervals were presented, separated by 300 ms. Each interval contained four consecutive 200 ms tones, separated by 100 ms. Both 'A' and 'B' tone complexes had an envelope repetition rate with equal F0, but differed in their TFS due to the deltaF. The starting phases of the components in each and every tone were random and a new random selection was used for every presentation. This prevented

envelope shape from being used as a discrimination cue. A background threshold-equalising-noise (TEN), extending from 200 to 16.000 Hz, was used to mask combination tones (Moore et al., 2000). DeltaF was the manipulated variable, initially set to 0.5F0. DeltaF varied from trial to trial according to a 2-down 1-up procedure, to estimate the value of deltaF producing 70.7% correct responses (Levitt, 1971). The value of deltaF was changed by a factor of 1.953 until the first reversal, then by a factor of 1.5625 until the second reversal, and by a factor of 1.25 thereafter (Moore and Sek, 2009a). After eight reversals, the run was terminated and the threshold was estimated as the geometric mean of deltaF values at the last six reversals. The maximum possible shift is 0.5F0 and if this was reached three times during a run, the shift was fixed at 0.5F0 and 40 more trials were presented; in this case the procedure changed to a non-adaptive procedure and a score was given as the proportion correct. A score of 25 or below was regarded as chance (Sek and Moore, 2012). The TFS1 test was installed on a DELL Latitude 6420 laptop and stimuli were presented via Sennheiser HD 25 1-ii headphones in a double-walled sound-attenuating booth. The stimulus was presented monaurally to the right ear at 65 dB SPL for the NH listeners. For listeners with SNHL the presentation level was 65 dB SPL or greater to ensure that the level was at least 30 dB SL (sensation level re: 1000 Hz pure tone threshold). The developers of the TFS1 test note that results do not depend critically on level, provided that the SL is at least 30 dB, at the centre frequency being tested (Moore and Sek, 2009a). The background TEN was presented at +15 dB SNR, started 300 ms before the first tone in the interval and ended 300 ms after the last tone in the second interval. All participants completed a practice run to ensure they understood the task. This involved discrimination of simple sine waves in a two-interval forced-choice task, with each interval containing four bursts of sound. Following the practice run, one run was completed for each stimulus condition, with the N6 condition completed first.

#### 2.4. Electrophysiology

#### 2.4.1. Stimuli

N6 and N12 evoked potential stimuli were generated using MATLAB 2012b (Mathworks, Inc.) replicating the stimulus parameters described in Section 2.2. In order to elicit an acoustic change



Fig. 2. Spectrograms of the presented stimuli. Top portion shows the deltaF values for the N12 stimulus condition and bottom portion shows the deltaF values for the N6 stimulus condition.

4

complex an 'ABA' stimulus sequence was used in contrast to the AAAA/ABAB sequences used in the behavioural TFS1 test. As shown in Fig. 3, stimuli generated for evoked potential recordings were a sequence of three bandpass filtered complex tones ('ABA' stimulus triplets). A total of six stimulus triplets, consisting of three deltaF values (0, 30, and 50 Hz), for each stimulus condition (N6, N12), were generated. Within each stimulus condition, the A-tone complex was always harmonic and the B-tone complex varied depending on the deltaF value. The ABA sequence with deltaF = 0 Hz served as a control stimulus with no pitch-based acoustic change. Both 'A' and 'B' tone complexes had an envelope repetition rate with equal F0, but they differed in their TFS due to the deltaF. Onset phases of the components in each tone were randomised from 0° to 360°. A new randomization was selected for every stimulus presentation. Each stimulus triplet was 600 ms long with no gaps between the A-B-A stimuli. A Hanning window of 2 ms was used to shape the onset and offset of each complex tone to ensure a smooth transition and avoid audible clicks at A-B-A transitions. There were phase discontinuities and a small amount of spectral splatter at the transitions within the stimulus triplets and hence the deltaF = 0 Hz condition was used as a comparison condition to control for these effects. The magnitude of the splatter was computed in Praat software (www.praat.org), using a 10 ms Gaussian window. The splatter at the transition of each stimulus triplet was 6 dBV (0 Hz), 8 dBV (30 Hz), and 13 dBV (50 Hz) for the N6 stimulus condition and 10 dBV (0 Hz), 15 dBV (30 Hz), and 16 dBV (50 Hz) for the N12 stimulus condition. TEN was used to mask combination tones. All sound stimuli were presented to the right ear using an ER-3A 10  $\Omega$  insert earphone. Stimulus triplets were presented at 65 dB SPL for the NH participants and at a level that was at least 30 dB SL for the SNHL participants, with background noise at +15 dB SNR. Calibration was based on overall RMS level. Two blocks of 150 trials for each stimulus triplet were presented to the participant. The sequence of the six stimulus triplets was randomized across each block and participants. Interstimulus interval (ISI) was set to 1150 ms.

#### 2.4.2. Recording and pre-processing of electrophysiological data

All testing was performed in a double-walled sound-attenuating booth. Participants were seated comfortably on a reclining chair while watching a close captioned DVD of their choice (Lavoie et al., 2008). The Neuroscan SCAN™ (version 4.5) software



**Fig. 3.** Time waveforms of the 600 ms ABA stimulus triplets for the two stimulus conditions are shown: N12 and its deltaF values (left), and N6 and its deltaF values (right).

and Synamps2 was used for recording electrophysiological data. Cortical responses elicited by the stimuli were obtained using three EEG channels with 10 mm silver-silver chloride disc electrodes placed at Cz and Fz, referenced to the ipsilateral mastoid (M2). These electrode sites were selected because of the robust nature of auditory evoked potentials at the midline location. The ground electrode was located on the forehead and eye blink activity was monitored using electrodes placed above and below the right eye. Electrode impedances were kept under 3 kΩ. EEG was amplified with a gain of 1000 and sampled at the rate of 1000 Hz. EEG data were pre-processed using Neuroscan's built-in functions. Trials with eye blink artefacts were corrected offline using the ocular artefact rejection function in Neuroscan software (Neuroscan Inc., 2007): the vertical electro-oculogram (VEOG) channel was scanned for the maximum eye movement potential. EOG deviations of more than 10% from the maximum were used as indicators of blinks. A minimum of 20 blinks was required to estimate an average blink. The procedure discarded artefacts starting <400 ms before a previous artefact, to avoid double detection. From the average VEOG ocular artefact, transmission coefficients were computed for each EEG channel by estimating the covariance of the averaged potentials of the VEOG channel with the EEG channels. The contribution of the average blink from the VEOG channel was then subtracted from all other channels on a point-by-point basis. EEG epochs with -100 ms pre-stimulus to 1500 ms poststimulus time windows were extracted post hoc from the continuous file. Before averaging, responses were digitally filtered at 0.1–30 Hz. All recordings were baseline corrected (-100 to 0 ms)before averaging. Trials containing artefacts exceeding ±75 µV were rejected from averaging. The remaining sweeps were averaged for each stimulus triplet.

#### 2.5. Data analysis and interpretation

Waves N1, P2, and acoustic change complexes were analysed at electrode sites Cz and Fz. N1 and P2 peak latencies were computed relative to the stimulus onset (0 ms) and peak amplitude relative to the baseline. Acceptable latency ranges were between 90 and 150 ms, and between 180 and 250 ms post stimulus onset for N1 and P2, respectively. Peak amplitudes were computed by locating the largest amplitude that is surrounded on both sides by smaller amplitudes within the latency window. Unlike the CAEPs which had robust amplitudes, the acoustic change complex was small relative to the noise floor in the recordings and hence window-based mean amplitudes were computed to improve SNR (Luck, 2005). For each stimulus triplet, the peak of the acoustic change complex was identified from the grand-averaged waveform and a time window was selected that included voltage points within +/-25 ms surrounding this peak. Using this time window each participant's mean acoustic change complex voltage was calculated and used for statistical analysis. Separate statistical analyses were performed for the obligatory components (N1, P2) and acoustic change complex amplitudes. Two (group: NH vs. SNHL)  $\times\,2$ (stimulus conditions: N6, N12)  $\times$  3 (stimulus triplets: deltaF)  $\times$  2 (electrode: Cz, Fz) mixed-model ANOVAs were used to find statistical differences for the evoked potentials.

Thresholds obtained from the behavioural TFS1 test for both groups were subjected to a 2 (group: NH vs. SNHL)  $\times$  2 (stimulus conditions: N6, N12) mixed-model ANOVA. Interaction effects were explored using one-way ANOVAs to examine each of the effects separately. Tests of simple effects were conducted using paired- and independent-samples *t*-tests. A significance level of 0.05 was used for statistical analyses. Greenhouse–Geisser corrections (Greenhouse and Geisser, 1959) were used when the assumption of sphericity was not met.

#### 3. Results

#### 3.1. Behavioural sensitivity to pitch cues

Table 2 shows the mean and individual thresholds of each subject group for the N6 and N12 stimulus conditions. Two of the NH participants and all nine of the SNHL participants were not able to discriminate the maximum deltaF (50 Hz) for the N12 stimulus condition. Moore and Sek (2009a) described a procedure to estimate deltaF values based on the detectability index, d', calculation in conditions where the participants were unable to reach a threshold less than deltaF = 50 Hz in the adaptive task. Only two participants (NH9 and SNHL2, Table 2) who failed the adaptive task had a score of >26 correct responses out of 40 trials for the fixed deltaF = 50 Hz value, indicating some ability to use TFS cues. The other participants failing the adaptive task performed at chance levels and hence, rather than estimating the deltaF using the dprime procedure for the statistical analysis, a fixed deltaF level of 55 Hz was assigned to all participants failing the adaptive task. The mixed-model ANOVA showed significant main effects for subject group [F(1,17) = 30.8, p < 0.001] and stimulus condition [F(1,17) = 56.5, p < 0.001]. Fig. 4 shows that the N12 condition was more difficult for both groups; however for the SNHL group the difference in performance was much greater. There was also a significant interaction between subject group and stimulus condition [F(1, 17) = 11.8, p = 0.003].

Post hoc *t*-tests were used to determine whether the mean thresholds differed between subject groups within each stimulus condition. For the N6 stimulus condition, the NH listeners typically performed somewhat better than the SNHL listeners and the difference in mean scores was statistically significant (t(17) = -2.47, p = 0.024). For the N12 stimulus condition, all of the participants in the SNHL group failed to do the task and hence overall performance was poorer than that of the NH group (Fig. 4).

#### 3.2. Electrophysiology

Electrophysiological recordings were used to investigate differences in neural encoding of pitch cues between the NH and SNHL groups and to explore pitch-related effects on the auditory evoked potentials. We hypothesised that group differences (NH vs. SNHL) would mainly be seen in the acoustic change complexes as the stimuli were all very detectable and hence should have generated robust CAEPs in both groups. We anticipated that pitch-related stimulus acoustic differences would primarily affect the P2 (Crowley and Colrain, 2004) component of the CAEPs and the amplitudes of the acoustic change complex (Martin and Boothroyd, 1999). Results of the mixed-model ANOVA, conducted

#### Table 2

Individual and mean TFS1 thresholds (deltaF, Hz) for the N6 and N12 stimulus conditions, for the NH and SNHL participants.

| Participants | NH        |            | SNHL      |                  |  |
|--------------|-----------|------------|-----------|------------------|--|
|              | N6        | N12        | N6        | N12 <sup>*</sup> |  |
| 1            | 5.2       | 9.7        | 9.7       | 19/40 (0.47)     |  |
| 2            | 6.5       | 5.8        | 12.0      | 30/40 (0.75)     |  |
| 3            | 10.5      | 17.0       | 9.4       | 19/40 (0.47)     |  |
| 4            | 8.3       | 22.9       | 29.3      | 20/40 (0.50)     |  |
| 5            | 8.3       | 5.8        | 24.7      | 23/40 (0.57)     |  |
| 6            | 6.9       | 14.1       | 13.0      | 19/40 (0.47)     |  |
| 7            | 5.7       | 13.6       | 8.1       | 25/40 (0.62)     |  |
| 8            | 11.6      | 23.6       | 12.9      | 25/40 (0.62)     |  |
| 9            | 17.1      | 28/40*     | 41.0      | 15/40 (0.37)     |  |
| 10           | 3.7       | 17/40*     |           |                  |  |
| Mean         | 8.38 (Hz) | 22.25 (Hz) | 17.7 (Hz) | 0.54             |  |
| (SD)         | (3.8)     | (18.3)     | (11.3)    | (11.2)           |  |

Number of correct responses out of 40.



**Fig. 4.** Mean TFS1 thresholds of each subject group for the N6 and N12 stimulus conditions. Error bars show the 95% confidence interval of the mean. \* = p < .05.

separately for the obligatory CAEPs and the acoustic change complexes are shown in Table 3.

#### 3.2.1. Obligatory CAEPs

Though no main effect of group was found for any of the CAEP components, there was a significant interaction between stimulus condition and group for N1 latency (Table 3). Overall N1 latency increased for the NH group for the N12 (144.5 ms) compared to the N6 (137.8 ms) condition but was essentially unchanged for the SNHL group (138.7 vs. 137.7 ms). To further explore the interaction between stimulus condition and group, response latencies were averaged across deltaF and electrodes and post hoc independent *t*-tests were conducted to comparing N1 latencies between NH and SNHL groups for the N6 and N12 stimulus conditions. These comparisons revealed no significant differences between groups for the N6 (t(17) = -0.1, p = 0.868) or N12 (t(17) = 1.1, p = 0.252) stimulus conditions.

The main effect of stimulus condition was significant only for P2 latency and amplitude (p < 0.05; see Table 3). P2 responses averaged across electrodes and groups were earlier and larger for the stimulus condition N6 [234 ms (SE: 4.1), 1.0  $\mu$ V (SE: 0.28)] compared to N12 [243 ms (SE: 4.6), .04  $\mu$ V (SE: 0.23)] (Fig. 5). Overall, stimulus condition effects on CAEPs were mainly seen for P2.

With regards to differences across electrodes, although there were no significant main effects, a significant two-way interaction was found for P2 latency, between stimulus condition and electrode (Table 3). Post hoc comparisons indicated that differences between stimulus conditions (N6 vs. N12) were evident at both Cz [t(18) = 4.0, p = 0.001] and Fz [t(18) = 2.9, p = 0.010], but the N6 vs. N12 difference was greater at Cz. There was also a three-way interaction between stimulus condition, electrode, and group for P2 amplitude (Table 3). In order to explore the effects of electrode site on differences across stimulus conditions, a  $2 \times 2$  ANOVA was conducted separately for each group. This analysis revealed that only Cz showed significant differences across stimulus conditions and this was present only for the NH group (F(1,19) = 4.7, p = 0.042). Overall, recordings at Cz were more affected by changes in stimulus condition than Fz.

#### 3.2.2. Acoustic change complex

Fig. 6 shows the average amplitudes of the acoustic change complexes to the various deltaF values for the two stimulus conditions in the NH and SNHL groups. As was observed for P2, stimulus conditions also had a significant effect on the acoustic change

6

# **ARTICLE IN PRESS**

#### A.K. Mathew et al./Clinical Neurophysiology xxx (2015) xxx-xxx

#### Table 3

Results of mixed-model ANOVA of N1, P2, and acoustic change complex for all conditions.

|   | N1 Latency               |                            | N1 Amplitude |          |  |
|---|--------------------------|----------------------------|--------------|----------|--|
|   | F(df)                    | р                          | F(df)        | р        |  |
| Group   | 0.298(1,17)              | 0.592                      | 0.012(1,17)  | 0.915    |  |
| Stimulus condition  | 2.794(1,17)              | 0.113                      | 2.659(1,17)  | 0.121    |  |
| Stimulus condition * group  | 4.866(1,17)              | 0.041                      | 2.226(1,17)  | 0.154    |  |
| deltaF  | 1.031(2,34)              | 0.368                      | 2.905(2,34)  | 0.068    |  |
| deltaF * group  | 0.639(2,34)              | 0.534                      | 0.555(2,34)  | 0.579    |  |
| Electrode   | 2.608(1,17)              | 0.125                      | 0.019(1,17)  | 0.891    |  |
| Electrode * group   | 0.033(1,17)              | 0.858                      | 0.966(1,17)  | 0.339    |  |
| Stimulus condition * deltaF   | 0.664(2,34)              | 0.521                      | 0.559(2,34)  | 0.577    |  |
| Stimulus condition * deltaF * group                                   | 2.358(2,34)              | 0.110                      | 1.191(2,34)  | 0.316    |  |
| Stimulus condition * electrode  | 0.287(1,17)              | 0.599                      | 2.802(1,17)  | 0.112    |  |
| Stimulus condition * electrode * group                                | 2.095(1,17)              | 0.166                      | 0.333(1,17)  | 0.571    |  |
| deltaF * electrode  | 1.649(2,34)              | 0.207                      | 1.698(2,34)  | 0.198    |  |
| deltaF * electrode * group<br>Stimulus condition * deltaF * electrode | 3.055(2,34)              | 0.060                      | 0.496(2,34)  | 0.613    |  |
| Stimulus condition * doltaF * electrode * group                       | .373(2,34)               | 0.090                      | 0.090(2,34)  | 0.420    |  |
| stimulus condition deltar electrode group                             | .145(2,54)               | 0.807                      | 0.901(2,54)  | 0.410    |  |
|   | P2 Latency               |                            | P2 Amplitude |          |  |
|   | F(df)                    | р                          | F(df)        | р        |  |
| Group   | .430(1,17)               | 0.521                      | 0.137(1,17)  | 0.716    |  |
| Stimulus condition  | 11.871(1,17)             | 0.003                      | 34.138(1,17) | 0.001    |  |
| Stimulus condition * group  | 0.404(1,17)              | 0.534                      | 0.020(1,17)  | 0.890    |  |
| deltaF  | 0.006(2,34)              | 0.994                      | 0.738(2,34)  | 0.486    |  |
| deltaF * group  | 1.212(2,34)              | 0.310                      | 0.089(2,34)  | 915      |  |
| Electrode   | 0.263(1,17)              | 0.615                      | 0.059(1,17)  | 0.811    |  |
| Electrode * group   | 2.498(1,17)              | 0.132                      | 1.194(1,17)  | 0.290    |  |
| Stimulus condition * deltaF * group                                   | 2.004(2,34)              | 0.150                      | 0.634(2,34)  | 0.537    |  |
| Stimulus condition * electrode  | 1.009(2,34)              | 0.215                      | 0.101(1.17)  | 0.176    |  |
| Stimulus condition * electrode * group                                | 2.500(1,17)<br>426(1,17) | 0.055                      | 7.026(1.17)  | 0.755    |  |
| deltaE*electrode  | 369(2.34)                | 0.525                      | 0.635(2.34)  | 0.017    |  |
| deltaF * electrode * group  | 721(2,34)                | 0.054                      | 1 174(2.34)  | 0.330    |  |
| Stimulus condition * deltaF * electrode                               | 1506(234)                | 0.434                      | 2106(2.34)   | 0.521    |  |
| Stimulus condition * deltaF * electrode * group                       | 545(2,34)                | 0.585                      | 0.879(2.34)  | 0.137    |  |
| summus condition dental electrode group                               | ACC amplitude            | 0.505                      | 0.075(2,54)  | 0.421    |  |
|   |                          |                            |              | <u> </u> |  |
|   | F(df)                    |                            | p            |          |  |
| Group   | 0.869(1,17)              |                            | 0.364        |          |  |
| Stimulus condition  | 9.966(1,17)              |                            | 0.006        |          |  |
| Stimulus condition * group  | 0.046(1,17)              | 0.046(1,17)                |              | 0.834    |  |
| deltaF  | 1.588(2,34)              | 1.588(2,34)                |              | 0.219    |  |
| deltar ' group  | 2.821(2,34)              | 2.821(2,34)                |              | 0.0/4    |  |
| Electrode * group   | 1/.05/(1,17)             |                            | 0.001        |          |  |
| Stimulus condition * doltaE   | 1.029(1,17)              |                            | 0.037        |          |  |
| Stimulus condition * deltaF * group                                   | 5 329(2 34)              |                            | 0.000        |          |  |
| Stimulus condition * electrode  | 0.512(1.17)              |                            | 0.484        | 0.484    |  |
| Stimulus condition * electrode * group                                | 2.024(1.17)              | 0.312(1,17)<br>2 024(1 17) |              | 0.173    |  |
| deltaF * electrode  | 0.547(2.34)              |                            | 0.584        |          |  |
| deltaF * electrode * group  | 0.432(2.34)              |                            | 0.653        |          |  |
| Stimulus condition * deltaF * electrode                               | 6.731(2.34)              |                            | 0.003        |          |  |
| Stimulus condition * deltaF * electrode * group                       | 4.712(2.34)              |                            | 0.016        |          |  |
| a contract and a contract group                                       |                          |                            |              |          |  |

complex (see Table 3). The acoustic change complex evoked by the stimulus condition N6 was more robust  $[-1.5 \,\mu\text{V} (\text{SE: } 0.17)]$  than that evoked by N12  $[-1.8 \,\mu\text{V} (\text{SE: } 0.17)]$ . Although there were no significant main effects of group and deltaF, an interaction effect was found between stimulus condition, deltaF, and group (Table 3). Fig. 7 illustrates the interaction between stimulus condition and deltaF values separately for the NH and SNHL groups. From this figure it is evident that for the N6 stimulus condition, the NH group showed a monotonic increase in acoustic change complex amplitude with increase in deltaF from 0 to 50 Hz (0 < 30 < 50 Hz). Mean acoustic change complex amplitudes for each stimulus triplet for the NH group were 0 Hz:  $-1.8 \,\mu V$  (SE: 0.27), 30 Hz:  $-1.6\,\mu V$  (SE: 0.31), and 50 Hz:  $-0.7\,\mu V$  (SE: 0.31). Thus, as expected robustness of the acoustic change complex increased with increasing pitch shift in the NH group. This pattern was not observed for the N12 condition for the NH group and was not evident for either condition for the SNHL group. To further explore the three-way interaction between stimulus condition, deltaF, and group, a  $3 \times 2$  ANOVA was conducted separately for each stimulus condition. This analysis showed that a group difference was present with significantly higher acoustic change complex amplitude only for the 50 Hz deltaF, N6 condition (*F*(1,18) = 7.7, *p* = 0.013). No other significant differences were observed between subject groups.

A main effect of recording electrode on acoustic change complex amplitudes was also found (Table 3). Mean acoustic change complex amplitude at Cz, averaged across stimuli was more positive [ $-1.6 \mu$ V, SE: 0.17] than at Fz [ $-1.8 \mu$ V (SE: 0.17)]. The analysis also revealed a four-way interaction between stimulus condition, deltaF, group, and electrode (Table 3). Fig. 7 illustrates this fourway interaction. The pattern of ACC amplitudes differed, as already noted, between groups for one combination of stimulus condition and deltaF (N6, deltaF = 50 Hz), however, the effect of deltaF and stimulus condition varied across electrode and group. For the

A.K. Mathew et al. / Clinical Neurophysiology xxx (2015) xxx-xxx



**Fig. 5.** Grand mean Cz waveforms for the adults with NH (n = 10) and SNHL (n = 9) elicited in response to the N6 (solid line) and N12 (dashed line) stimulus conditions, averaged across the three stimulus triplets. Arrow marks approximate N1, P2 peaks corresponding to the stimulus onset, and acoustic change complex. Overlaid time waveform of the stimulus demonstrates the correspondence to the ERP waveform.



Fig. 6. Grand mean Cz waveforms are displayed as a function of deltaF stimulus triplets (N6 stimulus condition), for the participants with NH and SNHL. The acoustic change complex is indicated by the grey inset box.

SNHL group the effect of deltaF differed between electrodes for the N6 but not the N12 condition. For the NH group results were consistent across electrode.

#### 4. Discussion

The current study showed differences in pitch discrimination abilities for bandpass-filtered harmonic (A) and inharmonic (B) tone complexes, containing resolved (N6) and mostly unresolved (N12) components, for NH and SNHL participants. Overall results indicate that listeners in the SNHL group showed poorer pitch processing abilities than the NH group for all stimulus conditions. Furthermore, perceptual processing abilities and neural encoding of pitch information depended on the stimulus condition (pitch salience). There was a strong association between the P2 component of the CAEPs and pitch salience; across both groups P2 was smaller and later for the weak pitch (N12) stimulus condition. Acoustic change complexes were equally sensitive to the stimulus conditions and to the frequency shift in the stimulus triplets



Fig. 7. Mean acoustic change complex amplitudes (Cz and Fz) for the N6 and N12 stimulus conditions plotted across stimulus triplets are shown for the NH and SNHL groups.

(deltaF 30 and 50 Hz) for the N6 stimulus condition only, for NH participants. For the SNHL group the frequency shift in the stimulus triplets did not produce a consistent acoustic change complex response.

#### 4.1. Behavioural sensitivity to pitch cues

Discrimination thresholds for the stimulus condition N6 were significantly better than for N12 for both subject groups. Thus the ability to extract pitch using shifts in excitation pattern and TFS cues are better for stimuli containing resolved components (N6). This is in agreement with previous reports describing TFS sensitivity (Bernstein and Oxenham, 2003; Houtsma and Smurzynski, 1990; Moore and Moore, 2003). Peripheral pitch encoding of complex tones containing low-numbered harmonic components (e.g. N6 stimulus condition) involves two processes (Moore and Gockel, 2011). Firstly, it is presumed that the harmonic components are spatially resolved on the basilar membrane, and secondly neural firing patterns phase lock to the TFS peaks at the envelope maxima. This results in a clear pitch percept and changes in deltaF are easier to discriminate (Houtsma and Smurzynski, 1990; Shackleton and Carlyon, 1994). In contrast, tones with high-numbered harmonics (e.g. N12 stimulus condition) produce a weaker pitch percept and poorer deltaF detection thresholds (Brenstein and Oxenham, 2003; Houtsma and Smurzynski, 1990; Moore et al., 2009b), consistent with the results of the current study for both NH and SNHL participants.

The NH group performed significantly better than the SNHL group for all stimulus conditions. For the N6 condition, the listeners with NH had an average discrimination threshold of 8.3 Hz (0.7% of centre frequency). This is consistent with the literature (1% or less) for tone complexes containing resolved harmonics (Moore et al., 2006a). This discrimination threshold was much lower than that obtained by listeners with SNHL (17.7 Hz, 1.5%). Poorer discrimination thresholds for the SNHL group, with only a

slight hearing loss in the mid frequencies (0.5, 1, 2 kHz), could be explained by broader auditory filters and/or decrease in phase locking in the auditory nerve compared with listeners who have NH (Moore, 2008). While most listeners in the NH group were able to perform the TFS1 task for the N12 stimulus condition, most listeners in the SNHL group scored no better than chance (Table 2). Poor discrimination scores suggest that participants with SNHL could not perceive differences in TFS cues between A and B tone complexes. These results corroborate findings of previous studies showing lack of sensitivity to TFS cues in adults with SNHL compared to NH controls (Ardoint et al., 2010; Hopkins and Moore, 2007, 2010; Hopkins et al., 2008; Lorenzi et al., 2006). These earlier studies showed reduced TFS sensitivity in adults with mild to moderate SNHL; the current study showed similar effects in adults with lesser degrees of hearing loss.

Previous studies have reported that TFS information is independent of the audiometric configuration (Hopkins and Moore, 2007; Strelcyk and Dau, 2009). Two of the participants aged 24 and 36 years with normal hearing thresholds (PTA < 15 dB HL) were not able to do the behavioural discrimination task for the N12 stimulus condition. The comparison of TFS1 thresholds for the N12 stimulus condition with audiometric thresholds assessed by means of Pearson correlations also showed no significant association between these variables (r = 0.040, n = 10, p = 0.913). Poor TFS1 performance could be indicative of a subclinical hearing loss that was not detected using conventional audiometry. To further explore this, we measured distortion-product otoacoustic emission (DPOAE) for all participants in the NH group. Interestingly, the two participants in the NH group who could not do the N12 task showed lower-amplitude and/or absent DPOAEs at higher frequencies compared to other NH participants (Fig. 8). Within the NH group, there was greater variation in DPOAE strength (Fig. 8) and audiometric thresholds (Fig. 1) at the higher frequencies. Moore (2007) proposed that limited ability to use TFS information for SNHL listeners relates to lower-amplitude OAEs. In the two NH participants described here,

a sub-clinical hearing loss as indicated by the DPOAEs, may account for their poor performance on the N12 task. Thus adults with audiometrically-normal hearing can still experience TFS deficits. Füllgrabe (2013) similarly showed evidence of reduced sensitivity to TFS cues in young adults with clinically normal hearing. The TFS1 test may be a good screening tool for either mild or sub-clinical hearing impairment (Hietkamp et al., 2010).

#### 4.2. Obligatory CAEPs

Obligatory CAEPs are sensory responses that depend on the physical characteristics of the stimulus (Martin et al., 2008). The presence of CAEPs indicated that the stimulus was detected at the auditory cortex (Hyde, 1997). In the current study CAEPs were present for each individual in each subject group and there were no substantive morphological differences in P1–N1–P2 across subject groups. This confirmed that stimuli were presented at a suprathreshold level, making them audible and equally detectable for all participants.

CAEPs have been used to show differential neural encoding of stimulus onset characteristics (Agung et al., 2006; Beukes et al., 2009; Digeser et al., 2009; Purdy et al., 2005; Whiting et al., 1998). N1–P2 CAEPs recorded using signal triplets (ABA) showed some onset-dependent changes when compared across stimulus conditions (N6 vs. N12). Previous studies have shown that N1 morphology mainly reflects changes in stimulus envelope/rise time (Kodera et al., 1979; Onishi and Davis, 1968), but we gated stimuli on (and off) using a constant rise time, and onset phases of the components were selected randomly for every complex which could account for the lack of stimulus effects on N1.

Previous investigations have associated P2 with pitch processing and musical training (Istók et al., 2013; Tong et al., 2009); consistent with our finding that P2 differed between clear (N6) and weak (N12) pitch stimuli (see Fig. 3). The N6 and N12 conditions tested here had the same centre frequency and fixed bandwidth but differed in their absolute F0 and harmonic components, resulting in pitch differences (Fig. 2). P2 sources have been identified in the planum temporale and the lateral part of Heschl's gyrus (Crowley and Colrain, 2004; Ross and Tremblay, 2009), and functional magnetic resonance imaging (fMRI) has shown enhanced activity in in these sites response to stimulus pitch differences (Barker et al., 2011; Schadwinkel and Gutschalk, 2010).

We found P2 to be significantly earlier and larger for the N6 stimulus condition than N12, which could be due to the better

resolution of the components on N6 producing a clearer pitch percept, and inducing faster neural processing and stronger neural activation. Penagos et al. (2004) has also showed evidence of lower cortical activation for complex tones with unresolved than resolved components. Alternatively, P2 differences between N6 and N12 conditions could have also occurred because F0 differed across stimulus conditions. Although differences in P2 arising from contrasts in pitch salience (N6 vs. N12) and F0 were not separately studied here, the results suggest that P2 is reflective of pitch processing.

#### 4.3. Acoustic change complex

Acoustic change complexes were recorded to examine the processing of pitch differences in two stimulus conditions with varying pitch shifts (deltaF), comparing adults with NH and SNHL. Overall results indicated that responses were larger and more discriminable at Cz than at Fz. This is consistent with previous studies showing larger ACC amplitudes near the vertex; at or lateral to Cz and FCz (Martin et al., 2010; Tremblay et al., 2006). However, amplitude differences seen across electrodes may result from the underlying volume conduction and inverse problems. As was seen for P2 amplitude and latency, acoustic change complexes were dependent on the salience of the pitch-evoking stimuli. Acoustic change complexes evoked using N6 stimuli were significantly more robust and produced clearer waveforms than those evoked by N12 stimuli (Fig. 3). This suggests that neural encoding of pitch information at the auditory cortex is predominantly driven by the presence of resolved harmonic components. This is supported by a recent fMRI study that showed stronger activation of cortical pitchsensitive regions in response to spectrally resolved harmonic tones than to frequency-matched noise and unresolved harmonic tones (Norman-Haignere et al., 2013).

4.3.1. Acoustic change complexes evoked using deltaF = 0 Hz control stimulus

From Fig. 9 it can be seen that acoustic change complexes were recorded even with the control stimulus (AAA) for both subject groups. This could reflect the phase discontinuities, the brief temporal gap due to ramping off and on of the stimuli at the transition points, and/or spectral splatter at the transition points within the stimulus triplets. However, this would not have led to artifactual results because the phase randomisation at each stimulus triplet transition meant that the amplitude discontinuity varied



**Fig. 8.** Distortion-product otoacoustic emission signal-to-noise ratio (DPOAE SNR) values for the right ear in the NH group (n = 10). The dashed lines show the results of the two participants with lower DPOAE SNR values who had difficulty with the N12 behavioural discrimination task.



**Fig. 9.** Grand mean Cz waveforms are displayed as a function of deltaF stimulus triplets (N6 stimulus condition), are overlaid for the participants with NH and SNHL. The acoustic change complex is indicated by the grey inset box.

10

A.K. Mathew et al. / Clinical Neurophysiology xxx (2015) xxx-xxx

randomly, independent of the frequency shift size and was thus evenly distributed across groups and conditions. Thus the group difference observed only for the deltaF = 50 Hz condition are likely to reflect differences in processing of pitch cues.

#### 4.3.2. Acoustic change complexes evoked by increasing deltaF

Acoustic change complexes demonstrated cortical sensitivity to pitch change only for the N6 stimulus condition with strong pitch salience. As expected, the NH group showed a monotonic increase in acoustic change complex amplitude with increasing pitch change (0 < 30 < 50 Hz). The 50 Hz change was perceptually discriminable but did not elicit an acoustic change complex for the N12 condition for the NH participants. Results for the N12 stimulus condition are supported by the findings of neuroimaging studies showing weak and distributed pitch responses in the auditory cortex when using unresolved pitch-stimuli (Barker et al., 2011; Norman-Haignere et al., 2013). Unlike the NH group, the SNHL group didn't show an increase in amplitude with increasing pitch shifts for either condition.

The finding of significantly larger acoustic change complex amplitudes in the NH group compared to the SNHL group (N6 stimulus condition, deltaF = 50 Hz) provides objective evidence for differences in the processing of complex acoustic cues between subject groups (see Fig. 9). Although the acoustic change complexes were evoked using a stimulus condition that produced a clear pitch percept (N6 stimulus condition), the response amplitude differed between NH and SNHL participants. This aligns with the results from the behavioural measures in the current study. These findings suggest that pitch processing can be affected in frequencies where the absolute audiometric thresholds are only slightly affected.

Overall, the acoustic change complexes measured here did not show significant differences consistently for all perceptually discriminable pitch shifts in the NH (N12) and SNHL (N6 and N12) groups. Although the behavioural and electrophysiological measure did not produce parallel results, the absence of a significant difference does not indicate a lack of discriminability. Rather, discriminability is more likely for the deltaF shift that shows differential neural encoding which is essentially a prerequisite for successful perception. For example, on comparing the responses evoked using the largest shift (deltaF = 50 Hz, N6 stimulus condition), the NH group showed significantly larger amplitude responses and better behavioural thresholds than the SNHL group. Additionally, evoked potentials were recorded using a passive listening paradigm as we were interested in obligatory encoding of pitch cues. It may be easier to demonstrate differential neural encoding to pitch change with an active oddball paradigm, in which participants are required to focus attention on the stimulus change.

#### 5. Conclusion

The current study utilised behavioural and electrophysiological measures to show processing of complex acoustic cues important for pitch perception. Both behavioural performance and neural representation depended on stimulus pitch salience. Overall the study showed that sensitivity to TFS cues is adversely affected in individuals with hearing loss. This is the first time a relationship between stimulus triplets of varying deltaF and amplitude of acoustic change complexes has been described, and hence further research is required to clarify these findings. The combined electrophysiological and behavioural approach may be a useful for evaluating the benefit of training and amplification in individuals who experience difficulties understanding speech in noise.

#### Acknowledgments

This research was supported by the Oticon Foundation, Denmark.

None of the authors have potential conflicts of interest to be disclosed.

#### References

- Agung K, Purdy SC, McMahon CM, Newall P. The use of cortical auditory evoked potentials to evaluate neural encoding of speech sounds in adults. J Am Acad Audiol 2006;17(8):559–72.
- Ardoint M, Sheft S, Fleuriot P, Garnier S, Lorenzi C. Perception of temporal finestructure cues in speech with minimal envelope cues for listeners with mild-tomoderate hearing loss. Int J Audiol 2010;49(11):823–31.
- Barker D, Plack CJ, Hall DA. Human auditory cortical responses to pitch and to pitch strength. NeuroReport 2011;22(3):111–5.
- Bernstein JG, Oxenham AJ. Pitch discrimination of diotic and dichotic tone complexes: harmonic resolvability or harmonic number? J Acoust Soc Am 2003;113(6):3323–34.
- Beukes EW, Munro KJ, Purdy SC. Duration-sensitive neurons in the auditory cortex. NeuroReport 2009;20(13):1129–33.
- Chasin M, Russo FA. Hearing aids and music. Trends Amplif 2004;8(2):35-47.
- Crowley KE, Colrain IM. A review of the evidence for P2 being an independent component process: age, sleep and modality. Clin Neurophysiol 2004;115(4):732–44.
- Digeser FM, Wohlberedt T, Hoppe U. Contribution of spectrotemporal features on auditory event-related potentials elicited by consonant-vowel syllables. Ear Hear 2009;30(6):704–12.
- Festen JM, Plomp R. Effects of fluctuating noise and interfering speech on the speech-reception threshold for impaired and normal hearing. J Acoust Soc Am 1990;88(4):1725–36.
- Friesen LM, Tremblay KL. Acoustic change complexes recorded in adult cochlear implant listeners. Ear Hear 2006;27(6):678–85.
- Füllgrabe C. Age-dependent changes in temporal-fine-structure processing in the absence of peripheral hearing loss. Am J Audiol 2013;22(2):313–5.Greenhouse SW, Geisser S. On methods in the analysis of profile data.
- Greenhouse SW, Geisser S. On methods in the analysis of profile data. Psychometrika 1959;24(2):95–112.
- Gordon-Salant S. Phoneme feature perception in noise by normal-hearing and hearing-impaired subjects. J Speech Lang Hear Res 1985;28(1):87–95.
- Harris KC, Mills JH, He NJ, Dubno JR. Age-related differences in sensitivity to small changes in frequency assessed with cortical evoked potentials. Hear Res 2009;243(1):47–56.
- Hietkamp RK, Andersen M, Kristensen MS, Pontoppidan NH, Lunner T. The TFS1-test reveals mild hearing loss. Poster presented at the American Speech-Language-Hearing Association Convention (ASHA), November 2010, Philadelphia, USA; 2010.
- Hopkins K, Moore BC. Moderate cochlear hearing loss leads to a reduced ability to use temporal fine structure information. J Acoust Soc Am 2007;122(2):1055–68.
- Hopkins K, Moore BC, Stone MA. Effects of moderate cochlear hearing loss on the ability to benefit from temporal fine structure information in speech. J Acoust Soc Am 2008;123(2):1140–53.
- Hopkins K, Moore BC. The importance of temporal fine structure information in speech at different spectral regions for normal-hearing and hearing-impaired subjects. J Acoust Soc Am 2010;127(3):1595–608.
- Houtsma AJ, Smurzynski J. Pitch identification and discrimination for complex tones with many harmonics. J Acoust Soc Am 1990;87(1):304–10.
- Hyde M. The N1 response and its applications. Audiol Neurootol 1997;2(5):281–307.
- Istók E, Friberg A, Huotilainen M, Tervaniemi M. Expressive timing facilitates the neural processing of phrase boundaries in music: evidence from event-related potentials. PLoS One 2013;8(1):e55150.
- Kim JR, Ahn SY, Jeong SW, Kim LS, Park JS, Chung SH, et al. Cortical auditory evoked potential in aging: effects of stimulus intensity and noise. Otol Neurotol 2012;33(7):1105–12.
- Kochkin S. MarkeTrak VII: obstacles to adult non-user adoption of hearing aids. Hear J 2007;60(4):24–51.
- Kodera K, Hink RF, Yamada O, Suzuki JI. Effects of rise time on simultaneously recorded auditory-evoked potentials from the early, middle and late ranges. Int J Audiol 1979;18(5):395–402.
- Lavoie BA, Hine JE, Thornton RD. The choice of distracting task can affect the quality of auditory evoked potentials recorded for clinical assessment. Int J Audiol 2008;47(7):439–44.
- Levitt HCCH. Transformed up-down methods in psychoacoustics. J Acoust Soc Am 1971;49(2B):467–77.
- Lorenzi C, Gilbert G, Carn H, Garnier S, Moore BC. Speech perception problems of the hearing impaired reflect inability to use temporal fine structure. Proc Natl Acad Sci USA 2006;103(49):18866–9.
- Lorenzi C, Debruille L, Garnier S, Fleuriot P, Moore BC. Abnormal processing of temporal fine structure in speech for frequencies where absolute thresholds are normal. J Acoust Soc Am 2009;125(1):27–30.
- Luck SJ. An introduction to the event-related potential technique. Cambridge MA: MIT Press; 2005.

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#### A.K. Mathew et al. / Clinical Neurophysiology xxx (2015) xxx-xxx

- Martin BA, Boothroyd A. Cortical, auditory, event-related potentials in response to periodic and aperiodic stimuli with the same spectral envelope. Ear Hear 1999;20(1):33–44.
- Martin BA, Boothroyd A. Cortical, auditory, evoked potentials in response to changes of spectrum and amplitude. J Acoust Soc Am 2000;107(4):2155–61.
- Martin BA, Tremblay KL, Korczak P. Speech evoked potentials: from the laboratory to the clinic. Ear Hear 2008;29(3):285–313.
- Martin BA, Boothroyd A, Ali D, Leach-Berth T. Stimulus presentation strategies for eliciting the acoustic change complex: increasing efficiency. Ear Hear 2010;31(3):356.
- Moore BCJ, Huss M, Vickers DA, Glasberg BR, Alcántara JI. A test for the diagnosis of dead regions in the cochlea. Br J Audiol 2000;34(4):205–24.
- Moore BC, Moore GA. Discrimination of the fundamental frequency of complex tones with fixed and shifting spectral envelopes by normally hearing and hearing-impaired subjects. Hear Res 2003;182(1):153–63.
- Moore BC, Glasberg BR, Flanagan HJ, Adams J. Frequency discrimination of complex tones; assessing the role of component resolvability and temporal fine structure. | Acoust Soc Am 2006a;119(1):480–90.
- Moore BC, Glasberg BR, Hopkins K. Frequency discrimination of complex tones by hearing-impaired subjects: evidence for loss of ability to use temporal fine structure. Hear Res 2006b;222(1):16–27.
- Moore BC. Cochlear hearing loss: physiological, psychological and technical issues. John Wiley & Sons; 2007.
- Moore BC. The role of temporal fine structure processing in pitch perception, masking, and speech perception for normal-hearing and hearing-impaired people. J Assoc Res Otolaryngol 2008;9(4):399–406.
- Moore BC, Sek A. Development of a fast method for determining sensitivity to temporal fine structure. Int J Audiol 2009a;48(4):161–71.
- Moore BC, Hopkins K, Cuthbertson S. Discrimination of complex tones with unresolved components using temporal fine structure information. J Acoust Soc Am 2009b;125(5):3214–22.
- Moore BC, Gockel HE. Resolvability of components in complex tones and implications for theories of pitch perception. Hear Res 2011;276(1):88–97.
- Moore BCJ. Auditory processing of temporal fine structure: effects of age and hearing loss. Singapore: World Scientific; 2014.
- Neuroscan Inc. Offline analysis of acquired data (Document number 2203, Revision E). SCAN 4.4 vol. II, Edit 4.4. Charlotte, NC: Compumedics Neuroscan; 2007. p. 141–8.
- Norman-Haignere S, Kanwisher N, McDermott JH. Cortical pitch regions in humans respond primarily to resolved harmonics and are located in specific tonotopic regions of anterior auditory cortex. J Neurosci 2013;33(50):19451–69.
- Onishi S, Davis H. Effects of duration and rise time of tone bursts on evoked V potentials. J Acoust Soc Am 1968;44(2):582–91.
- Ostroff JM, Martin BA, Boothroyd A. Cortical evoked response to acoustic change within a syllable. Ear Hear 1998;19(4):290–7.

- Penagos H, Melcher JR, Oxenham AJ. A neural representation of pitch salience in nonprimary human auditory cortex revealed with functional magnetic resonance imaging. J Neurosci 2004;24(30):6810–5.
- Picton TW, Stuss DT, Champagne SC, Nelson RF. The effects of age on human eventrelated potentials. Psychophysiology 1984;21(3):312–26.
- Plack CJ, Oxenham AJ, Fay RR. Pitch: neural coding and perception 2005;vol. 24. Springer; 2005.
- Purdy SC, Katsch R, Dillon H, Storey L, Sharma M, Agung K. Aided cortical auditory evoked potentials for hearing instrument evaluation in infants. In: A sound foundation through early amplification. Chicago, IL: Phonak AG; 2005. p. 115–27.
- Ross B, Tremblay K. Stimulus experience modifies auditory neuromagnetic responses in young and older listeners. Hear Res 2009;248(1):48–59.
- Schadwinkel S, Gutschalk A. Activity associated with stream segregation in human auditory cortex is similar for spatial and pitch cues. Cereb Cortex 2010;20(12):2863–73.
- Schouten JF, Ritsma RJ, Cardozo BL. Pitch of the residue. J Acoust Soc Am 1962;34(9B):1418–24.
- Seppänen M, Hämäläinen J, Pesonen AK, Tervaniemi M. Music training enhances rapid neural plasticity of N1 and P2 source activation for unattended sounds. Front Hum Neurosci 2012;6(43).
- Sek A, Moore BC. Implementation of two tests for measuring sensitivity to temporal fine structure. Int J Audiol 2012;51(1):58–63.
- Sharma A, Marsh CM, Dorman MF. Relationship between N1 evoked potential morphology and the perception of voicing. J Acoust Soc Am 2000;108(6):3030–5.
- Shackleton TM, Carlyon RP. The role of resolved and unresolved harmonics in pitch perception and frequency modulation discrimination. J Acoust Soc Am 1994;95(6):3529–40.
- Strelcyk O, Dau T. Relations between frequency selectivity, temporal fine-structure processing, and speech reception in impaired hearing. J Acoust Soc Am 2009;125(5):3328–45.
- Tremblay KL, Kalstein L, Billings CJ, Souza PE. The neural representation of consonant-vowel transitions in adults who wear hearing aids. Trends Amplif 2006;10(3):155–62.
- Tremblay KL, Billings C, Rohila N. Speech evoked cortical potentials: effects of age and stimulus presentation rate. J Am Acad Audiol 2004;15(3):226–37.
- Tong Y, Melara RD, Rao A. P2 enhancement from auditory discrimination training is associated with improved reaction times. Brain Res 2009;1297:80–8.
- Whiting KA, Martin BA, Stapells DR. The effects of broadband noise masking on cortical event-related potentials to speech sounds/ba/and/da. Ear Hear 1998;19(3):218–31.
- Wilson BS, Dorman MF. Cochlear implants: current designs and future possibilities. J Rehabil Res Dev 2008;45(5):695–730.