Optimizing the stimulus used to elicit the Acoustic Change Complex: evaluation of the pre-transition duration and stimulus complexity in normal hearing adults

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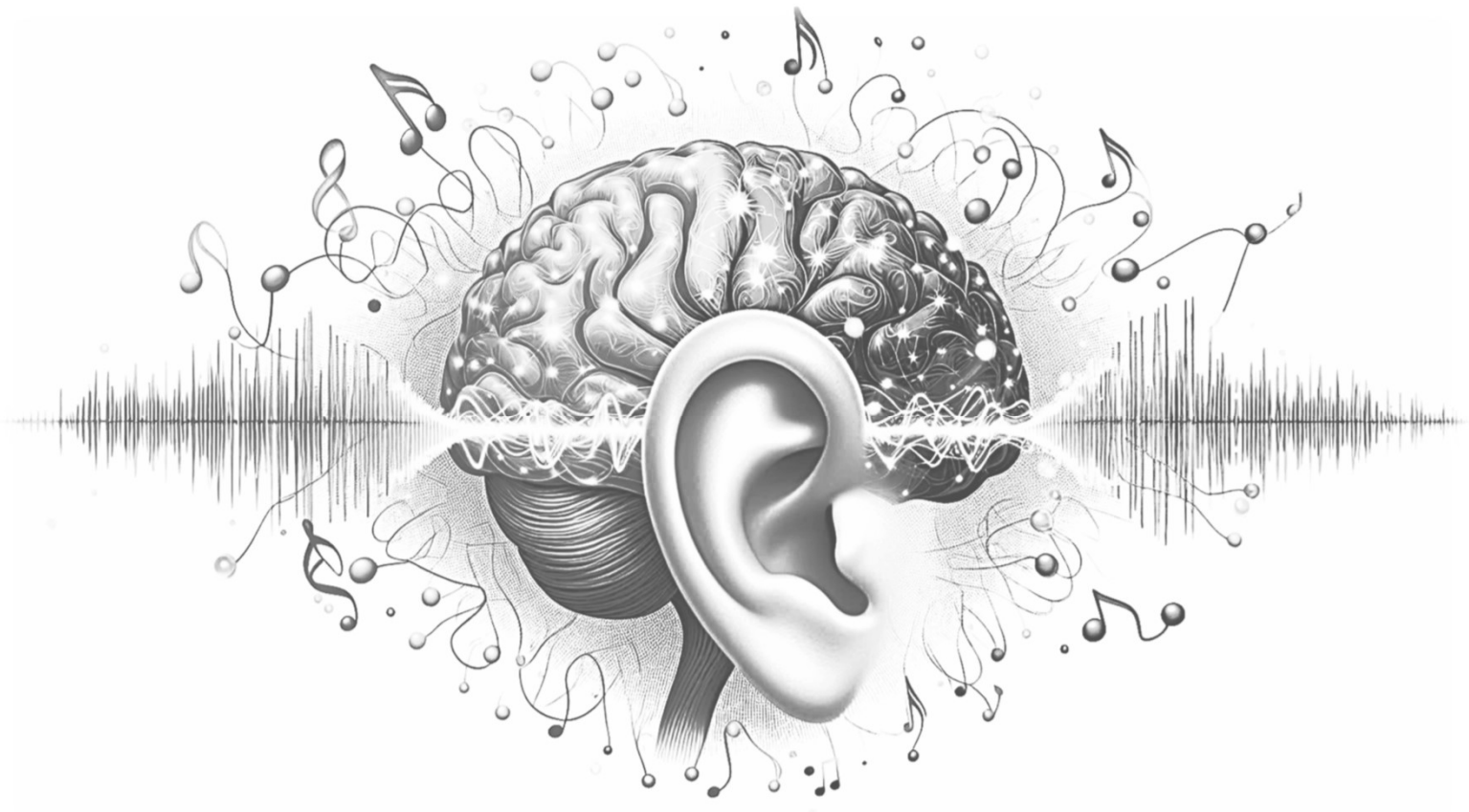

Optimizing the stimulus used to elicit the Acoustic Change Complex: evaluation of the pre-transition duration and stimulus complexity in normal hearing adults

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Preface and Acknowledgements

The third of July 2022 I was on a phone call with Marloes Adank (my soon-to-be daily supervisor), to discuss whether I was interested in researching the acoustic change complex for my thesis. A few days later I made the decision to say yes. Since then, quite some time passed. Most time I happily spent working on my thesis; delving into the wide range of literature on the acoustic change complex, having memorable clinical experiences, figuring out the measurement setup, programming in Matlab, making lots of decisions and having wonderful interactions with the people that work at the ENT department in the Erasmus Medical Center.

I am very proud that at this moment, this thesis is on your screen or in your hands. However, without the help of the following people it would not be. Firstly, I would like to genuinely thank my supervisors Jantien Vroegop and Marc van der Schroeff. Finishing this thesis, especially after needing to take a step back from working on it, would not have been possible without your patience and flexibility. You were always willing to give timely and valuable feedback and squeeze in an extra meeting when needed. I would like to thank Marloes Adank just as much for her critical thinking, personal feedback and willingness to discuss topics. Furthermore, I would like to thank all nineteen (whom for obvious reasons I cannot state by name..) individuals that participated in this study for their time and company. It was heartwarming that in no time there were so many people willing to contribute! A special thanks to Sarah Yorke-Smith, Mathijs van Geerenstein and Bart Formsma for proofreading my thesis. Additionally, a special thanks to Karlijn Scheepens for making time last-minute to have a discussion with me about my results. Furthermore, I want to thank Mathijs van Geerenstein for always being there for me, whether it was by brainstorming, giving a pep talk, a helping hand or simply going for a walk, run or bike ride. Without you it would have been a lot harder. Lastly, I would like to thank my friends and family for their support, warmth, feedback and encouragement. Having expressed my gratitude, the last thing I have left to say is: Happy reading! :)

Laura Schellekens

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Abstract

Introduction The Acoustic Change Complex (ACC) is a cortical auditory evoked potential elicited by a change in an ongoing sound that consists of a P1-N1-P2 complex. The ACC holds promise as a non-invasive, passive, and objective measure to monitor speech discrimination. This can improve the treatment of hearing loss for young children and adults that are not able to execute gold standard speech perception tests. However, the reported measurement times of the ACC are lengthy, which might impede the clinical feasibility of measuring young children and adults with behavioural issues that are difficult to test. Measurement time can be reduced by enhancing the signal to noise ratio (SNR). Furthermore, enhancement of the SNR might increase the sensitivity and specificity of the ACC as a measure of speech discrimination. Two stimulus parameters that might increase the SNR are an increase in the pre-transition duration (PTD) and stimulus complexity. The PTD is the duration between the onset of the stimulus and the change in the acoustic characteristics of the stimulus. Besides increasing the SNR, measurement time directly increases with an increase in PTD. Therefore, the optimal PTD regarding efficiency should be studied. **Objectives** The aims are to study the effect of 1) the PTD and 2) tonal complexity on the N1-P2 peak-to-peak amplitude, baseline noise and SNR of the ACC. To evaluate the optimal PTD, efficiency was included as an outcome measure for the first objective. **Methods** The ACC was measured in eighteen normal hearing adults to pure tone stimuli with a frequency change from 1 kHz to 1.1 kHz. The studied PTDs were 0.25, 0.5, 1, 2 and 3 s. Furthermore, a complex tone with the same center frequencies and a PTD of 1 s was presented. Efficiency was measured as the SNR divided by the total measurement time. **Main results** An increase in PTD significantly increased the N1-P2 peak-to-peak amplitude up to a PTD of 2 s. PTD 0.25 s was excluded from all analyses due to overlap with the onset response. The SNR of PTD 0.5 s was significantly smaller than all other measured PTDs. The PTD of 1 s was significantly more efficient than a PTD of 0.5 s, had a measurement time of 6.67 min and the ACC was present in 58.8 % of the participants. ACC presence increased (to 100 % for PTD 3 s) with an increase in PTD. There was no significant difference in the N1-P2 peak-to-peak amplitude or SNR between the complex and pure tone. However, ACC presence increased with 22.5 percentage points for the complex tone compared to the pure tone. **Conclusion** The ACC is affected by the PTD. The PTDs of 2 and 3 s generated the significantly largest responses. We recommend utilizing a PTD of 1 s instead of 0.5 s, as it resulted in a significantly higher N1-P2 peak-to-peak amplitude, SNR and efficiency. Furthermore, increasing tonal complexity or the PTD beyond 1 s seems promising to increase presence of the ACC without significantly decreasing the SNR or efficiency.

List of Abbreviations

ACC	Acoustic change complex
CAEP	Cortical auditory evoked potential
dB	Decibel
EEG	Electroencephalography
ERP	Event related potential
HEOG	Horizontal electrooculogram
HL	Hearing level
ICA	Independent component analysis
Md	Median
PTA	Pure tone audiometry
PTD	Pre-transition duration
SD	Standard deviation
SNR	Signal to noise ratio
SPL	Sound pressure level
VEOG	Vertical electrooculogram

1 Introduction

In the Netherlands, over 1 in 1000 children are born with permanent hearing loss [1, 2]. Language development starts at birth, with a critical period lasting until around age seven [3]. Children with hearing loss may face speech and language delays due to auditory deprivation, impacting social-emotional growth and school performance [4]. Early rehabilitation is key to support their development [5].

Auditory discrimination is the ability to recognize differences between two sounds. Besides detectability of a sound, auditory discrimination is essential for children to distinguish phonemes in words and thus to develop and understand spoken language [6]. Current gold standard speech perception tests cannot be conducted until the age of around three to four years old [7, 8]. Therefore, current clinical tests for this age group solely evaluate detectability of the sound. This is because speech perception tests require a minimum level of language ability, attention, motivation and motor skill [9, 10]. Additionally, current tests are behavioural and thus subjective [8].

A non-invasive, passive, and objective measure of speech discrimination is essential to evaluate if a child has sufficient discrimination abilities for speech language development. It could be used to monitor and optimize the treatment of hearing loss earlier on in the critical period of language development. Furthermore, it would also be a valuable tool to optimize hearing rehabilitation for adults that are not able to execute speech perception tests, such as people with a language barrier, cognitive impairment and intellectual or developmental disabilities [11, 12]. For these adults, adequate treatment of hearing loss can be crucial to prevent negative impact on communication, cognition, socialization, safety, mental health and integration into society [11, 12].

Measurements that hold promise as a non- invasive and objective measure of auditory discrimination are cortical auditory evoked potentials (CAEP) recorded by electroencephalography (EEG) [13]. The Acoustic change complex (ACC) is an CAEP elicited by a change in an ongoing sound that consists of a P1–N1–P2 complex, similar to the onset response to sound onset, see Figure 1. There are two other CAEP's that are frequently used to examine auditory discrimination: P3 and mismatch negativity [13]. Unlike the P3 component, the ACC can be elicited without active participation. Compared to mismatch negativity, ACC requires relatively few repetitions, has a higher amplitude, higher test-retest reliability and is sensitive on an individual level [13]. The ACC can be elicited by a broad variety of acoustic changes and can be recorded in adults, children, infants and patients with a hearing aid or cochlear implant [14, 13, 15]. In numerous studies, the ACC is already significantly correlated with speech perception tests, see Appendix A. The ACC thus holds promise as a clinical tool to objectively assess auditory discrimination ability.

A wide variety of methods and sound stimuli are used to elicit and measure the ACC. Many studies report lengthy measurement procedures. A systematic review by Meehan et al. (2024) [15] reported an average total ACC measurement time of $1.7\,\mathrm{h}$ in children, with a maximum of $3\,\mathrm{h}$. For adults, the average total ACC measurement time is $2.3\,\mathrm{h}$, with a maximum of $8\,\mathrm{h}$ that was reported by Scheperle and Abbas (2015) [16][1]. For young children that cannot participate in lengthy measurement sessions as well as for adults with behavioural issues due to intellectual or developmental disabilities, this might be too time consuming for a clinical application [19, 20, 21, 22, 23, 12]. Furthermore, a decrease in measurement time increases patient comfort and lowers financial costs of the measurement. An additional constraint for children is that the average number of EEG epochs that is rejected due to artefacts is much higher (43–$48\,\%$) than for adults (5–$8\,\%$), as shown by Chen and Small (2015) [23]. This leads to an increase in the number of stimulus repetitions necessary to achieve the minimal number of EEG epochs, resulting in a longer measurement duration. Reducing the measurement time potentially increases clinical feasibility of measuring the ACC on infants and adults that are difficult to test [23, 20].

A factor that can decrease measurement time is an increase in the signal to noise ratio (SNR). Fewer stimuli repetitions are required for recording when the SNR is increased [23]. Furthermore, increasing the SNR might increase the percentage of patients in which the ACC is distinguishable from the noise. This might increase threshold precision and the number of patients in which supra-threshold amplitude and latency outcome measures can be evaluated. The ACC threshold can be described as the smallest measured magnitude of acoustic change that elicits an ACC [19]. Two stimulus parameters that might influence the amplitude and thus the SNR, are the pre-transition duration (PTD) and stimulus complexity.

The PTD is the duration between the onset of the stimulus and the change in the acoustic characteristics of the stimulus, as shown in Figure 1 (yellow double arrow) [24]. The PTD used in studies that compare the ACC to speech perception tests varies from 200 to $3000\,\mathrm{ms}$. A PTD of $400\,\mathrm{ms}$ is most common, as can be seen in Table A1 in Appendix A. Vonck et al. (2019) [25] reported that in pilot data of three participants, prolonging the PTD from $1000\,\mathrm{ms}$ to $3000\,\mathrm{ms}$ increased the amplitude of the resulting ACC by a factor ~ 1.5. This raises the hypothesis that increasing the PTD will increase the amplitude of the ACC.

To the best of our current knowledge, the effect of the PTD on the ACC amplitude is rarely studied. Ganapathy et al. (2013) [24] studied the minimum PTD needed for successful elicitation of the ACC. They

[1] This mean is based on publications included in a review submitted for publication by Meehan et al. (2024) [17], of the 66 included publications, 29 reported measurement duration [18]

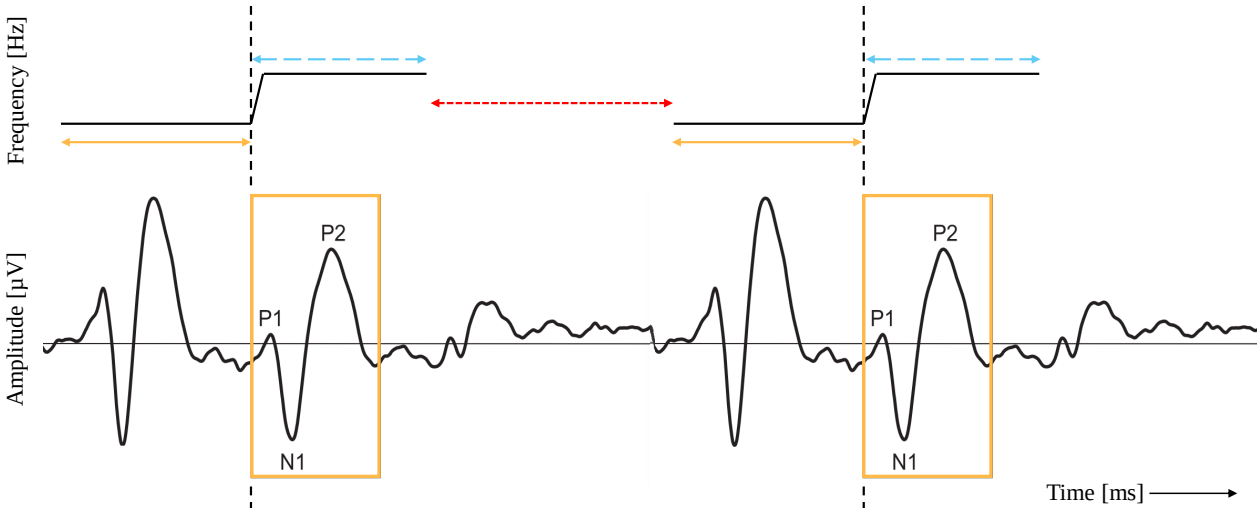

Figure 1: A sketch showing the onset response and the Acoustic change complex (ACC). The top half shows the stimulus, and the bottom half shows the measured electroencephalography (EEG). As a response to sound onset an onset response is measured in the EEG: first a positive peak (P1), followed by a negative peak (N1) and a second positive peak (P2). As a response to the frequency change an ACC is measured (yellow box). This ACC has the same morphology as the onset response. The yellow double arrows indicate the pre-transition duration, the blue dotted double arrows indicate the post-transition duration, and the red dotted double arrow indicates the inter stimulus interval. The figure is altered from Martin et al. (2008) [13].

studied PTDs between 50 and 150 ms in steps of 10 ms and concluded that the minimum PTD was 100 ms for the tonal stimulus and 80 ms for the consonant- vowel stimulus. This study thus used relatively short PTDs in comparison to other studies.

Decreasing the PTD shortens measurement time. However, the amplitude of the ACC might decrease with a shorter PTD, leading to an increased number of trials needed to obtain the same SNR. Therefore, the optimal PTD regarding measurement time and SNR should be studied.

Another factor that might influence the amplitude and therefore the SNR is spectral complexity of the stimulus used to elicit an ACC. Bardy et al. (2015) [26], found that the amplitude of the onset response to a complex tone was significantly larger than the amplitude of the onset response to a pure tone. This raises the hypothesis that the amplitude of the ACC might be bigger when elicited by a change in a complex tone compared to a pure tone. To our current knowledge, no studies evaluated this for the ACC.

In this work the aims are to study the effect of 1) the PTD and 2) tonal complexity of the stimulus on the N1-P2 peak-to-peak amplitude, baseline noise and SNR of the ACC. Furthermore, efficiency is used as an outcome measure for the first objective due to the possible trade-off between measurement duration and the resulting SNR. Efficiency is defined as the SNR divided by the total measurement time.

Our hypothesis is that the amplitude and SNR of the ACC will increase with increasing stimulus complexity and PTD. We do not expect the baseline noise to differ between the stimuli since measurement conditions (except total recording time) were the same. Regarding the efficiency, our hypothesis is that there will be one optimal PTD for which the increase in SNR is not cancelled out by an increase in measurement time.

2 Materials and methods

2.1 Participants

Normal hearing adult subjects participated in the study. Participants were recruited colleagues, relatives and acquaintances from the author. Informed consent was obtained from all participants. Inclusion criteria were: age ≥ 18 years old, normal hearing defined by an average hearing threshold < 20 Decibel Hearing Level (dB HL) over the frequencies 0.5, 1, 2 and 4 kHz in the better hearing ear [27] and a hearing threshold of < 20 dB HL in the better hearing ear at a frequency of 1 kHz. Exclusion criteria were a known neurological or mental disorder or the use of anticonvulsant or psychotropic drugs.

2.2 Stimuli

To study the objectives, the ACC was measured for two types of stimuli: pure tones that varied in PTD and a complex tone with a fixed PTD. For all stimuli, the acoustic change was a logarithmic frequency increase with a duration of 5 ms. The post-transition duration was 495 ms and the inter stimulus interval was 500 ms. Furthermore, to make the signal rise and fall smoothly, a Hanning window of 10 ms was applied to the onset and offset of the stimuli, thereby minimizing spectral splatter. At the start of the acoustic change and at the start of the post-transition frequency, phase transitions were applied to the waveforms to ensure a smooth transition between subsequent frequencies.

The pure tones with varying PTDs had a pre-transition frequency of 1 kHz and a post-transition frequency of 1.1 kHz. The PTDs that were used were: 250, 500, 1000, 2000 and 3000 ms. The pure tone with a PTD of 1000 ms was used in a test-retest measurement.

The complex tones used were defined by Bardy et al. (2015) [26] and created by adding four sinusoids. These sinusoids were 1 and 1/3 octave band around the center frequency, thus uniformly distributed around the center frequency on a logarithmic frequency scale. The center frequency was 1 kHz for the pre-transition frequency and 1.1 kHz for the post-transition frequency, equal to the pure tones. All added sinusoids had an equal amplitude and a zero-phase time delay at $t = 0$ ms. The complex tone with a center frequency of 1 kHz contained sinuses with frequencies of 707, 891, 1123, and 1414 Hz and the complex tone with a center frequency of 1.1 kHz contained sinuses of 778, 980, 1235 and 1556 Hz. The PTD of this complex stimulus was 1000 ms.

Two complex tones with intensity alterations were presented to the participants to account for possible intensity differences between pure and complex tones. The rationale behind this can be read in Text box 2 in Appendix E. The first is the above-mentioned complex tone presented 3 dB Sound pressure level (SPL) lower (67 instead of 70 dB SPL). The second is the above-mentioned complex tone with during the 5 ms frequency change an additional logarithmic intensity decrease of 3 dB.

All stimuli were equalized in terms of the root mean square energy and presented at 70 dB SPL (except for the complex tones with intensity alterations). Calibration was executed on the complex tones (Bruel and Kjaer 2250 sound level meter). Sound stimuli were made using Matlab (version R2022b, The MathWorks) at a sample frequency of 50 kHz. The Matlab code that was used for generation of the stimuli is available on Github[2].

2.3 Procedures

All participants underwent a manual pure tone audiometry (PTA) test for frequencies of 0.5, 1, 2, 4 and 8 kHz using a clinical audiometer that was calibrated according to ISO standard 389-1 (Decos audiology workstation, version 210.2.6). Sounds were presented with a headset (TD-39P Telephonics) in a sound-attenuated booth that met the maximum permissible ambient SPLs of ISO standard 8253-1. Hearing thresholds were measured according to the shortened ascending method based on ISO standard 8253-1, meaning that thresholds were defined by the intensity level at which the tone was heard in two out of three ascents.

Participants underwent a short interview to review the inclusion and exclusion criteria. They were comfortably seated in a chair with a headrest and optional head pillow and watched a silent non-captioned nature documentary of their choice (three options available). Prior to the recording, participants were instructed to not talk, sit as still as possible, minimize eye movements and fixate on the movie to minimize muscle and eye moving artefacts. Sound stimuli were presented binaurally through a speaker (Genelec 8020D) at ear height, 0° azimuth and one meter distance from the ears. EEG recordings were performed in a room without electrical shielding and sound attenuation. Stimuli were presented via STIM2 software (Compumedics) with 200 repetitions per stimuli. The complex tone without intensity alterations and the pure tones with varying PTDs were presented first. The order of first presenting the complex stimulus or varying PTD stimuli was switched between consecutive participants. Furthermore, the five pure tones with varying PTDs were presented in a random order to each participant. After a break of ≈10 min, the test- retest and the stimuli with intensity alterations were presented in the following order: complex tone presented at 67 dB SPL, complex tone with additional logarithmic intensity decrease of 3 dB and the test-retest pure tone. Participation took a total time of around 2 hours and 45 minutes. This can be subdivided into 1 hour of preparation (PTA, interview, placement of electrode net and impedance check), 1 hour of stimuli before the break and 45 remaining minutes that included a break, an impedance check, the stimuli after the break and disassembling.

2.4 EEG recording

Per stimulus, a continuous EEG was recorded using a Neuvo 128- channel amplifier (Compumedics) and CURRY 8 Acquisition software (Compumedics). Stimulus onset was monitored via a StimTracker (Cedrus Corporation). The EEG was recorded from 128 scalp electrodes using the 128-channel HydroCel Geodesic Sensor Net with sponge inserts (v.1.0, Electrical Geodesics, Inc.). Following the Electrical Geodesics manual, the net was placed using the tape measured electrode Cz (according to the International 10-20 system) as a landmark [28]. The reference electrode was located at Cz and the common mode electrode was located between Pz and POz [28]. The EEG was recorded in direct coupled mode with a sampling rate of 1 kHz and lowpass filtered with a 400 Hz cut off during acquisition.

Electrode numbers that were used for analyses and their corresponding approximate International 10-10 naming were: external canthus of the right eye (1), Fcz (6), right supra-orbital (8), Fz (11), F3 (24), left supra-orbital (25), external canthus of the left eye (32), C3 (36), T7 (45), left mastoid (57), Pz (62), right mastoid (100), C4 (104), T8 (108), F4 (124), right infra orbital (126) and left infra orbital (127) [29]. The remaining recorded electrodes were not used for the analyses. The vertical electrooculogram (VEOG) was derived from the differential signal between the electrodes located supra and infraorbital of the right eye [30, pg. 196-197]. The horizontal electrooculogram (HEOG) was derived from

[2] GitHub code

the differential signal between the electrodes located lateral to the external canthus of the left and right eye [31].

The impedances of above mentioned electrodes used for analyses were kept $\leq 50\,\mathrm{k}\Omega$. Impedances of the remaining electrodes were kept $\leq 100\,\mathrm{k}\Omega$. Unintentionally, impedances of the following electrodes used for analyses were kept $\leq 100\,\mathrm{k}\Omega$: the electrodes lateral to the external canthus of the left and right eye, and the left infra- and- supra- orbital electrodes. Impedances were checked prior to the start of the recording, once between the stimuli presented before the break (after an estimated duration of $20-30$ minutes) and prior to recording after the break.

2.5 Data analyses

2.5.1 Signal processing

All data was processed and analyzed in Matlab (version R2022b, MathWorks) using the EEGLAB toolbox (version 2022.1 Delorme and Makeig (2004) [32]) and ERPLAB toolbox (version 9.00 Lopez-Calderon and Luck (2014) [33]). The EEG signals were down sampled to $265\,\mathrm{Hz}$ to speed data processing and re-referenced offline to common mastoid [31]. The DC offsets were removed and the data was bandpass filtered (non-causal Butterworth infinite impulse response function, high pass half amplitude cutoff: $0.1\,\mathrm{Hz}$, low pass half amplitude cutoff: $30\,\mathrm{Hz}$, $12\,\mathrm{dB/oct}$ roll-off slope) and Notch filtered at $50\,\mathrm{Hz}$ (stop-band Parks-McClellan, 180th order) [30, pg. 245][34, 35].

Eye movements and blinks were corrected using independent component analysis (ICA) on parallel down sampled re-referenced data. In preparation for ICA, the DC offsets were removed and the data was bandpass filtered with a higher high-pass amplitude cut-off (non-causal Butterworth infinite impulse response function, high pass half amplitude cutoff: $1\,\mathrm{Hz}$, low pass half amplitude cutoff: $30\,\mathrm{Hz}$, $48\,\mathrm{dB/oct}$ roll-off slope) [36, 37, 34][38, Chap. 9.5]. Portions of EEG containing large artefacts or voltage offsets, and periods of recording prior and after presentation of the sound stimuli were identified by a semi-automatic ERPLAB algorithm and removed. Subsequently, ICA was performed and components that had a $>90\,\%$ probability of being an eye artefact, as classified by an automated EEG ICA classifier (IClabel, Pion-Tonachini et al. (2019) [39], were removed [40, 36]. From the ICA corrected data, corrected bipolar HEOG and VEOG signals were computed.

The continuous data was segmented into epochs using a window from -100 to 500 relative to acoustic change onset and baseline corrected from -100 to 0 relative to acoustic change onset. Artefacts that remained in the data after eye artefact correction were detected and excluded using automated ERPLAB algorithms. General artefacts, like electromyography bursts, movement artefacts, skin potentials, and sudden voltage changes of unknown origin were detected using two algorithms. The first was a simple voltage threshold algorithm that excludes any trials that had voltage excursions exceeding $\pm 200\,\mu\mathrm{V}$ on all channels except the bipolar eye channels [31]. The second was a moving window peak-to-peak algorithm on all non-eye channels and the supra-orbital eye channels with a threshold of $125\,\mu\mathrm{V}$ [31][38, Chap. 8.12]. ICA is known to not always correct eye movements perfectly, especially in participants who rarely make eye movements [31]. Therefore, trials with eye movements greater than approximately 4° of visual angle in the corrected HEOG channel were discarded using an algorithm that detects step-like artefacts [31][30, pg. 197-201]. The measurement time of our shortest stimulus was ≈ 4 minutes. Eye blinks during this stimulus might also be rare for participants that do not blink often, resulting in ICA not sufficiently correcting eye blinks. Therefore, an additional step-like artefact detection algorithm was applied to detect blinks on the corrected VEOG channel using a threshold of $50\,\mu\mathrm{V}$ [38, Chap. 8.9]. Per stimulus type, participants that exhibit artefacts on more than $25\,\%$ of trials were excluded [31][30, pg. 209-210]. Additionally, per stimulus type, participants that did not have a minimum number of 150 epochs were excluded. The average event related potential (ERP) for each stimulus per participant was computed and saved. The link to the Matlab code that was used to analyze the data is provided in the previous footnote[2]. Further details of data processing and the artefact detection parameters are provided in the comments of this code.

2.5.2 Quantification of signals and noise

Electrode FCz was used as the electrode to measure the outcome measures [31, 41, 42, 43]. Three local peaks were measured: P1, N1 and P2. To determine the time windows for the peaks, a collapsed localizer was made that averaged all but the test-retest stimulus [44][30, pg. 335-336]. Of this collapsed localizer the zero crossings were determined. For each peak, the surrounding zero time points were used as boundaries extended with 25 ms and rounded to the nearest multiple of five. Because there might be a large amplitude difference between the stimuli, the collapsed localizer might be dominated by the stimuli that elicit the largest amplitudes [30, pg. 335-336]. Therefore, the time windows of the peaks were visually checked on three randomly selected participants to see if they were suited for individual responses and all stimuli. To determine if the ACC was present, a cut-off value for the N1-P2 peak-to-peak amplitude of $4\,\mu\mathrm{V}$ was applied [19, 45, 46]. However, when on visual inspection an ACC waveform was unambiguous it was included, and when the ACC was not distinguishable from the noise, it was excluded. Responses were reviewed by a Technical medicine student (LS). When it was uncertain whether a response was present this was determined by discussion with the coordinating investigator (JV). Regardless of whether an ACC was present, the amplitude values of all participants were included for statistical analyses.

The latency values of ACCs that were not present were assigned a missing value and were excluded from further analyses. N1-P2 peak-to-peak amplitude was chosen as an outcome measure for amplitude and the signal portion of the SNR. N1-P2 peak-to-peak amplitude is the outcome measure most frequently used by studies that compare the ACC to speech perception tests (Appendix A). The remaining individual P1, N1 and P2 peaks were descriptively analyzed to minimize comparisons [30, pg. 312] [44]. Noise was defined as the standard error of the voltage during the baseline period of 100 ms prior to the acoustic change in the averaged ERP waveform calculated separately for each participant [47, 48].

The SNR was calculated with equation 2.1, with both the dividend and divisor in µV. Per stimulus, the measurement time was calculated in seconds with equation 2.2. The 200 repetitions per stimuli were multiplied with the PTD in ms plus 1000 ms which consisted of the acoustic change duration of 5 ms plus the post-transition duration of 495 ms and the inter-stimulus interval of 500 ms. This measurement time in ms was then divided by 1000 which resulted in the measurement time in seconds. Efficiency was then calculated with equation 2.3 [20].

$$\text{SNR} = \frac{\text{N1-P2 peak-to-peak Amplitude}}{\text{Baseline noise}} \tag{2.1}$$

$$\text{Measurement time} = \frac{200 \times (PTD + 1000)}{1000} \tag{2.2}$$

$$\text{Efficiency} = \frac{\text{SNR}}{\text{Measurement time}} \tag{2.3}$$

2.5.3 Statistical analyses

Statistical analyses was performed with SPSS (version 29.0.2.0, IBM). The Friedman test was used to compare the N1-P2 peak-to-peak amplitude, baseline noise, SNR and efficiency over all PTDs. When significant, post-hoc comparisons were performed with the Wilcoxon Signed Rank test. We used the Bonferroni correction for each post-hoc test to control the false discovery rate for multiple comparisons. To analyze the N1-P2 peak-to-peak amplitude, baseline noise and SNR between the complex and pure tone and test and retest stimulus, the one-sample Wilcoxon signed Rank test was used. Efficiency was not analyzed for the latter since the compared stimuli have the same measurement time. The significance threshold was set at $p < 0.05$.

3 Results

3.1 Participant characteristics

Nineteen subjects participated in this study. One participant was excluded due to an average hearing threshold of 26.75 dB HL, and a hearing threshold of 40 dB HL at 1 kHz in the better hearing ear. The remaining eighteen participants were included. Twelve participants were female and 7 were male. The mean age was 29.06 years (standard deviation (SD)$= 10.61$, range$= 19 - 60$ years). The mean Fletcher Index was 3.6 dB HL in the right ear (SD$= 3.8$) and 6.0 dB HL in the left ear (SD$= 9.3$).

3.2 Signal processing

After data recording, and before signal processing, three out of 162 measurements were excluded due to irregularities in the sound. A measurement is one measured stimulus type per participant, thus the mean of 200 repetitions.

Artefact correction, as described in subsection 2.5.1, resulted in the removal of one to five of the 15 independent components per measurement, resulting in a total of 381 removed independent components. For one measurement, no components exceeded the $90\,\%$ probability of being an eye artefact, and therefore, no artefact correction was applied on this measurement (ACC0014 retest stimulus). The mean probability of being an eye artefact of the removed components was 0.976 (SD 0.026, range $0.901 - 1.000$).

Artefact rejection, as described in subsection 2.5.1 resulted in a mean artefact rejection of $3.309\,\%$ (SD $5.081\,\%$, range $0 - 23\,\%$). The mean, SD and range of artefact rejection percentages per stimulus can be reviewed in Subsection B.2 of Appendix B. Two measurements were excluded due to artefacts on more than $25\,\%$ of the trials.

The PTD of 250 ms was not further analyzed due to a visual overlap of the onset response with the baseline period of the ACC. In Subsection B.1 of Appendix B, two figures showing this overlap can be reviewed.

To summarize all of the above, Table B1 in Appendix B gives an overview of the in and exclusion of measurements.

A summary of the signal processing is provided in Table 1, showing the number of participants, percentage of participants with a response and the mean artefact rejection percentage per stimulus. Table B3 in Subsection B.3 of Appendix B shows more detailed results of the ACC presence determination based on visual inspection as described in Subsection 2.5.2.

After signal processing, the collapsed localizer was computed, which can be viewed in Figure C.1 in Appendix C. This collapsed localizer resulted in the following time windows for the peaks (min-max [ms]): P1 $(10 - 105)$, N1 $(55 - 170)$, P2 $(120 - 315)$. These time windows were visually checked on three randomly selected participants (ACC0001, ACC0010 and ACC0013) for all stimuli and were appropriate. Furthermore, per stimulus, a grand average with SD was computed, which can be reviewed in Figure C.2 in Appendix C.

3.3 Pre-transition duration

A boxplot with the the baseline noise is shown in Figure 2a and a boxplot with N1-P2 peak-to-peak amplitude per PTD is shown in Figure 2b. Boxplots of the N1-P2 SNR and Efficiency are shown in Figures

Table 1: The number of participants, mean artefact rejection percentage, percentage of present responses of all included measures per stimulus and measurement time calculated with formula 2.2, converted to minutes. PTD = pre-transition duration in ms. The PTD for the complex and retest tones was 1000 ms.

	Stimulus					
	PTD 500	PTD 1000/ Pure tone/Test	PTD 2000	PTD 3000	Complex tone	Retest
Number of participants	17	17	17	18	16	18
Participants with response [%]	35.3	58.8	88.2	100.0	81.3	61.1
Mean artefact rejection [%]	2.9	3.4	3.6	4.1	3	3.8
Measurement time [min]	5.00	6.67	10.00	13.33	6.67	6.67

2c and 2d. Table 1 shows the number of participants for which an ACC was present, the mean artefact rejection percentage and the measurement time per PTD. Presence of the ACC ranged from 35.3 to 100 %. The grand averages of all PTDs are included in Figure 3.

There was a statistically significant difference in N1-P2 peak-to-peak amplitude (Friedman test: $x2(3)=40.36$, $p<0,001$), Baseline noise (Friedman test: $x2(3)=10.76$, $p<0,013$), SNR (Friedman test: $x2(3)=28.52$, $p<0,001$) and Efficiency (Friedman test: $x2(3)=12.84$, $p<0,005$) across the PTDs. Results of the post-hoc Wilcoxon Signed Rank test on N1-P2 peak-to-peak amplitude, baseline noise, SNR and Efficiency between the PTDs are shown in Table 2. An increase of the PTD resulted in a significant increase in N1-P2 peak-to-peak amplitude between all measured PTDs, except for an increase in PTD from 2000 to 3000 ms, which was not significant ($p=0.530$). Regarding the SNR, this effect remained for the difference between PTD 500 ms and all other measured PTDs, but diminished between the remaining pairs of PTDs. The baseline noise was not significantly different between the PTDs, except that for PTD 3000 ms the baseline noise was significantly smaller than for PTD 500 ms ($p=0.032$). When looking at the Efficiency, only the difference between PTDs 500 and 1000 ms ($p=0.013$) was statistically significant (Table 2).

Appendix D includes figures of the amplitude, latency, SNR and Efficiency boxplots for the remaining P1, N1 and P2 peaks. Remarkably, the P1 amplitude for PTD 500 ms was relatively high in comparison with PTDs 1000, 2000 and 3000 ms.

3.4 Tonal complexity

Figure 2b includes boxplots of the N1-P2 peak-to-peak amplitude for the complex and pure tone. Figure 4 includes the grand averages of the complex and pure tone. A Wilcoxon Signed Rank test revealed that N1-P2 peak-to-peak amplitude scores were not significantly different for the complex (Median (Md)$=4.943$ µV, n$=16$) compared to the pure tone (Md$=4.789$ µV, n$=16$), z$=-0.621$, p$=0.535$. The complex tone was present in 81.3 % of the cases and the pure tone was solely present in 58.8 % of the cases (see Table 1).

A boxplot of the baseline noise for the complex and pure tone is shown in Figure 2a. A Wilcoxon Signed Rank test indicated no significantly different baseline noise level for the complex (Md$=0.308$ µV, n$=16$) compared to the pure tone (Md$=0.329$ µV, n$=16$), z$=-0.103$, p$=0.918$.

A boxplot of the N1-P2 SNR for the complex and pure tone is shown in Figure 2c. A Wilcoxon Signed Rank test indicated no significantly different SNR for the complex (Md$=14.941$, n$=16$) compared to the pure tone (Md$=14.709$, n$=16$), z$=-0.362$, p$=0.717$.

Appendix D includes figures of the amplitude and latency boxplots for P1, N1 and P2. The P1 amplitude for the complex tone seemed to be slightly higher than that of the pure tone.

The descriptive results (table with a summary of the signal processing, grand averages and boxplots) of the ACCs elicited to complex tones with intensity alterations, as described in subsection 2.2 and Text box 2 in Appendix E.1, can be reviewed in Appendix E. This data was not further analyzed due to the absence of statistical significance between the N1-P2 peak-to-peak amplitude or SNR of the complex and pure tone.

3.5 Repeatability

The boxplots of the N1-P2 peak-to-peak amplitude to the pure tone and retest pure tone can be reviewed in Figure 2b. Figure 4 includes the grand averages of the test and retest tone. A Wilcoxon Signed Rank test revealed that N1-P2 peak-to-peak amplitude scores were not significantly different for the retest pure tone (Md$=4.512$ µV, n$=17$) compared to the pure tone (Md$=4.492$ µV, n$=17$), z$=-0.639$, p$=0.523$.

A boxplot of the baseline noise for the test and retest tone is shown in Figure 2a. A Wilcoxon Signed Rank test indicated no significantly different baseline noise level for the retest pure tone (Md$=0.507$ µV, n$=17$) compared to the pure tone (Md$=0.412$ µV, n$=17$), z$=-1.728$, p$=0.084$.

A boxplot of the N1-P2 SNR for the test and retest tone is shown in Figure 2c. A Wilcoxon Signed Rank test indicated no significantly different SNR for the retest pure tone (Md$=8.437$, n$=17$) compared to the pure tone (Md$=12.676$, n$=17$), z$=-1.775$, p$=0.076$.

Subsection D.1 of Appendix D includes figures of the amplitude and latency boxplots for P1, N1 and P2 for the test and retest tones. Visually, there were no remarkable findings regarding these peaks.

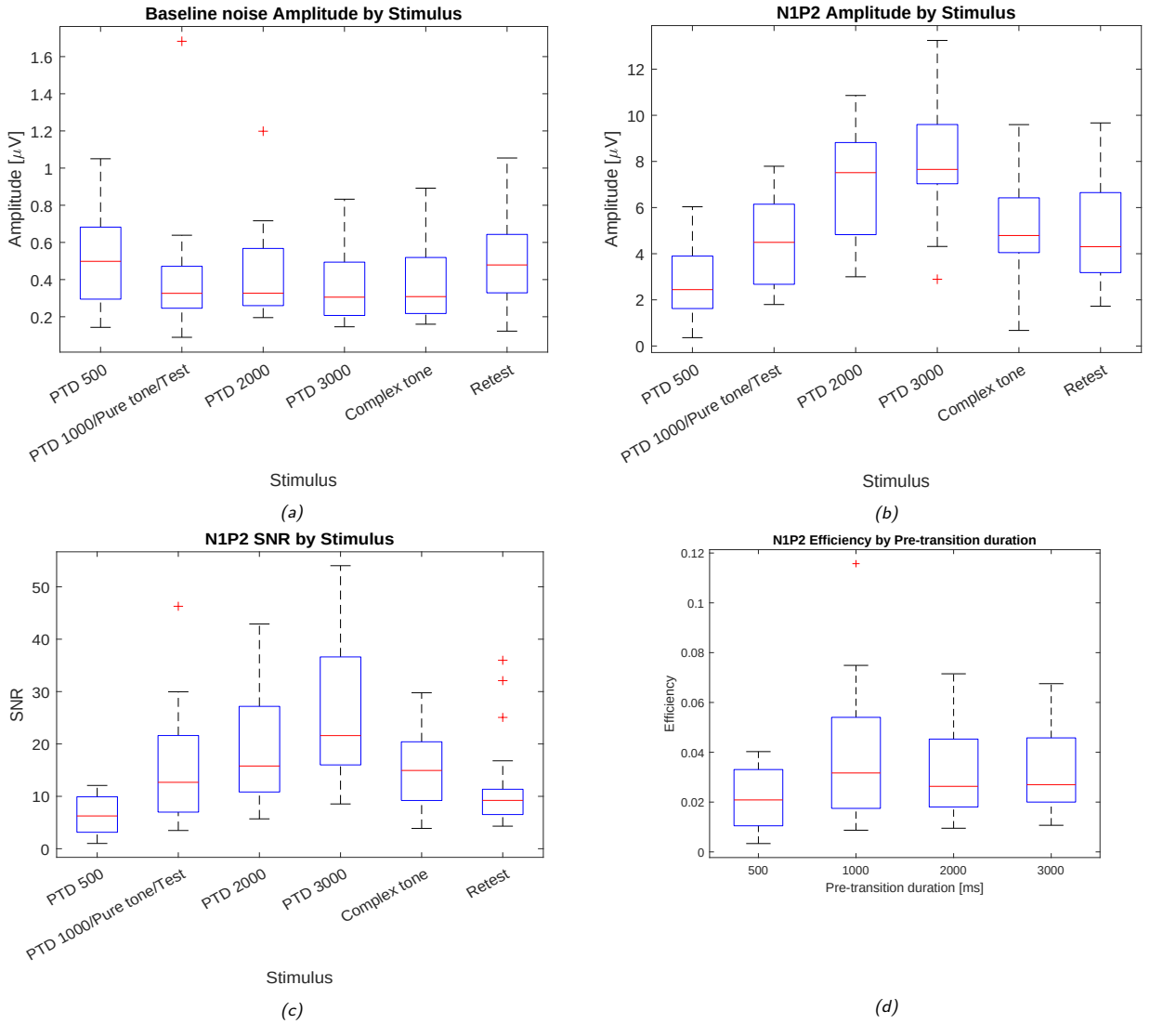

Figure 2: Boxplots of: 2a the baseline noise amplitude, 2b N1-P2 peak-to-peak amplitude, 2c N1-P2 peak-to-peak signal to noise ratio (SNR) and 2d N1-P2 peak-to-peak Efficiency per stimulus with varying pre-transition duration in ms (PTD) or tonal complexity. These outcome measures were derived from the acoustic change complex elicited to a (center) frequency change from 1 to 1.1 kHz. The baseline noise was the standard error measured from −100 to 0 ms relative to acoustic change onset. The PTD of the complex and retest tone was 1000 ms. SNR is calculated with formula 2.1 and Efficiency is calculated with formula 2.3.

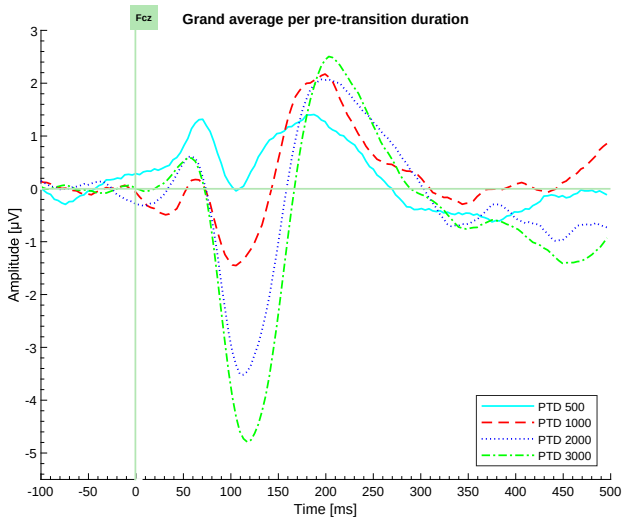

Figure 3: Grand averages of the acoustic change complex (ACC) of all stimuli with varying pre-transition durations (PTD). The ACC was elicited to a frequency change from 1 to 1.1 kHz that started at 0 ms.

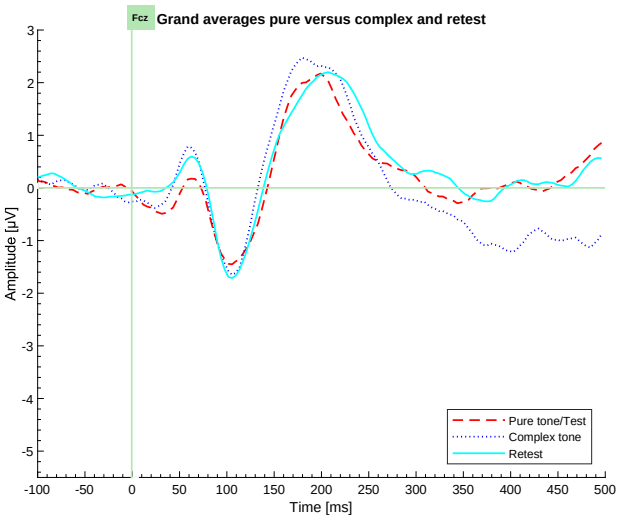

Figure 4: Grand averages of the acoustic change complex (ACC) of the complex, retest and pure/test stimuli. The ACC was elicited to a (center) frequency change from 1 to 1.1 kHz that started at 0 ms. The pre-transition duration was 1000 ms.

*Table 2: Results of the post-hoc Wilcoxon Signed Rank test between pre-transition durations (PTDs) for N1-P2 peak-to-peak (N1-P2) amplitude, signal to noise ratio (SNR) and efficiency and the baseline noise (N=15). *Using Bonferroni correction per (the number of comparisons per) outcome measure.*

	PTD [ms]		Median [µV]			
Outcome measure	Group 1	Group 2	Group 1	Group 2	Z	Adjusted* p value
N1-P2 Amplitude	1000	500	5.394	2.597	−3.351	0.005
	2000	500	7.748	2.597	−3.408	0.004
	3000	500	9.027	2.597	−3.408	0.004
	2000	1000	7.748	5.394	−3.408	0.004
	3000	1000	9.027	5.394	−3.408	0.004
	3000	2000	9.027	7.748	−1.704	0.530
Baseline noise	1000	500	0.326	0.502	−1.931	0.321
	2000	500	0.376	0.502	−1.193	1.00
	3000	500	0.309	0.502	−2.783	0.032
	2000	1000	0.376	0.326	−1.42	0.934
	3000	1000	0.309	0.326	−0.057	1.00
	3000	2000	0.309	0.376	−1.533	0.751
Outcome measure	PTD [ms]		Median		Z	Adjusted* p value
N1-P2 SNR	1000	500	16.742	6.672	−3.351	0.005
	2000	500	15.79	6.672	−3.351	0.005
	3000	500	22.62	6.672	−3.408	0.004
	2000	1000	15.79	16.742	−1.306	1.00
	3000	1000	22.62	16.742	−2.556	0.064
	3000	2000	22.62	15.79	−1.874	0.365
N1-P2 Efficiency	1000	500	0.042	0.022	−3.067	0.013
	2000	500	0.026	0.022	−2.613	0.054
	3000	500	0.028	0.022	−2.215	0.161
	2000	1000	0.026	0.042	−1.533	0.751
	3000	1000	0.028	0.042	−1.136	1.00
	3000	2000	0.028	0.026	−0.17	1.00

4 Discussion

Our objectives were to study the effect of 1) the PTD and 2) tonal complexity of the stimulus on the N1-P2 peak-to-peak amplitude, baseline noise and SNR of the ACC in normal hearing adults. Furthermore, for evaluation of the PTD, efficiency was included as an outcome measure. In the next two subsections, we will discuss our findings and compare them to previous studies and our hypothesis. Additionally, we did not find a significant difference between the baseline noise, amplitude and SNR of our test and retest pure tone, indicating that our setup seems to have a good test-retest reliability.

4.1 Pre-transition duration

Our results show that an increase in PTD significantly increased the N1-P2 peak-to-peak amplitude up to a PTD of 2000 ms, for which the ACC was present in 88.2 % of participants and the measurement time was 10.00 min. The baseline noise did not significantly differ between the PTDs, except the significantly higher baseline noise level for PTD 500 compared to PTD 3000 ms. The only significant difference in SNR was a significantly smaller SNR for PTD 500 ms compared to all other PTDs. A PTD of 1000 ms was significantly more efficient than a PTD of 500 ms. Efficiency for all other pairs of PTDs did not significantly differ. A PTD of 1000 ms had measurement time of 6.67 min, and the ACC was present in 58.8 % of the participants (Table 1 and 2).

In our data, the median N1-P2 peak-to-peak amplitude significantly increased by a factor 1.67 between PTDs 1000 and 3000 ms Table (2). This is in line with the findings of Vonck et al. (2019) [25]. They found in pilot data from three participants, that prolonging the PTD from 1000 to 3000 ms increased the amplitude of the resulting ACC by a factor of ~ 1.5 (using a 1 kHz pure tone with an unknown frequency increase). Ganapathy et al. (2013) [24] measured the ACC to PTDs ranging from 50 to 150 ms, in a pure tone with a frequency increase from 1 kHz to 2 kHz. Inconsistent with our findings, they did not find a significant effect of PTD on N1 and P2 amplitude [24]. The increase in PTD of 100 ms used by Ganapathy et al. (2013) [24], might not have been sufficient to increase the amplitude of the ACC.

4.2 Tonal complexity

There was no significant N1-P2 peak-to-peak amplitude, baseline noise and SNR difference between the complex and pure tone. However, the presence of ACC responses increased by 22.5 percentage points for the complex tone compared to the pure tone (Table 1). We expected that

an increase in presence would be a result of an increase in SNR. Bardy et al. (2015) [26] did find an increase in onset response presence and amplitude comparing the complex to the pure tone. However, we used other stimulus parameters and outcome measures, making it difficult to draw conclusions on why our findings are not in line with their findings.

4.3 Limitations and Recommendations

We found an increase in presence between the complex and pure tone, however, amplitude and noise levels did not significantly differ. This might indicate that our widely used but subjective visual inspection method for determining presence relies on more signal parameters than solely N1-P2 peak-to-peak amplitude and baseline noise such as morphology, distinctness and sharpness of the peaks. It would be interesting to see if our presence determination is reproducible with objective methods that do not rely on experience of the examiner. For example, the Hotellings t-squared test which is a multi-dimensional equivalent of the (squared) univariate t-statistic [49]. However, this method is not yet used much in ACC research.

Furthermore, as described in Textbox 2 of Appendix E, there was a possible intensity difference between the pure and complex tones due to measuring in the free field. We chose speakers for our setup to be able to measure individuals with a hearing aid or cochlear implant in the future. However, possible interference may have caused a change in the intensity of the pure tone, either overall or during the acoustic transition. Therefore, a possible intensity increase of the pure tone might have negatively influenced an amplitude difference between the pure and complex tone. To rule out this possible effect, it would be interesting to study if the results are reproducible when the sound is presented via headphones or inserts. Furthermore, this would rule out a possible increased ACC presence of the complex compared to the pure tone due to an intensity decrease of the pure tone. Comparing ACC presence for the complex tones with intensity alterations to ACC presence of the pure tone would also give insight in this.

Comparison of the amplitude values between the PTDs resulted in more significant p-values compared to the SNR values between the PTDs (Table 2). It is known from literature that peak amplitude levels become both more variable and systematically larger as the noise level increases [30, Chap. 9 Suppl.][38, Chap. 10.6]. An increase in peak-to-peak amplitude values due to an increased noise level therefore might have leveled out a decrease in SNR, leading to a decrease in the effect size [30, Chap. 9 Suppl.]. However, measuring mean amplitude was not possible due to alternating positive and negative peaks and N1-P2 peak-to-peak amplitude is the most frequently used outcome measure by studies that compare the ACC to speech perception tests (Appendix A) [30, Chap. 9 Suppl.].

The SNR increases in proportion to the square root of the number of trials [30, pg. 261]. We did not equalize the number of trials per measurement since this would exclude a large percentage of the trials [50]. Furthermore, mean artefact percentage slightly increased with an increase in PTD (Table 1, not statistically tested). Therefore, a possible effect of the number of trials on the SNR is expected to be small and would undermine our hypothesis.

We included the N1-P2 peak-to-peak amplitude values of participants in which no ACC was elicited. As a general outcome measure for efficiency and SNR this can be substantiated, since a low signal is of clinical relevance. However, when solely investigating the peak amplitudes it is interesting, and might be scientifically more rigorous to only include the amplitude values of participants in which the peaks were present. Due to missing data, more advanced statistics, such as linear mixed models, would then be required.

The significantly larger baseline noise level for PTD 500 in comparison with PTD 3000 ms, and the remarkably high P1 amplitude for PTD 500 ms (Figure D.1(a) in Appendix D, not statistically tested) might be due to overlap with the onset response. Overlap can alter the peak-to-peak amplitude levels and increase baseline noise. To study if overlap contributed to our results, the morphology and overlap should be evaluated on individual averages using techniques to recover the original overlap-free waveform [30, chap. 11].

4.4 Clinical implications and future work

Based on our results, we recommend using a PTD of 1000 ms for elicitation of the ACC rather than a PTD of 500 ms. This will significantly increase N1-P2 peak-to-peak amplitude, SNR and efficiency and thus is likely to increase sensitivity, specificity and clinical feasibility of difficult to test patients. When aiming for the same SNR, measurement time will be decreased by an estimated percentage of 78.8 % when the PTD is increased from 500 to 1000 ms, see Textbox 1. Though we did not measure the most commonly used PTD of 400 ms, we expect that this advise is generalizable for an increase in PTD from 400 to 1000 ms.

Increasing the PTD above 1000 ms did not result in significant SNR changes between subsequent PTDs and it did not lead to a significant change in efficiency. Furthermore, the complex tone was not significantly different in N1-P2 peak-to-peak amplitude or SNR from the pure tone. However, presence of the ACC did increase with an increase in tonal complexity and PTD (not statistically tested). We observed that ACC presence can reach 100 % for PTD 3000 ms in normal hearing adults. This raises the hypothesis that specificity of the ACC as a measure of speech perception can be increased with an increase in PTD or tonal complexity,

without negatively influencing the SNR or efficiency. However, this should be confirmed by future research.

To improve clinical applicability, the SNR might be further increased by optimizing other stimulus parameters, the paradigm, signal acquisition and data analysis, with the prerequisite that efficiency is maintained. Depending on the required SNR for a sufficient sensitivity and specificity of the ACC as a measure of speech discrimination, the measurement time may be reduced by decreasing the number of repetitions

The ACC to a frequency change in a pure tone is related to speech perception measures [45, 19, 43, 51, 52, 53]. Further research is needed to study the relationship between the ACC elicited by a complex tone and speech perception measures.

Feasibility of the total test time and the relationship between ACC outcome measures and speech perception measures in hearing impaired participants will eventually determine the clinical value of the ACC as a non-invasive, passive, and objective measure of speech discrimination.

The ACC would be valuable to assess sound discrimination capacity in children. However, the results of this study are not directly generalizable to children. This is because the effect of PTD on the resulting ACC is expected to be age dependent due to changes in myelination, cortical fiber density and synaptic refinement [23]. The morphology, detectability and amplitude of the onset response in children changes when the inter stimulus interval is altered, which is comparable to the PTD of the ACC [6, 54]. Therefore, a follow up study should investigate the effect of PTD on the ACC in children. For this study it is relevant to look at the presence of individual peaks and to analyse P1 besides N1 and P2. This is because for the onset response, P1 is significantly higher in children compared to adults and compared to N1 it is present in the first year of life with a lower inter stimulus interval [6, 54, 55].

5 Conclusion

We studied the effect of PTD and tonal complexity on the N1-P2 peak-to-peak amplitude, baseline noise, SNR and efficiency of the ACC in normal hearing adults. The ACC is affected by the PTD. An increase in PTD significantly increased the N1-P2 peak-to-peak amplitude up to a PTD of 2000 ms. The only significant difference in SNR was a significantly smaller SNR for PTD 500 ms compared to all other PTDs. A PTD of 1000 ms was significantly more efficient than a PTD of 500 ms. ACC presence increased with an increase in PTD and was 100 % for a PTD of 3000 ms (not statistically tested). The complex tone was not significantly different in N1-P2 peak-to-peak amplitude or SNR compared to the pure tone. However, ACC presence increased by 22.5 percentage points for the complex tone compared to the pure tone.

We recommend utilizing a PTD of 1000 ms instead of 500 ms, as it resulted in a significantly higher N1-P2 peak-to-peak amplitude, SNR and efficiency. Furthermore, an increase in tonal complexity or the PTD beyond 1000 ms seems promising to increase presence of the ACC without significantly decreasing the SNR or efficiency.

Follow up research is needed to study the effect of the PTD on the ACC in children and to relate ACCs elicited by complex tones to speech perception measures.

Our results add knowledge to the effects of stimulus parameters on the elicited ACC. This brings the field one step closer to implementing the ACC as a non-invasive, passive, and objective clinical measure of speech discrimination.

$$\text{Scaling factor repetitions} = \left(\frac{\text{Median SNR PTD } 1000}{\text{Median SNR PTD } 500}\right)^2 \tag{5.1}$$

$$\text{New repetitions PTD } 1000 = \frac{\text{Original repetitions}}{\text{Scaling factor repetitions}} \tag{5.2}$$

$$\text{New MT PTD } 1000 = \frac{\text{Old MT PTD } 1000 \times \text{New repetitions PTD } 1000}{\text{Original repetitions}} \tag{5.3}$$

$$\text{MT decrease} = \left(\frac{\text{New MT PTD } 1000 - \text{MT PTD } 500}{\text{MT PTD } 500}\right) \times 100 \tag{5.4}$$

In which the original repetitions (number of times the sound was presented and recorded) were 200 trials, the measurement time (MT) of PTD 500 ms was 5.00 min and the old measurement time of PTD 1000 ms was 6.67 min.

Text box 1: Calculation of the estimated change in measurement time.

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Appendices

A Findings extracted from the literature study conducted in preparation for this master thesis

The work done for this Appendix A was part of another course and therefore should not be graded.

In preparation for this master thesis a literature study was conducted named: *Procedures used for the Acoustic change complex as a measure of speech perception and its correlation with speech perception tests: a scoping review*. This Appendix contains extracted findings from this literature study.

A.1 Objectives, methods, and main results

Objectives The aim of this review is to provide an overview of procedures used for the Acoustic change complex (ACC) as a measure of speech perception. The procedures examined are the stimuli used for eliciting an ACC, what methods are used to determine the presence of the ACC, how missing data is managed and what outcome measures are used. The second aim is to compare the results of ACC as a measure of speech perception with speech perception tests regarding correlation between both measures. **Methods** A literature search was conducted to identify papers for inclusion in Embase, Medline ALL, Web of Science Core Collection, Cochrane Central Register of Controlled Trials, and Google Scholar. Studies that measured an ACC on participants with any age with normal hearing or hearing loss and that compared the outcomes of the ACC to a speech perception test were included. The reference lists of included articles were screened for additional relevant studies. Information is extracted and the altered methodological index for nonrandomized studies was assessed to evaluate methodological quality. **Main results** The search revealed 89 records and after selection and citation screening 20 relevant studies were included. Stimuli are presented with a change in a finite sound, multiple sequential changes in a continuous sound or using an oddball paradigm. Stimulus types used are speech and nonspeech stimuli and the latter can be divided in spectral modulation, temporal modulation, and intensity modulation. For determination of the presence of the ACC and the handling of missing data, diverse strategies are used. The ACC outcome measures can be divided in threshold and supra threshold measurements and the most used is the N1-P2 peak-to-peak amplitude followed by N1 latency. Speech perception tests are significantly correlated with ACC outcome measures in 42% of the statistical tests conducted. The mean correlation between ACC outcome measures and the outcomes of speech perception tests is 0.58.

A.2 Pre-transition durations used in studies that compare the ACC to speech perception test

Of the studies included in the literature review there were sixteen studies that measured the ACC to a single change in a finite sound. Of those 16 studies one study (Liang et al. (2016) [56] did not mention the pre-transition duration. The pre-transition durations of all other studies are included in Table A1. Ten used a pre-transition duration of 400 ms, three used a pre-transition duration of $\sim$ 3000 ms, one used a pre-transition duration of 500 ms and one of 200 ms. Four studies are not included in this table because they used an alternative paradigm. Cone et al. (2022) [9] and Cone (2015) [57] used an oddball paradigm and Dimitrijevic et al. (2011) [43] and Han and Dimitrijevic (2020) [58] used multiple acoustic changes in a continuous sound. As mentioned before, when the ACC is measured to multiple changes in a continuous sound the ISI is the same as the pre-transition duration. Dimitrijevic et al. (2011) [43] used an ISI of 1400 ms and Han and Dimitrijevic (2020) [58] used a random inter-stimulus interval that varied from 1800 to 2600 ms, with an average ISI of 2200 ms.

Table A1: Pre-transition durations of the studies that measured the ACC to a single change in a finite sound included in the literature study conducted in preparation for this master thesis.

Study	Pre-transition duration [ms]
Xie et al. (2022) [53]	400
Vonck et al. (2021) [19]	3000
Vonck et al. (2022) [45]	2997
Brown et al. (2015) [59]	400
He et al. (2014) [60]	400
He et al. (2013) [61]	400
He et al. (2015) [62]	400
McGuire et al. (2021) [52]	500
Kirby and Brown (2015) [63]	400
Shalaby et al. (2022) [64]	200
Heteren et al. (2022) [46]	2997
Mathew et al. (2017) [41]	400
Mathew et al. (2018) [42]	400
Mussoi and Brown (2019) [65]	400
Scheperle and Abbas (2015) [66]	400

B Signal processing results

This Appendix gives details about the artefact rejection and in and exclusion of measurement results. A measurement is a sound stimulus for one participant and thus includes 200 repetitions of one sound. Table B1 gives a summary of all included and excluded measurements. The pre-transition duration (PTD) of 250 ms is not included in this table because this PTD was excluded due to overlap with the onset response, which is outlined in Subsection B.1. Subsection B.2 gives the mean and standard deviation artefact rejection percentage of all included measures per stimulus. After artefact rejection, the included measures were evaluated on presence of the Acoustic change complex, of which the results can be reviewed in Subsection B.3.

*Table B1: Overview of which measurements were in and excluded. Green and orange indicate included measurements. Orange means that the acoustic change complex was rated as not present, as defined in Subsection 2.5.2. Blue indicates that the measurement was excluded due to sound irregularities. Red indicates that the measurement was excluded due to an artefact rejection percentage that exceeds the threshold of 25% (exact percentage is displayed in the table), as stated in Subsection 2.5.1. *2 labels were removed from the eventlist due to an abnormal first tone, which led to a double label. Therefore, there were 199 trials remaining in this measurement. ** Between the first two tones, the inter stimulus interval was <500 ms. Therefore, the first two labels were removed from the eventlist and there were 198 trials remaining in this measurement. PTD= pre-transition duration in ms.*

	Stimulus							
ID	PTD 500	PTD 1000/ Pure tone/Test	PTD 2000	PTD3000	Complex tone	-3dB Complex tone	Complex tone -3dB intensity change	Retest
ACC0001								
ACC0002								
ACC0003								
ACC0004				*				
ACC0005					**			
ACC0006								
ACC0007								
ACC0008								
ACC0009								
ACC0010								
ACC0012								
ACC0013								
ACC0014								
ACC0015								
ACC0016		38.5%			62.5% rejected			
ACC0017								
ACC0018								
ACC0019								

B.1 Exclusion of pre-transition duration 250 ms

The PTD of 250 ms was excluded from further analyses due to overlap with the onset response. As can be seen in Figure B.1, at time of the baseline period of the acoustic change, the grand average was still in the midst of the onset response. This phenomenon can be seen in individual responses as well, of which an example is shown in Figure B.2.

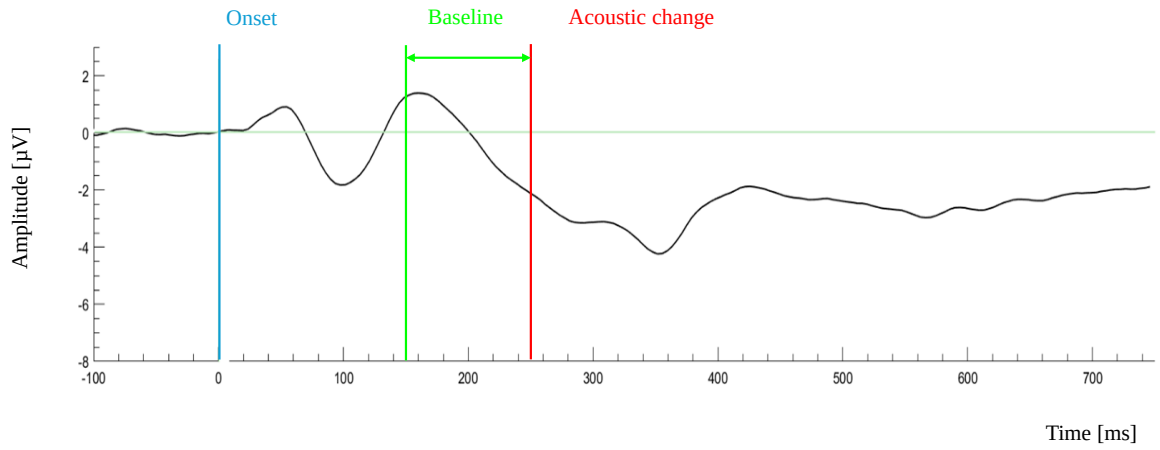


Figure B.1: Grand average of electrode Fcz for pre-transition duration 250 ms. At time point zero the sound started (Blue, onset), at 250 ms the acoustic change occurred in the sound (Red, acoustic change). The baseline period was 100 ms prior to the acoustic change (green arrow, baseline). The colored lines are sketches.

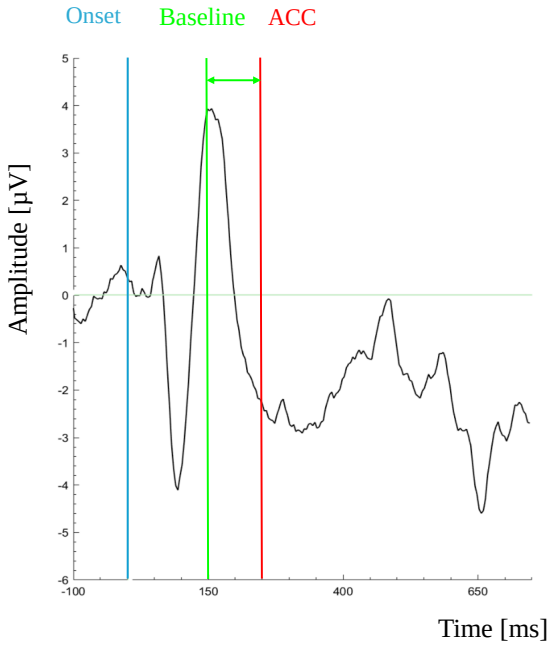


Figure B.2: Average of electrode Fz for pre-transition duration 250 ms from subject ACC0013. At time point zero the sound started (Blue, onset), at 250 ms the acoustic change occurred in the sound (Red, acoustic change). The baseline period was 100 ms prior to the acoustic change (green arrow, baseline). The colored lines are sketches.

B.2 Artefact rejection percentages per stimulus

Table B2 gives the mean, standard deviation and range of artefact rejection percentages of all included measures per stimulus. Included measures were the green and orange measurements of Table B1. Artefact rejection methods are described in Subsection 2.5.1. Percentages were calculated in Matlab (version R2022b, MathWorks).

Table B2: Mean, standard deviation and range of artefact rejection percentages of all included measures per stimulus. Included measures were the green and orange measurements of Table B1. PTD= pre-transition duration in ms.

	Stimulus							
	PTD 500	PTD 1000/ Pure tone/Test	PTD 2000	PTD 3000	Complex tone	-3dB Complex tone	Complex tone -3dB intensity change	Retest
Mean [%]	2.882	3.441	3.559	4.083	3.031	1.753	4.861	3.778
Standard deviation [%]	4.679	4.451	5.071	6.750	4.562	2.492	7.338	5.867
Minimum [%]	0	0	0	0	0	0	0	0
Maximum [%]	19	12	20	23	16	10	21	20

B.3 Presence evaluation of the Acoustic change complex

The included measures were evaluated on presence of the ccoustic change complex, as described in Subsection 2.5.2. Table B3 gives an overview of the number of measurements per stimulus that were above the threshold, were discussed with the principal investigator after the first review of the student and the number of measurements that were included or excluded despite the threshold. This resulted in a total number of present responses that can be reviewed in the last column.

Table B3: Results of the acoustic change complex presence evaluation. PTD= pre-transition duration in ms.

Stimulus	Participants [n]	Above threshold (4µV) [%]	Discussed [%]	Extra excluded [%]	Extra included [%]	Participants with response[%]
PTD 500	17	17.6	47.1	5.9	23.5	35.3
PTD 1000/Pure tone/Test	17	58.8	23.5	11.8	11.8	58.8
PTD 2000	17	82.4	11.8	0.0	5.9	88.2
PTD3000	18	94.4	5.6	0.0	5.6	100.0
Complex tone	16	75.0	12.5	6.3	12.5	81.3
-3dB Complex tone	18	72.2	0.0	0.0	16.7	88.9
Complex tone -3dB intensity change	18	38.9	27.8	0.0	33.3	72.2
Retest	18	55.6	11.1	5.6	11.1	61.1

C Grand averages and collapsed localizer

This Appendix includes the collapsed localizer and the grand averages of all stimuli, except for the stimuli with intensity alterations, which can be reviewed in Subsection E.3 of Appendix E. Table C1 in Subsection C.1 gives the number of participants and trials, as background information for the collapsed localizer and grand averages. Subsection C.2 shows the collapsed localizer on which the time windows for the peaks were determined, as described in Subsection 2.5.2. Subsection C.3 gives the grand averages of all stimuli.

C.1 Number of trials per grand average

Table C1: The number of accepted trials, participants and the total percentage of trials excluded after signal processing per stimulus. The total percentage of excluded trials is based on artefact rejection and sound irregularities as described in Appendix B. PTD= pre-transition duration in ms.

	Stimulus							
	PTD 500	PTD 1000/ Pure tone/Test	PTD 2000	PTD3000	Complex tone	-3dB Complex tone	Complex tone -3dB intensity change	Retest
Number of accepted trials	3302	3283	3279	3452	3101	3522	3425	3464
Number of participants	17	17	17	18	16	18	18	18
Trials excluded [%]	2.9	3.4	3.6	4.1	3	1.8	4.9	3.8

C.2 Collapsed localizer

Figure C.1 shows the collapsed localizer on which the time windows for the peaks were determined, as described in Subsection 2.5.2. Pre-transition duration 250 ms is not included in this collapsed localizer since presence of the onset response in the baseline period of the acoustic change complex, as described in Subsection B.1 of Appendix B.

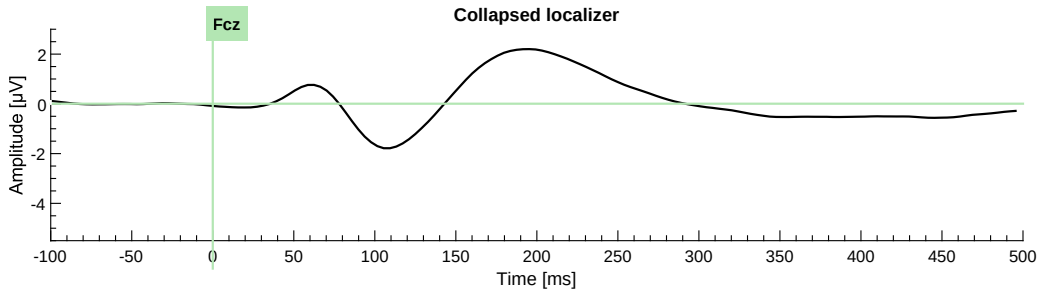
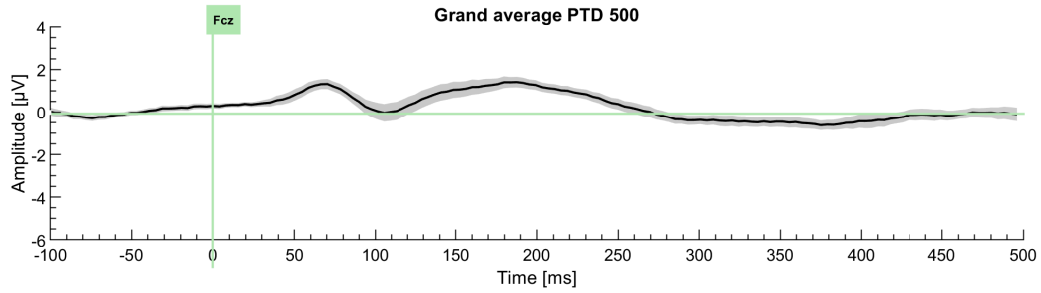
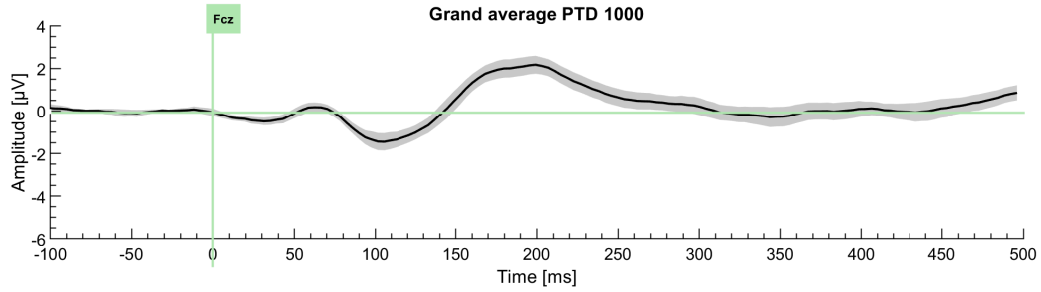


Figure C.1: Collapsed localizer without pre-transition duration 250 ms and test-retest stimulus.

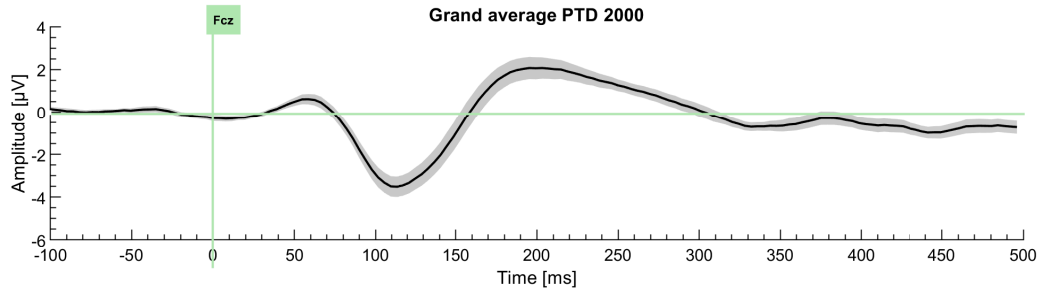
C.3 Grand averages



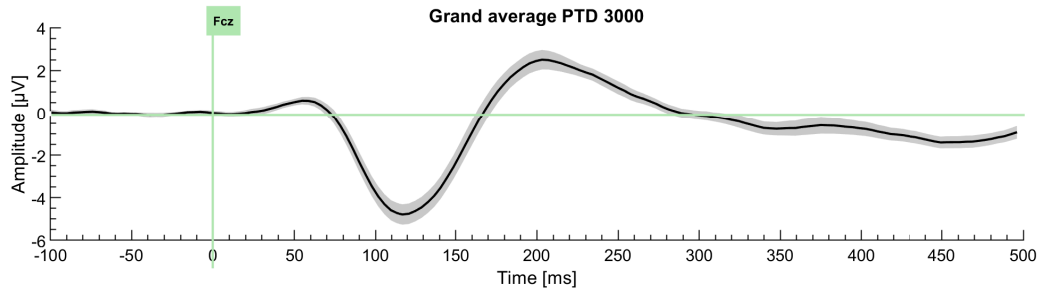
(a) Grand average of the pure tone with pre-transition duration (PTD) 500 ms with the standard error of the mean in grey.



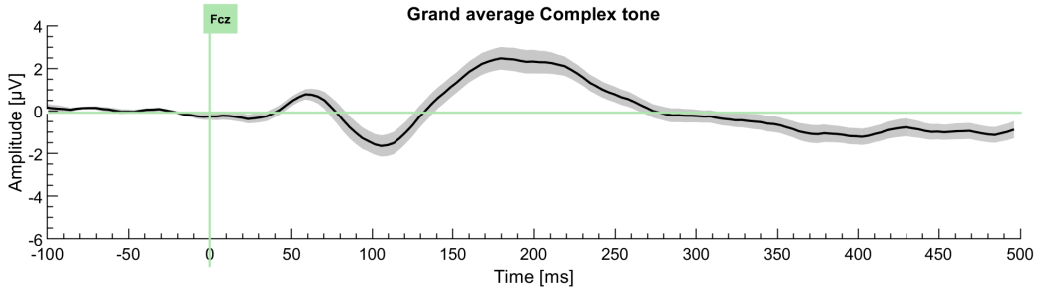
(b) Grand average of the pure tone with pre-transition duration (PTD) 1000 ms with the standard error of the mean in grey.



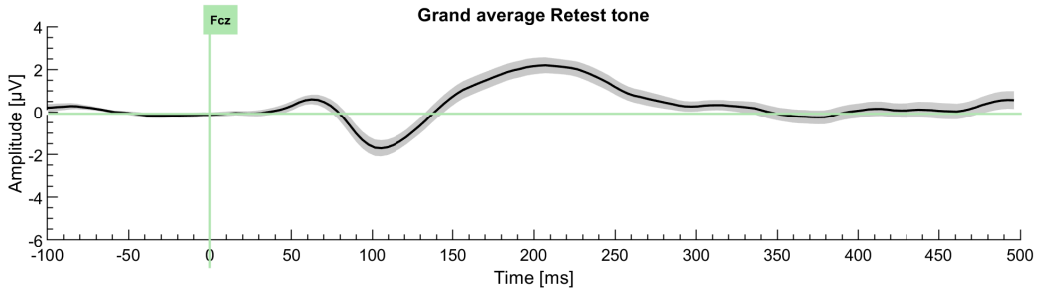
(c) Grand average of the pure tone with pre-transition duration (PTD) 2000 ms with the standard error of the mean in grey.



(d) Grand average of the pure tone with pre-transition duration (PTD) 3000 ms with the standard error of the mean in grey.



(e) Grand average of the complex tone with the standard error of the mean in grey.



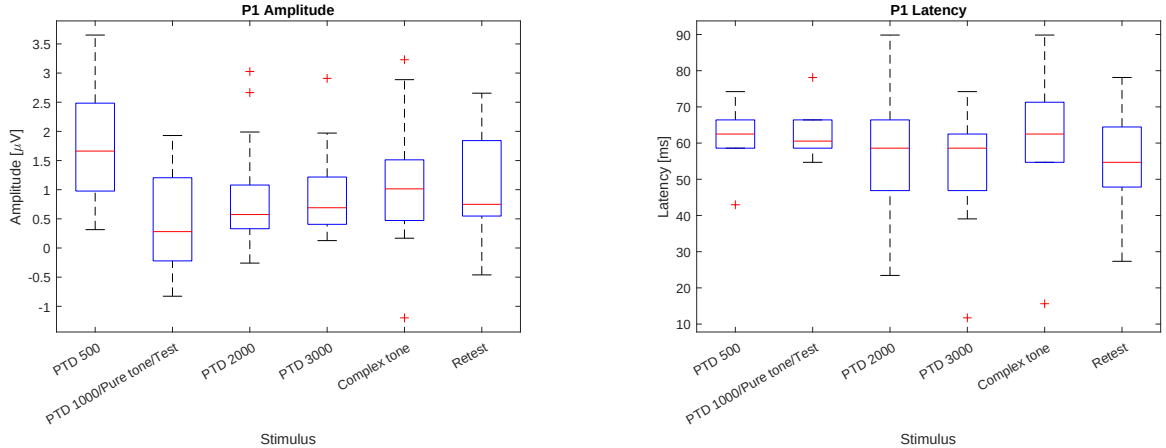
(f) Grand average of the retest pure tone with the standard error of the mean in grey.

Figure C.2: Grand averages for the pure tones with pre-transition durations (PTDs) of 500 (C.2a), 1000 (C.2b), 2000 (C.2c) and 3000 ms (C.2d) and the complex (C.2e) and retest (C.2f) tones with the standard error of the mean in grey.

D Boxplots

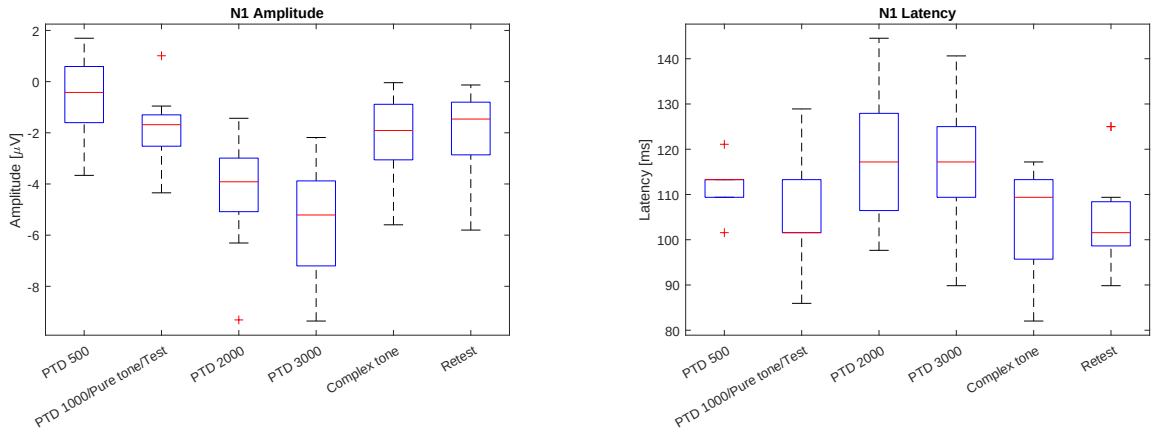
Subsection D.1 includes figures of the Amplitude and Latency boxplots for each peak and all stimuli. Subsection D.2 includes boxplots of the Signal to noise ratio (S/N) and Efficiency for each peak and pre-transition duration. The red lines indicate the medians, the upper and lower limit of each box are the 25th and 75th percentiles. The dotted whisker lines above and below the plot indicate the maximum and minimum values (excluding the outliers) and the Red crosses are outliers (defined as more than 1.5 times the interquartile range away from the upper and lower limit of the box) [67].

D.1 Amplitude and Latency boxplots of P1, N1 and P2



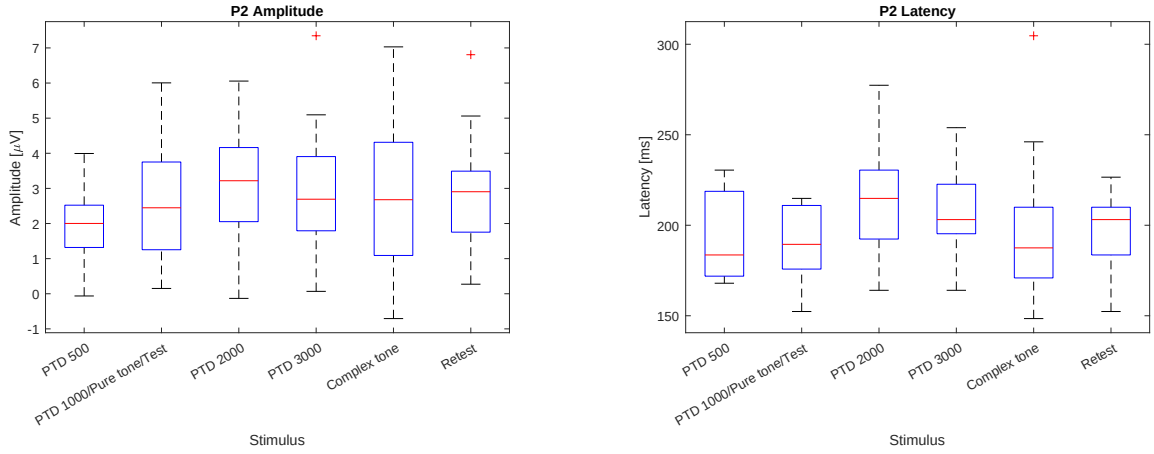
(a) *(b)*

Figure D.1: Boxplot of the P1 Amplitude (a) and Latency (b) per stimulus. PTD = pre-transition duration in ms.



(a) *(b)*

Figure D.2: Boxplot of the N1 Amplitude (a) and Latency (b) per stimulus. PTD = pre-transition duration in ms.



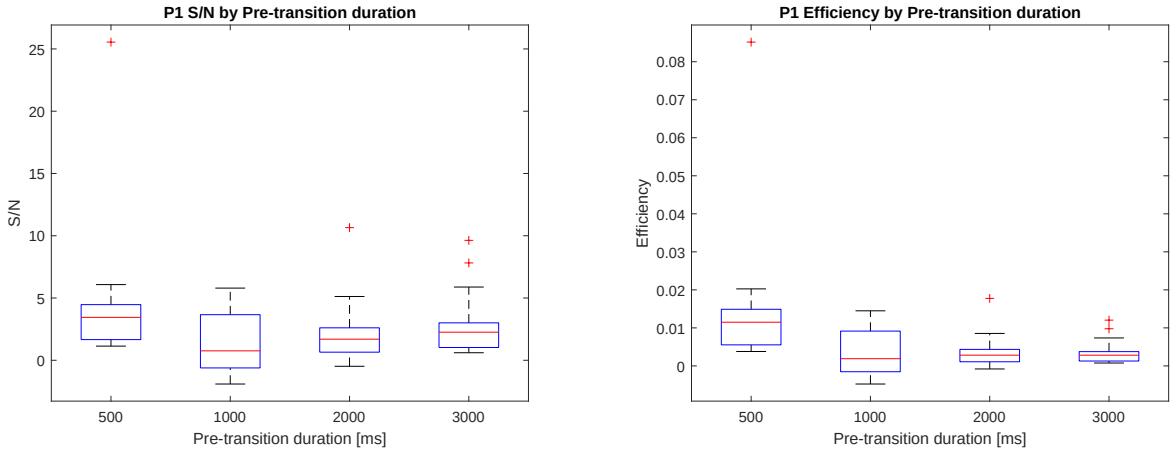
(a) *(b)*

Figure D.3: Boxplot of the P2 Amplitude (a) and Latency (b) per stimulus. PTD = pre-transition duration in ms.

D.2 Signal to noise and Efficiency boxplots per pre-transition duration of N1-P2 peak-to-peak, P1, N1 and P2

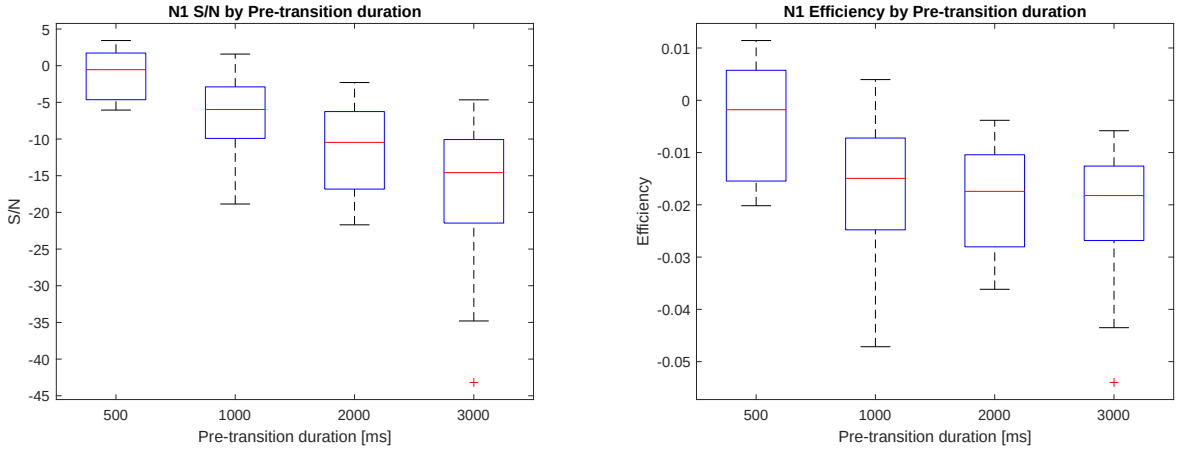
Boxplots of the Signal to noise ratio (S/N) and Efficiency for each peak and pre-transition duration. Efficiency is defined as:

$$\text{Efficiency} = \frac{\text{S/N}}{\text{Measurement time}} \tag{D.1}$$



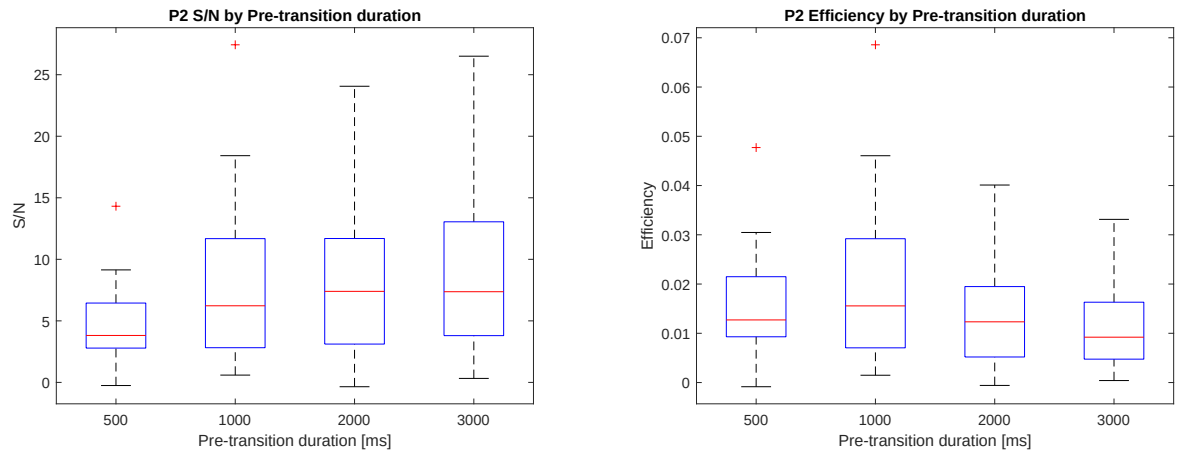
(a) *(b)*

Figure D.4: Boxplot of the P1 signal to noise ratio (S/N) (a) and Efficiency (b) per pre-transition duration.



(a) *(b)*

Figure D.5: Boxplot of the N1 signal to noise ratio (S/N) (a) and Efficiency (b) per pre-transition duration.



(a) *(b)*

Figure D.6: Boxplot of the P2 signal to noise ratio (S/N) (a) and Efficiency (b) per pre-transition duration.

E Complex stimuli with intensity alterations

Acoustic change complexes (ACCs) to complex tones with intensity alterations were measured to account for possible intensity differences between pure and complex tones. The rationale behind this can be read in Text box 2 in Subsection E.1. Table E2 in Subsection E.2 summarizes the results of signal processing as background information for the grand averages and boxplots. Subsection E.3 includes a plot with the grand averages of the tones with dB differences and the pure and complex tone and it includes plots of the grand averages with standard deviation for each stimulus. Boxplots of the Amplitude and Latency of all peaks for all stimuli with intensity differences are displayed in Subsection E.4.

E.1 Rationale behind complex tones with intensity alterations

When measuring pure tones in the free field, the sound can reflect against the walls and ceiling [68]. Therefore, there is a risk of interference resulting in possible (partial) cancellation or reinforcement of the intensity of the sound [69]. This can make the intensity of the sound unreliable [68]. The possible effect of intensity alterations on the measured pure tone Acoustic change complexes (ACCs) between pre-transition durations (PTDs) is expected to be negligible. This is because all measurements are done with the participant in the same position and all PTDs are measured with the same frequencies. The risk of a possible intensity effect is higher for pure tones than for complex tones, since complex tones consist of multiple frequencies and therefore the effect of nodes and anti-nodes will average out to some extend [68]. Our hypothesis is that complex tones will elicit Acoustic change complexes with a higher Amplitude and shorter Latency compared to pure tones. If this hypothesis is underlined by our data, this might be caused by a possible lower intensity of the pure tone instead of solely the difference between sound complexity.
To account for possible intensity differences between complex versus pure tones two additional sounds are presented. Firstly, the complex tone is offered at a lower intensity than the pure tone. Secondly, the post-transition frequency of the complex tone is offered at a lower intensity. This is done because there might be an intensity difference between the 1000 Hz and 1100 Hz pure tones, resulting in an ACC that is possibly elicited by an intensity and frequency change instead of only the latter. An intensity difference of 3dB is chosen for both additional sounds. Having two sources with the same intensity results in an intensity increase of +3dB [70]. The worst-case scenario is when the reflected wave is in perfect phase or anti-phase with the presented sound, resulting in the formation of standing waves and therefore the formation of nodes and anti-nodes [71, 68]. In this scenario the intensity can increase with +6dB or zero out to 0dB [70, 69]. However, because a reflected wave will lose energy, and the chance that they are in perfect phase or anti-phase is small and expected to be noticed, an intensity difference of 3dB is chosen. The exact properties of the sound attenuation in the room regarding the frequencies are not known. Therefore, the 3dB is an estimation.

Text box 2: Rationale to account for possible intensity differences when measuring complex and pure tones in the free field.

E.2 Summary of signal processing results for stimuli with intensity alterations

Table E2: The number of participants, percentage of present responses, accepted trials and the total percentage of trials excluded after signal processing per stimulus. PTD= pre-transition duration in ms.

	Stimulus			
	PTD 1000/ Pure tone	Complex tone	-3dB Complex tone	Complex tone -3dB intensity change
Number of participants	17	16	18	18
Participants with response [%]	58.8	81.3	88.9	72.2
Number of accepted trials	3283	3101	3522	3425
Mean artefact rejection [%]	3.4	3	1.8	4.9

E.3 Grand averages of stimuli with intensity alterations

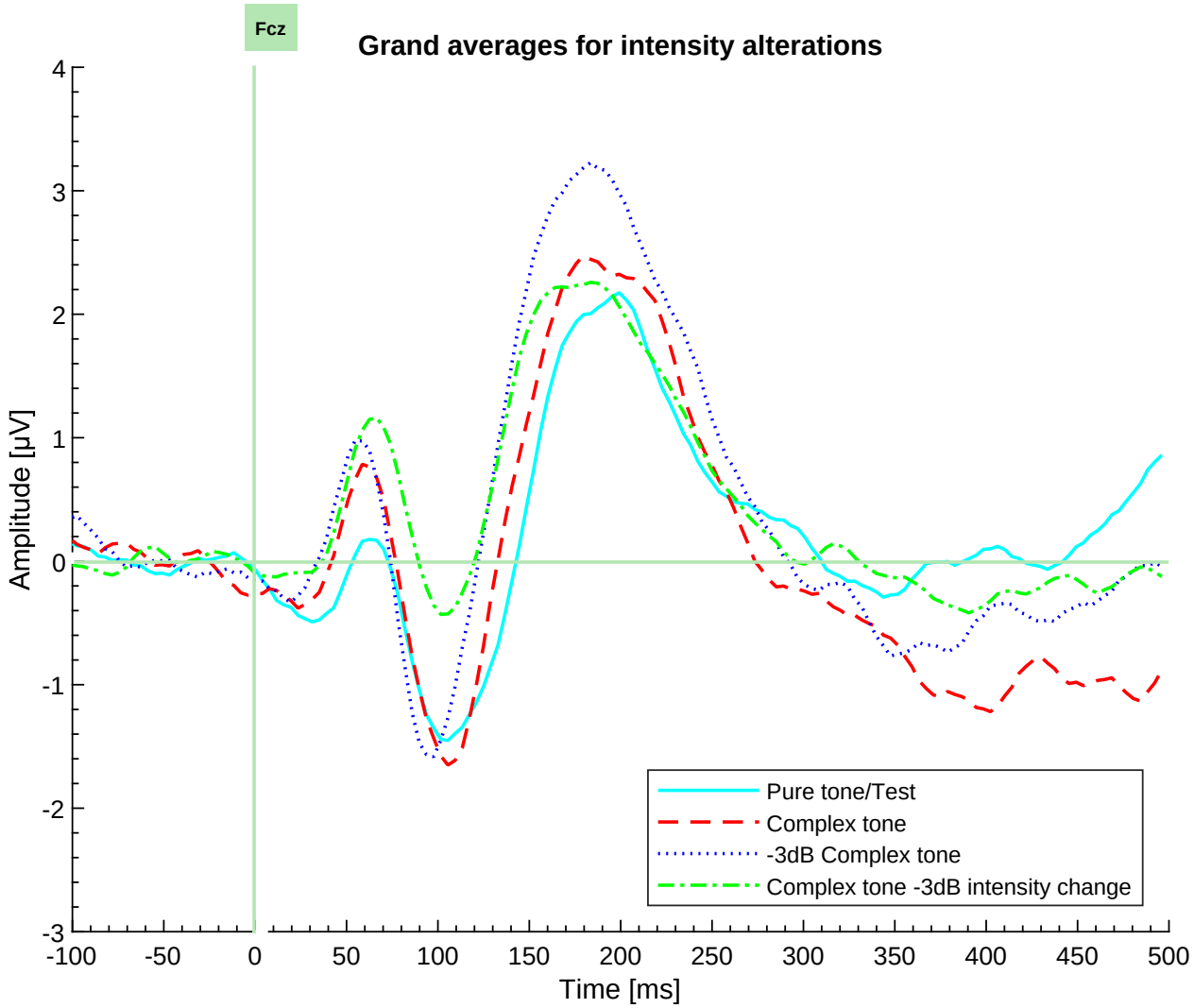
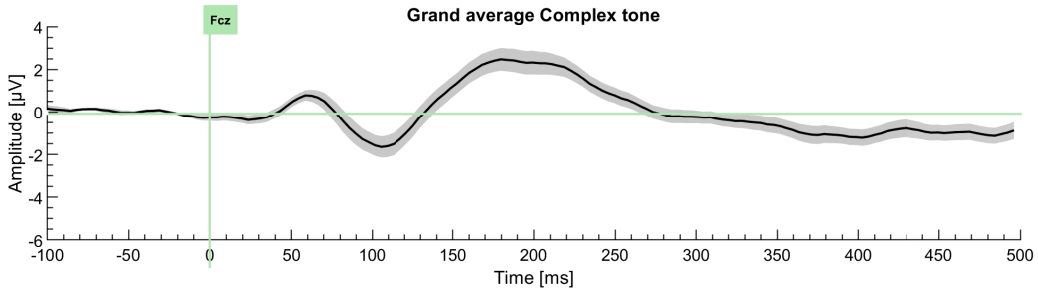
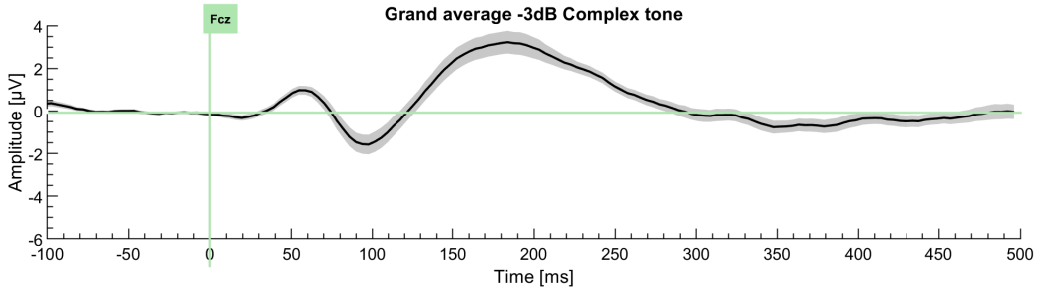


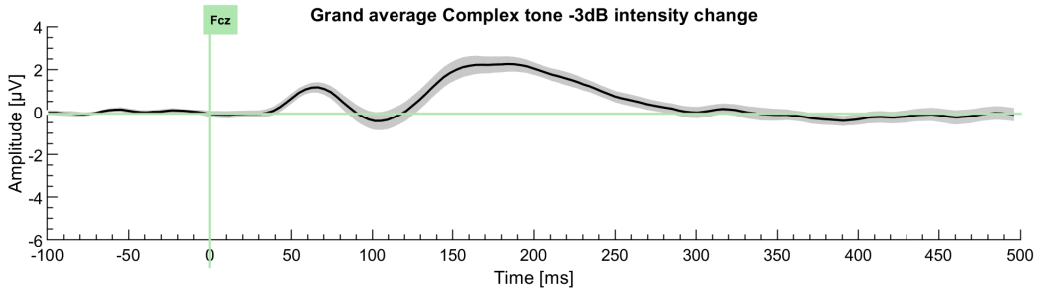
Figure E.1: Grand average of the complex tone, pure tone, and two complex tones with intensity alterations with the standard error of the mean in grey. -3dB is the tone presented 3dB lower than the complex tone, and -3dB intensity change is the tone that had an additional intensity decrease of 3dB during the acoustic change.



(a) Grand average of the complex tone with the standard error of the mean in grey.



(b) Grand average of the complex tone that is presented 3dB lower with the standard error of the mean in grey.



(c) Grand average of the complex tone with an additional intensity decrease of 3dB during the acoustic change with the standard error of the mean in grey.

Figure E.2: Grand averages for the complex tone E.2a, the complex tone that is presented 3dB lower E.2b and the complex tone with an intensity decrease of 3dB during the acoustic change E.2c with the standard error of the mean in grey.

E.4 Boxplots of stimuli with tonal complexity and intensity alterations

Boxplots of the Amplitude and Latency of all peaks for all stimuli with complexity and intensity differences and of the baseline noise are displayed in the figures below. The The red lines indicate the medians, the upper and lower limit of each box are the 25th and 75th percentiles. The dotted whisker lines above and below the plot indicate the maximum and minimum values (excluding the outliers) and the red crosses are outliers (defined as more than 1.5 times the interquartile range away from the upper and lower limit of the box) [67].

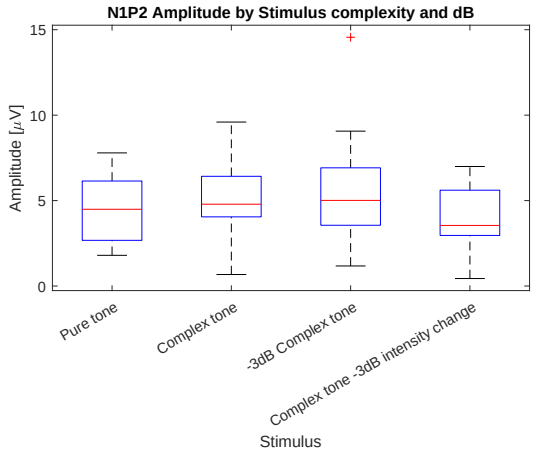


Figure E.3: Boxplot of the N1-P2 peak-to-peak Amplitude per stimulus.

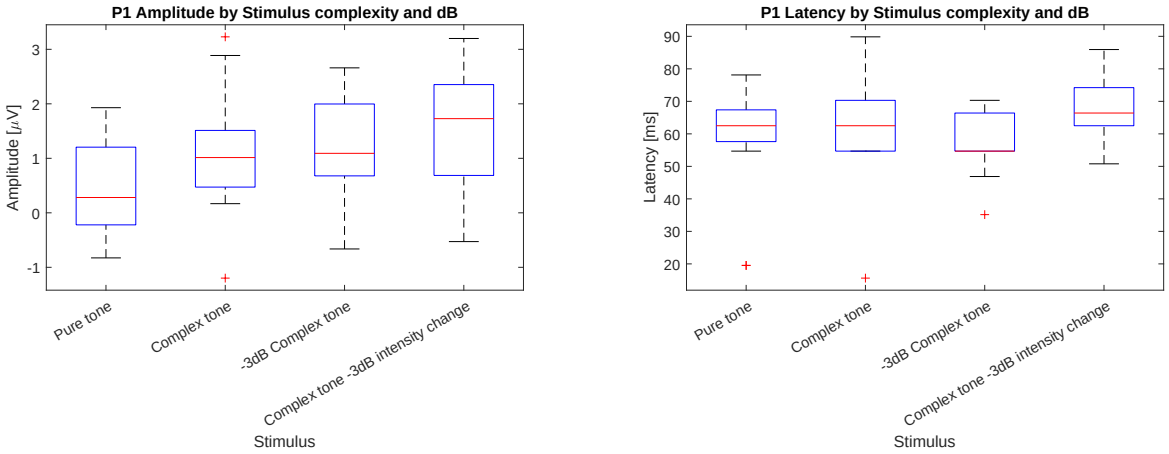


Figure E.4: Boxplot of the P1 Amplitude (a) and Latency (b) per stimulus.

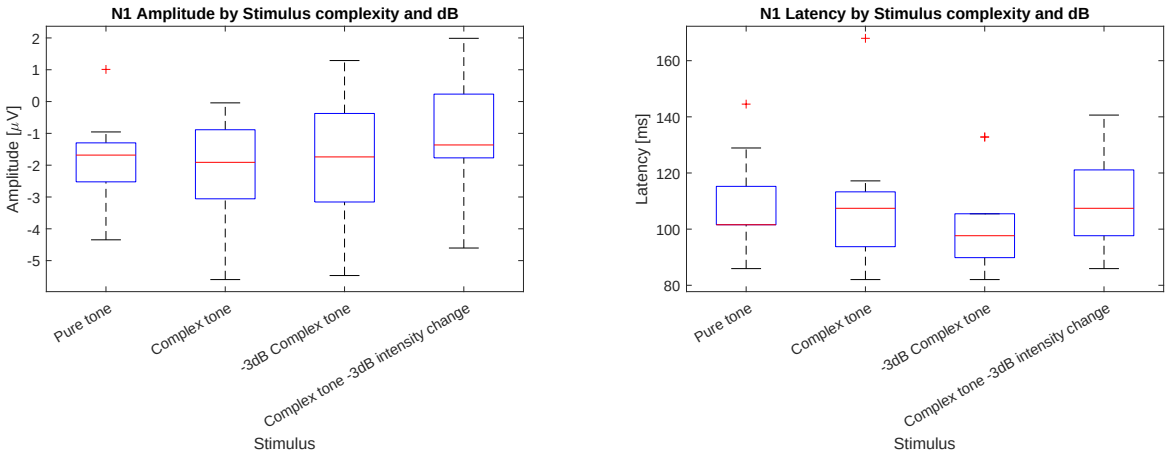


Figure E.5: Boxplot of the N1 Amplitude (a) and Latency (b) per stimulus.

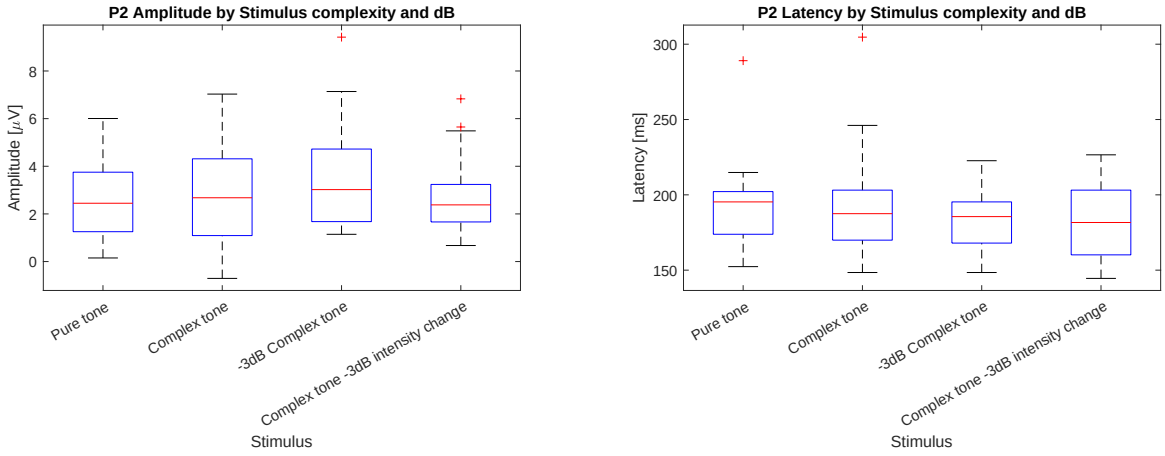


Figure E.6: Boxplot of the P2 Amplitude (a) and Latency (b) per stimulus.

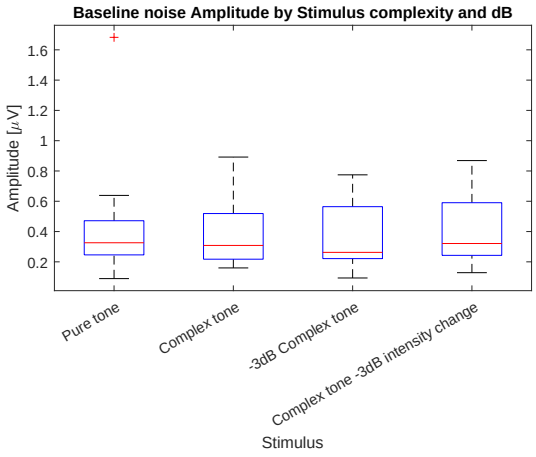


Figure E.7: Boxplot of the baseline noise Amplitude per stimulus.