EFFECT OF DIFFERENT INTER-STIMULUS INTERVALS (ISI) ON CORTICAL AUDITORY EVOKED POTENTIAL IN NORMAL HEARING ADULTS: A PRELIMINARY FINDING

'AFAF EZZATY ABDUL RAHIM, BAud (Hons)
DEPARTMENT OF AUDIOLOGY AND SPEECH-LANGUAGE PATHOLOGY, KULLIYYAH OF ALLIED HEALTH SCIENCES, INTERNATIONAL ISLAMIC UNIVERSITY MALAYSIA, JALAN SULTAN AHMAD SHAH, 25200, KUANTAN, PAHANG, MALAYSIA
afafezzaty@gmail.com

AHMAD AIDIL ARAFAT DZULKARNAIN, PhD (Corresponding author)
DEPARTMENT OF AUDIOLOGY AND SPEECH-LANGUAGE PATHOLOGY, KULLIYYAH OF ALLIED HEALTH SCIENCES, INTERNATIONAL ISLAMIC UNIVERSITY MALAYSIA, JALAN SULTAN AHMAD SHAH, 25200, KUANTAN, PAHANG, MALAYSIA
ahmadaidil@iium.edu.my

ABSTRACT

The aim of this study was to investigate the effect of different inter-stimulus intervals to the Cortical Auditory Evoked Potential (CAEP) findings in adult participants. Nineteen normal hearing individuals aged between 20 and 24 years old participated in this study. CAEP were measured by presenting 1000 Hz tone burst stimulus at 70dBnHL at three different inter-stimulus intervals (ISI)s of 2000, 909 and 555 ms in randomized order. Results revealed significant changes in the CAEP's amplitude as a function of ISI with a reduction of P1-N1 amplitude of up to 50%. N2 peak was absent in some subjects using short ISI (555 ms). This study concluded that the use of very short ISI (e.g. 555 ms) may not be appropriate clinically because it can reduce the CAEP wave amplitude and can cause an absence of peak N2. In contrast, the use of short ISI may be useful for other clinical applications that may benefit from neural habituation and refractoriness, for example to predict the potential future outcome of speech and mental disorders.

KEYWORDS: Cortical Auditory Evoked Potential, Stimulus Repetition Rate, Inter-stimulus Interval, Neural Inhibition, Habituation.

INTRODUCTION

Cortical Auditory Evoked Potential (CAEP) is a non-invasive, objective measure that can provide detailed information on the integrity of the central auditory nervous system in general and auditory cortex specifically. The auditory cortex appears to be the executor to process complex combinations of information for auditory perception or integration with other sensory pathway. These may include the analysis of complex sounds, localization, perception of temporal patterns, and identification of auditory stimuli. (Kaas & Hackett, 1999; Zatorre & Belin, 2001). CAEP consists of two biphasic waveforms that is represented by P1, N1, P2 and N2 peaks.

In audiology, CAEP is used to estimate hearing sensitivity with the predicted thresholds to be on average 10 dB higher than the behavioral threshold (Van Dun, Dillon, & Seeto, 2015). CAEP has also been used by clinicians as a tool to measure the effectiveness of audiology intervention either for hearing aid or cochlear implant (Chang, Dillon, Carter, Van Dun, & Young, 2012; Dorman, Sharma, Gilley, Martin, & Roland, 2007; Korczak, Kurtzberg, & Stapells, 2005), for measuring the effectiveness of auditory training (Tremblay & Kraus, 2002) and for differential diagnosis to differentiate between auditory processing disorder (APD)with other higher order function disorder such as Learning Disability (LD) (Purdy, Kelly, & Thorne, 2001).

Whilst CAEP has been proven to be an effective and promising tool in many audiology applications, the acquisition of the CAEP signal requires longer time to be completed. Given the CAEP last peak (N2) occurs around 200 ms and the potential of existence of any pathologies that may delay the CAEP components, the maximum inter-stimulus interval (ISI) to be presented is set to 500 ms (0.5/secs) with recommendation to set the ISI to be even longer of at least 1000 ms (1/secs) (Hall, 2007; Lightfoot, 2016). The recommendation to have longer ISI is because of the factors that include neural habituation that leads to absence of certain CAEP peak and the reduction to the CAEP amplitude peak components (Gilley, Sharma, Dorman, & Martin, 2005). Because of that, a longer ISI (e.g. more than 1000 ms) is typically used although there were scant scientific evidences in supporting this recommendation particularly in testing adult population.

The literature investigating the effect of ISI to the CAEP in adult population is limited with (i) two studies conducted to investigate the influence of the conventional ISI (up to only 500 ms) to CAEP (Davis, Mast, Yoshie, & Zerlin, 1966; Surwillo, 1981), (ii) only few studies that looked into the use of very short ISI (lower than 500 ms) and the use of novel algorithm to disentangle the overlapping CAEP presented through a pair of tone burst stimulus (Bardy, Van Dun, Dillon, & Cowan, 2014) and (iii) other studies investigated the effect of ISI to CAEP using speech syllables (Didone, Oppitz, Folgearini, Biaggio, & Garcia, 2016). To the author's knowledge, only Surwillo (1981) and Davis et al. (1966) investigated the effect of different ISI in adult population using standard ISI within its maximum limit (up to 500 ms) or using shorter ISI than 500 ms (up to 50 ms) without any mathematical property to disentangle the overlapped CAEP signals.

Based on the above literature, the knowledge of the effect of ISI to the CAEP using non-speech stimulus in adult population is limited to (i) studies that used very short ISI than the standard ISI, in which these ISIs are not available in most commercialized clinical AEP equipment (Bardy et al., 2014) (ii) studies that only reported the presence of P1 peak rather than the other two major peaks (N1 and P2) that can also be reliably recorded in CAEP (Davis et al., 1966) and, (iii) studies that used standard ISI (available in the commercial equipment) but without reporting its effect to the CAEP amplitude or only certain CAEP peaks were included in their analysis (Davis et al., 1966; Surwillo, 1981). Because of the limited studies that investigated the influence of different ISI to all of the four CAEP peaks with full report on its effects to the waves' amplitude, a study to investigate the effect of different ISIs in adult population is therefore warranted. This study therefore aimed to investigate the effect of different ISIs to the all of the CAEP major peaks amplitudes (P1, N1, P2 and N2) among normal hearing adult population.

MATERIAL AND METHODS

Subject

CAEP were recorded in 19 normal-hearing individuals in age ranged between 20 and 24 years old. This study received unconditional ethical approval from the International Islamic University Malaysia (IIUM) Research Ethics Committee (approval ID: IREC 687). All study participants had no significant medical history that indicates any pathological conditions that may influence the CAEP findings. This includes no otological, speech, language, or any psychological disorders. All study participants have normal hearing threshold (below 20 dBHL) at all octave frequencies (250 Hz – 8000 Hz), had Type A tympanogram suggesting no conductive element and normal acoustic reflex thresholds (<105 dBHL).

Stimulus Paradigm

The recording parameters used in the present study were based on recommendation as described in IIUM audiology protocol (International Islamic University Malaysia, 2017). Cortical auditory evoked responses were recorded in the response to a 1000Hz tone burst stimulus at 70dBnHL. The stimulus was presented at a constant level which was delivered via insert-phone. The sound was presented in a randomized order of 3 ISIs

presentations (2000, 999, and 505 ms). These 3 ISIs were chosen to represent very long ISI (2000 ms), medium ISI (999 ms) and short ISI (505 ms) that are typically available in a commercial AEP equipment.

CAEP recording procedures

Participants were placed in a position they were comfortable with. They sat on a soft cushion chair facing the laptop. The test preparation started while they were watching a no audio (silent) movie. Electrode sites were generally prepared by abrading the patient scalp with a gauze-pads and Nuprep skin preparation gels. Subject's skin was prepared carefully at the skin surfaces. Three different areas were prepared and placed with electrodes based on vertical electrode montage at the vertex (Cz) for the active electrode, nape of neck for the reference electrode and high forehead (Fz) for the ground electrode. To maintain electrode contact especially at the vertex area, a headband was used to keep the electrode in place.

Electrical impedance was examined and maintained below 5000Ω for each of the electrode. Inter-electrode impedances between each electrode was also maintained equal or below 2000 ohm throughout the testing to provide an optimum common mode rejection. Three different ISIs at 555 ms, 909 ms and 2000 ms were used in a train of stimulus sequences throughout the recording. The sequences of ISIs were randomized across study participants to avoid any potential order effect (Lee, Whang, Yoon, Park, & Kim, 2016). The raw CAEP signal was amplified 50,000 times at the electrode box. The CAEP then was further filtered using low frequency band-pass filter at 0.1 – 35 Hz, to remove unwanted component or noise caused by background electroencephalogram (EEG) activity, muscle activity or any electrical interference.

The CAEP signals were averaged up to 300 counts to differentiate the CAEPs by repetitive acoustic stimulation from the noise. Following that, the final averaged CAEPs data replaced the previous sub-averages data and was converted to digital signal using Analog-Digital Converter (ADC) through 512 data points along 500 ms time epoch. This translates to 1 ms temporal resolution equivalent to 100 Hz sampling frequency. The digital versions of the CAEP waveforms resolved from the ADC conversion were displayed in the Neurosoft time window of 500 ms. Any unwanted activities exceed ±50 µV; will result to the entire time epoch of data to be rejected. Eye blinking rejection or assignment of a specific electrode to the ocular region was not considered in the study. The potential contaminations from the low frequency electrooculography to the CAEP findings may be happen because of this limitation. Participants however were advised as much as possible to avoid any eye movements or blinks and any muscular related activities.

Waveform Analysis

The presence and absence of CAEP waveforms were determined by evaluating the repeatability of the CAEP recorded under two identical test parameters. Specifically, this was done by looking into the area of overlapping between the two overlay CAEP waveforms. To determine a correct CAEP peak selection and to distinguish the presence and absence of the peaks, normative data from previous reports were referred (Ponton, Eggermont, Kwong, & Don, 2000; Van Dun, Kania, & Dillon, 2016). In general, the authors determined the overall pattern of the CAEP, whether it has biphasic or single phase components. The plotted CAEP peaks were determined by two experienced audiologists who regularly conduct and analyze CAEP tests. For CAEP amplitude, amplitude of P1-N1, N1-P2 and P2-N2 were selected based on peak-to-peak amplitude technique. Peak-to-peak amplitude calculates the change between peak (highest amplitude value) and trough (lowest amplitude value) (Afra, Cecchini, Sandor, & Schoenen, 2000).

Statistical Analysis

The collected data was analyzed using SPSS version 17.0 software. The presence and absence of all peaks (P1, N1, P2, and N2) were analyzed using descriptive analysis to determine whether all peaks are presence or absence at all ISIs. The mean differences in the CAEP's results (Amplitude) between three ISIs were compared

using Repeated Measure ANOVA (RM ANOVA) because all the parametric assumptions were met. The test was conducted with Bonferroni correction to account for multiple comparisons to avoid type I error.

RESULTS

P1, N1, P2 and N2 complex

The general biphasic components of CAEP with three to four peaks were identified in all participants. P1, N1, and P2 structures were identified in all study participants at all ISIs. N2 peak were absent in four participants using the shortest ISI (555ms) and absent in one participant using the longest ISI (2000ms). Figure 1 showed an example of CAEP waveform at three different ISI from one study participant.
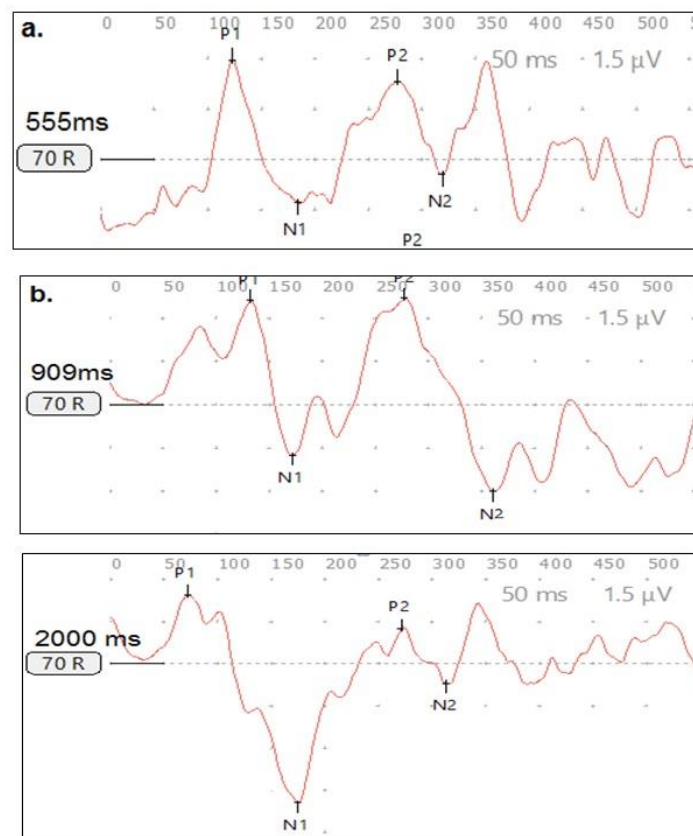
Figure 1 Examples of CAEP waveform recorded from one study participants at ISI of 555 ms (a), 909 ms (b) and 2000 ms (c).

Effects of different ISI to the CAEP peak amplitudes

Statistically significant difference in CAEP peaks amplitudes of P1-N1 and N1-P2 were identified between the three ISIs (F (2, 34) = 28.990, p < 0.01). This analysis in general (Table 1) indicates that the ISI affects the P1-N1 and N1-P2 peak to peak amplitudes but not the P2-N2 peak to peak amplitude.

Pairwise comparison was used to further identify pair of variables with significant differences as summarized in the table 2. For P1-N1 complex, significant differences in the peak-to-peak amplitudes were only found between the CAEP elicited from the longest ISI (2000ms) and the other two ISIs (shortest ISI (555ms) and the medium ISI (909ms)) (p<0.0001). As the ISI decreases, the P1-N1 complex peak-to-peak amplitude was reduced by approximately 56.37%. For N1-P2 complex, only CAEP elicited from the shortest ISI (500ms) and the longest ISI (2000ms) were identified to be statistically different. The CAEP N1-P2 peak-to-peak amplitude reduced by approximately 35.10% between these two ISIs.

Table 1 Mean and (standard deviation) for CAEP's amplitude at different ISIs condition. The *p*-values of the RM ANOVA analysis are shown in the last column.

ISI (ms)	Mean (sd)	*p-value*
P1-N1		
555	3.478 (0.296)	
909	4.339 (0.371)	<0.0001
2000	7.972 (0.721)	
N1-P2		
555	3.389 (0.260)	
909	4.183 (0.352)	0.002
2000	5.222 (0.550)	
P2-N2		
555	2.150 (0.207)	
909	2.289 (0.240)	0.355
2000	2.511 (0.199)	

Table 2 Pairwise comparison for amplitude of P1-N1 and N1-P2 in each ISIs conditions, min and max values and the percentage changes between ISIs. The last column is *p*-value.

P1-N1 Complex						
ISI 1 (ms)	**ISI 2 (ms)**	**Min**	**Max**	**Percentages of changes (%)**	**Mean Difference (2-1)**	***p-value***
555	909	-94.74	66.67	19.84	0.861	0.33
555	2000	32.73	84.21	56.37	4.494	<0.0001
909	2000	8.57	65.45	45.57	3.633	<0.0001

N1-P2 Complex						
ISI 1 (ms)	**ISI 2 (ms)**	**Min**	**Max**	**Percentages of changes (%)**	**Mean Difference (2-1)**	***p-value***
555	909	-62.07	73.68	18.98	0.794	0.15
555	2000	-30.56	77.45	35.10	1.833	0.01
909	2000	-50.00	53.92	19.89	1.039	0.16

DISCUSSION

The aim of this present study was to investigate the effects of different ISIs to the CAEP test result in normal hearing adults. In general, the present study found the following (i) the N2 from P2-N2 complex were not present in all subjects (ii) short ISI significantly reduces the overall CAEP amplitude.

All of these findings were consistent with the effect of repeated stimulation to the central nervous systems that cause neural habituation and/or refractoriness. Neural habituation refers to the neural activity reduction as a result of the subsequent stimulus lost its novelty following repeated stimulation causing some of the neurons to stop responding (Okamoto & Kakigi, 2014), where refractoriness refers to the presentation of the subsequent stimulus during the neurons refractory period. Presentation of the stimulus during this time may cause neurons to not respond and decrease overall amplitude of CAEP following signal averaging. The neural habituation can cause reduced contribution of the neurons when stimulated and a longer time is needed to re-activate the neurons (Sable, Low, Maclin, Fabiani, & Gratton, 2004; Zhang, Eliassen, Anderson, Scheifele, & Brown, 2009). Additionally, neural habituation and/or refractoriness may cause reduction in the amplitude of N2 peak that perhaps increase the possibility of the N2 peak to be absent than the other peaks in some of the subjects.

Besides neural habituation and/or refractoriness, the absence of N2 peak in four participants especially using short ISI at 500 ms might be because of other plausible factors. The first potential factor is the fact that the N2 peak is not a CAEP component that is usually reported in the literature and this peak is subjected to much variability (Hall, 2007). The most reproducible CAEP peaks are the P1-N1-P2 complexes (Lightfoot, 2016). The N2 peak is affected more with ISI may be due to its instability, less sensitive to the onset of stimulus and has complex variation than NI-P1 complex even in normal auditory function subjects (Baltzell & Billings, 2014; Lightfoot, 2016). The instability in P2-N2 complex may be potentially confounded from the fluctuation in the attention state and sleeping stage (Manunta & Edeline, 1999; Otazu, Tai, Yang, & Zador, 2009; Picton & Hillyard, 1974). When subject is consciously attending to the stimulus or fall asleep, the amplitude of the CAEP will generally change because the negative or positive waves may be amplified or de-amplified (Otazu et al., 2009; Picton & Hillyard, 1974). Patient's attention state and state of arousal was monitored throughout the recording in the present study (subject being asked to watch video clips with no audio), especially if the participant seems drowsy to avoid false result at the end of recording. However, the patient's state of attention was not being monitored overtime as EEG may fluctuate through the recording and may cause the absence of N2 peak in the four study participants (attention state and state of arousal may fluctuate even patient seems to be awake during the test). The second factor that may contribute to the absence of N2 peak is due to the possibility of poor signal to noise ratio in the P2-N2 complex. The researcher only monitored the N1-P2 amplitude complex signal to noise ratio (SNR) over the remaining residual noise, not for the P2-N2 SNR. Given the amplitude of P2-N2 are smaller than the N1-P2 complex, it is possible that the ratio of P2-N2 to the noise are less than the 3:1 as per recommended CAEP recordings (Billings, Tremblay, Stecker, & Tolin, 2009; Lightfoot, 2016). The third factor is the possibility of N2 peak could be recorded in these four study participants but at the other locations over the scalp or it will only be visible by having a summation response from vertex (Cz) and nearby location at C3 and C4 (Wunderlich, Cone-Wesson, & Shepherd, 2006). This is the limitation of the study as the CAEP was acquired using a commercialized AEP system with single channel recording not a multiple-channel (32-256 channels) EEG system with the capability of measuring scalp topography and to calculate spectral density power.

In the present study, the P1-N1 CAEP complex amplitude reduced from the longest ISI of 2000 ms to 500 ms with a reduction of amplitude of approximately 50%. This finding is expected and the reduction of P1-N1 as a function of ISI has also been reported in the literature (Näätänen & Picton, 1987; Zhang et al., 2009). It has been highlighted earlier that N2 peak is more affected with ISI because this peak was not presence in all study participants, however it appears in the present study that the N1 amplitude (from P1-N1 and N1-P2 complex) was affected more by the short ISI than the other peaks (especially P2-N2). To our knowledge, this is

one of the first studies that investigated the effect of ISI to the P2-N2 complex, as most of previous studies only investigated the influence of conventional ISI to the CAEP results in adult by analyzing only either P1 or N1 peaks (Davis et al., 1966; Surwillo, 1981). The largest reduction found in the N1 amplitude than the N2 is possibly because of the amplitude of the presently small N2 and unstable (response fluctuate overtime) relative to the N1 (even with longest ISI). Given the smaller amplitude of the N2 peak, chances of the peak to be absent would be higher than the N1 peak as the ISI decrease. On the other hand, given the robustness of the N1 amplitude, shorter ISI may affect more to its amplitude, although it is not to the extent that may cause absence to their peak as compared to the N2 that happen in some of the study participants.

The present study, the optimum ISI for recording CAEP were identified by evaluating the ISI that offer the fastest recording and ISI that maintain the accuracy of the CAEP test findings. CAEP with short ISI consequently is considered as the test that offers the shortest test duration to record the neural response from the brain as compared to the long ISI. However, the disadvantage of using short ISI is that it may affect the accuracy of the overall results. When short ISI was used, some of the study participants' N2 peaks were diminished and the amplitude of N1-P1, N1-P2 and N2-P2 were reduced. Therefore, the use of short ISI may not be suitable for general clinical applications with the exception of clinical application that highly depends on the neural habituation such as investigation of sensory gating in patient with attention deficit hyperactivity disorder.

CONCLUSIONS

This study concluded that the use of very short ISI below than 900 ms (e.g. 555 ms ISI) may not be appropriate for audiology or other relevant clinical applications that depends highly on the presence of all CAEP peaks. In contrast, the use of short ISI may be useful for other clinical applications that may benefit from neural habituation and refractoriness for example to possibly predict the potential outcome of speech and mental disorders. The conclusions of this study are limited to the equipment, test parameters, stimulus types, ISIs and test protocols used in the present study.

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REFERENCES

Afra, J., Cecchini, A. P., Sandor, P., & Schoenen, J. (2000). Comparison of visual and auditory evoked cortical potentials in migraine patients between attacks. *Clinical Neurophysiology, 111*(6), 1124-1129.

Baltzell, L. S., & Billings, C. J. (2014). Sensitivity of offset and onset cortical auditory evoked potentials to signals in noise. *Clinical Neurophysiology, 125*(2), 370-380.

Bardy, F., Van Dun, B., Dillon, H., & Cowan, R. (2014). Least-squares (LS) deconvolution of a series of overlapping cortical auditory evoked potentials: a simulation and experimental study. *J Neural Eng, 11*(4), 046016. doi:10.1088/1741-2560/11/4/046016

Billings, C. J., Tremblay, K. L., Stecker, G. C., & Tolin, W. M. (2009). Human evoked cortical activity to signal-to-noise ratio and absolute signal level. *Hear Res, 254*(1), 15-24.

Chang, H.-W., Dillon, H., Carter, L., Van Dun, B., & Young, S.-T. (2012). The relationship between cortical auditory evoked potential (CAEP) detection and estimated audibility in infants with sensorineural hearing loss. *International Journal of Audiology, 51*(9), 663-670.

Davis, H., Mast, T., Yoshie, N., & Zerlin, S. (1966). The slow response of the human cortex to auditory stimuli: recovery process. *Electroencephalogr Clin Neurophysiol, 21*(2), 105-113.

Didone, D. D., Oppitz, S. J., Folgearini, J., Biaggio, E. P., & Garcia, M. V. (2016). Auditory Evoked Potentials with Different Speech Stimuli: a Comparison and Standardization of Values. *Int Arch Otorhinolaryngol, 20*(2), 99-104. doi:10.1055/s-0035-1566133

Dorman, M. F., Sharma, A., Gilley, P., Martin, K., & Roland, P. (2007). Central auditory development: evidence from CAEP measurements in children fit with cochlear implants. *Journal of communication disorders, 40*(4), 284-294.

Gilley, P. M., Sharma, A., Dorman, M., & Martin, K. (2005). Developmental changes in refractoriness of the cortical auditory evoked potential. *Clinical Neurophysiology, 116*(3), 648-657.

Hall, J. W. (2007). *New handbook of auditory evoked responses*. Boston: Allyn&Bacon.

International Islamic University Malaysia. (2017). Hearing and Speech Clinic audiology protocol *AEP protocol*. unpublished.

Kaas, J. H., & Hackett, T. A. (1999). 'What'and'where'processing in auditory cortex. *Nature neuroscience, 2*(12).

Korczak, P. A., Kurtzberg, D., & Stapells, D. R. (2005). Effects of sensorineural hearing loss and personal hearing aids on cortical event-related potential and behavioral measures of speech-sound processing. *Ear and Hearing, 26*(2), 165-185.

Lee, J., Whang, M., Yoon, J., Park, M., & Kim, J. (2016). Optimized inter-stimulus interval (ISI) and content design for evoking better visual evoked potential (VEP) in brain-computer interface applications. *Brain-Computer Interfaces, 3*(4), 186-196.

Lightfoot, G. (2016). Summary of the N1-P2 Cortical Auditory Evoked Potential to Estimate the Auditory Threshold in Adults. *Seminar in Hearing,* 37(1), 1-8

Manunta, Y., & Edeline, J. M. (1999). Effects of noradrenaline on frequency tuning of auditory cortex neurons during wakefulness and slow-wave sleep. *European Journal of Neuroscience, 11*(6), 2134-2150.

Näätänen, R., & Picton, T. (1987). The N1 wave of the human electric and magnetic response to sound: a review and an analysis of the component structure. *Psychophysiology, 24*(4), 375-425.

Okamoto, H., & Kakigi, R. (2014). Neural adaptation to silence in the human auditory cortex: a magnetoencephalographic study. *Brain and behavior, 4*(6), 858-866.

Otazu, G. H., Tai, L.-H., Yang, Y., & Zador, A. M. (2009). Engaging in an auditory task suppresses responses in auditory cortex. *Nature neuroscience, 12*(5), 646-654.

Picton, T., & Hillyard, S. (1974). Human auditory evoked potentials. II: Effects of attention. *Electroencephalography Clinical Neurophysiology, 36*, 191-200.

Ponton, C. W., Eggermont, J. J., Kwong, B., & Don, M. (2000). Maturation of human central auditory system activity: evidence from multi-channel evoked potentials. *Clinical Neurophysiology, 111*(2), 220-236.

Purdy, S. C., Kelly, A. S., & Thorne, P. R. (2001). Auditory evoked potentials as measures of plasticity in humans. *Audiology and Neurotology, 6*(4), 211-215.

Sable, J. J., Low, K. A., Maclin, E. L., Fabiani, M., & Gratton, G. (2004). Latent inhibition mediates N1 attenuation to repeating sounds. *Psychophysiology, 41*(4), 636-642.

Surwillo, W. W. (1981). Recovery of the cortical evoked potential from auditory stimulation in children and adults. *Developmental psychobiology, 14*(1), 1-12.

Tremblay, K. L., & Kraus, N. (2002). Auditory training induces asymmetrical changes in cortical neural activity. *Journal of Speech, Language, and Hearing Research, 45*(3), 564-572.

Van Dun, B., Dillon, H., & Seeto, M. (2015). Estimating hearing thresholds in hearing-impaired adults through objective detection of cortical auditory evoked potentials. *Journal of the American Academy of Audiology, 26*(4), 370-383.

Van Dun, B., Kania, A., & Dillon, H. (2016). *Cortical auditory evoked potentials in (un) aided normal-hearing and hearing-impaired adults.* Paper presented at the Semin Hear.

Wunderlich, J. L., Cone-Wesson, B. K., & Shepherd, R. (2006). Maturation of the cortical auditory evoked potential in infants and young children. *Hear Res, 212*(1), 185-202.

Zatorre, R. J., & Belin, P. (2001). Spectral and temporal processing in human auditory cortex. *Cerebral cortex, 11*(10), 946-953.

Zhang, F., Eliassen, J., Anderson, J., Scheifele, P., & Brown, D. (2009). The time course of the amplitude and latency in the auditory late response evoked by repeated tone bursts. *Journal of the American Academy of Audiology, 20*(4), 239-250.