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Gaps in Noise: Effects on Early Auditory Transient and Steady-State Response

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UNIVERSITY OF MIAMI

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STEADY-STATE RESPONSES

By

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Psychophysical detection of silent gaps embedded in ongoing steady sounds is commonly used to measure temporal resolution in hearing tests. Long latency auditory responses to such gaps in a noise signal are routinely investigated as electrophysiological measures of temporal resolution. This study was conducted to investigate the characteristics of early transient responses (Auditory Brainstem and Middle Latency) as well as Auditory Steady State Responses to such stimuli. Young subjects were monaurally stimulated by three different duration (12ms, 9ms, 6ms) of silence gaps in a white noise. All stimuli in this study were presented with 40 Hz stimulation rate in isochronic or jittered sequences. Quasi ASSRs were deconvolved using the CLAD (Continuous Loop Averaging Deconvolution) algorithm to obtain early transient responses to individual gaps (Delgado & Ozdamar, 2004). Responses to conventional clicks were also recorded. All subjects evoked identifiable early transient responses characterized by two positive and three negative peaks (N_{g1}, P_{g1}, N_{g2}, P_{g2}, N_{g3}). Peaks were about 25 ms apart and the first positive peak P_{g1} was the most prominent. Results suggest that early responses to gaps in noise are composite ABR and MLR responses generated by noise onsets and offsets.   Amplitudes

and latencies of early transient responses and ASSR were affected by gap duration.

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CHAPTER 1: INTRODUCTION AND GOALS

The human brain is a very complex organ that performs highly advanced tasks. However, the current theories explaining how the brain functions and coordinates such tasks are not adequate to solve many scientific inquiries. Of particular importance is the question of how the brain processes and perceives sounds detected by the ears. One of the amazing and complex tasks that the brain performs is speech perception. People with normal hearing and neural function can distinguish and perceive spoken words easily. Yet how this amazing feat is accomplished is not well understood.

The discovery of the electroencephalogram (EEG) provided the most essential and powerful tool to form answers to many questions such as brain speech perception and understanding. EEG has been used to subjectively evaluate neural brain activities; by using EEG, the areas in the brain responsible for speech perception have been determined. However, many aspects of how the brain perceives speech need to be investigated.

The ability of the brain to process small changes of pitch in time provides cues that help a person in understanding speech (Moore & Moore, 2003). In other words, the temporal resolution, which is defined in Moore and Moore (2003) "An introduction to psychology of hearing" as the ability to detect changes in an auditory stimulus over time. One of the most commonly used methods to evaluate temporal resolution of hearing is the silent gap in noise test. This test stimulus, as the name indicates, consists of short gaps of silence embedded in

white noise. It is a behavioral test where the listener is asked to report the smallest gap duration he or she can perceive. Typically, the smallest perceived gap duration reported has been reported to be 2 to 3 ms, after extensive training (Moore, 2003). Normal gap detection threshold recorded without training is about 4 to 5 ms (Musiek, 2005).

Individuals with weak temporal processing abilities may not be able to benefit from small changes in sound over time that could provide cues to understand speech (Musiek, 2005). Moreover, poor temporal resolution has been shown to correlate with speech recognition difficulties (Gordon-Salant & Fitzgibbons, 1993). Factors that play a role in increasing the behavioral gap detection threshold have been explored in many studies. Older adults showed poorer gap detection thresholds compared to young adults (Schneider et al., 1994). Additionally, temporal resolution in normal hearing and impaired listeners has been investigated by using gaps in noise stimuli (Fitzgibbons & Wightman, 1982); the results of such studies showed that temporal resolution was considerably better for normal listeners than hearing-impaired listeners.

The use of the gap in noise test for measuring behavioral gap detection threshold is based on subjective patient feedback only. The use of an alternative method that provides objective measures is desirable and greatly needed. Cortical evoked potentials to gaps in noise are typically recorded to provide such objective measures of temporal resolution. Such tests also allow for analysis of higher order skills in the central auditory system.

Several studies recorded long latency responses to gaps in noise stimuli to evaluate the temporal resolution as well as study the effect of different gap duration with respect to age (Pratt et al., 2005; Lister et al., 2007; Atcherson et al., 2009; Lister et al., 2011; Harris et al., 2012; Palmer & Musiek, 2013;) . Similarly, gaps in noise were also used to stimulate the auditory system to study the effect on auditory brainstem responses (Poth et al., 2001; Werner et al., 2001). However, such studies did not investigate the effect of high rate stimulation on auditory middle latency or steady state responses.

The aim of this study is to investigate the effects of short silent gaps in noise on early transient responses as well as auditory steady state responses. As mentioned earlier, all studies that investigated the effect of gaps in noise on auditory evoked potentials used low stimulation rates. The use of such low rate stimuli has some limitations, one of which includes the recording time needed to reach adequately high signal to noise ratios to get reliable auditory evoked potentials (Daniels, 2011). The long recording time needed when such low rates are used decreases the clinical feasibility of such current testing protocols. To avoid this limitation we used a high stimulation rate to shorten the recording time needed to achieve the recording of reliable evoked potentials. Moreover, the use of high stimulation rates provides a chance to compare the results of high rate to low rate stimuli. In fact, we were able to use stimulation rate as high as 40 Hz, which provides the generation of high amplitude middle latency and steady state responses (Galambos et al., 1981). Such responses can be easily analyzed in the frequency domain, thus, providing sufficient information for objective testing.

This rate ,however, causes overlapping of transient responses. We were able to extract transient responses by using Continuous Loop Averaging Deconvolution (CLAD), an algorithm developed in our laboratory (Özdamar & Bohórquez, 2006).

Consequently, this study aims to investigate the effects of embedded silent gaps of varied durations (6, 9, 12 ms) in an ongoing white noise signal as an auditory stimulus on the Middle-latency response and Auditory Steady-State Response. All stimuli are designed with 40 Hz stimulation rate in this study. 40 Hz isochronic gaps stimuli were designed to evoke real steady state responses. Additionally, 40 Hz low jittered gaps stimuli were designed to meet the CLAD conditions to allow the extraction of transient responses from overlapped (convolved) responses. To demonstrate the validity of the deconvolved responses, synthetic ASSRs were constructed from deconvolved transient response then compared to real ASSRs.

CHAPTER 2: REVIEW OF LITERATURE

2.1 Anatomy of Hearing System

The first step to understanding how the human ear perceives sound is to understand the nature of sound itself. The study of the relationship between the auditory system response and the precise characteristics of sound is the key to recognizing how the sound is perceived. Sound, as the human ear perceives it, is essentially composed of vibrations traveling in the air causing compression and rarefaction in air particles. However, the extent to which the ear can perceive sound principally depends on the functionality of the hearing system. The hearing system is characterized into two parts that transduce the sound to be perceived; the first one is the peripheral auditory system while the second part is the central auditory system.
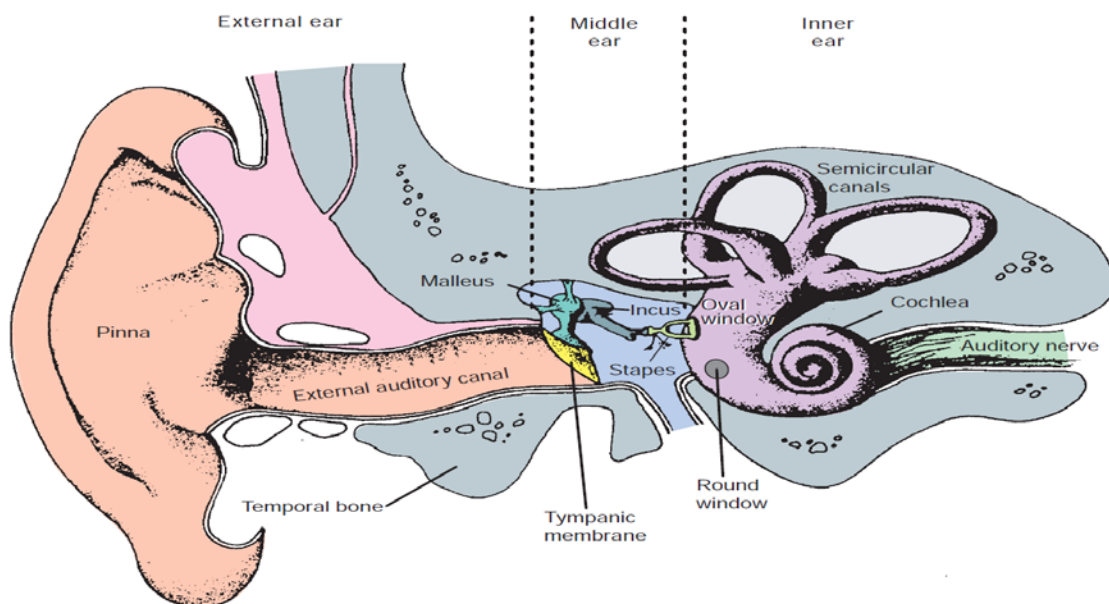
FIGURE 2.1 Drawing of the auditory periphery within the human head. The external ear (pinna and external auditory canal) and the middle ear (tympanic membrane or eardrum, and the three middle ear ossicles: malleus, incus, and stapes) are indicated. From (Squire et al., 2012).

The peripheral auditory system is categorized into three parts as shown in Figure 2.1. The external ear, which includes the pinna and the ear canal in addition to the surface of the tympanic membrane, is considered the first part of the peripheral auditory system. The second part is the middle ear, which is an air filled compartment. The components of the middle ear as shown in Figure 2.1 are the inner surface of the tympanic membrane and the ossicles (malleus, incus and stapes).
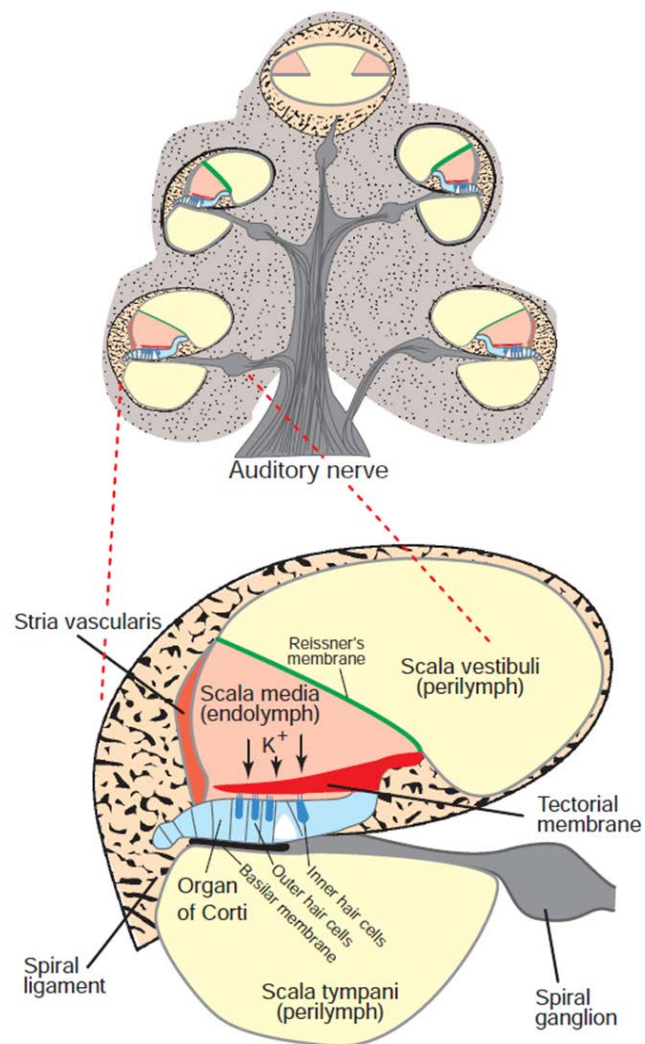
FIGURE 2.2 (Top) Cross-section through the cochlea. (Bottom) Cross-section through one cochlear turn to illustrate important cell groups (organ of Corti, spiral ligament, stria vascularis, and spiral ganglion). From (Squire et al., 2012)

Moreover, inside the middle ear there are two muscles (Tensor tympani muscle and Stapedius muscle). The middle ear is connected to the nasal cavity by the Eustachian tube. The third part of the peripheral auditory system is the inner ear that consists of the cochlea and other non-auditory structures. The cochlea has a spiral shape as shown in Figure (2.1). It is a fluid filled structure that is divided into three sections as illustrated in Figure (2.2), the two sections shaded with yellow color are Scala vestibuli and Scala tympani; both of them are filled with perilymph. The third section, which is between the Scala vestibuli and Scala tympani, is the Scala media which is filled with endolymph.

The cross section of the cochlea in Figure (2.2) also illustrates the basilar membrane between the scala tympani and scala media as well as the Reissner's membrane in between the scala vestibuli and scala media. Inside the scala media lie the tectorial membrane and organ of Corti. The Organ of Corti contains both the inner and the outer hair cells.

The central auditory system, or the auditory pathway, starts with the auditory nerve that carries the neural signals transduced by the peripheral auditory system. The auditory pathway carries the neural signals coming from the auditory nerve through the brain stem and midbrain, ending at the auditory cortex as illustrated in Figure (2.3).
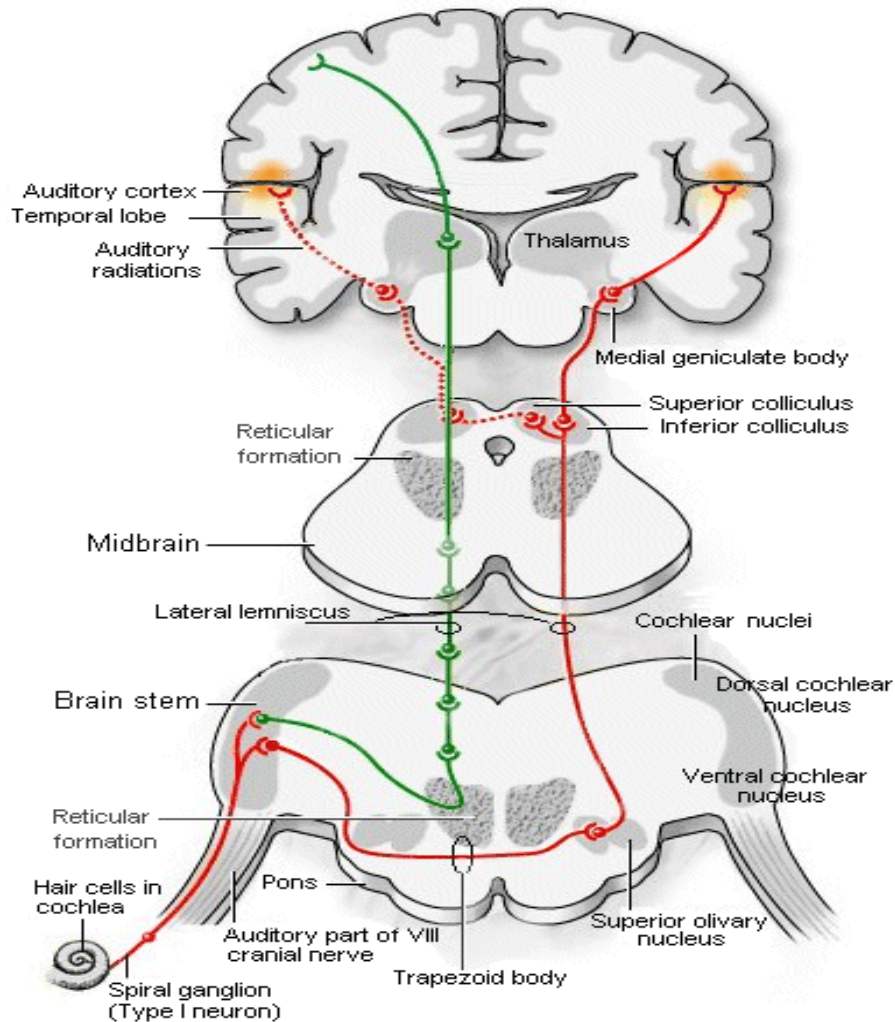
Figure 2.3 Illustration of the auditory pathway (central auditory system)
.Source http://firstyears.org/anatomy/ear.htm

2.2 Physiology of Hearing System

The sound waves propagated through air are collected by the Pinna and directed to the ear canal. The Pinna plays a significant role in collecting and focusing the sound waves into the ear canal and contributes to the sound's source localization. Then, the sound wave propagates down the ear canal toward the tympanic membrane. The tympanic membrane vibrates because of the acoustic characteristics of the sound waves.

On the other side of the tympanic membrane is the middle ear. At this stage, the acoustic energy coming from the external ear is transferred into mechanical energy. As shown in Figure 2.1, the tympanic membrane is attached to the Malleus, which moves in response to the movements of the tympanic membrane. Malleus, Incus and Stapes are all attached together in a very delicate style in which the acoustic energy is transferred into mechanical energy and the pressure is amplified around 25-30 dB (Squire et al., 2012). One of the factors that contribute mostly in the amplification process of sound pressure is the size difference between the Tympanic membrane and the footplate of the Stapes; the area of the eardrum is 35 times larger than the area between the Stapes and the Oval window (Squire et al., 2012) .

The mechanical energy from the middle ear is transferred to the next stage (cochlea) through the Oval window as shown in Figure 2.1. In the cochlea, the conversion of the mechanical energy into neural impulses occurs. The movement of the footplate of the stapes striking the oval window causes the movement of uncompressible fluids in the cochlea. As a Stapes move in and out, it creates a flow of the perilymph toward the scala vestibuli as shown in the uncoiled schematic representation of the cochlea in Figure 2.4. The basilar membrane is a flexible membrane that bends as result of the movements of the perilymph.

Uncoiled
cochlea

Apex

Base

Oval window

Helicotrema

Stapes

Scala vestibuli

Basilar membrane

Round window

Scala tympani
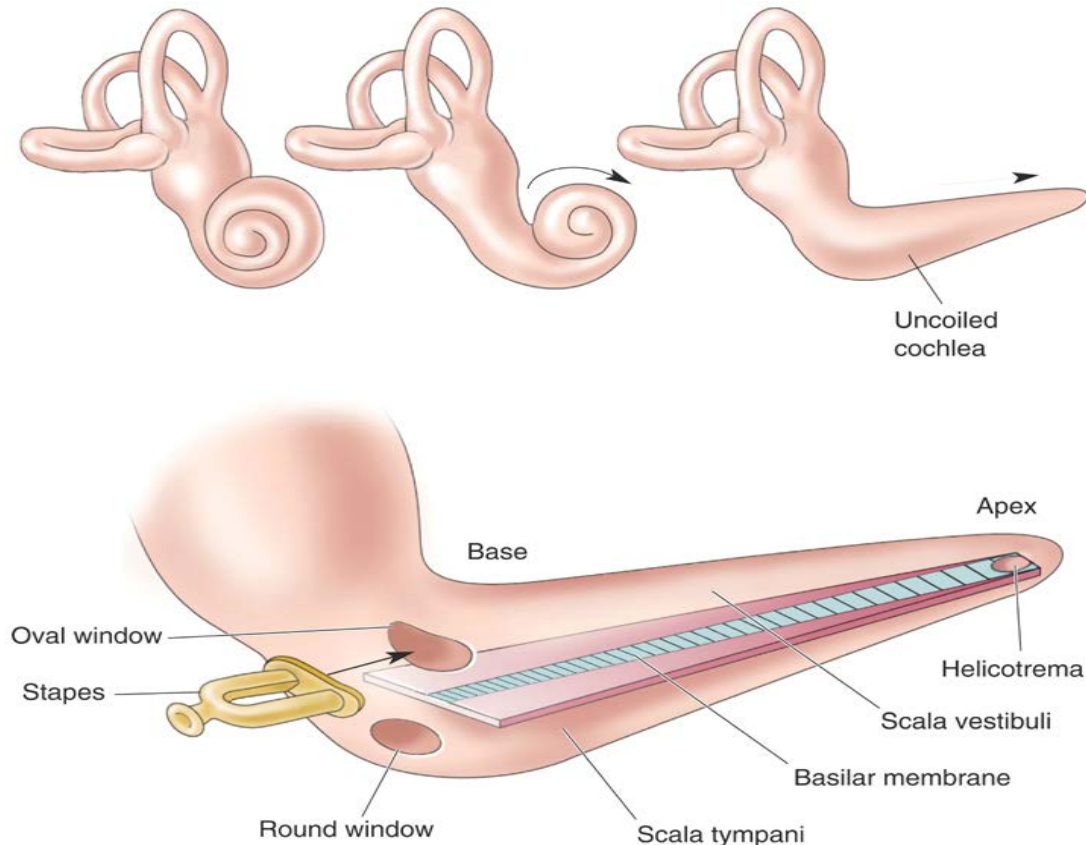
Neuroscience: Exploring the Brain, 3rd Ed, Bear, Connors, and Paradiso Copyright © 2007 Lippincott Williams & Wilkins

FIGURE 2.4 the basilar membrane in uncoiled cochlea. From (Bear et al., 2006)

The basilar membrane as shown in Figure 2.4 is wider toward the base and narrow toward the apex. The basilar membrane has the additional property of being rigid in the base, gradually transitioning to flexibility towards the apex. The distance that the sound wave travels in the cochlea depends on the sound frequency. If the sound wave has high frequencies, the stiffer part of the cochlea near the base will vibrate and the signal will not travel very far. Conversely, if the signal has low frequencies, the signal will travel toward the flexible part of the membrane (Bear et al., 2006).
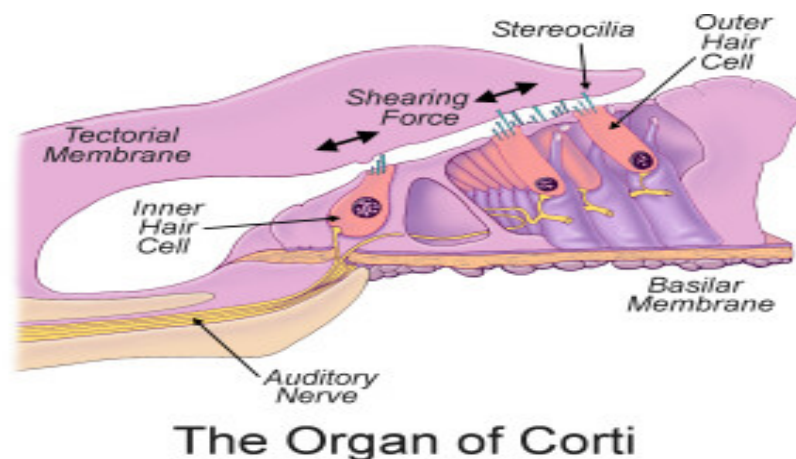
FIGURE 2.5 Illustration of organ of Corti. Source:
http://oghalailab.stanford.edu

The movements of the basilar membrane cause a deformation of the organ of Corti, which forces the tectorial membrane to move back and forth as shown in Figure 2.5. The movements of the tectorial membrane are sensed and converted into electrical impulses by specialized inner hair cells that have stereocilia attached to the tectorial membrane. The electrical impulses are collected by the auditory nerve travelling to the auditory path way as illustrated in Figure 2.3.

2.3 Auditory Evoked Potentials (AEP)

Electroencephalography (EEG) is an experimental approach to measure the electrical activities on the scalp using non-invasive electrodes. When a stimulus is introduced to the brain through the hearing system, minute changes in the spontaneous activities of the brain's electrical activities (EEG) occur. These changes are called Auditory Evoked Potentials (AEPs) and sometimes they are normal auditory evoked responses. Stimuli coming to the brain from the visual

system are called visual evoked potentials. However, our concern in this thesis is focused on the auditory system only.

Auditory evoked potentials are time locked responses that appear in the brain's EEG after the auditory stimulus is presented. One of the major obstacles to detecting AEPs is the ongoing unrelated electrical activity of the brain that obscures the relatively small electrical response to the auditory stimulus. The ongoing EEG activities in this case are considered as unwanted background noise. Since the EEG activities have random characteristics in terms of time and magnitude while the AEPs are assumed to have a synchronized appearance with the auditory stimulus presentation, methods such as signal averaging are utilized to improve the Signal to Noise Ratio (SNR).

In this technique, an auditory stimulus is presented to the ear (click, tone burst, speech...etc.) and repeated many times. In the repetitive presentation of the stimulus to ear, time intervals are calculated in a way to ensure that each response is completed and the AEP is settled down again and ready for the second stimulation. When the EEG responses are recorded and stored in a computer, signal averaging is applied by summing all the responses such that the random nature of the background noise causes it to cancel out, and the consistent AEP is preserved. This type of AEP is called transient evoked potential since each response is recorded in response to one stimulus.

A different type of AEP called Auditory Steady State response (ASSR) is also considered a promising diagnostic tool for the audiology field. In this type of AEP, an auditory stimulus is delivered to the ear at a characteristic frequency

such that responses overlap each other, creating repetitive peaks that correspond to the stimulation rate. In this chapter, we will discuss some of the different types of AEPs and how they can be evoked as well as understanding interpretation of their amplitudes and latencies.

2.3.1 Auditory Brainstem Response (ABR)

Auditory brainstem responses (ABRs), or short latency responses, are a set of wave components that appear in the first 9 ms following the stimulus onset (Jewett & Williston, 1971) . In humans, ABRs consist of seven vertex-positive wave components, named with Roman numerals from wave I to wave VII (Jewett & Williston, 1971). Identification of each peak in ABRs depends on their latencies. Peak V is the most remarkable peak and typically has the highest amplitude in comparison with the rest of the auditory brainstem response components. Moreover, studies have been conducted to focus on identifying the neural generators of each peak in ABRs as shown in Figure 2.6.

The first peak that appears after the stimulus onset is believed to be generated from the distal portion of the 8th cranial nerve (Møller & Jannetta, 1981). Wave two of the auditory brainstem response is believed to originate from the proximal portion of the 8th cranial nerve as it enters the brainstem (Møller & Jannetta, 1981). Peak III is believed to be generated from the activity in superior olivary complex (Drummond et al., 2010). Wave IV of the auditory brainstem response is believed to be generated from the cochlear nucleus and nucleus of lateral lemniscus (Drummond et al., 2010). The fifth wave is believed to be generated from inferior colliculus as indicated in Figure 2.6 (Picton et al.,

1977).Peak V in the auditory brainstem response is the most stable component because of its insensitivity to the higher rate stimulation (Picton et al., 1977).
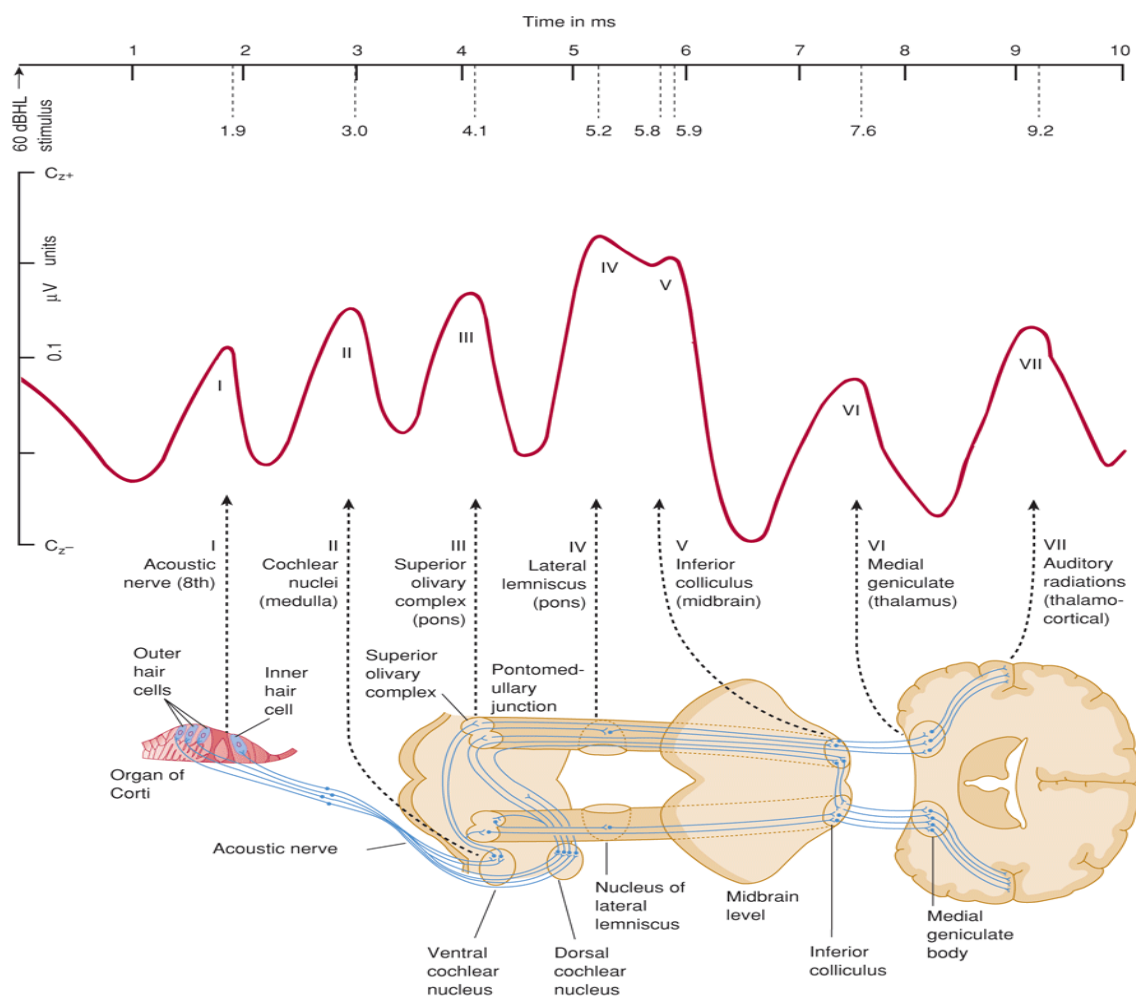
FIGURE 2.6 Illustration of the auditory brainstem responses generators in central auditory system from (Drummond et al., 2010)

Auditory brainstem responses are widely implemented in clinical diagnosis. ABRs are a sensitive way to examine the condition of brainstem structures as well as, identify abnormalities or lesions in the auditory pathway (Markand, 1994). Furthermore, ABRs are used as a tool for diagnosing patients with different brainstem disorders as well as neurological disease diagnosis

(Markand, 1994). Moreover, because of the stability of the ABRs with different recording conditions such as arousal, attention or sedation, it is a decent tool for diagnosing young children or children who are difficult to test (Picton et al., 1977)

2.3.2 Middle Latency Response (MLR)

Middle latency responses (MLRs) are the auditory evoked potentials recorded after the auditory brainstem responses; usually MLRs are recorded between 10 and 50 ms after the stimulus onset (Picton et al., 1974). In response to the click stimulus, the MLRs usually contain a set of five wave components that are named according to its positivity or negativity. The five MLR components are commonly named respectively as (No, Po, Na, Pa, and Nb) (Picton et al., 1974a); Figure 2.7 illustrates the wave components of the middle latency response.
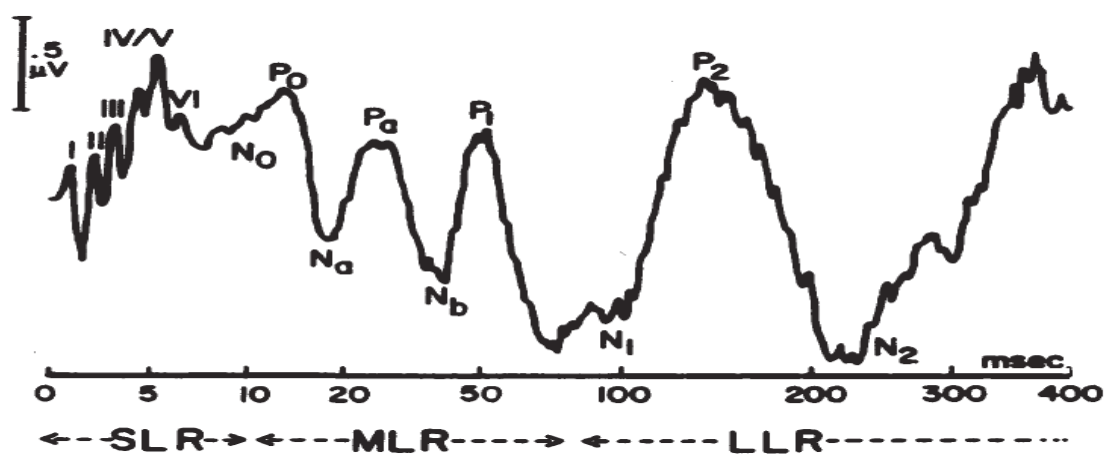
FIGURE 2.7 Short latency response, middle latency response and long latency response. Modified and redrawn from (Michelini et al., 1982)

The neural generators of MLR components are less understood compared to the ABR's neural generators; it is currently believed that the MLRs are generated by the combination of multiple generators. The thalamocortical pathways are held to be the major contributors to the MLR waveform, with the inferior colliculus and reticular formation as minor contributors (Kraus et al., 1994). Furthermore, in a study conducted by (Hashimoto, 1982) indicates that Po and Na are generated from the midbrain region while Pa most probably originates in the auditory cortex. Moreover, a study conducted by (Kraus et al., 1982) on patients with cortical lesions suggested that Pa is most likely to originate bilaterally in the temporal lobes.

Attempts have been made for clinical applications based on employing the middle latency responses as diagnostic method for neural problems. Diagnosing patients with cortical deafness has been investigated by (Özdamar et al., 1982). Moreover, assessments of patients with cortical lesions using middle latency responses have been also investigated by (Kraus et al., 1982). Additionally, middle latency responses have been utilized to approximate hearing sensitivity threshold (Zerlin & Naunton, 1974). Furthermore, middle latency responses have been investigated to be utilized in determination of depth of anesthesia (Thornton & Newton, 1989).

2.3.3 Long Latency Response (LLR)

Long latency responses (LLRs), sometimes called late latency responses, are evoked potentials recorded after 50 ms from the stimulus onset. Historically, LLR was the first auditory evoked responses observed while recording electroencephalograms during sleep in the presence of auditory stimuli (Davis et al., 1939).

Long latency responses usually contain a set of four wave components that are named according to their positivity or negativity. The four LLR components are commonly named P1, N1, P2, and N2, respectively (Picton et al., 1974b) . N1 and P2 are generally referred together as the N1-P2 complex. The long latency responses are easy to identify because of their distinguishable amplitudes with respect to the earlier auditory evoked responses, as shown in Figure 2.7. Studies have suggested that long latency responses origins are largely associated with frontal cortex (Picton et al., 1974b).

2.3.4 Auditory Steady State Response (ASSR)

An auditory steady state response is a cyclic response that has a relatively consistent phase relation with respect to the rate of the auditory stimulation, and is only generated when the stimuli is presented at a rate high enough to cause an overlapping of the transient evoked responses (Galambos et al., 1981). Moreover, a modulated amplitude and frequency tone stimulus presented at a rate between 1 Hz and 200 Hz can be used to evoke an auditory steady state response from the human scalp (Picton et al., 2003).

Figure 2.8 shows the results of the study conducted by (Galambos et al., 1981); the figure illustrates the effect of increasing a rate of tone burst stimulus from 3.3 stimuli per second up to 40 stimuli per second. Additionally, Figure 2.8 shows the transient response to a click stimulus which includes peak V as well as middle latency responses. As mentioned in (Galambos et al., 1981) study, auditory steady state responses evoked by a 40 Hz stimulus are the most robust responses because of their prominent peaks.
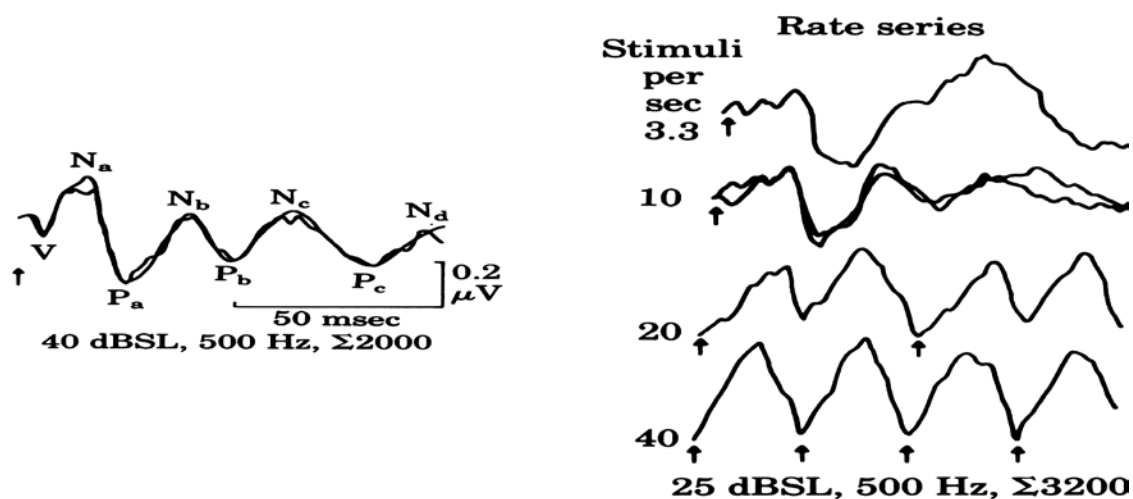
FIGURE 2.8 response to 500 Hz tone burst, different rate series shown between 3.3 Hz up to 40 Hz. Modified from (Galambos et al., 1981).

In contrast to the transient evoked responses which are described with respect to their amplitudes and latencies, the auditory steady state responses are described based on their magnitudes and phase after quantifying the signal in the frequency domain. To extract the signal phase and magnitude, the signal is transformed from time domain into frequency domain using Fourier transformation theory. By applying Fourier transform mathematical operations, the time domain signal is transform to form the frequency spectrum (Schimmel et

al., 1974) . Moreover, from a particular frequency of the signal, a magnitude versus the phase representation can be plotted on a unit circle (Picton et al., 2003).

Several clinical applications exist that implement auditory steady state response to assess hearing threshold. The ASSR has been used to predict hearing threshold in infants (Rance & Rickards, 2002; Rance, 2005). Moreover, ASSRs have been implemented clinically in fitting hearing aids as well as diagnosing young children in need of cochlear implants. Additionally, ASSRs may also be useful to evaluate the functionality of hearing aids (Picton et al., 2003). ASSRs recorded in response to high rate stimuli (80 Hz) are more useful than ASSRs recorded to low rate stimuli in diagnostic applications because they are not affected by sleep or sedation, which make it useful for diagnosing newborn infants (Picton et al., 2003).

2.4 Continuous Loop Averaging Deconvolution (CLAD)

In general, conventional averaging calls for the transient auditory evoked potentials to be recorded using a stimulation rate low enough to prevent the overlapping of the transient responses. In other words, a time interval should be considered while presenting a sequence of stimuli; this time interval should be designed to allow the completion of the first response before applying the second stimulus.
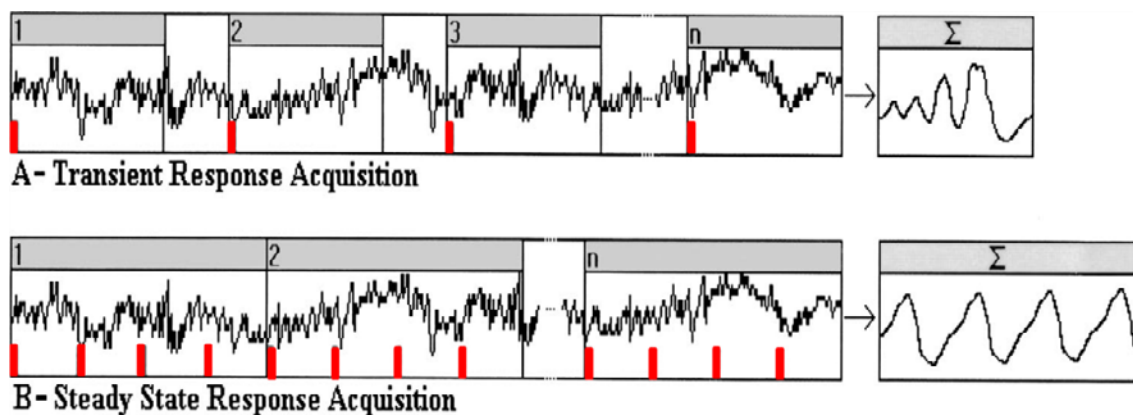
FIGURE 2.9 A) transient responses conventional averaging method . B) Steady state responses conventional averaging method. Modified from (Delgado & Ozdamar, 2004)

For example, to record ABRs which last usually 12-15 ms without causing the responses to overlap, the stimulation rate generally should be below 67-83 Hz. On the other hand, to record MLRs (usually lasting 50-80 ms) without overlaps, the stimulation rate generally should be below 12.5-20 Hz (Ozdamar et al., 2007). Considering the above-mentioned limitations, it is clear that conventional averaging has a limitation imposed on the rate of stimulation for any given paradigm below which one must stay to prevent overlapping of the responses (Delgado & Ozdamar, 2004).

Furthermore, Figure 2.9 (A) shows how the conventional averaging is acquired by making stimuli sequence (in red) far enough to allow the completion of the transient response. Transient responses extracted from the EEG using conventional averaging are analyzed in the time domain by analyzing the latencies and amplitudes. On the other hand, by increasing the stimulation rate while using conventional averaging the resulting response will be the steady state response as shown in Figure 2.9 (B). Steady state responses extracted from EEG Using Conventional averaging are analyzed in the frequency domain by identifying the magnitude and the phase of the signal (Delgado & Ozdamar, 2004).

The limitations of conventional averaging prevent obtaining transient response using high rate stimuli. Moreover, steady state responses gained by using conventional averaging can never be decomposed to obtain its transient responses because of multiple stimulus overlapping. To overcome this limitation Delgado & Ozdamar (2004) proposed a novel generalized acquisition method called Continuous Loop Averaging Deconvolution (CLAD). As proposed in this study, the CLAD method has the ability to deconvolve the overlapped transient evoked responses evoked by high stimulation rate sequences.

The deconvolution method works based on the presentation of the high rate stimulation to the auditory system in which the responses will overlap. However, the stimulation sequence used in the deconvolution method are not equally spaced. In other words, the time intervals between each stimulus are nonisochronic. Each individual response is obtained by applying the CLAD

algorithm to the overlapped resulting signal from high rate stimulation using a nonisochronic sequence. The main assumption and condition are that the single response is independent; and the overlapped responses represent the sum of all single responses (Delgado & Ozdamar, 2004).

In Delgado & Ozdamar (2004), the data acquisition process is explained mathematically in the time domain by using matrices. The deconvolution method requires data to be obtained using a continuous acquisition loop buffer v[t] that contains the sum of all individual responses. The assumption is that each individual a[t] is independent. The convoluted measured response vector v[t] is related to the desired deconvoluted response vector a[t] with the following matrix equation:

$$\mathbf{v}[t] = \mathbf{M} \, \mathbf{a}[t]$$

Where M is a multidiagonal matrix with a sequence of ones and zeros related to the stimulus sequence. Deconvoluted responses to individual stimuli can be obtained by solving the equation for a[t] as follows:

$$\mathbf{a}[t] = \mathbf{M}^{-1} \, \mathbf{v}[t]$$

Although the continuous loop averaging deconvolution method in time domain was able to deconvolve the overlapped transient evoked responses evoked by high stimulation rate sequences, it has some limitations. First, some sequences produce unwanted noise. Second, the time taken to execute CLAD computations is relatively long. To resolve these issues, Özdamar & Bohórquez (2006) proposed an upgrade of the time domain deconvolution method to a frequency domain deconvolution method.

In this study, Özdamar & Bohórquez (2006), explained the origin of unwanted noise in the time domain deconvolution method and they offered faster computation time in the frequency domain. They developed a generalized method to calculate the signal-to-noise ratio (SNR) for any desirable sequence and analyze the noise amplification factor (NAF) of the averaged deconvolution processes. A brief description of how the computations of the deconvolution method in frequency domain are processed is illustrated in Figure 2.10.
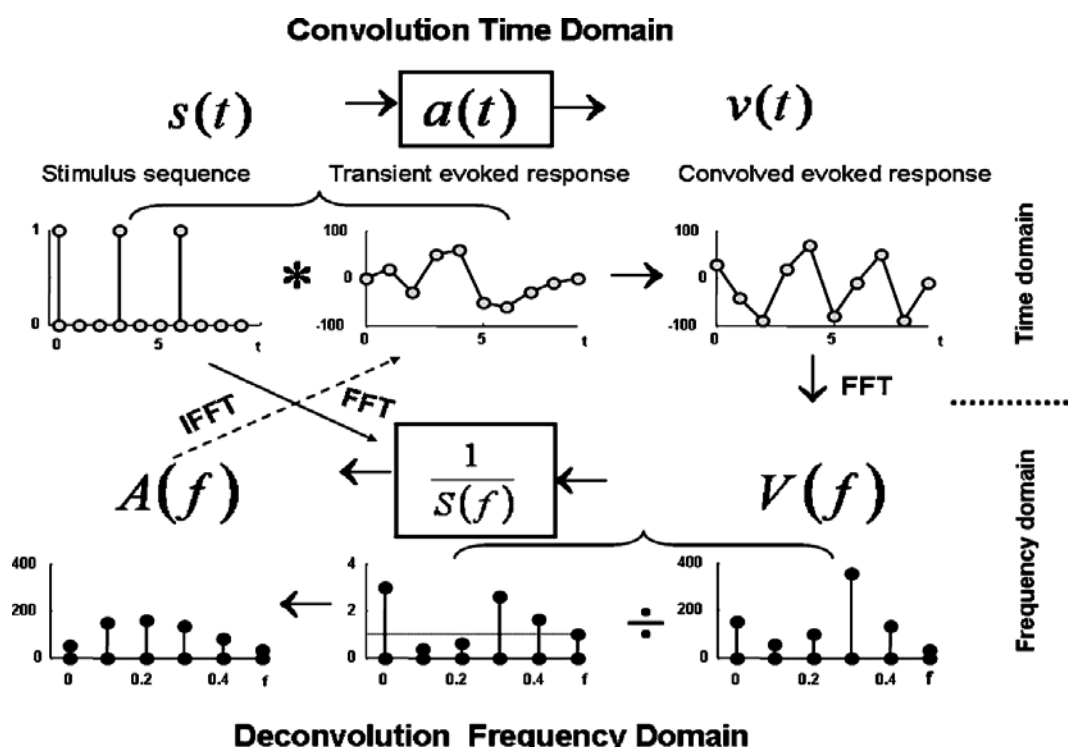
FIGURE 2.10 Convolution of the elementary responses to a stimulus sequence in the time domain produces a convolved response (top) and the deconvolution of the convolved response into the elementary response in the frequency domain (bottom). From (Özdamar & Bohórquez, 2006)

Furthermore, in another study conducted by (Bohórquez & Ozdamar, 2008) the deconvolution method was implemented to investigate the superposition theory of 40 Hz steady state generation. In this study, low jitter sequence (near isochronic) was used in addition to medium and high jittered sequences. Figure 2.11 illustrate the difference between high, medium and low jittered sequences in addition to the isochronic sequence.
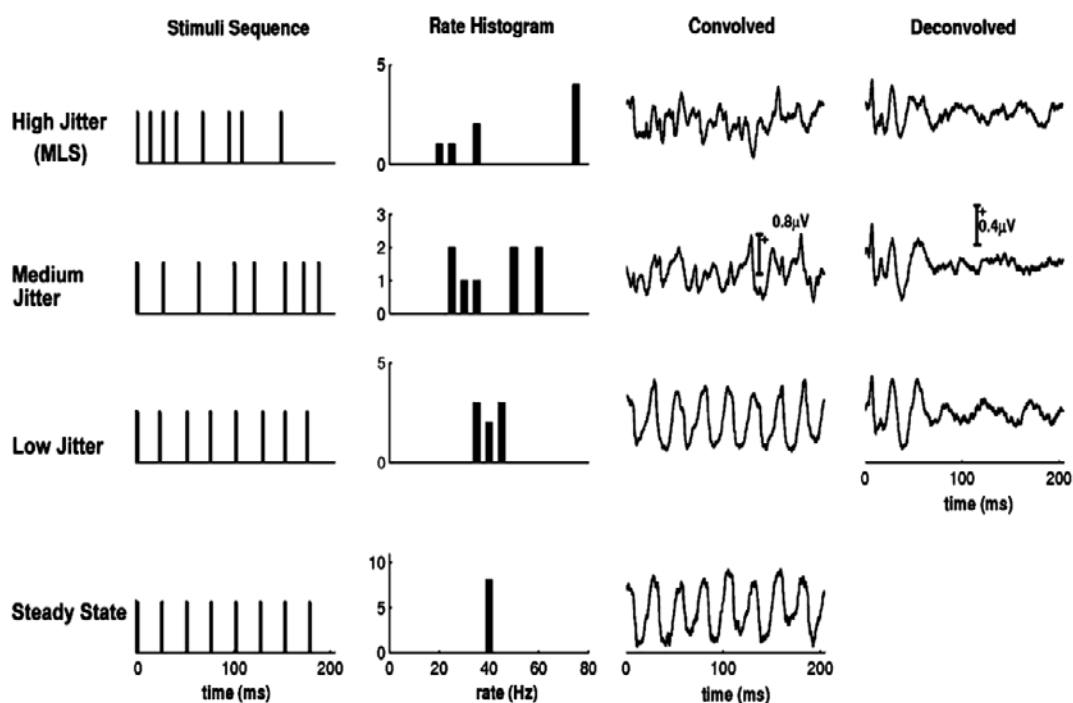
FIGURE 2.11 Effects of different jittered sequences (high, medium and low), in addition to steady state sequence. From (Bohórquez & Ozdamar, 2008)

The deconvolution method allows for the investigation of high rate stimulation using almost any sequence except the strictly isochronic sequences. In Delgado & Ozdamar (2004), ABRs and MLRs have been recorded in response to high rate stimuli with a quality comparable to ABRs and MLRs obtained from

low rate stimuli. Moreover, one of the advantages proposed in (Delgado & Ozdamar, 2004) is the flexibility to design any desired sequence including sequences very similar to the isochronic sequences that provide results comparable to the previous studies based on conventional averaging. Moreover, application of CLAD is not limited to auditory evoked potentials but it provides a general nonsynchronous excitation and deconvolution technique that can be applied to any technique requiring excitation and time averaging of acquired signals.

2.5 Gaps in noise studies

The study of silent gaps embedded in noise was widely explored in order to form some sort of understanding of how the auditory nervous system reacts to a sudden silence in the auditory stimulus. The gap-in-noise (GIN) test has been used as a behavioral test to examine temporal processing. Processing time of changes in sound reflects information that can be used in speech recognition for different situations (Palmer & Musiek, 2013). In this section, we are going to describe how gap-in-noise has been used as a test to measure temporal processing. We are also going to review the literature on how gaps embedded in noise have been used as a stimulus to study the effect of aging. Moreover, in this section we will cover the studies that explored the effect of gaps in noise stimulus on patients with hearing loss or neural disorders. Additionally, we will review and compare the auditory evoked responses reported by different studies to gaps in noise stimulus.

2.5.1 Gaps-In-Noise (GIN) test

The GIN test has been used as a tool to evaluate temporal resolution (Musiek, 2005). The temporal resolution is defined according to (Moore & Moore, 2003) as "the ability to detect changes in stimuli over time, for example, to detect a brief gap or detect that sound is modulated in some way." Poor temporal resolution has been shown to correlate with speech recognition difficulties (Gordon-Salant & Fitzgibbons, 1993).

The GIN test was developed to introduce a clinically feasible measure for assessing the ability of various patient populations to detect gaps, particularly patients who are known for central auditory disorders (Musiek, 2005). Several experts recommended including the temporal resolution evaluation as a part of the diagnosis of patients at risk for auditory processing disorders (Jerger & Musiek, 2000). They demonstrated the importance of temporal resolution evaluation because it could provide insights into the integrity of the central auditory system. Moreover, identifying the deficits in temporal resolution abilities can provide helpful clues to direct rehabilitative planning (Jerger & Musiek, 2000)

Musiek, (2005) proposed an example of a GIN test used to evaluate temporal resolution in normal-hearing subjects and subjects with confirmed neurological hearing impairments of the central auditory nervous system. The test consists of 0 to 3 silent gaps ranging from 2 ms up to 20 ms embedded in white noise with duration of 6 seconds as illustrated in Figure 2.12. The location, number, and duration of the gaps in each white noise band differ during the course of the testing for a total of 60 gaps presented in each of four lists.
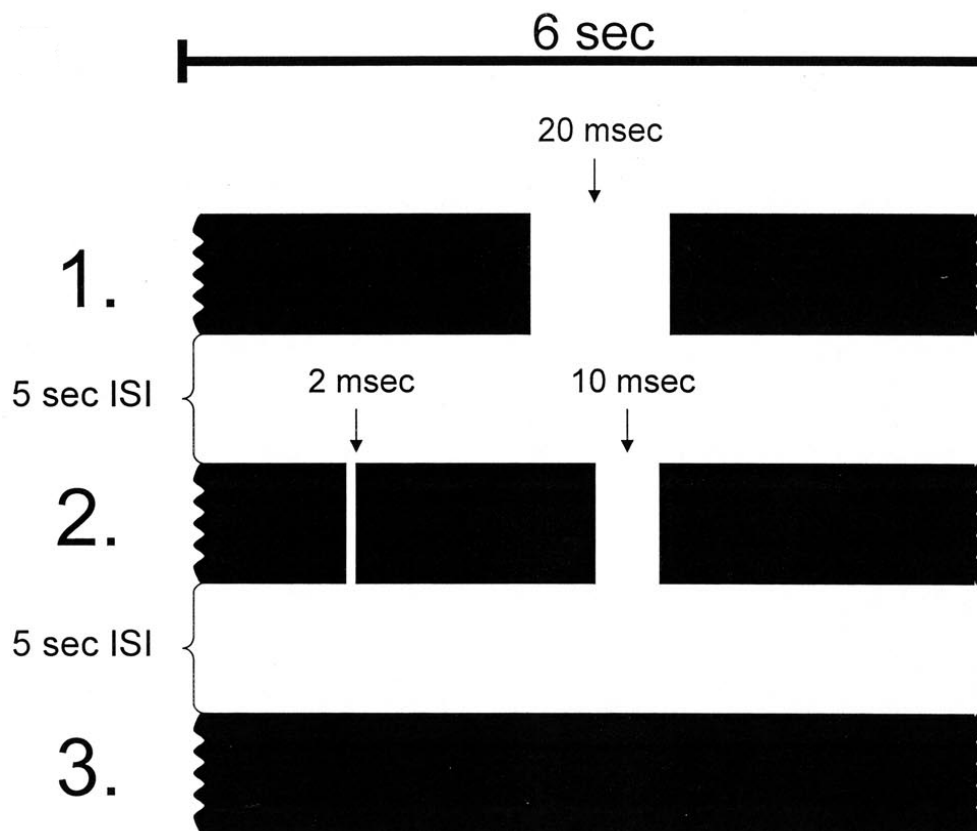
FIGURE 2.12 Samples of three GIN items demonstrating the duration of the stimuli, Inter-Stimulus Intervals (ISI), and varying durations. Modified from (Musiek, 2005).

Results from the (Musiek, 2005) study showed mean gap detection threshold to be 4.9 ms for right ears and 4.8 ms for left ears in normal-hearing subjects. In the other side, subjects with confirmed neurological hearing impairments of the central auditory nervous system had higher gap detection thresholds approximately 7.8 ms for left ears and 8.5 for right ears. This study proposed the GIN test as a reliable test based on the achieved results. Moreover, this study showed the feasibility using GIN test for temporal resolution evaluation because it can be performed in a period of time suitable for clinical application. Additionally, it showed that the GIN test is sensitive and specific to central auditory nervous system lesions.

2.5.2 Age-Related Differences in Gaps-in-Noise Studies:

Several studies have consistently demonstrated the differences between young and older adults in response to silent short gaps embedded in white noise or two bursts of noise band separated by short gaps (Harris et al., 2010; Harris et al., 2012; Poth et al., 2001; Schneider et al., 1994; Snell, 1997).

One of the latest studies of gaps embedded in noise was conducted by Harris et al. (2012). The focus of this study was to measure the effect of age variability on the ability to detect gaps in noise, as well as to use gap detection as a tool to identify the speed of temporal processing in younger and older adults. In Harris et al. (2012) study, the cortical Event Related Potentials (ERPs) were examined in terms of amplitudes and latencies. The ERPs were recorded from 50 subjects; half of them were young adults and the other half were old adults. This study implemented two conditions of recording: passive and active. In the active recording condition, subjects were given a push button and asked to press the button when they sense the gap in the stimulus. While in passive recording condition, they were asked to ignore the stimulus and read quietly. Temporal processing speed was calculated as the percent of gaps detected in the active condition. The stimulus was designed in such that 3, 6, 9, 12, 15 ms gap durations are separated by 2 to 2.2 second white noise bands; each gap duration was presented in a sequence 250 times(see Figure 2.13). When the first gap duration completed a cycle of 250, other gap duration took place in a random manner. In this study, the right ear was stimulated monaurally by the stimulus presented in all condition and to each subject (Harris et al., 2012).
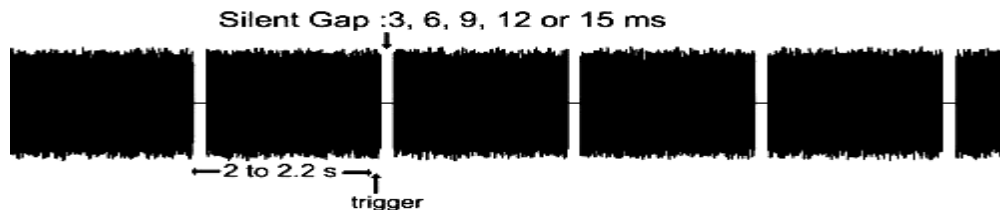
FIGURE 2.13 Continuous noise was presented with silent gaps distributed every 2 to 2.2 second, modified from (Harris et al. 2012)

The findings of the (Harris et al., 2012) study has shown that the differences between younger and older adults were observed in temporal processing speed; the older adults had slower speed of detection of gaps compared to young adults. The neurophysiological responses obtained to gap onset from older adults were irregular in which the amplitude of P2 was reduced with the absence of N2 wave. On the other hand, in younger adults and in both active and passive recording conditions, response latencies were shorter for N1 and P2.This study concluded that older adults exhibited poorer temporal processing speed and gap detection with the increase of task complexity (Harris et al., 2012).

Findings of (Harris et al., 2012) were consistent with the previous study conducted by (Harris et al., 2010), which showed the differences in gap detection abilities between younger and older adults. The differences have been shown to increase when the complexity of the auditory task increased. In this study, older adults showed poorer abilities to detect short gaps in white noise. However, this study in particular tested different factors that may have contributed to the ability to detect gaps in noise for both younger and older adults. One of the possible factors was the precise gap location in the stimulus noise burst (beginning,

middle and end). In addition, gap detection threshold was measured; processing speed for gap detection was quantified by measuring how fast individuals reacted when they detected gaps in ongoing noise by pressing the push button. Based on the results of this study, the authors believed that age related differences in gap detection were associated with changes in the central auditory system (Harris et al., 2010).

Poth et al., (2001) have tested the auditory brainstem responses in younger and older adults with stimuli consisting of broadband noise separated by silent gap. They used a stimulus designed by using 50 ms of broadband noise bursts separated by silent gaps of different durations (4, 8, 32 and 64 ms), see Figure 2.14. They reported that all subjects had a measurable peak V of the auditory brainstem response while three out of eight older adults did not show a measurable peak V to the second noise burst after the silent gap of durations 4 and 8 ms. Additionally, one of eight younger adults did not have a measurable peak V for the second noise burst after 4 ms gap durations. When there is measurable peak V, all subjects showed similar latencies but older adults showed smaller amplitudes.
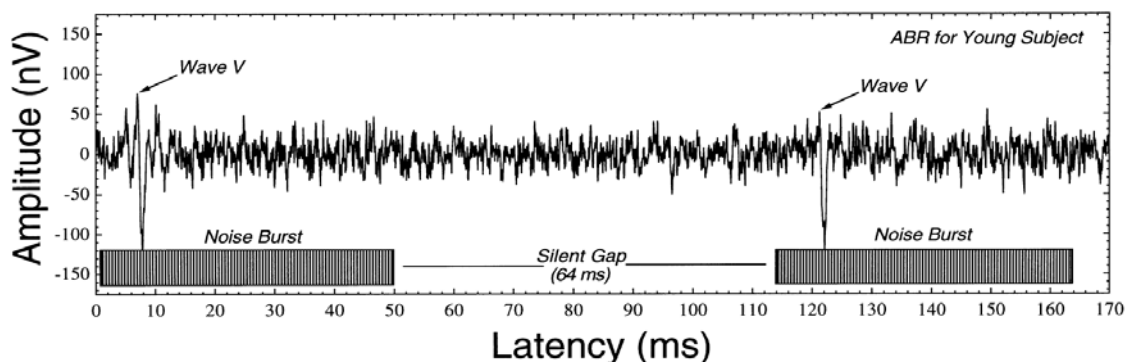
FIGURE 2.14 ABR waveform to two noise bursts separated by a 64-ms silent gap for a young subject. Arrows indicate wave V to the first and second noise bursts. Modified from (Poth et al., 2001)

2.5.3 Gaps in Noise Studies with Hearing Loss

Temporal resolution in normal hearing listeners and impaired listeners has been investigated by using gaps in noise stimuli (Fitzgibbons & Wightman, 1982); temporal resolution was considerably better in normal-hearing listeners. Moreover, two studies (Lister & Roberts, 2005; Roberts & Lister, 2004) examined different groups of listeners including normal hearing young adults, normal hearing older adults and older adults with hearing loss. Findings from both studies were consistent with other studies that showed age-related differences in gap detection. Furthermore, both studies showed that older listeners with hearing loss performed more poorly in gap detection.

Another animal study conducted by Yin et al. (2008) on animal subjects with sensorineural hearing loss to evaluate the temporal resolution. Responses to gaps in noise were recorded in the inferior colliculus and auditory cortex of guinea pigs through implanted electrodes. Findings from this study indicate that a high-frequency hearing loss showed an impact on temporal processing in the low-frequency region of the auditory system.

2.5.4 Auditory Evoked Responses to Gaps in Noise

As shown previously in this section, several studies have used silent gaps in noise stimuli to evaluate the subject's temporal resolution. Some of these studies were based on the participant's feedback to report gap detection threshold. Other studies like (Harris et al., 2012) built their findings based on the participant's feedback and compared cortical evoked responses to gaps embedded in white noise. Some studies have recorded the auditory brainstem

response to silent gaps in noise (Poth et al., 2001; Werner et al., 2001). Other studies have recorded long latency responses to silent gaps in noise (Atcherson et al., 2009; Harris et al., 2012; Lister et al., 2007; Lister et al., 2011; Palmer & Musiek, 2013; Pratt et al., 2005). There were no reachable studies on the effect of silent gaps embedded in white noise on the middle latency responses.

Auditory brainstem responses were recorded in a Werner et al. (2001) study in response to gaps in broadband noise; gap durations varied between 0 - 125 ms with 1 ms increments. In addition, psychophysical responses to gaps were evaluated to measure the gap detection threshold. They reported that the ABR threshold to gaps in noise and the psychophysical gap detection threshold were similar. The auditory evoked response threshold to gaps was 2.4 ms while the gap detection threshold was 2.9 ms. In addition, the age related study described earlier recorded auditory brainstem responses to gaps embedded in white noise (Poth et al., 2001) as well.

Different studies have focused on studying the late electrophysiological responses to gaps in white noise stimuli. The (Harris et al., 2012) study is an example of studies that used gaps in noise stimulus to study age-related differences as described earlier. Moreover, a study conducted by Pratt et al. (2005) compared the behavioral gap detection threshold to the recorded late latency responses. Recorded evoked potentials were compatible with the behavioral measures of the average of gap detection thresholds. In this study, N_1-P_2 components were clearly recorded to gaps of 5 ms duration or longer. However, N_1 showed an inflection, or showed a bifid peak, (see Figure 2.15).
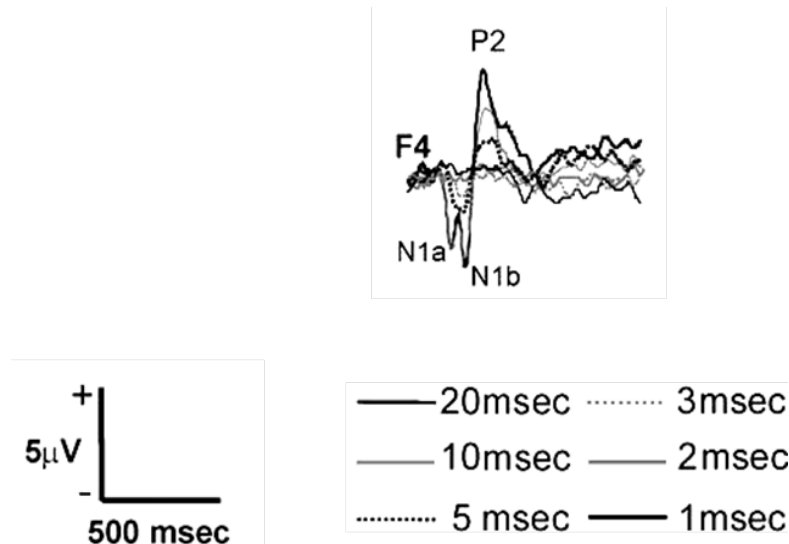
FIGURE 2.15 Grand averaged waveforms (13 subjects) of potentials to short gap durations in the passive condition. Note that N1 was inflected or bifid, consisting of N1a and N1b. Modified from (Pratt et al., 2005)

Another study showed consistency with previously mentioned studies in which the N_1 component can be elicited by gaps in narrowband noise. Additionally the electrophysiological gap detection thresholds and psychophysical gap detection thresholds showed compatibility (Atcherson et al., 2009). Finally, Palmer and Musiek (2013) conducted one of latest studies on gaps in noise stimuli for long latency responses. The focus of their study was to focus on recording N1- P2 responses to gaps in broadband noise in normal-hearing young adults. They compared N1- P2 amplitudes, latency and morphology to different gap durations. They evaluated the electrophysiological responses to see if it could be used to evaluate the temporal resolution. They found that N1- P2 amplitudes decreased with decreasing gap durations. Additionally, they reported that latencies of N1- P2 remained stable as gap durations changed.

CHAPTER 3: METHODS

3.1 Study Population

Six young adult participants were included in the study population. The age of the participants varied between 21 and 27, with the mean age of 23.66. All six participants were right-handed males with normal hearing level, without any reported hearing loss or neurological diseases. All participating subjects signed informed consent forms in accordance with the Institutional Review Board of the University of Miami. During the experiment, each subject was lying comfortably inside a sound-solated room while watching sound-muted movie with closed captions. All six participants were instructed to relax as much as they could while the stimulus was delivered monaurally to the right ear.

3.2 Stimuli Description

As mentioned previously, this study mainly focused on exploring the effect of gaps embedded in ongoing white noise on the Middle Latency Responses (MLRs) and Auditory Steady State Responses (ASSRs), as well as studying the variability effect of gap duration on both MLRs and ASSRs. Moreover, as it has been discussed earlier, it is difficult to extract MLRs efficiently with a high rate stimulus such as 40 Hz (Delgado & Ozdamar, 2004). This being the case, two sets of stimuli were designed as described in the following sections, 3.2.1 and 3.2.2. Both sets include three different gap durations.

3.2.1 Steady State sequence

The steady-state (isochronic) sequence is designed in a way that the time intervals between gaps are equal. Figure 3.1 below illustrate the isochronic sequence in which the time intervals between each stimulus are constant. The interval time period between each stimulus in this sequence is 25.6 ms, making the stimulation rate equal to 39.06 Hz. The histogram in Figure 3.1 shows the rate of the steady-state (isochronic) sequence and how it is located at 39.06 Hz.

3.2.2 Quasi Steady State sequence

The Quasi Steady State (QSS) sequence, also referred to as the low-jittered sequence, was designed according to the Deconvolution method (Delgado & Ozdamar, 2004) in which the time between gaps appearance is not exactly the same throughout stimulation but jittered slightly. In contrast to Isochronic sequence, Figure (3.1) illustrates the inequality of time intervals in low jittered sequence.

The mean interval time period of the QSS sequence is 25.6 ms. As a result of the low jittering in the sequence, the blue bars in rate histogram in Figure 3.1 show how the frequency is distributed around 40 Hz while the Isochronic sequence rate is 39.06 Hz. The mean deconvolution gain factor (cdec) or Noise Amplification Factor (NAF) of this sequence is 0.4807 and it has very few noise amplification bands as seen in the Figure 3.1.
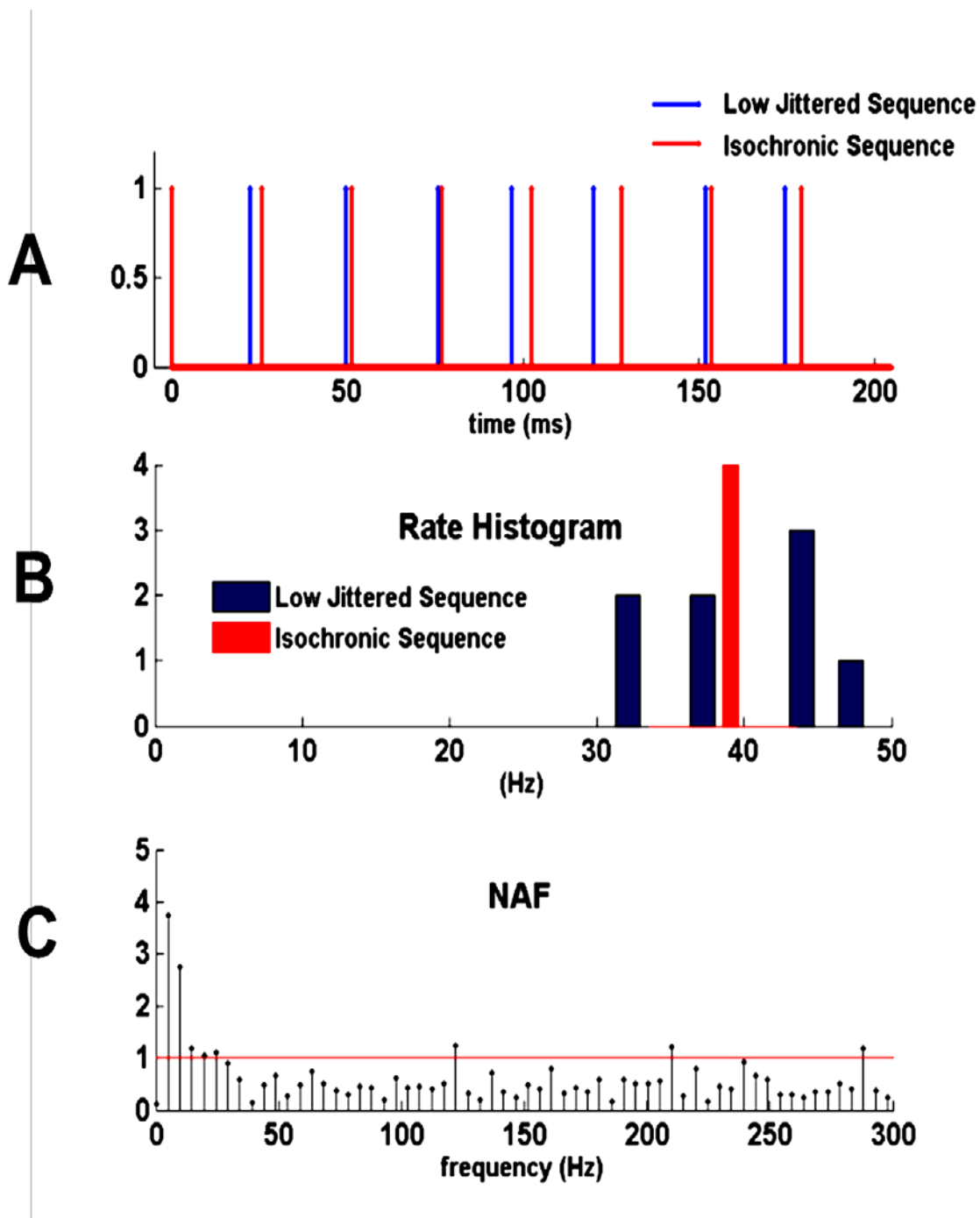
FIGURE 3.1 Comparison of the isochronic and low-jittered stimulus paradigms. A) Temporal occurrences of each sequence. B) Comparison of isochronic and low-jittered rate histograms. C) Noise Amplification Factor (NAF) of the low-jittered sequence used in this study.

In order to design each stimulus, a random number generator function was used to produce a uniformly distributed white noise signal. Then, the signal was low pass filtered to (5 KHz) to remove all frequency components beyond the Nyquist criteria. The white noise signal having been created, we modulated the white noise signal by inserting gaps according to the two different sequences (SS and QSS).
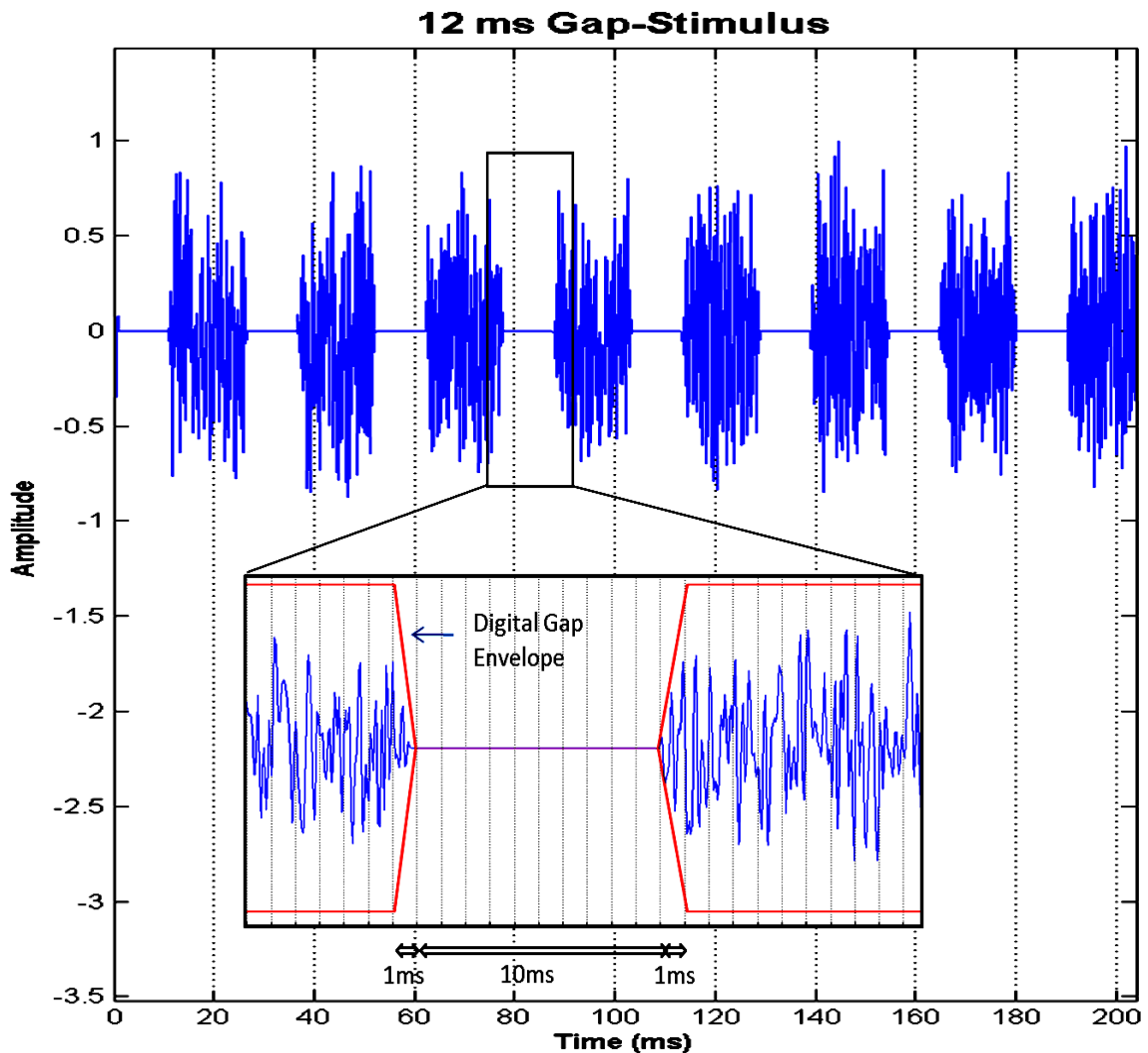
FIGURE 3.2 Top trace shows the12 ms gap stimulus presented at 40Hz. The zoomed window displays the digital gap envelope. The gradual offset of 1ms is followed by 10 ms silence and then 1ms of gradual onset. The presentation of these gaps occurs at 40Hz.

The key property of the gap's design was the onset and the offset of the gap. The 12 ms gap stimulus consisted of a 1 ms onset fall followed by a 10 ms gap, and ending in a 1 ms offset rise. Figure 3.2 illustrates the design of the entire stimulus of the 12 ms gap. The gaps have been designed for three different durations 6, 9, and 12 ms to be embedded in the 204.8 ms white noise signal with a range of rate approximately equal to 40 Hz.

In addition, a conventional click stimuli (100 µs) have been designed with QSS sequence and Isochronic sequence with rate of 40 Hz. The following Table 3.1 summarizes eight sets of stimuli delivered to each subject based on the different gap durations. Moreover, the table shows the age of each individual subject.

Table 3.1: illustrates the age of each individual subject included in this study and the total different stimuli sent to each subject

Subjects ID	Age	12 ms GAP		9 ms GAP		6 ms GAP		Clicks	
		Isochronic sequence	Jittered Sequence	Isochronic sequence	Jittered Sequence	Isochronic sequence	Jittered Sequence	Isochronic sequence	Jittered Sequence
S 1	27	√	√	√	√	√	√	√	√
S 2	25	√	√	√	√	√	√	√	√
S 3	21	√	√	√	√	√	√	√	√
S 4	21	√	√	√	√	√	√	√	√
S 5	22	√	√	√	√	√	√	√	√
S 6	26	√	√	√	√	√	√	√	√

3.3 Instrumentation and Recording

3.3.1 Subject Preparation

Experiment preparations started with explaining the purpose of this study to the volunteer participant. Following the explanation, the participant was given the time needed to read and sign the informed consent form. After that, the four gold cup electrodes were placed firmly on the skin by using a medical grade conductive gel. The montage of the electrodes placements is in accordance with the 10-20 system as in Figure 3.3. Each participant's head was measured by tape from Nasion to Inion to locate Cz which is half way between them. The ground electrode (G) was placed on forehead just above the area between the eyebrows. The other two electrodes were placed on both right (A2) and left (A1) earlobes.
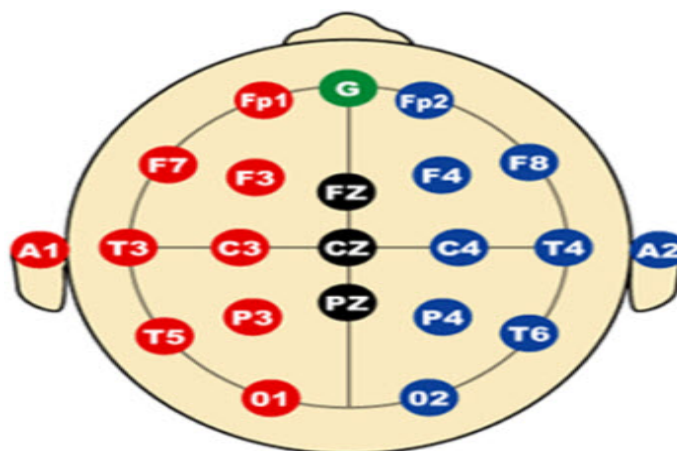

FIGURE 3.3: 10-20 International Electrode Placement Systems

Skin abrading was applied to remove dead skin or oil by using alcohol swabs (Electrode Prep Pad). After electrode placement, the participant was walked to the recording chamber which is a dim double walled sound-attenuated room. At that point, an impedance test was applied to insure that the impedance

limits were within reasonable values: between 1 and 3 Kilo-Ohms. Earphones (ER-3 A, Ethymotic Research, Elk Grove Village, IL) were inserted into the right ear. The participant was then instructed to lie down on the bed in a comfortable position and relax while listening passively to the sound in the right ear.

The electrodes were assigned as active (+) or reference (-) and ground. We recorded from a pair of electrodes, Cz to A1 and Cz to A2 for middle-latency responses. The electrode placement montage and the acquired EEG channels as well as the stimulated ear are illustrated in Figure (3.4).
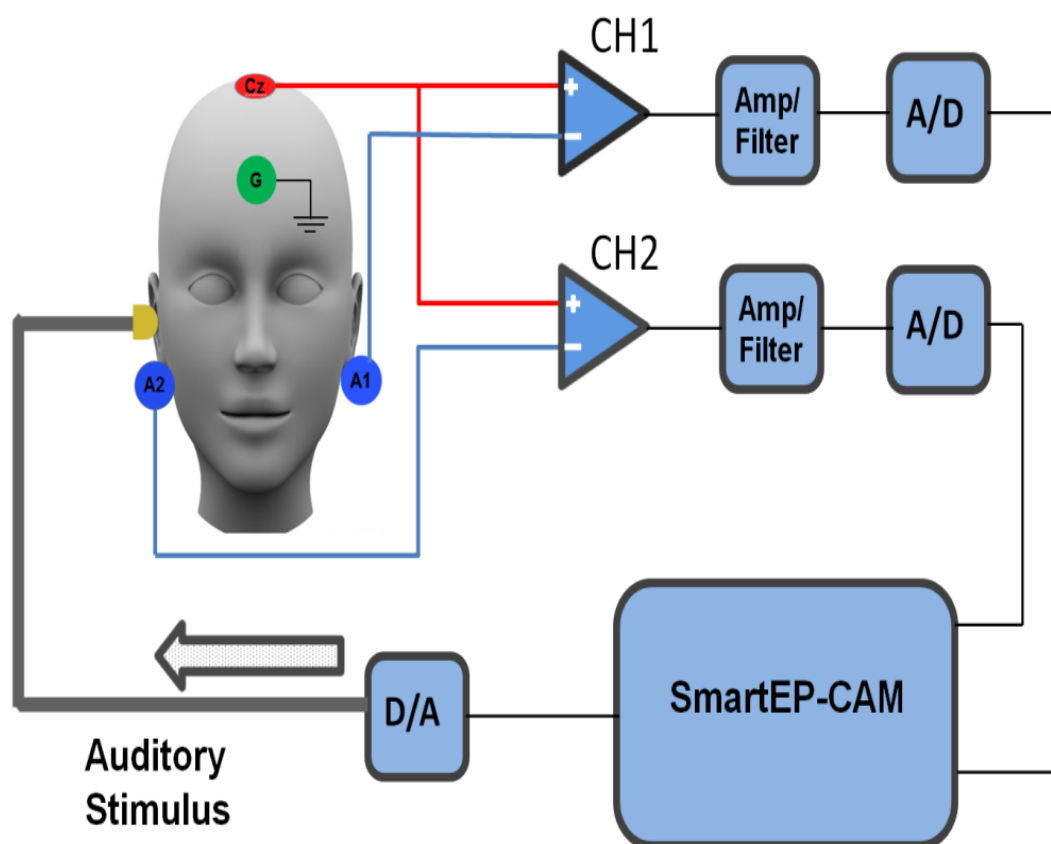

FIGURE 3.4 experimental setup and electrodes configuration. Amplifier gain: 100 K, Filters: 10-1500 Hz

3.3.2 Instrumentation

The acquisition system used to send stimuli and acquire EEG signals was SmartEP-CAM. Which is an auditory evoked potential system developed by (Intelligent Hearing Systems, Miami, FL).The built in features in SmartEP-CAM system enabled us to control the recording settings such as the number of sweeps sent to the subject, the ear that we were stimulating, and intensity of the stimulus. Moreover, the gain and filters settings were controllable in addition to the ability to set artifact rejection value.

3.3.3 Data Collection Process

The process of sending stimuli and obtaining EEG signals included six recording sessions for 6 different gap stimuli. Since we were testing three gap durations (6, 9, and12) with two different sequences (SS and QSS), there were a total of 6 recording sessions for 6 stimuli. In addition to the six stimuli, two click stimuli recordings in both sequences were acquired. The sweep length of each stimulus was 204.8 ms. During each recording session, 2048 sweeps were acquired. The number of sweeps makes up the total time for each session to be 6.99 minutes. The order in which the stimuli were sent was randomized. The EEG recordings were amplified by a gain of 100,000, band pass filtered from 1 to 1500 Hz and digitized with sampling frequency at 5000 Hz. While acquiring EEG signals, an artifact rejection feature in SmartEP-CAM was activated.

3.4 Signal Processing

All EEG signals were stored as unprocessed raw data files. In this step we describe how we process these data files by using (MATLAB, R 2012a) to extract the desired auditory evoked potentials. Using MATLAB, signals with artifacts are eliminated by setting an artifact rejection value of ±30 µV.

Firstly, EEG responses of the isochronic sequence were averaged to extract the real ASSR. Then, by using the CLAD Algorithm, transient evoked potentials were extracted from EEG responses of the jittered sequence. Finally, synthetic ASSRs are constructed using the 40 Hz stimulus.

3.4.1 Auditory Steady State Response

The EEG signals were recorded in response to 40 Hz isochronic sequence stimuli for 6, 9 and 12 ms gap durations and clicks. The recorded EEG signals were digitally averaged to extract Auditory Steady State Responses (ASSRs). Each sweep consists of 1024 data points with 204.8 ms duration. All the acquired sweeps after artifact rejection were then averaged for each stimulus recording. Further filtering to ASSRs is applied in the frequency domain. By using FFT function in Matlab, the Fourier transform of the signals were filtered by a comb filter. Signals were digitally denoised by keeping only the main frequency (39.06 Hz) and the first two harmonics (f1 = 78.12 Hz and f2 = 117.18 Hz).

3.4.2 Transient Evoked Potentials

The total number of sweeps recorded in response to the 40 Hz low-jittered sequence stimuli for each 6, 9 and 12 ms gap durations and clicks were averaged. The averaged signals represent the convolved responses to each stimulus. By using the Continuous Loop Averaging Deconvolution (CLAD) (Delgado & Ozdamar, 2004); these responses were deconvolved to produce the transient evoked potentials. To remove the residual noise which could not be removed effectively by analog filtering, the signals were passed through a band pass filter computed in the frequency domain; the filter designed to cancel out the first pins of the signal spectrum (0 Hz-9.7 Hz) and frequencies above 150th (737 Hz) spectral pins. In this frequency band, the Noise Amplification Factor (NAF) of the sequence is low, see Figure (3.1).

3.4.3 Predicted Auditory Steady State Response

The predicted responses, or synthetic steady state responses, are responses constructed by using the cyclical time shifted MLR waveform (Hari et al., 1989). The deconvolved transient response recorded in response to the low jittered sequence stimuli are divided to eight segments, then shifted by 25.6 ms in cyclic mode to create eight consecutive recordings; eventually these sequentially shifted recordings are added up linearly to form the synthetic ASSR as shown in Figure (3.5) and described in Bohorquez & Ozdamar (2008) .
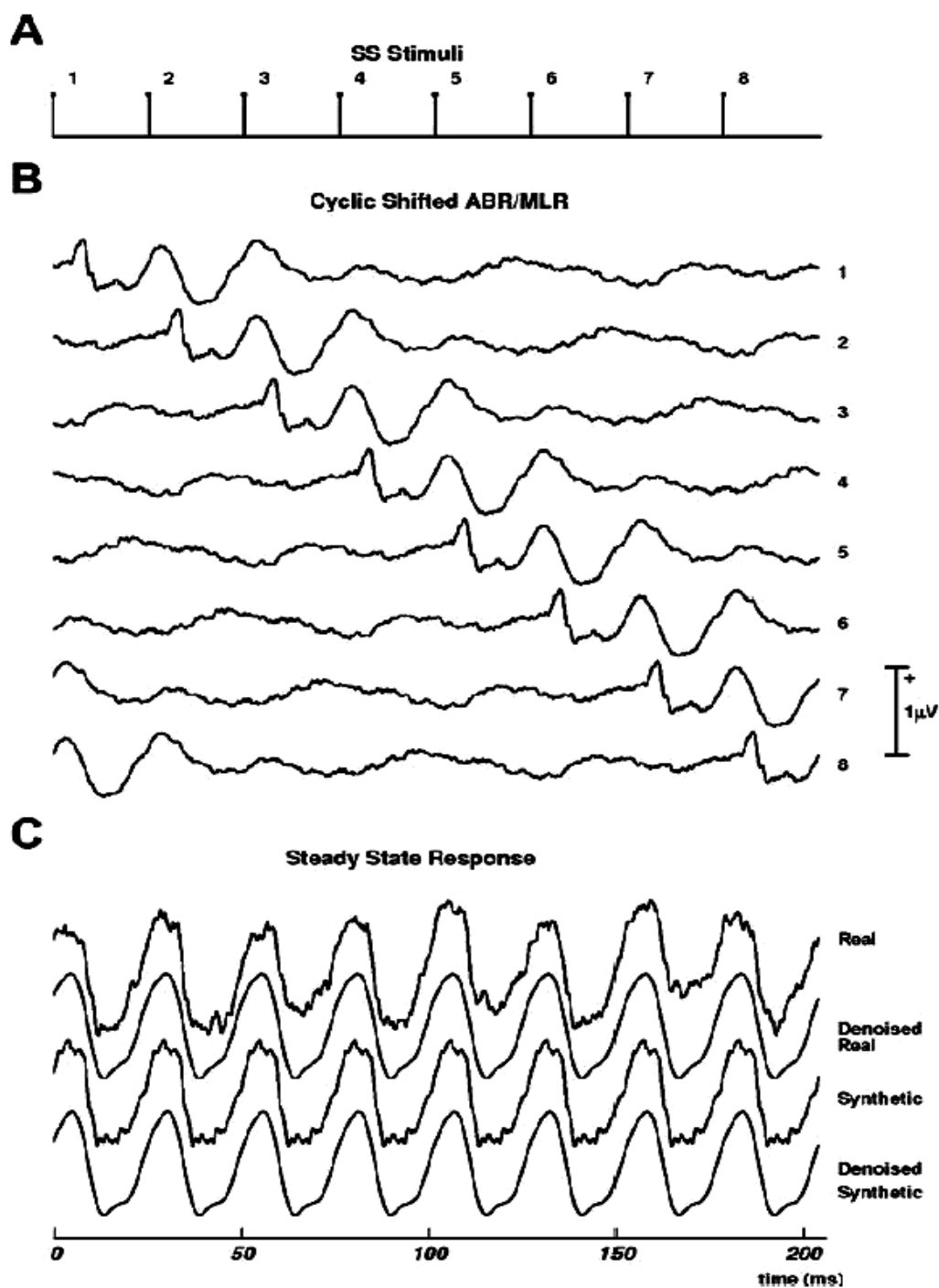
FIGURE 3.5 "Time domain construction of the synthetic ASSR using the low- jitter 39.1 Hz response. (A) The 39.1 isochronic stimulus sequence with each click in the sweep labeled from 1 through 8. The following eight rows in (B) correspond to the cyclic time shifted low-jitter 39.1-Hz deconvolved responses. (C) The first two rows show the separately acquired ASSR (raw) and its spectral filtered version (denoised). The bottom two rows show the summated response (synthetic) obtained by adding all the eight shifted responses shown in (B) and its filtered version (denoised synthetic)". From (Bohórquez and Ozdamar, 2008).

CHAPTER 4: RESULTS

This chapter presents the results obtained based on the goals mentioned in Chapter 1 and by implementing the methods and material explained in Chapter 3. As it has been described, this study aims to investigate the effects of a 40 Hz stimulation rate of silent gaps embedded in white noise on ASSRs and gap transient early responses. The transient early responses were obtained by implementing the continuous loop averaging method (Ozdamar & Bohorquez, 2006). Transient responses were deconvolved from overlapped (convolved) responses to jittered stimuli sequences of 12, 9, and 6 and click. In a parallel effort, auditory steady state response (ASSRs) were recorded in responses to 12, 9, 6 and click isochronic stimuli. Finally, Gap and click responses to isochronic stimuli were simulated using synthesized deconvolved gap responses to jittered stimuli as done in Bohorquez and Ozdamar (2008) and compared to real isochronic gap responses.

4.1 Transient Early Responses to Gap in Noise

In this section, the deconvolved response of jittered 40 Hz Click stimuli is presented. In addition, deconvolved responses to 40 Hz jittered stimuli of the three gap durations (12, 9 and 6 ms) are presented. Amplitudes and latencies of MLRs are described in this section for all the different stimuli responses. all responses are recorded from six young adult subjects with ages range between 21 and 26, each subject has a subject number as shown in Table 3.1. Middle latency responses to 100-μs conventional click stimulus with jittered sequence

are illustrated in Figure 4.1. Responses shown in the figure are averaged responses of about 2048 sweeps, top to bottom traces are deconvolved responses recorded from S1 to S6 followed by grand population average of all six responses. All six responses from each subject showed a consistent peak V with latency of 7.6 ms as labeled in Figure 4.1. Middle latency responses are also labeled according to their negativity and positivity, N_a component shown with latency of 18 ms while P_a had 32 ms latency. Furthermore, N_b component showed latency of 48 ms while P_b showed a latency of 63 ms.

The next Figure 4.2 illustrates the deconvolved responses from each subject to 12 ms gap stimulus and the grand population average of all six responses. All subjects elicited repeatable and consistent responses to 12 ms gaps. The population average of six subjects to the 12 ms gap response consisted of two positive peaks (P_{g1}, P_{g2}) and three negative peaks (N_{g1}, N_{g2} and N_{g3}) before and after as shown in the figure. The two positive peaks had latencies of 20 and 43 ms, respectively. On the other hand, the three negative peaks had 13, 36 and 58 ms, respectively.

The responses to 9 ms gap stimuli are presented in Figure 4.3. The bottom trace of this figure show the population average of six subjects; the response is similar to 12 ms gap responses but it is slightly reduced. Moreover, the first positive peak P_{g1} had a latency of 17 ms while the second positive peak P_{g2} had a latency of 42 ms. The 6 ms gap responses are shown in Figure 4.4; unlike 12 and 9 ms gap responses, responses to 6 ms gap are much reduced. Additionally, some subjects showed absent or poor responses.

Averaged deconvolved responses to 12, 9 and 6 ms gaps are shown in Figure 4.5 coupled with schematic representations of each gap stimulus envelope. Gap stimulus envelope showed in the figure illustrates the gap onset with slope of 1 ms then period of silence followed by slope of 1 ms gap offset (see section 3.2 for details). Latency of the first positive peak P_{g1} of all three transient responses shown varies with respect to gap duration. As indicated by arrows in the figure, gap durations are 12, 9 and 6 ms; latencies of P_{g1} were about 8 ms later for all gaps stimuli. Additionally, P_{g1} is the most prominent peak to all gap stimuli (12, 9, and 6 ms) but its amplitude reduces when gap duration is reduced. The second positive peak P_{g2} exists only in the 12 and 9 ms gap responses and greatly diminished in the 6 ms gap response.
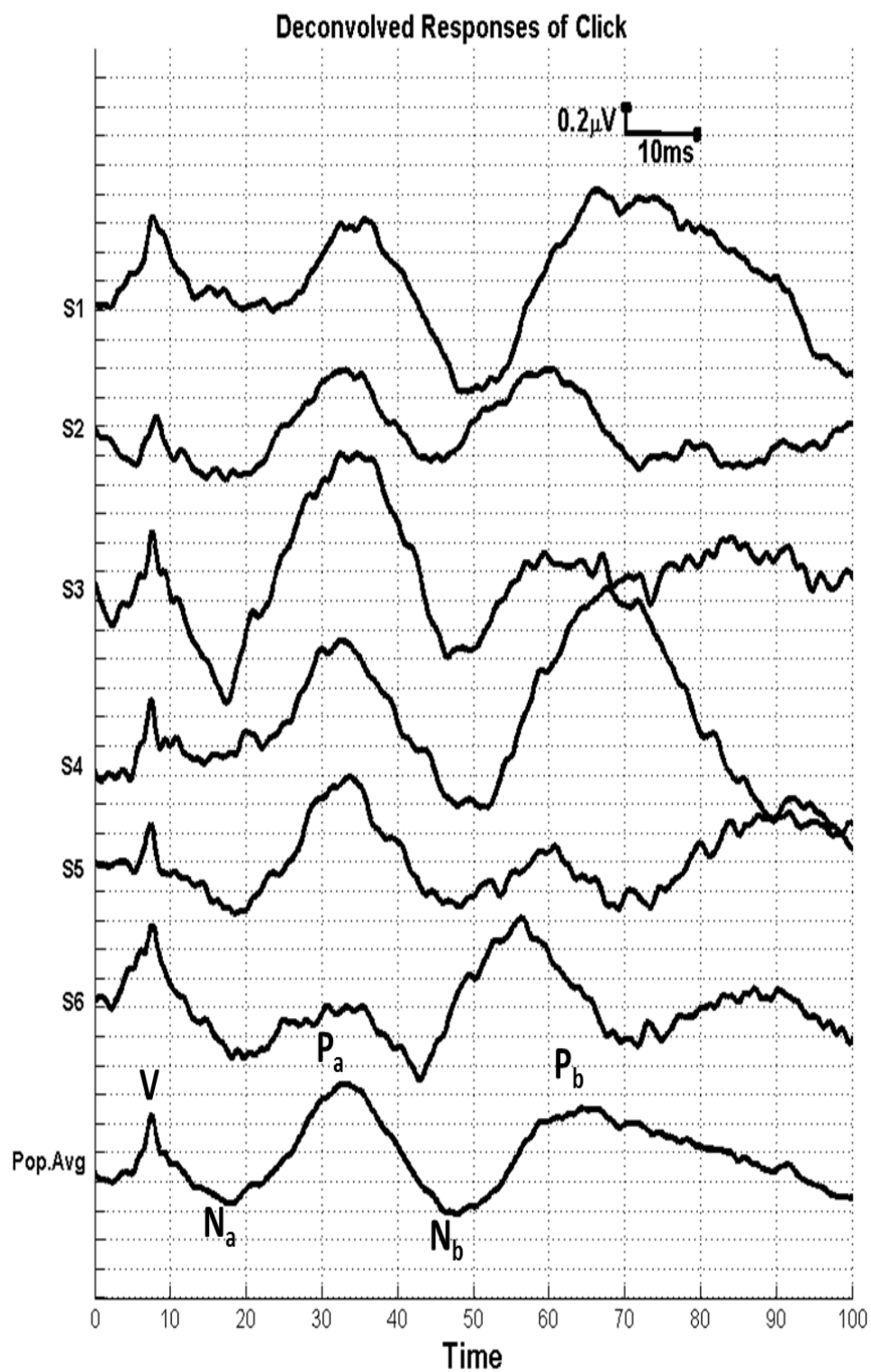
FIGURE 4.1 of deconvolved responses to jittered click stimulus. Individual subject responses are shown in addition to the population response.

Deconvolved Responses of 12ms Gaps

FIGURE 4.2 Deconvolved responses to 12 ms gap stimulus. Individual subject responses are shown in addition to the population average.

Deconvolved Responses of 9ms Gaps

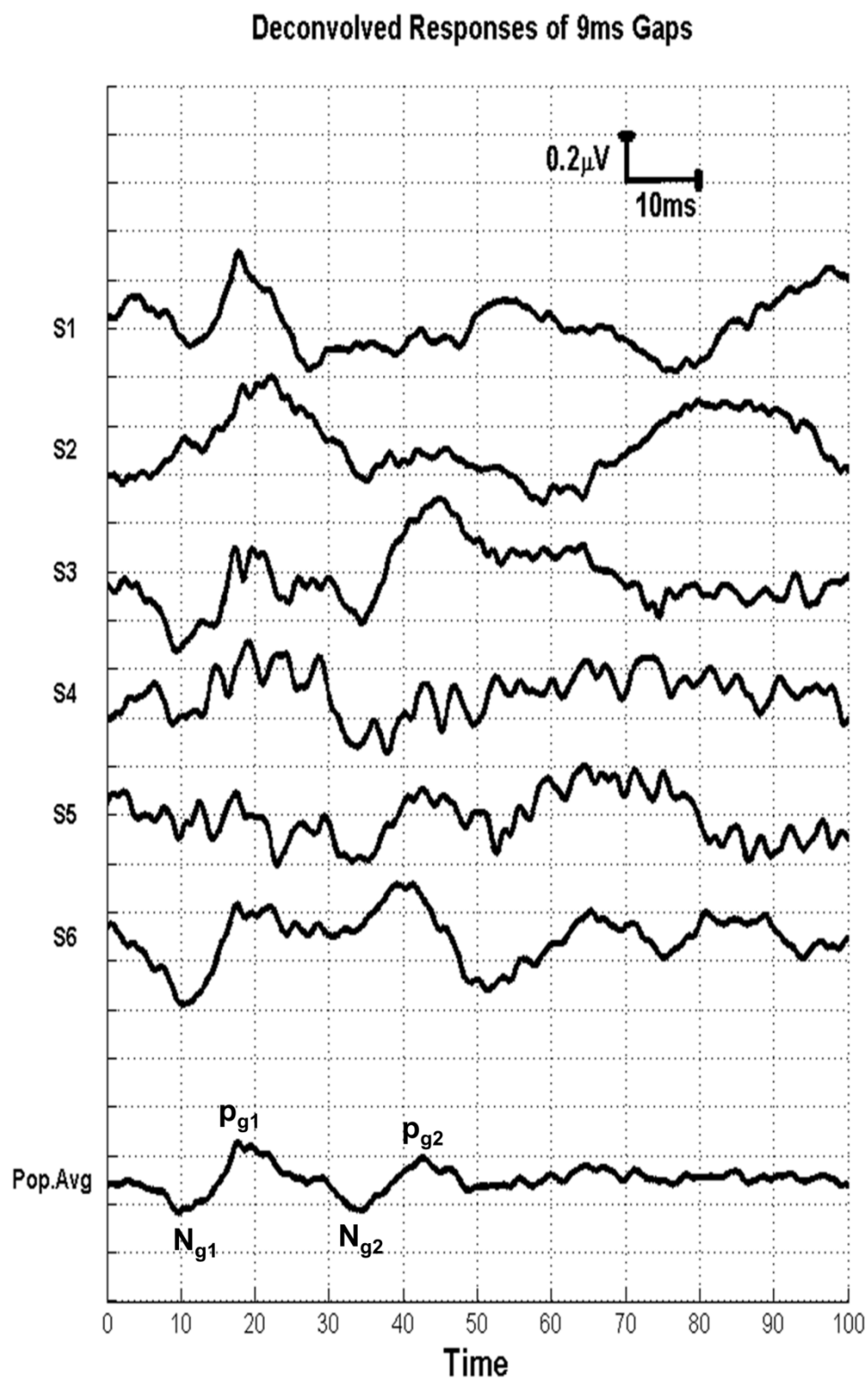FIGURE 4.3 Deconvolved responses to 9 ms gap stimulus. Individual subject responses are shown in addition to the population average.
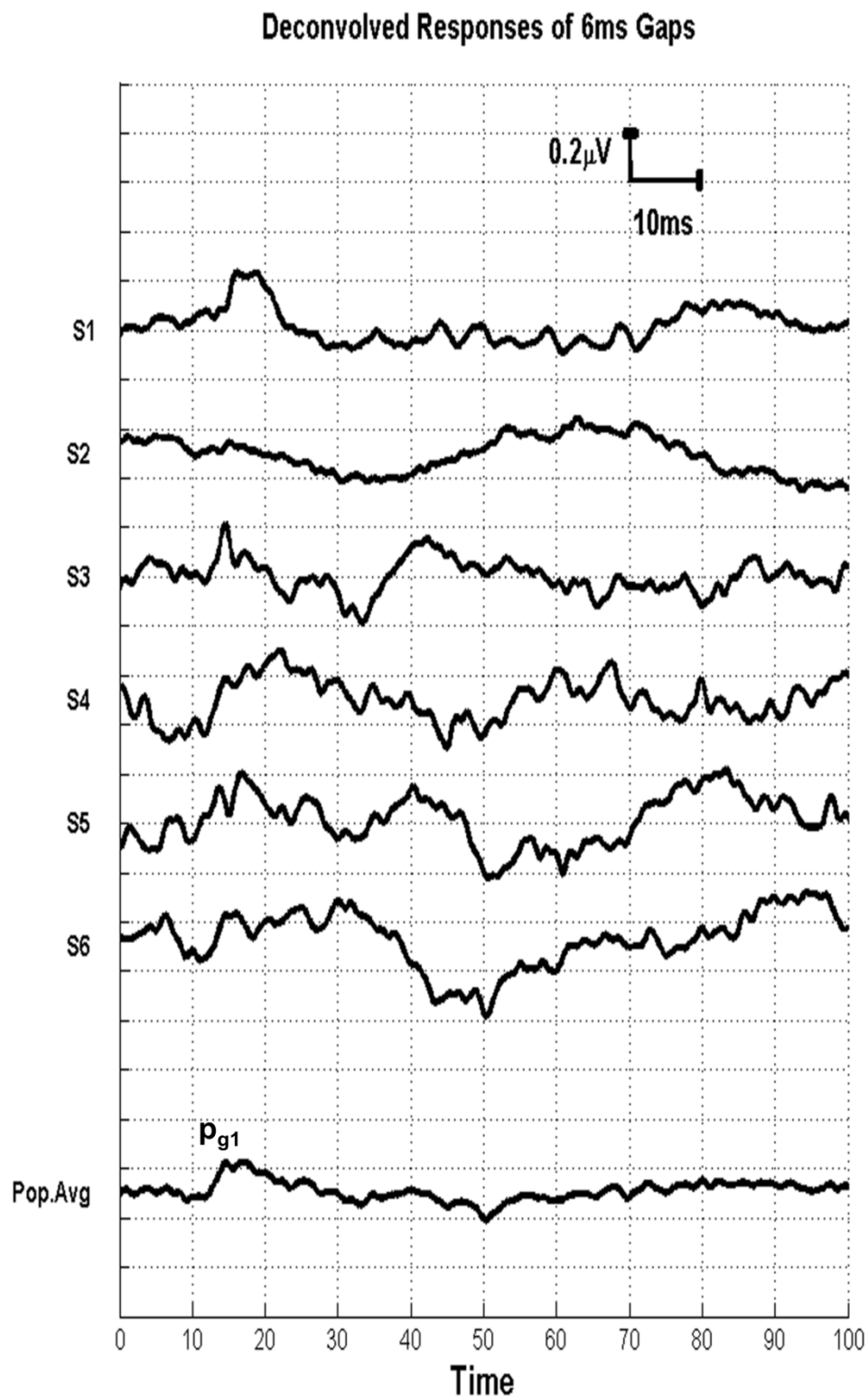
FIGURE 4.4 Deconvolved responses to 6 ms gap stimulus. Individual subject responses are shown in addition to the population average
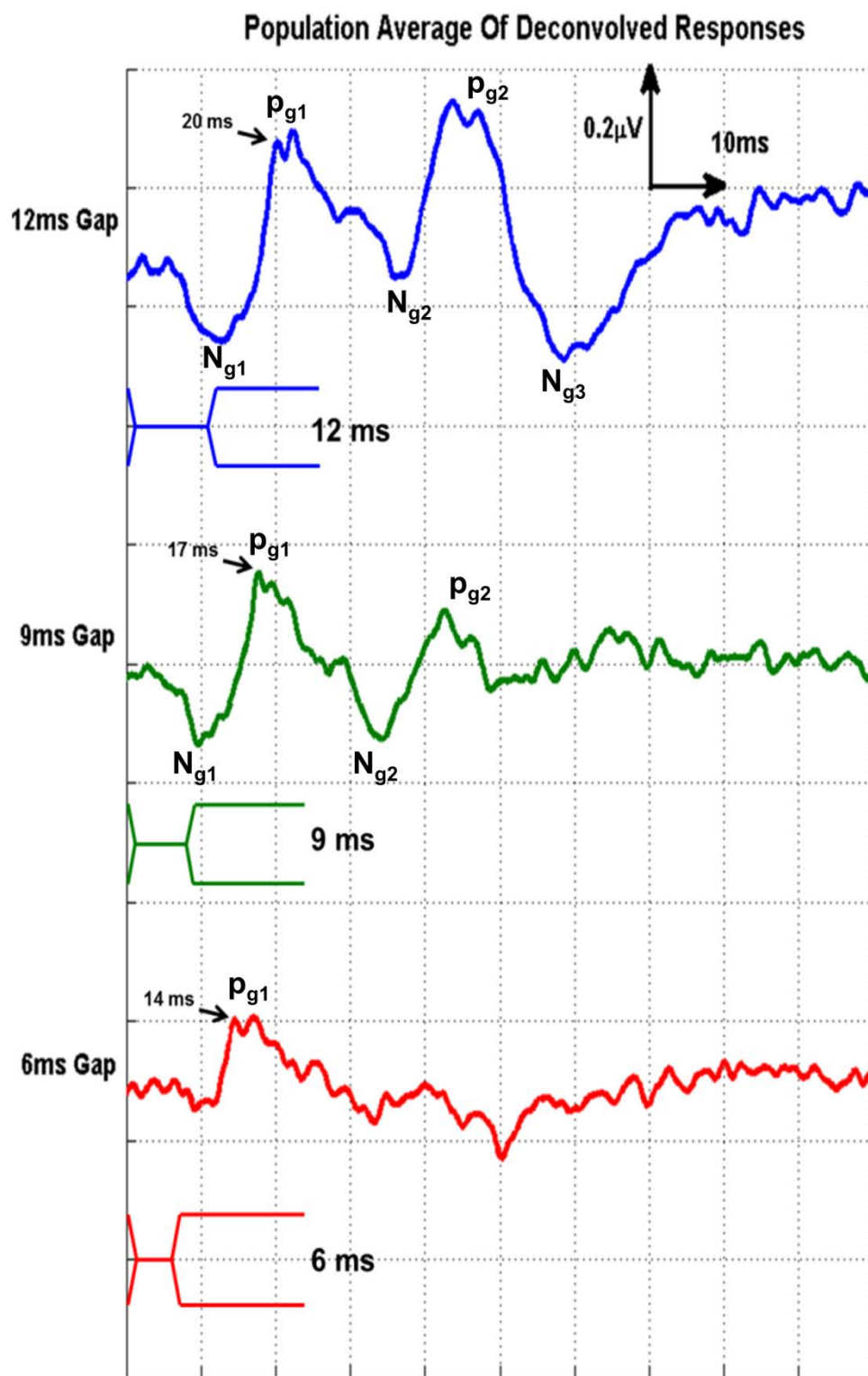
FIGURE 4.5 Averaged deconvolved responses of 12, 9 and 6 ms gap stimuli with the gap stimulus shown below.

4.2 Gap Auditory Steady State Responses:

Auditory steady state responses to isochronic gap stimuli are shown in Figure 4.6, with the top trace illustrating ASSR's to click stimulus followed by the three gap stimuli (12, 9 and 6 ms). Isochronic stimuli are designed conventionally to elicit real ASSRs (for details see section 3.2). Magnitudes of click ASSRs are much larger than the gap ASSRs. Notably, longer gap durations have larger ASSR magnitudes.

Furthermore, Figure 4.7 gives phasor analysis of ASSRs by illustrating the phase and magnitude of click, 12, 9 and 6 ms gap responses. Additionally, Figure 4.8 shows a bar chart comparison of the peak-to-peak magnitudes between all different responses. Clicks had the largest magnitude of 1.38 µV, while 12, 9 and 6 ms gaps had magnitudes of 0.64, 0.42 and 0.22 µV, respectively. Real ASSRs magnitudes values obtained from each subject individually are shown in Table 4.1.

40 Hz ASSRs
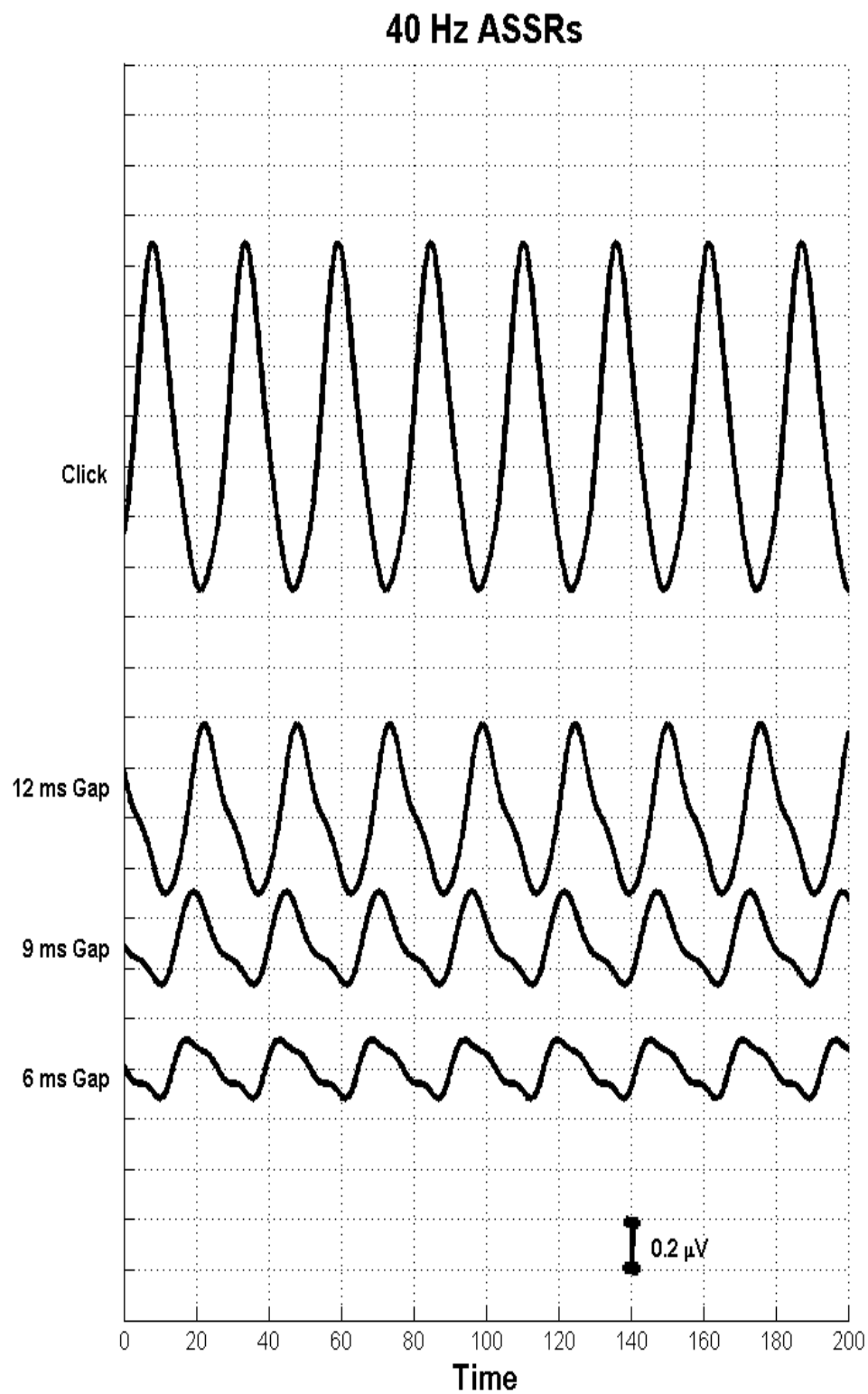
FIGURE 4.6 Filtered Steady State responses to click (top), 12 ms gap (second), 9 ms gap (third) and 6 ms gap (bottom).
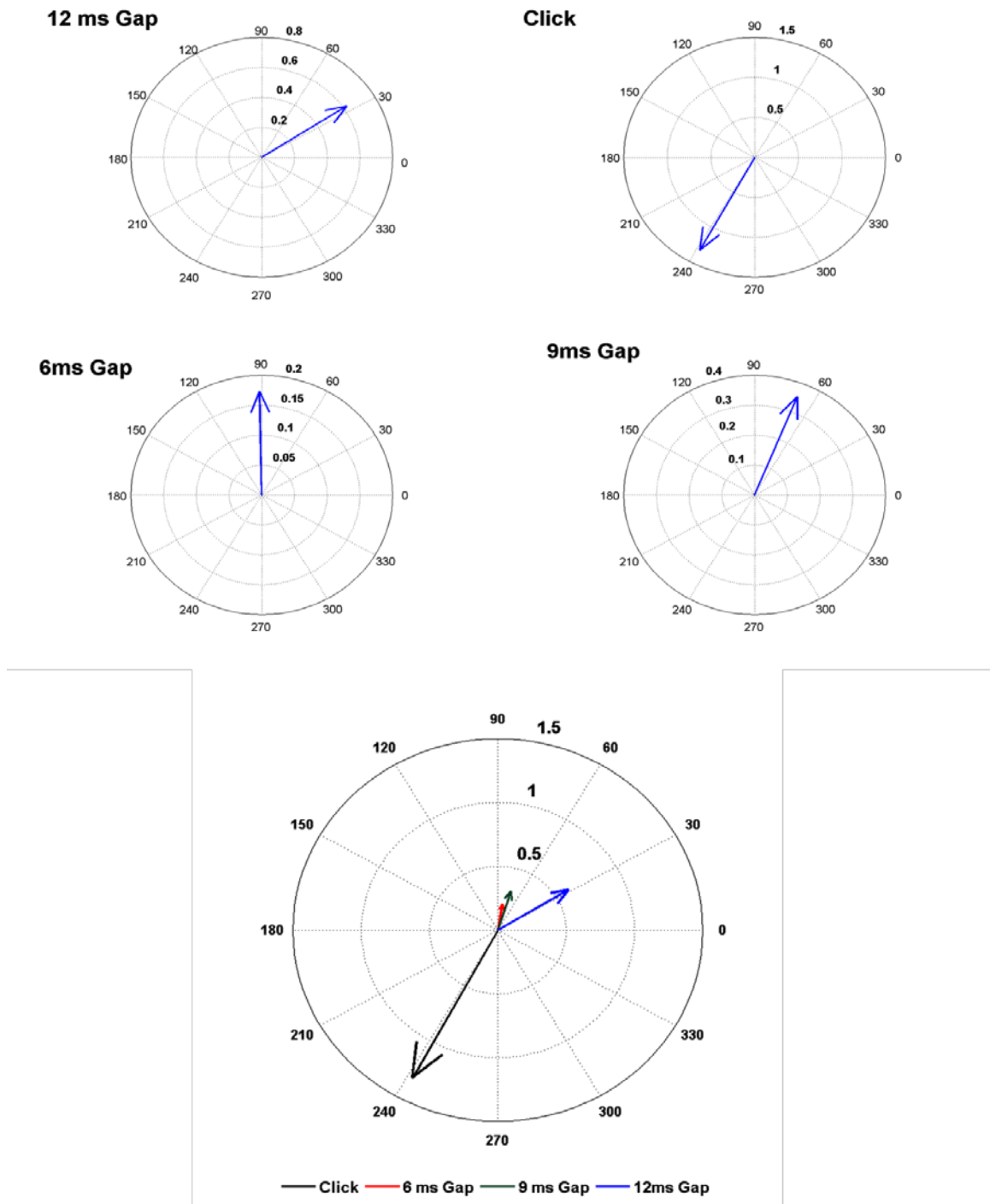
FIGURE 4.7 (Top plots) four Phasor plots of real ASSRs to click, 12, 9, and 6 ms gaps. (Bottom plot) phasors of all ASSRs (click, 12, 9 and 6 ms gaps).

FIGURE 4.8 Comparison between the magnitude of Click ASSRs and 12, 9 and 6 ms gap ASSRs. Columns indicate average peak-to-peak magnitudes with vertical bars showing standard deviation. Numerical values in columns indicate average magnitude response.
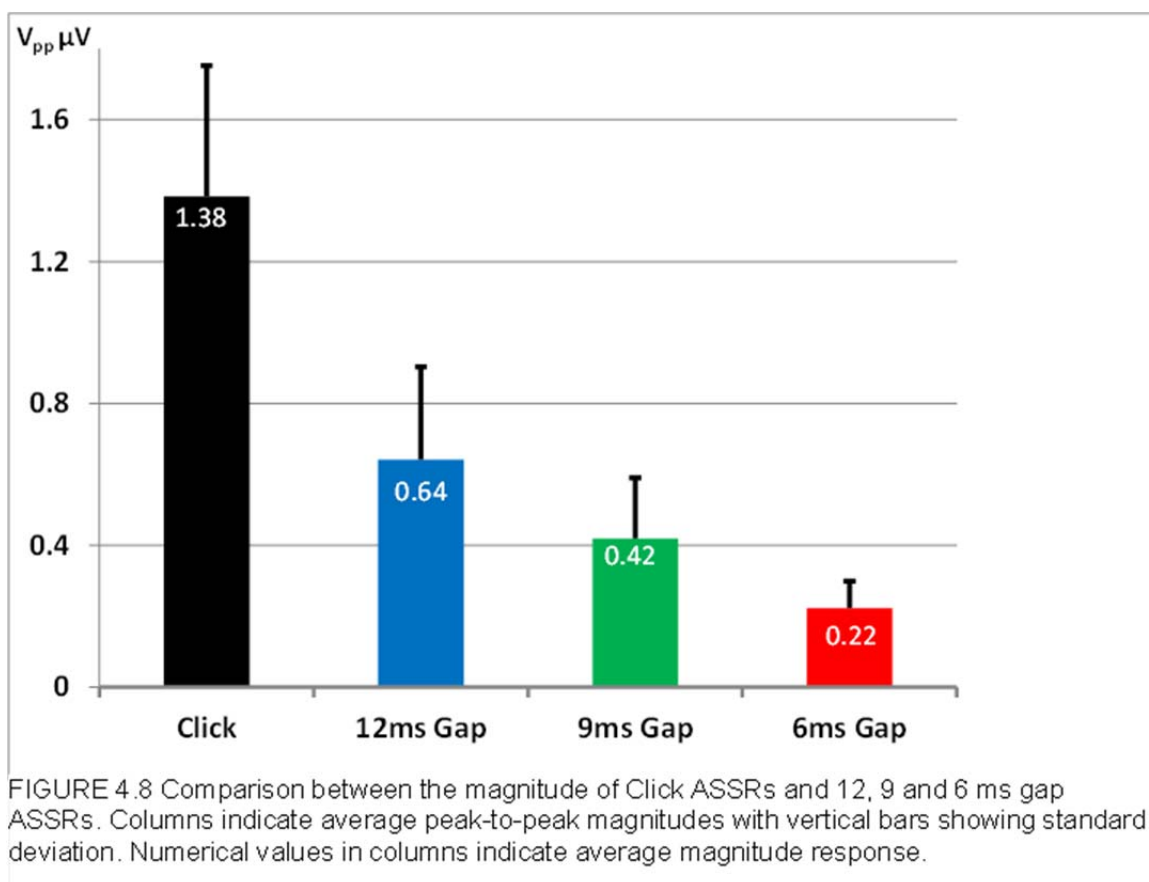
Table 4.1-Real ASSR magnitude values (µV) obtained from each subject as a response to Click, 12ms, 9ms and 6ms gaps (S: Subject, S.D: Standard Deviation)

Stimulus	S1	S2	S3	S4	S5	S6	MEAN	S.D
Click	1.31	1.06	2.01	0.98	1.45	1.50	1.38	0.36
12ms Gap	0.54	0.31	1.04	0.48	0.85	0.64	0.64	0.26
9ms Gap	0.32	0.21	0.64	0.31	0.60	0.44	0.42	0.17
6ms Gap	0.16	0.211	0.36	0.16	0.25	0.20	0.22	0.07

4.3 Synthetic Gap Steady State Responses:

Synthetic gap responses to isochronic stimuli were constructed using deconvolved gap responses to jittered stimuli as done in Bohorquez and Ozdamar (2008) and compared to real isochronic gap responses. The bar chart in Figure 4.9 illustrates the comparison between real and synthesized ASSRs to gap stimuli and click stimuli. Figure 4.10 shows the 40Hz phasor comparisons for 12ms and 9ms gap ASSRs. Predicted measurements of magnitudes and phases were very close to real ASSR measurements as shown in Figure 4.9 and Figure 4.10. Synthetic ASSR magnitudes for individual subjects and population average and standard deviation are listed in Table. 4.2.
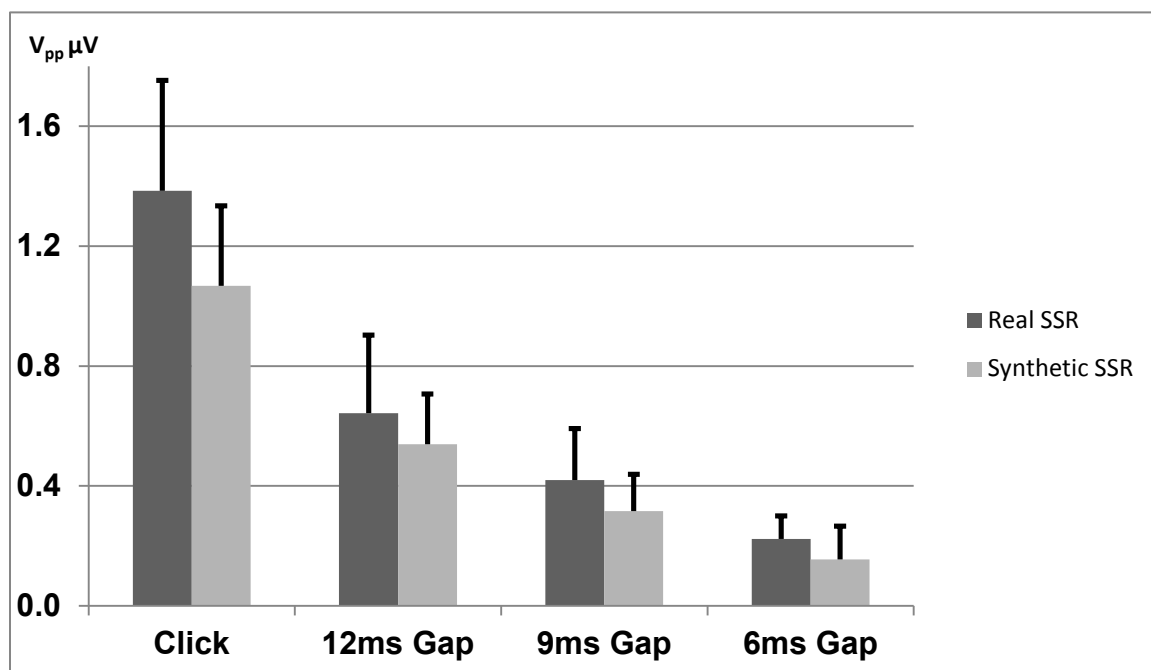
FIGURE 4.9 Comparison between the magnitude of real and synthetic Click, 12, 9 and 6 ms gap ASSRs
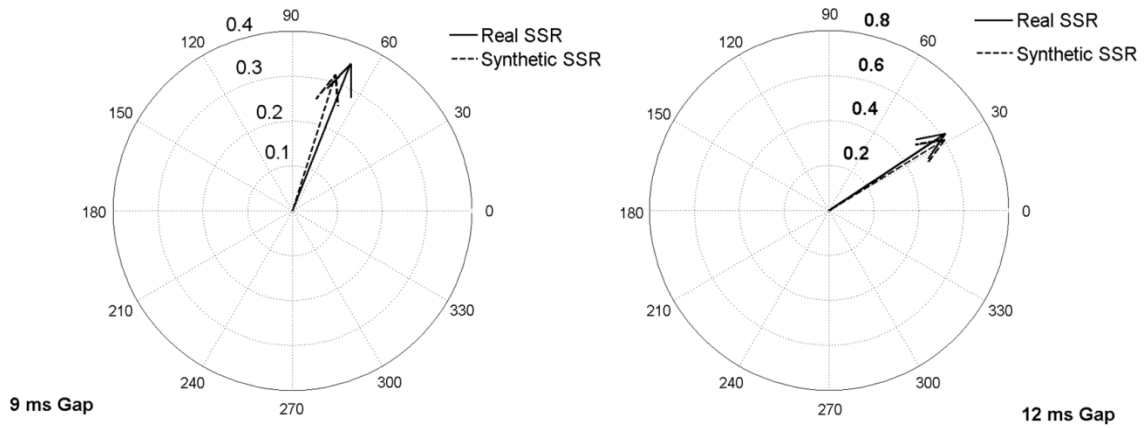
FIGURE 4.10 12ms gap phase and magnitude plot of both real and synthetic ASSRs (Right). 9ms gap phase and magnitude plot of both real and synthetic ASSRs (Left).

Table 4.2 Synthetic ASSR magnitude values (µV) obtained from each subjects

Stimulus	S1	S2	S3	S4	S5	S6	MEAN	S.D
Click	1.06	0.99	1.58	0.81	1.00	0.94	1.06	0.27
12ms Gap	0.52	0.30	0.81	0.47	0.59	0.51	0.54	0.17
9ms Gap	0.17	0.17	0.46	0.30	0.40	0.37	0.32	0.12
6ms Gap	0.09	0.04	0.32	0.06	0.24	0.15	0.15	0.11

CHAPTER 5: DISCUSSION & SUMMARY

In this study, early transient responses to varying duration gaps in noise at 40 Hz were investigated using the deconvolution method (Ozdamar and Bohorquez, 2006). In addition, 40 Hz auditory steady state responses were investigated as a response to isochronic gap stimuli. Finally, a simulation technique has been used to validate the deconvolved transient responses. The validation technique was based on constructing auditory steady state responses by using the cyclical time shifted transient waveform. The resultant ASSR was called the synthetic ASSR. By comparing the synthetic ASSRs to real ASSRs as a response to isochronic stimulation, the validity of the transient responses can be illustrated.

5.1 Early Transient Responses

Long latency responses to gaps in ongoing noise have been investigated in different studies (Palmer & Musiek, 2013; Harris et al., 2012; Pratt et al., 2005). Findings of Palmer & Musiek (2013) showed a relationship between N_1-P_2 component amplitudes and different gap durations in broadband noise. As the duration of gap decreased, the N_1-P_2 responses decreased. Moreover, they reported that the latencies of N_1-P_2 remained relatively stable with variable gap durations. In a different study conducted by Harris et al. (2012), similar findings were observed. Consistent N_1-P_2 -N_2 components were obtained in response to gaps as short as 6 ms. As reported in Harris et al. (2012), amplitudes of N_1-P_2 -N_2 components decreased by decreasing the gap duration. In Pratt et al. (2005),

similar conclusions were reported. N_1-P_2 components were obtained in responses to gaps of 5 ms or longer. Additionally, amplitudes of N_1-P_2 increased with elongation of gap durations.

Similarly, auditory brainstem responses have been investigated as a response to gaps in noise stimuli (Poth et al., 2005; Warner et al., 2001). The recorded amplitudes of peak V in the ABRs to gaps in noise stimuli reported by Poth et al. (2005) also correlated to gap duration. As a result of decreasing gap duration, amplitude of peak V decreased.

Earlier latency responses to short silent gaps in white noise were investigated in this study. In terms of amplitude, the effect of gap duration on early transient responses was relatively similar to the effect on long latency responses reported by previous studies. As shown in Figure 4.5, 12 ms gap stimuli showed larger responses compared to 9 ms and 6 ms gaps. 9 ms gap response showed similar wave shape but relatively smaller amplitudes. 6 ms gap responses were the smallest of all tested responses. In general, the first positive peak P_{g1} was the most prominent peak in all gap durations with very small amplitude in the 6 ms gap duration response. Transient responses to 9 ms gaps showed an absence of N_{g3} while responses to 6 ms gaps showed only the first positive peak P_{g1} with absence of all other peaks.

Moreover, as observed in Figure 4.5, deconvolved gap responses at 40 Hz consists of two major positive peaks (P_{g1},P_{g2}) about 25 ms apart. Small high frequency (400-800 Hz) waves are superimposed on these peaks. As shown on Figure 4.5 gap duration affects the latencies of these waves indicating that they

are possibly the ABRs generated by the onset of the noise bursts (gap offset).
The preceding negativity N_{g1} possibly corresponds to the off response of the
noise offset. The major positive/negative (N_{g1}- P_{g1}) peaks possibly correspond to
slow negativity of the ABR and the P_a and P_b peaks of the MLR. The earlier
appearance of these waves with shorter gap durations provides evidence to this
hypothesis.

It is important to notice that Pratt et al., (2005) have found that long
latency responses to gaps embedded in noise showed a bifid N_1 , potential to gap
onset N_1 including two negativities about 60 ms apart (N_{1a}, N_{1b}). In this study, the
first positive peak P_{g1} of the early transient responses also showed a bifid shape
with two peaks 2 ms apart. The bifid shape of P_{g1} was consistent in all grand
averaged responses (12, 9, and 6 ms) as shown in Figure 5.4.

Although gap responses showed no obvious relationship to conventional
ABR and MLR peaks, the results suggest that they are convolved responses
evoked by the onset and offset of the noise bursts separated by silent gaps. They
could be helpful in separating the effects of peripheral and central hearing in
relation to age differences in gap detection and temporal resolution of the
auditory system.

5.2 Gap Auditory Steady-State Responses

The second part of this study focused on auditory steady state responses
recorded in response to isochronic gap stimuli where ASSRs showed a
significant relationship to gap duration. As shown in Figure 4.6, magnitudes of
real ASSRs decreased when gap duration decreased. The isochronic 12 ms gap

duration showed the largest responses of the three gap durations recorded. Furthermore, the variation of magnitude and phase is clearly shown in Figure 4.7. The phases of each gap response are different, which may have occurred because of the change in gap duration. Further recordings of 15 and 18 ms gap stimuli are needed to confirm that ASSRs phase is changing with the same factor of changing gap duration.

Finally, synthetic steady state responses were constructed using transient deconvolved responses to click, 12 ms gap, 9 ms gap and 6 ms gap stimuli. Synthetic ASSR results are shown in Figures 4.9 and 4.10. The magnitudes of all synthesized ASSRs were very close to the magnitude values of real ASSRs. Moreover, as shown in magnitude and phase plots in Figure 4.10, phases of the synthetic ASSRs were closely similar to real ASSR phases. Consequently, measures of all predicted ASSRs were very closely similar to the real ASSRs recorded to isochronic stimuli. Such a degree of similarity between synthetic ASSRs and real ASSRs validates the use of the Continuous Loop Averaging Deconvolution method to extract gap-induced transient responses from overlapped responses resulting from high rate stimulation (40 Hz).

5.3 Summary and Future Directions

This study was conducted to explore the effect of 40 Hz gap stimuli embedded in white noise on auditory steady state responses and early transient responses. The gap durations investigated in this study were 12, 9 and 6 ms. In order to obtain transient responses from overlapped responses due to high rate auditory stimulation, the Continues Loop Averaging Deconvolution method was

implemented. To meet the deconvolution method conditions, stimuli were specially designed using low-jitter sequence (near isochronic). Moreover, isochronic gap stimuli were designed to evoke real auditory steady state responses. Finally, the validity of the deconvolved responses was shown by the close similarity of the synthesized auditory steady state responses to the real auditory steady state responses.

The findings of this study show that middle latency responses change when gap duration changes. The amplitudes and latencies of middle latency responses were affected by gap duration. Equally important, the auditory steady state responses were also affected by gap duration. Changes in magnitude and phase of auditory steady state responses to each gap stimuli were shown to result from different gap durations. Investigations and further work should be done to reach sufficient knowledge about the effect of short silent gaps in noise on middle latency responses and auditory steady state responses. One of the steps that we think should be taken towards this end would be to increase the gap duration range to include 3 ms gaps as well as 15 and 18 ms gaps.

Additionally, it will be beneficial to investigate temporal resolution by studying the behavioral gap detection thresholds side by side to the electrophysiological gap thresholds. Moreover, it will be advantageous to record long latency responses to the same gap stimulus design; by doing that we will be able to compare the effects of high rate stimuli to previously investigated low rate gap stimuli. Finally, subjects of this study were young adults, therefore we

recommend the inclusion of older adults in further studies to examine age-related

differences in auditory evoked potentials.

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