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AN OBJECTIVE MEASURE OF TEMPORAL RESOLUTION IN NORMAL SUBJECTS USING FREQUENCY MODULATED SIGNALS

Dissertation

Presented in Partial fulfillment of the Requirements for the Degree Doctor of Philosophy in the Graduate School of The Ohio State University

By

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1999

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ABSTRACT

The present investigation was conducted to determine whether an exogenous event-related potential called the mismatch negativity (MMN) would change systematically in response to frequency-modulated signals with varying temporal properties. Both N1 and P2 waveforms were recorded to 50 ms frequency modulated signals from normal hearing subjects without a history of neurological disease. The standard (frequent) stimuli for this investigation were continuous sweep tones with center frequencies of 1000, 2000, and 4000 Hz. The deviant (infrequent) stimuli were signals that traversed the frequency range in two, four, six, or eight discrete steps. To resolve the MMN, the averaged frequent response was subtracted from the infrequent. All conditions were recorded twice to ensure repeatability. Results suggest that in the three subjects: 1) mean MMN peak-to-peak amplitude decreased with decreases in step duration and was the best indicator of psychophysical performance for the two magnitude measures, 2) mean area decreased with a decreases in step duration, 3) Latency measure one demonstrated a slight trend to increase as step duration decreased, and 4) Latency measure two demonstrated a significant increase in latency as step duration decreased. Additionally, it was the best indicator of psychophysical performance for the two latency measures as well as all for all four measures.
To my parents, Daryl and Laurie, and my sisters, Shannon and Amy
ACKNOWLEDGMENTS

First, I would like to express sincere appreciation to my adviser Dr. Lawrence Feth. The assistance, guidance, and support throughout this project and the doctoral program were invaluable.

My thanks also go to Dr. Pamela Mishler for her insight, patience, personal warmth and help in securing funding for the study.

I would also like to thank Dr. Gary Jacobson for his careful readings and contributions in shaping and nurturing this project.

I would especially like to thank my mother; my two sisters, Shannon and Amy; and my lovely and talented girlfriend Heather. Finally, thanks to the Veterans Affairs Medical Center and National Institute of Health for the award of the pre-doctoral fellowships.
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PUBLICATIONS:


**BOOK CHAPTER**


**PUBLISHED ABSTRACTS**


FIELDS OF STUDY

Major Field: Speech and Hearing Science
Other Studies: Electrophysiology
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Audiologists routinely utilize auditory evoked potentials (AEPs) as an objective test of hearing. Objective audiometry is useful when patients are unable or unwilling to participate in typical behavioral testing paradigms. Examples include individuals that are mentally retarded, those who are severely physically handicapped and those with neurological diseases (e.g. aphasia and dysphasia).

Several different AEPs can be recorded in response to stimuli. The fundamental application of evoked potential audiometry is to obtain hearing thresholds without requiring a response from the subject. This is accomplished by presenting stimuli that decrease in the parameter being examined until the evoked response can no longer be identified. Often the audiologist obtains information that augments responses obtained with the pure tone tests by using an objective electrophysiological threshold measure. While pure tone information is certainly important, of equal importance is how well the patient processes complex auditory information (e.g. speech) at levels above “absolute” threshold. The development of an accurate objective test for quantifying impaired auditory processing that also enables the audiologist to measure the effectiveness of the remediation is greatly needed. For example, once an infant has been identified with a
hearing loss, the audiologist may suggest that the infant be fit with some type of amplification. If the child is young, it difficult to monitor how successful a chosen treatment is. The audiologist needs information concerning the infant’s ability to discriminate simple and complex sounds as well as the child’s capacity to learn to identify new sound patterns. Speech understanding requires the discrimination of different auditory parameters (e.g. temporal and spectral cues). The term discrimination refers to the process of comparing one stimulus to another and making a decision. The process of discrimination requires two mechanisms. The first is some type of comparator and the second uses working memory (Picton, 1995). In order to objectively derive auditory information the test must assess the patient's discrimination ability.

Since the pioneering work of Butler (1968), AEPs have been used to assess auditory discrimination. A negative going wave at 100ms following the onset of a train of repetitive stimuli, can be recorded from the scalp. This is referred to as the N1 potential. If a physically different stimulus is placed inside the repetitive stimulus sequence, a small negative deflection generated by the deviant is superimposed on the waveform in the latency range of a positive going wave known as P2. This additional negativity starting at 100ms and ending at approximately 250ms is isolated by subtracting the waveform obtained from the standard stimuli from that obtained for the train containing the deviant. This response is known both as N2a or the “mismatch negativity” (MMN). The MMN is thought to reflect the brain’s automatic process of encoding stimulus change. This response was originally described by Nätänen, Gaillard, and Mantysalo (1978). They have described some predictable characteristics of the MMN response. When the
difference between the frequent and infrequent stimulus is large, the MMN grows in amplitude and adds to N1. The MMN also occurs earlier in time. However, if the stimulus deviance is small the MMN occurs later and the MMN has no influence on N1. Sams, Paavilainen, Alho, and Nätäären (1985) demonstrated that the MMN could be recorded when the deviant stimuli were just discriminable from the standard stimuli but not when the difference was undetectable. These findings suggest that the MMN may be used as an objective neurophysiological test of auditory discrimination thereby giving the investigator some insight into the speech capabilities of a patient unable to participate in conventional audiometry tasks (e.g., dysphasia, Kraus and McGee, 1994; Korpilahti and Lang, 1994).

Speech information is conveyed by acoustic waveforms that change in frequency and intensity over time. When the speech mechanism produces a sound, alterations in the vocal tract result in changes in its resonant properties. These resonances in sound transmitted through the vocal tract are known as formants. Formant transitions are changes in the resonant properties created when moving from a consonant to a vowel or vice versa.

Previous work has demonstrated that the second formant transitions contain important information about the place of production for consonants (Delattre, 1958; Liberman, 1957; Liberman, Delattre, Copper, and Gerstman, 1954). Liberman, Cooper, and Shankweiler (1967) proposed that it is the second-formant transitions that are fundamental in listeners’ correctly perceiving and identifying consonants. Formant transitions also contain information pertaining to the slope and direction of frequency transitions. In order for listeners’ to correctly process speech, they must be able to detect
and identify short duration frequency transitions. The ability of the auditory system to process and discriminate these rapid changes in the acoustic signal over time is known as temporal resolution. In order for auditory information to convey meaning, it is crucial that the temporal structure of the signal be accurately represented when it reaches the listeners' auditory cortex. This requires that the temporal pattern of the signal arriving at the ear be relayed through the peripheral and central auditory nervous system (CANS) with as little change as possible.

Damage to the either peripheral or central structures may result in an inability to accurately encode the acoustic event. The failure of the auditory system to identify and maintain these discrete temporal changes in the acoustic stimulus may result in a misrepresentation of the original stimulus at the cortex where the event is ultimately perceived. This misrepresentation would manifest itself clinically as an inability to understand speech.

The purpose of this study is to investigate the use of the MMN as an objective neurophysiological measure of temporal resolution. Using an experimental paradigm developed by Feth, Neil, and Krishnamurthy (1989), the study will employ two discrimination tasks. The first was a psychophysical discrimination task in which subjects are asked to distinguish between two sinusoidal signals. One signal, the glide, makes a transition from a lower frequency to a higher frequency over a smooth linear path. The other signal is called a step signal. It begins and ends at the same frequencies as the glide, but does so in a series of discrete steps. That is, signal frequency remains at one value for a brief time before jumping to the next value. Figure 1 illustrates the linear glide and
Figure 2 shows an 8-step glide. The second discrimination task was an electrophysiological one. One response will be generated by the frequent stimulus, the linear glide. The second response was generated by the infrequent stimulus, a step signal. The two traces were collected and subtracted in order to derive the MMN.

Feth et al. (1989), Bicknell (1998) and Madden (1992) demonstrated that subjects with normal hearing thresholds are able to discriminate the step from the linear glide when the number of steps is small and the step duration is large. As the number of steps increases and step duration becomes smaller, performance will reach chance. It is assumed that when the subjects are unable to temporally resolve the differences between the linear glide and the step glide they have reached their temporal resolution threshold. Threshold is defined as the half way point between perfect performance (100%) and chance (50%).

The current study is designed to adapt the Feth et al. (1989) procedure in an electrophysiological paradigm that will generate an MMN and derive an objective temporal resolution threshold. The study is focused on two questions. The first is will the amplitude of the MMN decrease with decreasing step size? Second, will latency become longer with decreasing step duration? If the MMN performs as expected it may be useful in assessing temporal resolution in the difficult-to-test populations discussed above.
Figure 1: Representation of a linear glide with a center frequency of 1 kHz
Figure 2: Representation of a stepped glide with a center frequency of 1 kHz
A measure of hearing acuity is the temporal resolution of acoustic signals that change rapidly with time. Earlier studies have used the discrimination of amplitude and frequency-modulated signals as a psychophysical measure of temporal acuity. These studies will be discussed in the literature review. Clinically, temporal resolution could also be used to determine the status of the auditory system. A more rapid and efficient method of measuring temporal resolution, as opposed to psychophysical testing may be the use of evoked-potentials. The relevance of evoked-potentials to measure temporal acuity will be discussed in terms of their generator sites and stimulating paradigms. In addition, studies concerning the mismatch negativity's sensitivity to temporal changes is reviewed. Finally, literature concerning the mismatch negativity and its correspondence with behavioral discrimination is discussed.

2.1 Studies Examining Temporal Resolution using Amplitude Modulated Signals

Temporal resolution is the ability of the auditory system to process rapid changes in an acoustic signal over time. If the auditory system responds slowly or inaccurately, then the acoustic stimulus will be incorrectly coded resulting in an inability to accurately perceive the target sound. The temporal resolution of the human auditory system has been thoroughly investigated by psychoacousticians for approximately the last 20 years.
Several research paradigms have been employed to determine the threshold of auditory temporal resolution. The majority of studies examining temporal acuity utilize amplitude-modulated signals (e.g. gap-detection, temporal masking and temporal modulation transfer functions). These studies all have an underlying theme that it is the continuance of an auditory sensation, either from peripheral or central structures, which limit temporal resolution.

2.1.1 Forward Masking

Forward Masking is described by investigators as a change in a subject’s absolute threshold for detecting a probe stimulus due to the introduction of a prior masking stimulus (Nelson and Freyman, 1987; Jesteadt, Bacon, and Lehman, 1982; Fitzgibbons, 1979). Fitzgibbons (1979) describes two components to the psychophysical functions generated by forward masking studies. During the first component, the subject demonstrates little or no change in threshold for the probe stimulus for the initial 2.5 msec following presentation of the probe stimulus. The stability of the subject’s threshold during this time period suggests the masking stimulus have a constant effect on threshold. This span of time can be used as a measure of temporal acuity. A second component begins at the end of the first (2.5 msec) and subjects’ demonstrate a linear decrease in threshold up to unmasked levels at 150 to 200 msec at which point they plateau. In forward masking paradigms temporal resolution is typically presented as the time constant of the masking function.
2.1.2 Gap Detection

Gap-detection is another popular way to measure temporal resolution and the effect of both intensity (Florentine and Buus, 1984; Penner, 1977; Buus Florentine, 1985; Plomp, 1964) and frequency (Fitzgibbons, 1983; Shailer and Moore, 1983; Duifuis, 1973) on the detection of gaps has been investigated. Gap detection is technically a modification of the forward masking paradigm. This paradigm identifies the location of a single point on the forward masking function. This point occurs at the end of the initial plateau period discussed in the preceding section. Researchers believe that this is where the residual sensation level of the first signal decreases to a level at which it is just discriminable in intensity or frequency from a similar second signal. The duration of this gap is thought to represent the subject's temporal resolution threshold.

2.1.3 Temporal Modulation Transfer Functions

Another measure of temporal resolution is the temporal modulation transfer functions (TMTF) (Viemeister, 1973; Moore, 1988; Scott, 1986). This paradigm assesses the auditory systems' capacity to detect amplitude modulation at different modulation rates (Viemeister, 1979). As modulation rate increases, the modulation is less detectable. Depth of modulation as a function of modulation rate forms the transfer functions that can then be analyzed to determine the temporal resolution threshold.

Temporal resolution results using amplitude-modulated signals regardless of the paradigm used produce similar results. The temporal resolution thresholds for forward masking studies suggest that subjects are incapable of temporally resolving the probe stimulus anytime before the 2.5 msec window ends. Gap detection studies suggest that 2
to 3 msec is possible while TMTF studies suggest that temporal resolution thresholds can be anywhere from 2 to 8 msec depending on the experimental conditions. However, the above studies all describe temporal resolution using amplitude-modulated signals. Relatively few studies examine temporal acuity with FM signals even though frequency modulation occurs in nearly all sounds produced naturally.

2.2 Static versus Dynamic Stimuli

The preponderance of acoustic information found in a listener's environment is dynamic in nature. That is, stimuli exhibit a certain degree of change (i.e. in frequency and intensity) over a given time period. This concept presents problems inherent to those researchers who wish to make assumptions about speech processes using data derived from investigations utilizing static stimuli such as pure tones and clicks. Therefore, in order to understand the processes underlying speech perception, studies must incorporate stimuli whose physical characteristics closely approximate those of speech. Some of the dynamic acoustic cues, which are required for accurate perception of speech, are frequency and amplitude modulations.

When the vocal mechanism produces a speech sound, resonances known as formants are created during the transmission of the acoustic signal. The degree and locations of the constrictions in the vocal tract and the length of the pharyngeal-oral tract influence these resonances. These formants which make up speech sounds are numbered according to their frequency. The first formant or F1 is the lowest frequency while the second formant (F2) is higher in frequency and the third formant is higher yet. These
formants or frequency transitions connect the speech sounds when moving from a
c consonant to a vowel or vice versa.

There has been a recent trend for investigators to probe speech perception
processes of infants, children and adults using natural speech or synthesized speech
materials. An alternative to a speech stimulus which may provide the researcher with a
means to investigate the temporal resolving properties of the auditory system is the use of
a simple auditory stimulus (e.g. a pure tone) that changes some characteristic (e.g.
frequency) over time as does speech. This study is devoted to developing an
electrophysiological measure to evaluate a subject’s ability to process rapid frequency
transitions. Ideally, the stimuli of choice would be true recorded speech formants.
However, speech stimuli are extremely complex and contain many interactions making it
difficult for the researcher to say with any certainty exactly which parameter accounted
for the electrophysiological response. For example, the multiple interactions between
amplitude and frequency may actually cancel each other out or sum together making it
difficult for the investigator to say which accounted for what part of the response. One
possible solution to this problem inherent in frequency-modulated (FM) speech signals is
to start with the simplest forms of FM signals which are tone glides. One parameter may
be altered (e.g. rate of transition or duration) allowing the investigator to say with a great
dergree of confidence that any changes observed in the recorded potential is due to that
controlled alteration. The following studies have examined the capabilities of subjects’
to detect and discriminate differences in gliding signals.
2.3 Psychophysical Studies of Discrimination of Frequency Transitions

Pollack (1968) investigated subjects' ability to discriminate the direction of frequency change for tone-glides. Starting frequencies of the signals ranged from 125 Hz to 1 kHz with durations of .5, 1, 2, and 4 seconds. The subject's task was to determine the direction of the transition in a one interval task. The starting frequency of the glides was randomized so that responses would be based on the direction of the frequency transition, not on the difference in frequency at the end of the signals. Pollack's results demonstrated that subjects were able to discriminate the direction of the frequency transition. Additionally, he reported that there was an increase in the threshold of frequency change for two of the subjects when a random starting frequency was applied.

Collins and Cullen (1978) examined subjects' ability to detect frequency transitions using tone glides. The investigators stated that they considered as similar to the formant transitions of isolated stop consonants. F1 formants were represented using tone glides in the frequency region of 200-700 Hz and 1200-1700 Hz for F2 formants. Subjects detection thresholds were measured in three different conditions: 1) rising glides, 2) falling glides, and 3) steady-state tones. Two primary findings were reported. First, detection thresholds for falling glides were higher than those for rising glides when signals of short durations were used. Second, detection thresholds for falling and rising glides were higher compared to the steady-state tone condition.

Nabelek (1978) investigated masked thresholds for steady-state tones and rising and falling glides. The method of adjustment was used to determine thresholds in nine normal hearing listeners. Stimuli consisted of gliding tones presented monaurally in three overlapping frequency regions. The frequency regions consisted of 250 to 1000 Hz,
250 to 2000 Hz, and 825 to 3300 Hz. Duration of the signals varied between .5 msec and 5 seconds. The glides' frequency was linear in every case. The masker stimulus was a wideband noise presented monaurally at a level of 70 dB SPL. The author reported that discrimination thresholds for falling glides were higher than thresholds of both rising glides and steady-state tones. This finding of directionality is in line with findings presented by Collins and Cullen (1978). Nabelek observed that differences in threshold might be the result of a different time course of neural decay.

Dooley and Moore (1988) investigated the detection thresholds of linear-frequency glides as a function of frequency and duration. An adaptive 2AFC procedure was used that estimates the 70.7% correct point on the psychometric function. The experiment had four conditions: 1) two steady tones, 2) one steady tone and one up-glide, 3) one steady tone and one down-glide, and 4) one up-glide and one down glide. For listeners with normal hearing, frequency glide detection thresholds as a function of center frequency were obtained. The task for the subject was to indicate which of the two successive tones in a trial was higher in frequency. Signals had center frequencies of 500, 1000, 2000, 4000, and 8000 Hz with durations of .5 seconds. Results showed that discrimination performance was better for pulsed tones than for rising and falling glides at all frequencies. Additionally, discrimination thresholds for rising glides were higher than for falling glides which is in contrast to the findings of Collins and Cullen (1978) and Nabelek (1978). However, the difference was very small at frequencies of 4000 and 8000 Hz. The authors also examined frequency-glide thresholds as a function of duration. Stimuli consisted of 2000-Hz gliding signals shaped with rise/fall times of 50, 100, 250, 500, and 750 ms. The task of the subject was to indicate which stimulus was gliding.
Results showed that discrimination performance for frequency decreased monotonically for pulsed tones with increasing duration. Glide thresholds only decreased as duration increased from 50-100 ms.

Elliot, Hammer, Scholl, Carrell, and Wasowicz (1989) investigated the ability of a subject to discriminate synthesized frequency transitions that mimicked rising and falling single-formants. The subjects were to discriminate between two frequency transitions having different onset frequencies but similar offset frequencies. Onset frequencies of rising transitions moved from 942 to 1146 Hz in 17-Hz increments. The falling frequency transitions contained onset frequencies that ranged from 1772 to 1340 Hz in 36-Hz increments. Both rising and falling frequency transitions ended at a frequency of 1240 Hz. Three different stimulus durations (36, 60, and 120 msec) were used in two conditions. One condition consisted of a frequency transition followed by a steady-state tone, the second condition contained the frequency transition alone. The authors demonstrated several effects. First, no difference could be discerned between the lone transition and the transition followed by the steady-state tone. Second, the investigators noted slightly improved discrimination performance following practice with stimuli of short duration. Third, a significant increase in discrimination performance was noted for transitions with the 120 msec durations which is in contrast to findings presented by Dooley and Moore. Fourth, no difference was noted between rising and falling transitions which contradicts results found by Nabelek (1978), Collins and Cullen (1978) and Dooley and Moore (1988). The benefit of using this type of signal is that the problem observed in the previous studies with parameter interaction (transition rate, transition duration, and extent of frequency sweep) is negated.
Elliot, Hammer, and Carrell (1991) described the discrimination of signals similar to second-formant frequency transitions. Four conditions, consisting of two rising transitions and two falling transitions with two different durations were used for testing. Each of the four different stimuli had either the same frequency onset, but a different frequency offset or the same frequency offset but different frequency onset. Signal duration was either 60 or 120 msec, and all transitions had the same rate of frequency transition regardless of the duration. Results showed no evidence that discrimination ability differed between rising and falling transitions. Second, discrimination ability improved with the larger duration signals which is in agreement with the findings of Elliot et al., (1989). The authors concluded that these findings suggest subjects ability to discriminate an initial stop consonant preceding a vowel should be poorer than his or her ability to discriminate a final consonant following the same vowel.

Porter, Cullen, Collins, and Jackson (1991) examined subjects’ ability to discriminate the onset frequencies of formant transitions with signal durations of 30, 45 and 60 msec. The psychophysical procedure consisted of a two-alternative forced-choice (2AFC) paradigm in which subjects were instructed to identify a frequency transition having a different slope. Results demonstrated that subjects were able to discriminate falling transitions better than rising ones. Furthermore, when the target signals were set with transition rates greater than the reference, subjects demonstrated smaller JNDs than when the target stimulus had a transition rate less than the reference. Finally, JNDs decreased as the frequency transition became longer in duration. Porter et al. (1991) suggested that this increased performance with longer duration signals was due to the subject being able to better use timbre and pitch cues.
Cullen, Houtsma and Collier (1992) investigated two primary questions regarding discrimination of tone glides. First, they examined the subjects’ ability to discriminate tone glides having varying initial or final endpoints. The reference signal was either a rising or falling frequency transition with a center frequency of 1950 Hz. Each transition traversed 200 Hz and was 40 msec in duration. Second, the authors looked at the discrimination of tone glides having different transition rates. The transition rates of the signals consisted of 2.5, 5, or 10 Hz/msec for signals with durations of 40 msec. For the first question concerning endpoints, the discrimination ability improved just noticeable differences (smaller JNDs) for tone-glides with frequency differences at the final endpoints. Cullen et al. stated that this finding may be due to memory processes and or a backward-masking effect, which interfered with the subjects’ discrimination. With regard to the second question concerning transition rate, the JNDs increased with an increase in the transition rate of the reference glide. This finding in terms of transition rate is in line with findings by Porter et al. (1991).

One must be careful in interpreting the above findings. Different results can be obtained depending upon the stimulus used and the task employed. Examples include the conflicting results obtained when determining whether discrimination ability is better for rising or falling glides. Elliot et al., (1991) and Elliot et al., (1989) found no difference in the detection ability of subjects when the stimulus was a rising or falling glide. However, Nabelek (1978) and Collins and Cullen (1978) observed that detection thresholds for falling glides were higher than for rising glides. This contrasts with Dooley and Moore (1988) findings that subjects detection ability for rising glides was worse than for falling glides. Conflicting evidence is also observed according to the
duration of the signals used in the paradigm. Elliot et al. (1991) and Elliot (1989) demonstrated that as the duration of the glides increased, discrimination ability improved. Dooley and Moore (1988) presented data showing that thresholds for glide stimuli decreased as duration increased. Interestingly, there is corresponding evidence that JNDs increase with an increase in transition rate (Porter et al., 1991 and Cullen et al., 1992).

2.4 Temporal Resolution in Frequency Modulated Signals

Only a handful of studies have attempted to investigate temporal resolution using FM signals. The current study is based on a study by Feth, Neil, and Krishnamurthy (1989). They developed a FM signal procedure to measure temporal resolution thresholds. The task consisted of a nonadaptive two-cue, two-alternative forced-choice procedure (2Q, 2AFC) in which the subjects were asked to discriminate between two FM signals having the same endpoints. However, whereas the reference signal traversed the frequency region in a smooth linear path, the target signal moved through the frequency span in a series of discrete steps. As the number of steps increase, the signal becomes temporally smoothed. Thus, the step signal sounds more like the linear glide, and performance eventually drops to chance. Stimuli in this study were FM signals, 25, 50, 100 msec in duration, with frequency sweeps of 100, 200, or 400 Hz. Thresholds for discrimination of the stepped glide from the linear glide were found to be in the range of 7-10 ms for all frequencies except 4000 Hz, where thresholds were in the range of 15-20 msec. Using the same paradigm, temporal resolution thresholds in subjects with mild-to-moderate bilateral sensorineural hearing loss were obtained by Madden (1990) and Madden and Feth (1992). These investigators determined that hearing-impaired subjects
were able to discriminate between the two stimuli. However, the mean temporal resolution thresholds were nearly twice those of their age-matched normal hearing counterparts.

These studies using tonal glides have been used as a staging point for investigation into the processing of more complex formant transitions by the human auditory system. In order to fully understand the processing of speech, the absolute sensitivity of the auditory system must first be described. The primary objectives of the above studies were to determine the constraints imposed by the auditory system when it attempts to resolve the physical properties of FM stimuli. Furthermore, when absolute thresholds are derived in normal hearing listeners, theories can be constructed to deal with those problems experienced by the hearing-impaired. To avoid the cognitive and perceptual complications that are associated with speech stimuli, the studies described above have measured the JNDs in frequency and duration of tone glides. Comparison of these difference limens with those determined from static stimuli provide insight into the perceptual cues used in the discrimination of long and short dynamic stimuli which can be generalized to vocalic transitions. The literature describing the detection of frequency modulated signals present mixed results as does measures of temporal resolution using amplitude modulated signals. A technique that may offer some insight into the conflicting results is the development of an objective measure for temporal resolution using auditory evoked potentials. Audiologists' frequently employ auditory evoked potentials to obtain objective measures concerning the integrity of the auditory system. The current study will adapt the Feth et al. (1989) paradigm into an electrophysiological one and determine if objective electrophysiological thresholds derived from the cortex
are as sensitive to the differences between the step and the linear glides as the behavioral
data presented in that paper.

2.5 Auditory Evoked Potentials

The most common way to record auditory evoked responses is with scalp
electrodes. The majority of auditory evoked potentials used clinically are far-field
responses that are volume conducted (e.g. through brain, dura, cerebrospinal fluid,
muscle, and scalp) demonstrate short latencies (5.5 msec or less), and have small
amplitudes (1 uV or less). Examination of voltage fields of scalp-recorded responses
show that they have a broad distribution coupled with shallow voltage gradients. Short-
and-middle latency evoked potentials are generated from neural activity starting at the
end organ (i.e., cochlea) and traveling through the auditory (VIII) nerve, brainstem,
thalamus, and finally the auditory cortex.

Long-latency auditory-evoked potentials (LAEPs) have latencies greater than 50
msec and reflect processing of information by the auditory cortex. LAEPS can be
grouped into two categories, exogenous and endogenous. In exogenous evoked
potentials, the response parameters (latency/amplitude) are determined by physical
characteristics of the evoking stimulus; and they are insensitive to the significance of the
stimulus. Endogenous evoked potentials vary with the state of the subject (i.e drowsiness
or alertness), the meaning of the stimulus, and the demands of the task.

LAEPs provide a means of measuring the time and sequencing of speech-sound
processing. The LAEP N1 is an obligatory potential that is elicited approximately 100
ms after onset of the acoustic stimulus. The N1 is preceded by the positive P1 wave and
is followed by the positive wave P2 (Figure 3). Embedded inside these late components is another exogenous response known as the mismatch negativity (MMN).

2.5.1 Mismatch Negativity

If a physically deviant stimulus is placed inside a repetitive homogeneous stimulus sequence, a negative going waveform starting at 100 msec and ending at approximately 250 msec, is able to be recorded. This exogenous evoked response is known both as N2a and the “mismatch negativity” (MMN). Näätänen, Gaillard, and Mantysalo (1978) state that this response reflects the automatic process involved in the encoding of stimulus difference, or change, by the brain and may represent an objective electrophysiologic measure of auditory discrimination. Näätänen, Simpson, and Lovelace (1982) recorded the response in passive subjects and were the first to demonstrate that the MMN held the potential to be an objective measure of auditory discrimination. The MMN is typically presented by displaying a difference waveform derived by subtracting the waveform of the frequent stimulus from the waveform of the infrequent stimulus (Figure 4). For optimal MMNs, the deviant stimulus requires a large change in its physical characteristics, and the stimuli should be presented with short interstimulus intervals (ISI).

2.5.2 Applications for the Clinic

The current study investigates the viability of the MMN as an objective measure of temporal resolution using FM signals. Audiologists routinely assess the brainstem to obtain some objective measure of hearing sensitivity. Although objective,
Figure 3: Two typical N1-P2 responses produced by an oddball paradigm
Figure 4: Typical mismatch negativity response derived from N1-P2 responses
auditory brainstem recording techniques are relatively insensitive to very discrete changes in acoustic signal. Another evoked response often used by audiologists is the P300. This response can be recorded when a listener is required to detect an infrequent target signal that occurs unpredictably in a train of standard stimuli. However, this test is not objective since it requires that the subject pay attention to the stimuli. The MMN is a pre-attentive discrimination process that has been shown to be sensitive to small acoustic changes (Näätänen et al., 1978). Since the MMN is a cortical exogenous response best recorded in a passive condition, the response lends itself to evaluating patients who are unable to participate in psychophysical studies due to mental constraint (e.g. dementia and mental retardation). The MMN may be useful in identifying or evaluating children that are at risk for language disorders and persons suffering from aphasia. Additionally, disruptions in speech perception due to abnormalities or damage to the central nervous system may be capable of being objectively evaluated by clinical audiologists.

2.5.3 Generators of the MMN

Research in both animals and humans suggests that the MMN response emerges from both the primary and nonprimary auditory pathways. The primary pathway is comprised of neurons found in the ventral portion of the medial geniculate body (MGB) and the primary auditory cortex (AI). These neural units are known to respond specifically to auditory stimuli and to phase lock to the stimulus properties. Furthermore, these neurons are arranged tonotopically and demonstrate frequency tuning to tonal stimuli (Clarey, Barone, and Imig 1992). The nonprimary auditory pathway is comprised of the dorsal and medial portions of the medial geniculate body and the secondary
cortical area AII. Neurons in the nonprimary auditory system respond to many different modalities including visual, somatosensory, and auditory stimuli. The primary generator thought to contribute to the generation of the MMN is the auditory cortex, with contributions from both the hippocampus and thalamus. MMN responses have been recorded from the nonprimary subdivision of the MGB suggesting a thalamic contribution (Csepe, Karmos, and Molnar, 1987). This paper will focus on describing only the primary components.

The MMN consists of two primary components. The first component was identified from recordings made over the temporal lobes that produced large amplitude MMNs ( Näätänen, Gaillard, and Mantysalo, 1978). Sams and Näätänen (1991) and Pardo and Sams (1993) were able to record MMNs in response to changes in the direction of frequency glides. Further studies by Scherg, Vasjar, and Picton (1989) showed that MMNs could be elicited using slight changes in frequency of the infrequent stimulus. Hari, Joutsiniemi, Hamalainen, and Vilkman (1984) recorded similar findings using magnetoenchephalography (MEG), which is method capable of measuring magnetic field produced by neurons. MMNm (MEG recorded MMN) derived using tonal stimuli of different frequencies, durations, and intensities resulted in a reproducible equivalent current dipole (ECD) located in the supratemporal auditory cortex (Sams et al., 1991).

Paavilainen, Tiitinen, Alho, and Näätänen (1991) recorded MMNs from the lateral surface of the temporal lobe in response to changes in frequency, intensity, and duration using pure tones. These investigators hypothesized that these MMN responses may be the second primary component of the auditory cortex MMN generator. However,
because the neural units are oriented radially and MEG is unable to detect radial responses, this response could only be recorded electrically. Näätänen and Michie (1979) proposed the concept of a second component generating the MMN which is localized to the frontal lobe. Giard, Perrin, Pernier, and Bouchet (1990) provided evidence of the second component using scalp current density (SCD) maps localizing MMN responses to the frontal lobe. Additionally, this frontal component was found to produce larger amplitude MMNs that were shorter in latency in the right hemisphere, independent of the ear stimulated. These findings are in agreement with recordings obtained by Scherg, Hari, and Hämäläinen 1989; Paavilainen et al, 1991; and Giard et al. 1995).

2.5.4 MMNs Elicited by Temporal Changes in the Stimulus

The MMN can be evoked in response to any acoustic change, given that the stimulus difference is great enough to be detected by the brain. Investigators have demonstrated, as noted above, that changes in intensity (Näätänen et al., 1987; Ford, Roth, Dirks, and Kopell, 1976), frequency (Näätänen et al., 1978; Näätänen, Paavilainen, Alho, Reinikainen, and Sams, 1989, Raavilainen, Alho, Renikainen, Sams, and Näätänen, 1991; Woldorff, Hackley, and Hillyard, 1991), spatial location (Paavilainen et al., 1989) of a stimulus, and temporal differences (Näätänen, Paavilainen, and Reinikainen, 1989; (Ford and Hillyard, 1981; Nordby, Hammerborg, Roth, and Hugdahl, 1988) are all capable of producing MMNs. Of interest to our study is the sensitivity of MMN to changes in the temporal properties of a signal. Näätänen, Paavilainen, and Reinikainen (1989) recorded MMNs in response to changes in the
stimulus duration. An oddball stimulus paradigm was used with a constant interstimulus interval (ISI) 510 msec. The subject was distracted from the acoustic stimulus by reading. The frequent and infrequent stimuli were the same frequency but the duration of the infrequent stimulus was half that of the frequent stimulus. Other investigators (Ford and Hillyard, 1981; Nordby, Hammerborg, Roth, and Hugdahl, 1988) demonstrated that by disrupting a stimulus train with a constant ISI an MMN can be generated.

Nordby, Roth, and Pfefferbaum (1988a) presented a constant stream of stimuli with an ISI of 800 msec. Occasionally the ISI would be decreased to 400 msec. The averaged waveform to the earlier occurring stimuli produced a recordable MMN. Nordby, Roth, and Pfefferbaum (1988b) recorded MMNs when a stimulus repetition occurred in a sequence of two alternating tones. However, Ritter, Paavilainen, Lavikainen, Reinikainen, Alho, Sams, and Näätänen (1991) were unable to obtain an MMN when a repetition of the stimulus was inserted into an irregular train of five equiprobable tones.

Tervaniemi, Saarinen, Paavilainen, and Näätänen (1992) recorded MMNs in response to an infrequent reversal of the order of the stimuli in the stimulus train. An MMN was also recorded when the second member of the pair was infrequently identical to the first stimulus, or if it was omitted.

2.5.5 The MMN and its Correspondence with Behavioral Discrimination

The current study is concerned with the correspondence between MMN thresholds for amplitude and latency and behaviorally derived thresholds of temporal resolution using the Feth et al. (1989) signals. The preceding section details the
sensitivity of MMN to temporal changes in the stimulus. Investigators have also provided evidence that suggest the sensitivity of the MMN to acoustic change may closely correspond to the subject’s ability to detect the same changes behaviorally. Lang, Nyrke, Ek, Aaltonen, Raimo, and Näättänen (1990) investigated the MMN to determine if there was a correlation between the MMN amplitude and individual behavioral pitch-discrimination ability. This study focused on comparing behavioral and electrophysiological data using temporal differences and the authors demonstrated that the amplitude difference in the MMN and behavioral pitch discrimination performance was positively correlated. Six of the 26 subjects examined demonstrated poor discrimination performance behaviorally, and it was not possible to elicit a MMN. The nine subjects who showed good behavioral discrimination showed mixed ability to generate a MMN. The eleven subjects that demonstrated excellent discrimination had MMNs that were generated by the smallest stimulus deviance.

Aaltonen, Eerola, Hellstrom, Uusipaikka, and Lang (1995) also demonstrated that the same correlation between behavior and MMN exists when synthetic are used as stimuli. The authors demonstrated a relationship between pitch discrimination performance and the MMN amplitude in normal subjects when small pitch differences were used as the frequent and infrequent stimuli.

Additionally, Kraus et al. (1994) examined cochlear implant patients and normal-hearing subjects to determine the relationship between psychophysical performance and the amplitude and latency of the MMN. The authors presented a synthesized stimulus pair /da/,/ta/ to successful cochlear implanted subjects. A successful implant user was defined as one who could understand sentences in an open-set task. The responses obtained from

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the successful users were very robust and similar in morphology to those of normal hearing subjects. When the same stimulus pair was presented to subjects judged as unsuccessful users, the waveforms morphology was very poor and dissimilar from those of the normal hearing subjects and successful cochlear implant users. The authors explain that this finding implies that the processing of these stimuli by the brain is very similar in both successful implant users and normal-hearing subjects.

Additional evidence for a relationship between psychophysical performance and MMN amplitude is provided by Näätänen, Schroger, Karakas, Tervaniemi, and Paavilainen (1993). The investigators demonstrated that the MMN produced predictable changes using a intricate spectro-temporal pattern that followed the subject’s psychophysical performance. Auditory stimuli were presented in an oddball paradigm to subjects who were in a passive condition. At first, the pitch difference between the frequent and infrequent stimulus did not elicit a MMN. However, later in the recording session MMNs were resolvable. The authors suggest that this represented a ‘sharpening’ of sensory information processing by the brain.

Kraus, McGee, Carrell, and Sharma (1995) investigated the MMN in two hearing aid users with similar hearing losses but with different behavioral performance on discrimination tests. A stimulus pair (/da/,/ga/) was presented to both subjects while wearing their hearing aids. The subject with good discrimination demonstrated robust MMNs while the subject with poor discrimination had no MMNs. The authors suggest that the MMN provided a neurophysiologic measure of each subject’s ability to discriminate fine acoustic differences.
Further evidence that a relationship between behavioral discrimination performance and MMN amplitude is provided by studies from Winkler and Näätänen (1992) and Winkler, Reinikainen, and Näätänen (1993). Winkler and Näätänen (1992) used a backward-masking paradigm to examine the relationship between the time course for recovery of recognition memory and MMN amplitude. A MMN was recorded when the gap between the first and second tone of the pair was longer in duration (150, 300, or 400 msec). However, when the gap interval was short (20 or 50 msec) a MMN was not obtained. The investigators suggest that the inter-tone interval effect is consistent with the effects observed on psychophysical performance in backward-masking paradigms.

Winkler, Reinikainen and Näätänen (1993) applied a recognition-masking paradigm in which a masking stimulus was presented either before or after a target stimulus. The interval between the target and the masker was varied. Results indicated that the shorter the interval between the test signal and the masking stimuli, the more the recognition memory trace of the target stimulus degraded. Interestingly, the MMN amplitude was strongly correlated with the subject’s discrimination ability in the task. The authors suggest that this may represent an index of the strength of sensory memory.

The preceding section has presented evidence that the sensitivity of the MMN to acoustic change follows the subject’s ability to behaviorally detect these changes. This suggests that the MMN may potentially be an objective measure of normal and/or pathological discrimination ability. This objective measure may hold potential for investigating frequency and temporal resolution.
2.6 Statement of Problem

The MMN is believed to be an objective electrophysiologic measure of auditory discrimination, which occurs independently of attention (Näätänen, Gaillard, and Mantysalo 1978). To date, there have been no investigations of MMN using frequency modulated signals to determine MTRTs in cochlear implant subjects using FM signals. Pilot data obtained by our lab determined that the MMN is highly sensitive to the temporal differences in the step glides utilized by Feth (1989), Madden and Feth (1992), and Bicknell (1996) thereby allowing an objective measure of temporal resolution.

The proposed research is designed to study the central auditory processes that encode temporal changes important for speech perception in normal-hearing adults. This will be accomplished by extending the Feth et al. (1989) psychoacoustic paradigm to an electrophysiological one and determining if the results obtained using the behavioral task can be derived objectively using the MMN. If the MMN is sensitive to the temporal changes of the step signals, then the response holds promise for providing an objective index of temporal resolution characteristics of the auditory cortex. This could be a tool for assessing those who are at risk for auditory processing disorders but who are unable to be tested using conventional behavioral test techniques.

The purpose of the present investigation is to determine whether a correspondence can be established between the subject’s psychophysical ability to discriminate FM signals with varying temporal properties, and an exogenous event-related potential evoked by the same stimuli.
CHAPTER 3
METHODS AND PROCEDURES

Descriptions of the electrophysiological recording parameters and stimulating paradigms are presented in this chapter. Additionally, the two-cue, two-alternative, forced choice psychoacoustic task, which was used to determine temporal resolution thresholds is also presented. Generation and calibration of the frequency modulated signals is also described.

3.1 Subjects

The subjects in this experiment were three neurologically intact, adults with a mean age of 43 (30yrs-51yrs). They had no experience with ERP recordings. Normal hearing sensitivity was defined as pure tone thresholds better than 15 dB HL for the octave frequencies 250-8000 Hz. The subjects were tested in three 4 hour blocks (12 hours) for the electrophysiological portion and for a total of 43 hours for the psychophysical portion of the study. They were reimbursed for their participation in the study.
3.2 Procedures

3.2.1 Audiological Test Session

Electrophysiological and behavioral testing was completed at the Dayton Veterans Affairs Medical Center (VAMC) and Henry Ford Hospital in Detroit. The tests were completed in an Industrial Acoustic Company (IAC-402) sound treated audiometric suite. Initially, each subject was asked to read and sign a consent form (Appendix A). To ensure auditory sensitivity was within the guidelines established by the study, pure-tone and speech audiometric measures were obtained from the subjects using a GSI model 10 audiometer. Furthermore, in order to assess the integrity of the middle ear system, immittance measures were derived using a GSI-33 Middle Ear Analyzer. The behavioral screening portion of the test session lasted approximately 20-30 minutes.

3.2.2 Behavioral Test Session

A two-cue, two-alternative forced-choice procedure was used. The subject was presented with three linear FM signals and one step signal. The subject was asked to identify the step glide, which was always presented either in interval two or three. This procedure was not adaptive. The step signal duration remained constant throughout the block of 50 trials. The subject's percent correct scores for the 5 different step durations (or numbers of steps) were used to construct psychometric functions for each condition.

A minimum of three sets of three blocks was presented to each subject for each step signal. Only one set of three blocks for a particular signal was run during a session. If the subject was unable to demonstrate an increase in the percent correct performance
over the last two sets of three blocks, data collection was terminated for that condition. The percent correct performance for each condition was determined by calculating the mean of the percent correct scores from each of those six blocks. Typically, no significant improvement was demonstrated after the second set of blocks. In the event that improvement was shown to continue, the session was extended with additional sets of three blocks and run until no further improvement occurred. The percent correct performance was calculated as described above. The each data point on the psychometric functions are constructed from 300 discrimination trials.

The order of presentation of the five conditions was not randomized. This was done so as to optimize each subject’s performance. All sessions began with a two-step signal with a center frequency of 1000 Hz. This condition was then followed by decreasing step duration (four, six, eight, and finally linear). Step signal conditions were presented until the subject reached chance performance for two consecutive signals. This procedure was designed to obtain each subject’s optimal performance. By presenting the signals with the largest temporal contrasts, subjects learned discrimination cues before moving on to more difficult stimuli.

3.2.3 Event-Related Potential Test Session

All ERP measurements were made in the same audiometric suite at the Dayton VA Medical Center audiology clinic. Electrophysiological recordings were made with each subject sitting in a reclining chair in an electrically shielded and acoustically attenuated booth. To maintain vigilance and decrease random eye movement the subject viewed a
subtitled movie during the data collection. The amplifiers and experimenter were located in the adjoining room.

Prior to electrode application, the subject's scalp was measured and electrode sites marked with a wax marking pencil according to the International 10-20 electrode system (Jasper, 1956). Gold plated electrodes were applied to the scalp using conventional surface electrode preparation techniques. Electrode impedances were always less than 3000 Ωs and interelectrode impedances were always less than 2000 Ωs. Gold plated disk noninverting electrodes were placed at Pz, F3, F4, Fz, Cz, C3 and C4. Additionally, a pair of electrodes were placed below and lateral to the left eye to exclude electrooculographic interference. The inverting electrode was placed on the cheek or nose. The ground electrode was placed at A1.

The analysis period was 250 msec including a 50 msec pre-stimulus baseline interval. Electrical activity was amplified X500 and filtered (1-70 Hz) with a neurophysiological amplifier. The signals were digitized (sampling rate = 500 Hz, accuracy = 0.168 (μV/bit) and signal averaged with a commercially available signal averaging system (Neuroscan™ Scan System). Raw data were stored as a continuous EEG file with stimulus trigger pulses. The data were later offline epoched and signal averaged. The baseline was calculated as the mean voltages during the 50 msec prestimulus. Artifact rejection values were set at +/-75mV.
3.3 Stimuli

3.3.1 Linear Glide Signal parameters

The glide signals were sinusoidal sweep tones with center frequencies of 1000, 2000, and 4000 Hz. The frequency transition was 200 Hz and the signal had a fixed duration of 50 msec with a 5 msec rise/fall time (Figure 1). These stimulus parameter values translate to a rate of frequency change of 4 Hz per msec. Signal onsets and offsets were shaped with a cosine-squared function. Subjects were only tested with signals that changed from lower to higher frequencies (upsweeps).

3.3.2 Step Signal Parameters

The step signals were sinusoid with the same characteristics as the linear glides with the exception that they traversed the 200 Hz frequency range in two, four, six, or eight discrete steps. (Figure 2).

3.3.3 Signal Generation

The glide and step signals were created and stored in digital form as .wav files. The .wav files were then transferred to the Neuroscan STIM system where they were converted to .snd files. Both step and glide signals were generated using a Sound Blaster 16 signal acquisition board with a 16-bit D-A converter mounted in a Dell 200 megahertz computer. A sampling rate of 100 kHz was used for converting the digital signal to analog form.
3.3.4 Signal Delivery

The signals were sent from the Sound Blaster board to a Neuroscan attenuator. The auditory signals were presented monaurally at an average rate of 3 Hz (varying pseudorandomly between 2Hz and 4 Hz) through an Etymotic ER3-A dynamic insert earphone delivery system at an intensity of 60 dB SL.

3.3.5 Spectral Analysis

The glide and step signal were identifiable only by differences in their temporal fine structure. The long-term frequency spectra of the signals were kept essentially identical. According to Madden (1990) any abrupt frequency transition in the step signal could manifest itself in the form of an off-frequency spectral difference which could potentially be used by the subjects to help them discriminate. To eliminate these confounding cues, a program written by A. Krishanmurthy generated the step signal with rounded "corners". When the signals were spectrally analyzed, the long-term spectrum of the step signals were essentially identical to that of the linear glide signals.

Spectral comparisons were performed at a series of SPLs for the acoustic signals. A Sennheiser earphone was coupled to a sound level meter (Bruel and Kjaer 2204) with a flat-plate coupler. The signal from the AC output of the sound level meter was delivered to a Hewlett-Packard 3561A Spectrum Analyzer for analysis. The acoustic spectra of the step and linear glide signals were essentially identical.
3.4 Event-Related Tasks

The MMN paradigm employed two frequency glides with the same center frequency while one was stepped (infrequent) and the other was linear (frequent). The stimulus probability was maintained at a presentation ratio of 80% (frequent linear glide) and 20% (infrequent stepped glide). A total of 1200 stimuli were presented in a single run (960 each of the frequent stimuli and 240 each of the infrequent stimuli) with each run being replicated once to ensure repeatability. This resulted in two runs for each of the 12 recording conditions. If the two waveforms were repeatable, they were grand averaged. If they were not repeatable, they were excluded from further analysis. Repeatability was determined by the presence of the MMN within the same latency time frame for both repetitions.

3.5 Data analysis of the Mismatch Negativity Potential

The MMN is by definition, a derived response elicited by an infrequent deviant stimulus in an oddball paradigm. According to McGee, Kraus, and Nicol (1997), computing the area of the MMN waveform in combination with latency criteria resulted in a high hit rate when identifying and measuring the magnitude of the MMN. The multiple t-test was used as the gold standard. Furthermore, when this analysis procedure was compared with other popular analysis methods, area proved to be the most indicative single measure currently available to evaluate the MMN. With this in mind, the amplitude, latency and area of the MMN were measured from a difference wave computed by subtracting the standard response from the deviant response.
Two different latency measures and two different magnitude measures were used to describe the MMN response derived for each subject (Figure 3). The first latency measure (LM1) was marked at the first positive deflection of the waveform following 100 msec. The second latency measure (LM2) was marked at the most negative going deflection following 100 msec and occurring within 250 msec of the signal onset.

The amplitude measures were described in microvolts and calculated as the peak-to-peak amplitude between the two latency measures described above. Additionally, an area metric also was used to quantify the MMN response for the distance between the onset and offset of the MMN. The onset and offset were judged to be the points of greatest relative positivity preceding and following the peak (Figure 3). Three experienced investigators independently judged the two latency measures and the onsets and offsets for each subject's waveform without knowing which stimulus conditions accounted for the responses. These investigators demonstrated consistency across all stimulus conditions when marking the MMN latencies. The signal averaged response waveforms for each recording session were converted to ASCII format and transferred to an Excel spreadsheet for analysis. The following algorithm was used to obtain area measure of magnitude (Barrett and Fulfs, 1998).
The area of the MMN is defined as

\[ \sum_{t_1}^{t_2} = \text{ABS}(x_n - x) \]

where \( \text{ABS} \) is the absolute value, \( t_1 \) is represented in msec and is the start of summation, \( t_2 \) is also described in msec and represents the end of summation. \( x_n \) equals the instantaneous voltage at any point in time on the waveform between \( t_1 \) and \( t_2 \) and \( x \) is the mean of \( x_n \) determined by the rectified waveform.
Figure 5: Illustration of the method used to obtain the two magnitude measures as well as the two peak latency measures for the MMN.
CHAPTER 4

RESULTS

The electrophysiogical protocol described in chapter 3 was designed to investigate whether the MMN potential can be used to determine temporal resolution thresholds in adults with normal hearing.

The following chapter is divided into three primary sections each representing a frequency. Each section describes the psychophysical results for an individual frequency and how they compare to the electrophysiological data collected. Peak-to-Peak amplitude, area measurements and latency of the MMN are described and compared in detail.

4.1 Data Processing

The psychometric functions for all three subjects in response to step vs. glide signals at the center frequencies 1 kHz, 2 kHz, and 4 kHz for all experimental conditions are discussed in the following chapter. Percent correct discrimination is plotted as a function of step duration and each data point for the three subjects consists of at least 450 trials per subject. The horizontal dashed line in each graph marks the 75% discrimination point on the y-axis. The vertical dashed lines indicate the points on the x-axis at which the psychometric functions intercept the 75% correct discrimination level. It is assumed
that these points represent the average temporal resolution of the listeners at the test frequency.

Two amplitude measures were used to describe the magnitude of the MMN response. For the first measure the peak-to-peak amplitude between the two latency measures was calculated. The second amplitude measure consisted of the area between the onset and offset of the MMN. The onset and offset were judged to be the points of greatest relative positivity preceding and following the peak (see methods section). The signal averaged response waveforms for each recording session were converted to ASCII format and transferred to an Excel spreadsheet for analysis by an algorithm presented by Barrett and Fulfs (1998).

Two different latency measures were used to describe the MMN response derived for each subject. The first latency measure which is designated LM1 was marked at the first positive deflection of the waveform following 100 msec. The second latency measure designated LM2 was marked at the most negative going deflection following 100 msec and occurring within 250 msec of the signal onset. The individual latencies for LM1 and LM2 at each frequency, step duration and subject at all other electrode positions are illustrated in Appendix A.

4.2 Results for 1 kHz signals

4.2.1 Psychophysical Results

The mean psychometric functions for stimuli with center frequencies of 1 kHz for all three subjects are illustrated in Figure 6. When the figure is examined, the psychophysical thresholds in the figures closely correspond with data obtained from
Figure 6: Averaged psychometric function for signals with a 1 kHz center frequency
Madden (1992) whose five subjects had an average temporal resolution threshold of 7.0 msec. Individual psychometric functions for all three subjects in this study are illustrated in Appendix C. Temporal resolution thresholds consistently decrease with decreases in step duration up to six-steps resulting in an average temporal resolution threshold of 8.3 msec. At this point subjects are unable to distinguish 76% or more of the step glides from the linear glides.

4.2.2 Peak-to-Peak Amplitude Measures

The MMN peak-to-peak amplitude data were normalized in order to facilitate comparison with the psychometric functions. The peak-to-peak amplitude is greatest for the longest step duration and declines as the task is made more difficult. Thus, all amplitude values for a given subject were divided by the largest one and expressed as a percentage of the largest value. Figure 7 shows the peak to peak amplitude compared with the psychometric function. The psychometric function consists of the points connected by the solid line. The response which was always the largest in the 1 kHz condition was the MMN evoked by infrequents with a step duration of 25 msec (2-step glide). All three subjects were able to obtain a 100% discrimination score when they were asked to differentiate between the 2-step glide and the linear glide. When the infrequent stimulus had a step duration of 12.5 the MMN peak-to-peak response decreased by 20% whereas the psychometric function decreased only by 8%. A step duration of 8.3 msec demonstrated a 39% decrease compared to a 28% decrease in psychophysical performance. This greater change or steeper slope in the electrophysiological function compared to the one derived psychophysically suggests that
Figure 7: MMN peak-to-peak amplitude compared with the psychometric function for FM signals with center frequencies of 1 kHz plotted as a function of step size. The solid line represents the psychometric function and the filled circles represent percent of maximum amplitude of the MMN.
the MMN is somewhat less sensitive than thresholds obtained in a behavioral paradigm. However, both functions are very similar in shape.

4.2.3 Area measures

When the area measure for 1 kHz is compared with the psychometric function in Figure 8 the same normalization method is used as with the peak-to-peak amplitude. The largest area measure was always obtained from the MMN evoked in response to the stimulus with the largest deviance (25 msec step duration) and this was set as 100%. When the infrequent stimulus had a step duration of 12.5 (4-step) the MMN area measure decreased by 25% whereas the psychometric function decreased by 8%. Additionally, when a step duration of 8.3 msec was used as the infrequent the MMN area measure demonstrated a 51% decrease compared to only a 28% decrease in psychophysical performance. As with the peak-to-peak amplitude, the electrophysiological function has a steeper slope compared to the one derived psychophysically. This suggests that the MMN area measure is less sensitive than thresholds obtained in a behavioral paradigm. Furthermore, the area function does not appear to follow the behavioral function as closely as does peak-to-peak amplitude.

4.2.4 Latency Measure 1 (LM1)

Figure 9 compares LM1 with the psychometric function using a slightly different method of normalization than that used with the magnitude measures. Since performance decreases with decreasing step duration and latency shows a trend to increase, short
Figure 8: MMN area amplitude compared with the psychometric function for FM signals with center frequencies of 1 kHz plotted as a function of step size. The solid line represents the psychometric function and the filled circles represent percent of maximum amplitude of the MMN.
Figure 9: Mean MMN latency measure one compared with the psychometric function for FM signals with center frequencies of 1 kHz plotted as a function of step size. The solid line represents the psychometric function and the filled circles represent percent of maximum latency of the MMN.
latencies are measured for the best discrimination performance, with latency increasing as the task becomes more difficult. Thus, the 100% point for latency was designated as the shortest latency recorded. The reciprocal of each latency measure was calculated and divided into the reciprocal of the minimum latency. The shortest latency in the 1 kHz condition was always recorded from the MMN evoked using an infrequent glide stimulus with a 25 msec step duration. When MMNs were recorded using infrequent stimuli with step durations of 12.5 msec, the MMN latency increased by 12%. The point on the psychometric function representing a step duration of 12.5 msec only decreased by 8%. MMNs elicited using stimuli with 8.3 msec step durations demonstrated the same latency as that evoked by the 12.5 step duration which was a 12% increase. The point on the psychometric function illustrating 8.3 msec step durations dropped 28%. Figure 9 illustrates a high degree of agreement between psychophysical thresholds and LM1 latency for step durations of 25 and 12.5 msec. However, for 8.3 msec step durations the psychometric function continues to fall while the latency for LM1 stays stable.

4.2.5 Latency Measure 2 (LM2)

When the latency measure LM2 is compared with the psychometric function in Figure 10, the function derived using the latencies closely follows the function obtained psychophysically. The same normalization method used to calculate and display LM1 is used with LM2. The shortest latency LM2 was obtained from the MMN evoked by infrequents with a 25 msec step duration. When the infrequent stimulus had a step duration of 12.5 the degree of change was very similar. LM2 increased by 6% while the psychometric function decreased by 8%. When a step duration of 8.3 msec was
Figure 10: Mean MMN latency measure two compared with the psychometric function for FM signals with center frequencies of 1 kHz plotted as a function of step size. The solid line represents the psychometric function and the filled circles represent percent of maximum amplitude of the MMN.
employed as the infrequent, LM2 increased by 15% coupled with a 28% decrease in psychophysical performance. Figure 10 illustrates how closely the two functions follow each other suggesting that a LM2 increase is closely associated with decreasing stimulus deviance.

4.3 Results for 2 kHz signals

4.3.1 Psychophysical Results

The mean psychometric functions for stimuli with center frequencies of 2 kHz for all three subjects are illustrated in Figure 11. Individual psychometric functions for all three subjects in this study are illustrated in Appendix C. Temporal resolution thresholds consistently decrease with increases in step duration up to six-steps at which point subjects are unable to distinguish 76% or more of the step glides from the linear glides.

4.3.2 Peak-to-Peak Amplitude

The peak-to-peak amplitude using FM signals with a center frequency of 2 kHz is compared with the psychometric function in Figure 12. The psychometric function consists of the points connected by the solid line. The response which was always the largest in the 2 kHz condition was the MMN evoked by infrequents with a step duration of 25 msec (2-step). All three subjects demonstrated 100% discrimination performance when they were asked to differentiate between the 2-step glide and the linear. When the infrequent stimulus contained step durations of 12.5 msec the MMN peak-to-peak response decreased by 48% whereas the psychometric function decreased only by 15%. A step duration of 8.3 msec did not produce a measurable MMN. A 28% decrease in
Figure 11: Averaged psychometric function for signals with a 2 kHz center frequency
Figure 12: MMN peak-to-peak amplitude compared with the psychometric function for FM signals with center frequencies of 2 kHz plotted as a function of step size. The solid line represents the psychometric function and the filled circles represent percent of maximum amplitude of the MMN.
psychophysical performance was noted at this step duration. This extreme change in MMN peak-to-peak amplitude without an accompanying large change in the psychophysical measure suggests that the sensitivity of the MMN is less than responses derived behaviorally. Additionally, only the two stimuli having the largest stimulus deviance were capable of producing a measurable MMN whereas the three largest stimulus deviants were able to evoke a MMN in the 1 kHz condition.

4.3.3 Area Measures

The area measure is compared with the psychometric function in Figure 13. Again the largest area measure was from the MMN in response to the stimulus with the largest deviance from the frequent stimulus (25 msec step duration). Infrequent stimuli with step durations of 12.5 msec evoked MMNs with a mean area measure that decreased by 35%. Psychometric data produced a function which decreased by 15%. A step duration of 8.3 msec did not produce a measurable MMN. However, an additional 28% decrease in mean psychophysical performance was recorded. As with the peak-to-peak data in the 2 kHz condition the slope of the function is extremely steep yet the function does move in the direction hypothesized. While a robust MMN is capable of being generated in response to the largest stimulus deviance, the MMN responses degrade at a faster rate than psychophysical ones as step duration decreases.

4.3.4 Latency Measure 1 (LM1)

LM1 in the 2 kHz condition is compared with the psychometric function in Figure 14. Again the shortest latency was derived from the MMN in response to the stimuli with
Figure 13: MMN area amplitude compared with the psychometric function for FM signals with center frequencies of 2 kHz plotted as a function of step size. The solid line represents the psychometric function and the filled circles represent percent of maximum amplitude of the MMN.
Figure 14: Mean MMN latency measure one compared with the psychometric function for FM signals with center frequencies of 2 kHz plotted as a function of step size. The solid line represents the psychometric function and the filled circles represent percent of maximum latency of the MMN.
25 msec step durations. When LM1 was measured from MMNs evoked using the infrequent stimuli with step duration of 12.5, the MMN peak-to-peak latency increased by only 1%. However, a 15% decrease the psychometric function for the same stimuli was obtained. A step duration of 8.3 msec or less did not produce any measurable MMNs. A 28% decrease in psychophysical performance was found with stimuli having 8.3 msec step durations. This negligible change in LM1 from a 2-step glide to a 4 step glide in the 2 kHz condition suggests that this measure may not provide much insight into behavioral performance.

4.3.5 Latency Measure 2 (LM2)

When LM2 is compared with the psychometric function in Figure 15 the two mean latencies recorded follow the behavioral function very closely for 25 msec and 12.5 msec step durations. The shortest latency was again derived from those MMNs evoked in response to the stimuli with 25 msec step durations. When the infrequent stimulus had a step duration of 12.5 LM2 increased by 12% and the psychometric function decreased by 15%. A step duration of 8.3 msec did not generate a measurable MMN. However, subjects demonstrated a 28% decrease in psychophysical performance. LM2s close approximation to the subjects psychophysical function suggest that this measure may provide some insight into their temporal resolution thresholds.
Figure 15: Mean MMN latency measure two compared with the psychometric function for FM signals with center frequencies of 2 kHz plotted as a function of step size. The solid line represents the psychometric function and the filled circles represent percent of maximum amplitude of the MMN.
4.4 Results for 4 kHz signals

4.4.1 Psychophysical Results

The mean psychometric functions for stimuli with center frequencies of 4 kHz for all three subjects are illustrated in figure 16. Individual psychometric functions for all three subjects in this study are illustrated in Appendix C. Temporal resolution thresholds rapidly decrease with decreases in step duration up to four-steps at which point subjects are unable to distinguish 76% or more of the step glides from the linear glides.

4.4.2 Peak-to-Peak amplitude

The peak-to-peak amplitude is compared with the psychometric function in Figure 17. The psychometric function consists of the points connected by the solid line. The largest peak-to-peak response in the 4 kHz condition was always evoked by the infrequents with a step duration of 25 msec (2-step). When the infrequent stimulus had a step duration of 12.5 the MMN peak-to-peak response decreased by 45% compared to the 20% decrease exhibited by in the psychophysical condition. A step duration of 8.3 msec did not produce a measurable MMN. Both the psychophysical and the electrophysiological functions degrade quickly with decreasing step size. However, the Peak-to-peak amplitude measure decreases much more rapidly than the behavioral performance.
Figure 16: Averaged psychometric function for signals with a 4 kHz center frequency
Figure 17: MMN peak-to-peak amplitude compared with the psychometric function for FM signals with center frequencies of 4 kHz plotted as a function of step size. The solid line represents the psychometric function and the filled circles represent percent of maximum amplitude of the MMN.
4.4.3 Area measures

Area measures for the 2 kHz condition are compared with the psychometric function in Figure 18. As had been the case in the previous two conditions, the largest area measure was derived from the MMN evoked by stimuli with 25 msec step durations. When the infrequent stimulus consisted of 12.5 msec step durations, the MMN area measure decreased by 45% whereas the psychometric function decreased by 20%. Again a step duration of 8.3 msec did not produce a measurable MMN. As with the peak-to-peak amplitude area measures degrade at about the same rate and much more rapidly than the psychophysical results.

4.4.4 Latency Measure 1 (LM1)

When LM1 is compared with the psychometric function in Figure 19 it can be observed that the electrophysiological function follows the psychophysical one fairly closely for step durations of 25 and 12.5 msec. The shortest latency was again obtained from MMNs produced by infrequent stimuli with 25 msec step durations. When the infrequent stimulus had a step duration of 12.5 the MMN latency increased by only 9% compared to the psychometric function which decreased by 20%. A step duration of 8.3 msec or less did not produce a measurable MMN.

4.4.5 Latency Measure 2 (LM2)

The LM2 measures for the 4 kHz condition are compared with the psychometric function in Figure 20. The shortest latency in this case was again those measures from MMN derived from infrequent stimuli having step durations of 25 msec. When the
Figure 18: MMN area amplitude compared with the psychometric function for FM signals with center frequencies of 4 kHz plotted as a function of step size. The solid line represents the psychometric function and the filled circles represent percent of maximum amplitude of the MMN.
Figure 19: Mean MMN latency measure one compared with the psychometric function for FM signals with center frequencies of 4 kHz plotted as a function of step size. The solid line represents the psychometric function and the filled circles represent percent of maximum latency of the MMN.
Figure 20: Mean MMN latency measure two compared with the psychometric function for FM signals with center frequencies of 4 kHz plotted as a function of step size. The solid line represents the psychometric function and the filled circles represent percent of maximum latency of the MMN.
infrequent stimulus had a step duration of 12.5 msec LM2 increased by only 2% while the psychometric function decreased by 20%. A step duration of 8.3 msec did not produce a measurable MMN.
CHAPTER 5
DISCUSSION

This chapter includes a discussion of the results obtained in the present investigation as they relate to the research questions previously posed. In addition, further areas of research are discussed. Finally, the chapter concludes with the major findings of this study.

The purpose of this study was to examine whether the MMN could be used as a physiological index of temporal resolution. Frequency modulated signals were presented in an oddball sequence with the stepped glide being assigned as the infrequent stimulus. It was assumed that the magnitude of the MMN would change with changes in the step duration of the step glide. Secondly, comparisons between the psychophysical tasks and electrophysiological responses will be measured in terms of their sensitivity to the step signals. Thus the primary question was would predictable changes in the peak-to-peak amplitude and area measurements of the MMN accompany changes in step duration. A second question was the effect of step duration on the latency of the MMN. Finally, are changes in MMN descriptors comparable to listener performance in a psychophysical task.
5.1 Relationships Between Psychophysical and Electrophysiological Results

5.1.1 Peak-to-Peak Amplitude and Psychophysical Findings

The mean peak-to-peak amplitudes of identifiable MMNs in response to step signals for all three subjects decrease with decreases in discrimination performance across all frequencies. Figure 21 illustrates that as discrimination performance presented as percent correct in a 2AFC procedure decreases, so does mean peak-to-peak amplitude. Each point on the figure also represents one of the three center frequencies. In Figure 21 the points are tightly grouped around the regression line. An increase in the number of steps in the glide stimulus creates smaller step durations making the target or infrequent stimulus more difficult to distinguish from the standard which was always the linear glide. This decrease in MMN peak-to-peak amplitude is in line with previous research (Novak, Ritter, and Vaughan 1990 and Sams, Paavilainen et al. 1985) suggesting that as stimulus deviance decreases between the frequent and the infrequent stimulus, the amplitude of the MMN decreases as well. These findings suggest that MMN peak-to-peak amplitude may be a good predictor of the temporal resolving capabilities in normal hearing subjects. If an individual is incapable of participating in a psychophysical procedure, a MMN may be able to be recorded and insight may be gained into that subject’s ability to process temporal information.

5.1.2 Area Amplitude and Psychophysical Findings

As with the peak-to-peak amplitudes, the mean area amplitudes of measurable MMNs also demonstrate a trend to decrease with decreases in discrimination...
Figure 21: Mean MMN peak-to-peak amplitude plotted as a function of the psychometric performance for all frequencies. The circle represents the condition 1 kHz with two steps, the square is 1 kHz 4 steps, the right side up triangle represents 1 kHz 6 steps, the upside down triangle is 2 kHz with 2 steps, the rhombus represents 2 kHz 4 steps, the hexagon is 4 kHz with 2 steps and the circle with an X through it is 4 kHz with 4 steps.
performance across all frequencies. However, points constructing the area function are not as tightly clustered around the regression line as the peak-to-peak amplitude is. Figure 22 illustrates decreasing discrimination performance produces a decrease in mean area amplitude across all frequencies. Area does in fact decrease with decreases in psychophysical performance allowing the investigator to make objective assumptions about the temporal resolution of the subject.

5.1.3 Latency Measure 1 (LM1) and Psychophysical Findings

The mean LM1 latencies of identifiable MMNs in response to step signals for all three subjects demonstrate a slight trend to increase with decreases in discrimination performance across all frequencies. Figure 23 illustrates that as discrimination of the step glide from the linear becomes harder, the initial latency measure of the MMN becomes longer. All three frequencies demonstrate an increase in latency. 1 kHz has the largest initial change in latency followed by 4 kHz and then 2 kHz. An increase in the number of steps in the glide stimulus creates smaller step durations making the target or infrequent stimulus more difficult to distinguish from the standard which was always the linear glide. This finding that the latency of LM1 increases with decreasing step duration may allow the investigator or clinician to make some assumptions about the temporal resolving abilities of the subject or patient. Interestingly, Näätänen and Gaillard (1983) concluded that the MMN latency is a more reliable correlate of the magnitude of frequency difference that the MMN amplitude. These authors suggested that the MMN amplitude may saturate at a moderate magnitude stimulus deviation. Additionally, Sams and Paavilainen et al. (1985) presented data suggesting that the MMN peak latency for
Figure 22: Mean MMN area amplitude plotted as a function of the psychometric performance for all frequencies. The circle represents the condition 1 kHz with two steps, the square is 1 kHz 4 steps, the right side up triangle represents 1 kHz 6 steps, the upside down triangle is 2 kHz with 2 steps, the rhombus represents 2 kHz 4 steps, the hexagon is 4 kHz with 2 steps and the circle with an x through it is 4 kHz with 4 steps.
Figure 23: Mean MMN latency measure one plotted as a function of the psychometric performance for all frequencies. The circle represents the condition 1 kHz with two steps, the square is 1 kHz 4 steps, the right side up triangle represents 1 kHz 6 steps, the upside down triangle is 2 kHz with 2 steps, the rhombus represents 2 kHz 4 steps, the hexagon is 4 kHz with 2 steps and the circle with an X through it is 4 kHz with 4 steps.
changes in frequency are more closely correlated with psychophysical performance than MMN magnitude. The same effect may be occurring in response to the temporal stimulus deviations used in this study.

5.1.4 Latency Measure 2 and Psychophysical Findings

The mean LM2 latencies of identifiable MMNs in response to step signals for all three subjects demonstrate a dramatic trend to increase with decreases in discrimination performance across all frequencies. Figure 24 illustrates that as discrimination of the step glide from the linear becomes harder, the initial latency measure of the MMN becomes longer. All three frequencies demonstrate an increase in latency tightly grouped around the regression line except for the condition 4 kHz that employs the four-step infrequent stimulus. This grouping suggests there is a close correspondence between behavioral performance and MMN LM2 measures. If the signal-to-noise ratio is good and a robust MMN is present, the LM2 increase in latency in conjunction with decreasing step duration may afford clinicians to make some predictions about the temporal resolving abilities of the subject or patient.

5.2 Factors Influencing Variability in the MMN

5.2.1 Variation of the MMN in Individual Subjects

It has been determined from other studies as well as this one that even with no change in stimulation parameters, there is a certain amount of variability in individual MMN amplitudes and latencies from one recording session to another. The difference in subject variance is a concern for the investigator wishing to use this response clinically.
Figure 24: Mean MMN latency measure two plotted as a function of the psychometric performance for all frequencies. The circle represents the condition 1 kHz with two steps, the square is 1 kHz 4 steps, the right side up triangle represents 1 kHz 6 steps, the upside down triangle is 2 kHz with 2 steps, the rhombus represents 2 kHz 4 steps, the hexagon is 4 kHz with 2 steps and the circle with an X through it is 4 kHz with 4 steps.
Pekkonen, Rinne, and Nätänen (1995) investigated the variability and replicability of the MMN in ten subjects. Subjects were run twice with a one-month interval between the two runs with a duration and frequency condition. Results from this study demonstrated that the test-retest stability in individual subjects was only significant in the duration condition. Additionally, Lang, Eerola, Aaltonen (1995) also examined the reliability in three subjects over 5 days utilizing four stimulus blocks. Results indicated that the MMN amplitude had a higher coefficient of variation than that of latency. This suggests that the MMN amplitude is a less reliable response metric than latency.

Another important source of variability in the MMN is the vigilance of the subject during the recording session. Lang, Mikola, Eerola (1995) demonstrated that in various states of alertness, the MMN amplitude and latency changed in a predictable manner. In the initial stages of drowsiness, the MMN amplitude and latency increased. When the subject entered stage one sleep and slow eye movements started to occur, the MMN amplitude started to decrease while latency continued to increase. Additionally, the MMN demonstrated a significant although variable amplitude decrease when a monotonous recording session lasted for one to 1.5 hours (Lang et al., 1995). This investigation illustrates the importance of keeping a subject’s alertness and to avoid long monotonous recording sessions. This suggests that subjects who are noted to be tired should be run at another time when they are rested. The current study ran subjects for six hour sessions with 15 minute breaks every two hours. This may explain some of the high variability seen in this study. The MMN amplitude also depends on the stimulation parameters used and the degree of deviance of the deviant stimulus. To conclude, a
complicated interaction seems to exist between the individual's age, the MMN amplitude, and the stimulation parameters.

Another source of interindividual variation may be due to the inherent ability of the subjects to discriminate the stimulus used in the recording session. The focus of this study is on the correspondence between the behavioral and electrophysiological discrimination of temporal differences using frequency-modulated signals. In a similar study examining the relationship between behavior performance and the MMN, Lang, Nyrke, Ek, Aaltonen (1990) demonstrated that the amplitude of the MMN and behavioral pitch discrimination performance is positively correlated. This study examined 26 subjects behaviorally and electrophysiologically. Six of the subjects demonstrated poor discrimination performance behaviorally and it was not possible to elicit a MMN. The nine that showed good behavioral discrimination showed mixed ability to record a MMN. The 11 that demonstrated excellent discrimination MMNs were generated by the smallest stimulus deviance. Other investigators (Kraus, McGee, Micco, Carrell, Sharma, & Nicol, 1993; Näätänen, Schroger, Tervaniemi, Karakas, & Paavilainen, 1993) have also demonstrated the relationship between MMN amplitude and pitch discrimination.

Interestingly, this study screened seventeen subjects and only three demonstrated a robust MMN. All three of the subjects demonstrated very similar discrimination performance across all frequencies. Discrimination performance was not assessed in any of the screened subjects not included in the study.

Aaltonen, Eerola, Hellstrom, Uusipaikka, and Lang (1995) have also demonstrated that same correlation exists in MMNs when vowels created synthetically are used as stimuli. The authors demonstrated that there is a relationship between pitch
discrimination performance and the MMN amplitude in normal subjects when small pitch
differences are used as the frequent and infrequent stimulus.

The strong correspondence between the subject’s MMN amplitude and behavioral
discrimination of the frequency characteristics of a stimulus is of great interest to those
investigators who wish to use it clinically. Although the above research suggests that
discrimination abilities differ greatly in a subject pool of normal hearing subjects, the fact
that the MMN is sensitive to these acoustic differences is promising for clinical research.

Lang and Mikola (1994) suggest that the mechanisms responsible for
discriminating frequency differences in the stimuli are either poor or of short duration.
What is very interesting is that some of the subjects who showed small MMN amplitudes
at the beginning of the experiment were capable of improving their behavioral
discrimination performance with more practice. With these increases in discrimination
performance the MMN demonstrated an increase in amplitude.

5.2.2 Additional Sources of Variation of the MMN

Woods (1992) demonstrated that with increasing age, the MMN amplitude
decreases. This effect is further magnified if a long ISI is used. Additionally,
significantly greater proportions of the recorded MMNs were biphasic and the signal-to-
noise ratio became worse with age. Gender has been shown influence the MMN. Barrett
and Fulfs (1998) demonstrated that there were no significant gender differences in the
peak latency of the MMN. However, peak-to-peak amplitude and area under the curve
were significantly larger for woman than for men. Since the current study utilizes FM
signals and not pure tones, it is of interest that complex stimuli produce MMNs with significantly longer latencies if females rather than males (Aaltonen et al., 1994).

5.3 The Issue of Signal-to-Noise Ratio

A subject's just noticeable difference (JND) for a pure tone frequency is based upon the absolute frequency, intensity and duration of the stimulus. When a subject is presented a 1000 Hz pure tone stimulus during a behavioral task, he/she is able to discriminate a difference when the signal changes by 1 to 2 Hz (Wier, Jesteadt, & Green, 1977). When JNDs for more complex sounds are examined, the JND is influenced by the spectral composition of the stimulus as well as the perceptual masking effects of the ear. Flanagan (1965) described results for vowels that indicated the JND is 4% to 5% of the absolute formant frequencies.

Lang, Nyrke, Ek, Aaltonen, Raimo, and Näätänen (1990) have provided evidence that discrimination performance obtained through behavioral tasks correlates with the MMN amplitudes when using pure tones. Other investigators have found similar results utilizing more complex stimuli such as vowels (Aaltonen, Eerola, Hellstrom, Uusipaikka, & Lang, 1995). In theory, MMNs should be able to be generated by frequency deviations near or around the behavioral JND. However, the preceding section discussed how the signal-to-noise ratio of the recording can interfere with electrophysiologically derived thresholds. Tiitinen, May, Reinikainen, & Näätänen, (1994) investigated MMN threshold using pure tones as the stimulus. MMNs thresholds of 0.3 μV were generated in response to stimulus deviations of 5 to 10 Hz at 1000, 3 to 5 times greater than the JND derived from the behavioral task, and one could assume that much smaller frequency
deviations could evoke a minor MMN. In contrast to the previous study, Aaltonen, Eerola, Lang, Uusipaikka, & Tuomainen, (1994) presented evidence that when more complex stimuli are used a 4% deviation of the F2 formant frequency of /y/ vowel generated a measurable MMN.

5.4 Amount of Averaging Needed to Resolve an MMN

The MMN recorded from the scalp after each stimulus contains both the responses from the auditory pathways and other electrical potentials that are not associated with the auditory system. In scalp recorded electrophysiology, averaging is a common method used to extract the desired signal out of the unrelated background noise. The process of averaging requires that the stimulus is repeated and the electrical activities recorded after each stimulus is averaged. When the collected activity is subjected to averaging and filtering, the signal remains and noise should decrease the square root of the number of samples. However, due to the random nature of the background noise, all activity not time locked to the stimulus decreases in amplitude as the amount of averaging increases.

Regan (1989) has stated that the signal-to-noise ratio (SNR) of the averaging process increases by a factor of $\sqrt{\text{SQR}(N)}$ where $N$ equals the number of single trials that are in the average. The inherent noise of an electroencephalography (EEG) amplifier can be estimated to be Gaussian normal white noise in the approximately the same frequency region as the MMN (0.1 to 30 Hz). When the noise of a typical EEG amplifier is measured the amplitude is approximately 0.5 $\mu$Vp-p (Lang, 1994). Lang et al. (1994) explains that the MMN peak amplitude should be three times greater (SNR = 3:1) than
the sigma of the noise present in the EEG amplifier. If the investigator interested in resolving an MMN Uses these assumptions, detection threshold to derive a measurable MMN response would be about 0.3 µV, which is in agreement with results reported by Tiitinen et al., (1994).

5.5 Number of Trials Needed to Extract the Waveform

Besides amplifier noise the small response of the MMN response must also be extracted from the physiological EEG-background activity. Due to the background EEG activity not being time-independent random variable, it will not be 100% cancelled during the averaging process.

Lang and Mikola (1994) provide an equation that calculates the approximate number of trials an investigator would need in order to detect a MMN. The equation assumes that the frequency region of the MMN is very close to that of the alpha band. This equation is based on the assumption that the MMN threshold is 0.3 µV and in an eyes-open condition the mean alpha amplitude in the frontal areas is 10 µVrms.

$$\text{SNR} = \frac{U_{\text{rms}}}{U_{\text{rms}} \sqrt{N}}$$

Where:

- SNR = signal-to-noise ratio
- $U_{\text{rms}}$ = signal amplitude (rms)
- $U_{\text{rms}}$ = noise amplitude (rms)
- $N$ = number of trials in the average
If the investigator solves for $N$ and substitutes the values desired to reach a SNR of 3:1, more than 10,000 deviant responses would need to be averaged in order to resolve a 0.3 $\mu$V MMN response from the ongoing background EEG. In a clinical setting, however, 10,000 trials would take much longer than is normally provided for the average electrodiagnostic test. Currently most investigators collect 1200 or 2400 trials with 10% or 20% of these being deviants. Lang et al. (1994) states that a practical MMN threshold (peak value) in normal subjects is approximately 1.7 $\mu$V. Furthermore, MMN responses demonstrating a peak amplitude less than 2 $\mu$V are difficult to identify because of the poor SNR.

In order to find three subjects for this study that demonstrated robust MMN’s, several other subjects were screened using optimal recording methods to determine if a MMN was present. In order to expedite the process of recording the MMNs in a research setting it would be useful to know a priori whether or not and MMN can be identified in a particular subject using a simple “optimized” paradigm before the entire study is run (Jacobson, 1999 personal communication a).

5.6 Future Research

Several findings in this study should be investigated further. First, in order to accurately determine electrophysiological thresholds using these stimuli, all step sizes (1-8) should be used rather than just every other one.

Due to the often poor recordability of the MMN, the signal-to-noise ratio of the response should be examined and measured in order to determine if the subject is a good candidate for the study. One way this could be accomplished would be to establish the
minimum amplitude MMN that is detectable in a perfect (virtually "noiseless") setting for pure tone stimuli. This then demonstrates how small the residual unaveraged noise can be where you can expect to extract the MMN from the noise floor. Responses should then be recorded using a pre-stimulus baseline equal to the window. Compute the RMS value of the residual activity (post-averaging) in the pre-stimulus period and in the period during which the MMN should occur. Create the noise-to-signal ratio and determine whether it exceeds the criteria level based upon the smallest recorded MMN in an ideal condition. If the residual unaveraged (RMS) activity in the pre-stim period exceeds that in the MMN interval, then the likelihood would be low that a MMN would be able to be resolved (Jacobson, 1999 personal communication b).

Another technique used to determine the amount of noise in a waveform is by calculating the residual noise level (RNL) (Schimmel, 1967). The RNL in the average waveform can be estimated using what is known as the +/- reference. Unlike RMS measures where all the recorded waveforms are added together and then divided by the number of trials, this procedure alternately adds and subtracts each waveform prior to the division. Since the response to the stimulus is continually added to and then subtracted from the average, any recorded time locked response to the stimulus is canceled out. However, random activity is random regardless of its polarity and the (+/-) reference analysis creates an estimate of what the final average would appear as with no response present. A criterion level would need to be determined and if the RNL exceeded this level that the subject would be a poor candidate for the study.

Another aspect of the study should be further investigated is how hearing loss changes the responses. The effects of hearing loss on the MMN in response to the signals
used in this study should also be examined. Using hearing impaired subjects would contribute new insights into how long term peripheral hearing loss affects the temporal resolution of central auditory nervous system CANS. Specifically, this study would produce objective measures of temporal resolution in hearing impaired subjects utilizing the MMN. The data obtained would elucidate the implications of cochlear hearing loss on speech perception in the CANS thereby allowing more effective guidelines to be established for remediation and/or rehabilitation.

5.7 Conclusions

The following is a summary of the primary findings of this study.

1) The mean peak-to-peak amplitude of the identifiable MMN became progressively smaller as temporal differences between the frequent and infrequent stimulus decreased. More specifically, as step duration decreases MMN peak-to-peak amplitude decreases. Furthermore, peak-to-peak amplitude systematically decreases in magnitude with decreases in discrimination performance in the psychophysical 2AFC procedure. Of the two magnitude measures, peak-to-peak amplitude most closely approximated the psychophysical function.

2) The area measure for the amplitude of the identifiable MMN becomes progressively smaller as temporal changes between the frequent and infrequent stimulus decrease for all three subjects and all frequencies. As the step duration of the infrequent stimulus decreases, the area of the MMN response decreases. MMN area decreases with decreases in discrimination performance in the psychophysical 2AFC procedure.
3) For all frequencies the latency of LM1 in all three subjects increases when going from two steps to four steps. Additionally, increases in latency are observed in all three subjects when moving from four steps to six steps. There is no readily identifiable MMN in the eight-step or the linear condition. LM1 increases in latency follow decrease in discrimination performance in the psychophysical 2AFC procedure.

4) The mean latencies of LM2 increase as subjects must discriminate step glides with decreasing step sizes from the linear glide. LM2 increases in latency follow decrease in discrimination performance in the psychophysical 2AFC procedure. When the two latency measures are compared in terms of how closely they follow the psychophysical function, LM2 most closely approximated the psychophysical function.

5) MMNs were capable of being recorded using signals with a 8.3 msec step duration in the 1 kHz condition only. In the 2 kHz and 4 kHz condition MMNs were only able to be recorded in response to 25 and 12.5 msec step durations.
APPENDIX A

RAW DATA FOR ELECTRODE FZ
<table>
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</thead>
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<td></td>
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</tr>
<tr>
<td></td>
<td>4-Step</td>
<td>135</td>
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<tr>
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<td>113</td>
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<tr>
<td></td>
<td>8-Step</td>
<td></td>
</tr>
<tr>
<td>Latency 2 (msec)</td>
<td>2-Step</td>
<td>141</td>
</tr>
<tr>
<td></td>
<td>4-Step</td>
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Table 1: Peak-to-peak amplitude (μV) (latency 1 to latency 2), area in μV-msec and peak latency in msec (Latency 1 and Latency 2) for MMNs in response to stimuli with a center frequency of 1 kHz at electrode position FZ.
Measure at FZ | Stimuli | Center Frequency of 2 kHz
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<tr>
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</tr>
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<td>Peak-to-Peak Amplitude</td>
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<td>1.47</td>
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<td>8-Step</td>
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Table 2: Peak-to-peak amplitude (µV) (latency 1 to latency 2), area in µV-msec and peak latency in msec (Latency 1 and Latency 2) for MMNs in response to stimuli with a center frequency of 2 kHz at electrode position FZ.
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</tr>
<tr>
<td></td>
<td>8-Step</td>
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<td>Latency 2 (msec)</td>
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<td>8-Step</td>
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Table 3: Peak-to-peak amplitude (µV) (latency 1 to latency 2), area in µV-msec and peak latency in msec (Latency 1 and Latency 2) for MMNs in response to stimuli with a center frequency of 2 kHz at electrode position FZ.
APPENDIX B

RAW DATA FOR ELECTRODES F3,F4,C3,C4,CZ,PZ
<table>
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Table 4: Subject 1. Peak-to-peak amplitude (μV) (latency A to latency B), area in μV-msec and peak latency in msec (Latency 1 and Latency 2) for MMNs in response to stimuli with a center frequency of 1 kHz at additional electrode positions.
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<th>C4</th>
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<td>*</td>
<td>*</td>
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Table 5: Subject 1. Peak-to-peak amplitude (µV) (latency 1 to latency 2), area in µV-msec and peak latency in msec (Latency 1 and Latency 2) for MMNs in response to stimuli with a center frequency of 2 kHz at additional electrode positions.
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<td>Latency 2 (msec)</td>
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<td>Area (μV-msec)</td>
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Table 6: Subject 1. Peak-to-peak amplitude (μV) (latency 1 to latency 2), area in μV-msec and peak latency in msec (Latency 1 and Latency 2) for MMNs in response to stimuli with a center frequency of 4 kHz at additional electrode positions.
Table 7: Subject 2. Peak-to-peak amplitude (μV) (latency 1 to latency 2), area in μV·msec and peak latency in msec (Latency 1 and Latency 2) for MMNs in response to stimuli with a center frequency of 1 kHz at additional electrode positions.
<table>
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Table 8: Subject 2. Peak-to-peak amplitude (μV) (latency 1 to latency 2), area in μV-msec and peak latency in msec (Latency 1 and Latency 2) for MMNs in response to stimuli with a center frequency of 2 kHz at additional electrode positions.
Table 9: Subject 2. Peak-to-peak amplitude (µV) (latency 1 to latency 2), area in µV-msec and peak latency in msec (Latency 1 and Latency 2) for MMNs in response to stimuli with a center frequency of 4 kHz at additional electrode positions.
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<td>2-Step</td>
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<td>4-Step</td>
<td>.67</td>
<td>.72</td>
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<td>6-Step</td>
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<td>.68</td>
</tr>
<tr>
<td>8-Step</td>
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<td>*</td>
</tr>
<tr>
<td>Area (μV-msec)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2-Step</td>
<td>55</td>
<td>65</td>
</tr>
<tr>
<td>4-Step</td>
<td>46</td>
<td>44</td>
</tr>
<tr>
<td>6-Step</td>
<td>20</td>
<td>12</td>
</tr>
<tr>
<td>8-Step</td>
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<td>*</td>
</tr>
</tbody>
</table>

Table 10: Subject 3. Peak-to-peak amplitude (μV) (latency 1 to latency 2), area in μV-msec and peak latency in msec (Latency 1 and Latency 2) for MMNs in response to stimuli with a center frequency of 1 kHz at additional electrode positions.
Table 11: Subject 3. Peak-to-peak amplitude (μV) (latency 1 to latency 2), area in μV-msec and peak latency in msec (Latency 1 and Latency 2) for MMNs in response to stimuli with a center frequency of 2 kHz at additional electrode positions.

<table>
<thead>
<tr>
<th>Measure</th>
<th>Stimuli</th>
<th>Electrode Positions</th>
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</thead>
<tbody>
<tr>
<td></td>
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<td>F3</td>
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<tr>
<td>Latency 1 (msec)</td>
<td>2-Step</td>
<td>103</td>
</tr>
<tr>
<td></td>
<td>4-Step</td>
<td>104</td>
</tr>
<tr>
<td></td>
<td>6-Step</td>
<td>*</td>
</tr>
<tr>
<td></td>
<td>8-Step</td>
<td>*</td>
</tr>
<tr>
<td>Latency 2 (msec)</td>
<td>2-Step</td>
<td>115</td>
</tr>
<tr>
<td></td>
<td>4-Step</td>
<td>112</td>
</tr>
<tr>
<td></td>
<td>6-Step</td>
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<tr>
<td></td>
<td>8-Step</td>
<td>*</td>
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<td>Peak-to-Peak Amplitude</td>
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<td>4-Step</td>
<td>.33</td>
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<td>8-Step</td>
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<tr>
<td>Area (μV-msec)</td>
<td>2-Step</td>
<td>27</td>
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<td></td>
<td>4-Step</td>
<td>21</td>
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<td>6-Step</td>
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<tr>
<td>Measure</td>
<td>Stimuli</td>
<td>F3</td>
</tr>
<tr>
<td>--------------------------</td>
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<tr>
<td>Latency 1 (msec)</td>
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<td>4-Step</td>
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<tr>
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<td>6-Step</td>
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<td>*</td>
</tr>
<tr>
<td>Latency 2 (msec)</td>
<td>2-Step</td>
<td>115</td>
</tr>
<tr>
<td></td>
<td>4-Step</td>
<td>156</td>
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<td>4-Step</td>
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<tr>
<td></td>
<td>8-Step</td>
<td>*</td>
</tr>
<tr>
<td>Area (μV-msec)</td>
<td>2-Step</td>
<td>17</td>
</tr>
<tr>
<td></td>
<td>4-Step</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>6-Step</td>
<td>*</td>
</tr>
<tr>
<td></td>
<td>8-Step</td>
<td>*</td>
</tr>
</tbody>
</table>

Table 12: Subject 3. Peak-to-peak amplitude (μV) (latency 1 to latency 2), area in μV-msec and peak latency in msec (Latency 1 and Latency 2) for MMNs in response to stimuli with a center frequency of 4 kHz at additional electrode positions.
AN OBJECTIVE MEASURE OF TEMPORAL RESOLUTION IN NORMAL SUBJECTS USING FREQUENCY MODULATED SIGNALS

1. PURPOSE OF THE PROJECT

You have been asked to take part in a research study because you have normal hearing. The purpose of this study is to describe the characteristics of electrical responses produced by your brain when you hear two different sounds. The purpose of the study is to determine whether there is a relationship between the two types of signals and the responses recorded from the brain.

There will be a total of three persons participating in this research study at Dayton Veteran's Affairs Medical Center.

2. PROCEDURES OF THE PROJECT

You will undergo a series of simple hearing tests. For some tests we will ask you to let us know the softest loudness you can just detect beeping tones and words. Further, we will ask you to repeat back words that will be presented to one or both of your ears through earphones. In addition, skin surface electrodes will be taped to your forehead, the top, sides, and back of your head, beside and below one eye, and one to the cheek. We will ask you to sit in a comfortable reclining chair that is in our laboratory. The wires from the electrodes over your brain will then connected to a brainwave recording system. Further, we will place an additional electrode on your ear lobes. We will ask you to sit comfortably and watch TV. We will place comfortable sponge earphones in your ears. Tones will be presented through the sponge earphones. You will not be asked to respond to any of the sounds. The entire experiment should take no longer than 12 hours.

3. RISKS/DISCOMFORTS OF THE PROJECT

There will be negligible risk or discomfort to you as the subject. There is wall with a window between you and the brainwave-recording machine. The skin surface on the scalp and cheek will be prepared for surface electrode placement using a mild abrasive conductant liquid. There is an unlikely possibility that a skin abrasion might occur at those electrode sites. There are no known risks associated with any of the testing.

4. BENEFITS OF THE PROJECT

You may not be helped by this study. However, others may be helped by what is learned from this research. Specifically, it is hoped that the results of this experiment will provide the investigators with an objective measure to evaluate certain characteristics of speech that are important in understanding. The knowledge gained may better enable
professionals to evaluate those individuals who are incapable of participating in behavioral tests.

5. ALTERNATIVES TO PARTICIPATION

There are no alternative procedures that might be beneficial to you.

6. PRIVACY

Research data that include your name or other identifying information will not be published, released or seen by anyone other than an authorized representative of the Dayton Veteran's Affairs Medical Center unless you give permission in writing or unless there are legal requirements to disclose that information. If information from this study is published in a medical journal or presented at a scientific meeting, you will not be identified by name.

7. INJURY DUE TO PROJECT

If you have a medical problem as a result of being in this study, you should call Dr. Pamela Mishler at (937) 262-2149 or Devin McCaslin at (937) 262-2149. If you have a medical emergency as a result of participating in this study while at Dayton Veteran’s Affairs Medical Center, emergency treatment will be given to you. If the adverse reaction, illness, or injury occurs somewhere else, you should go to an emergency room.

There is no federal, state, or other program that will compensate you or pay for your medical care if you are injured as a part of participating in this study. You and/or your medical insurance may have to pay for your medical care if you are injured as a result of participating in this study.

8. INFORMATION ABOUT THE PROJECT

Dr. Pamela Mishler or Devin McCaslin has explained this research project and has offered to answer any questions. If you have additional questions about the research, you may contact Dr. Pamela Mishler at (937) 262-2149.

9. VOLUNTARY PARTICIPATION

Your participation in this research study is voluntary. You do not have to take part in the study, and if you decide to participate, you can stop at any time. If you decide not to participate, or if you enter the study but then later decide to stop, you will get the same medical care from Dayton Veteran’s Affairs Medical Center that you would have without consenting to take part in the study. There will be no penalties or loss of benefits to which you would otherwise be entitled if you choose not to participate or if you choose to stop your participation once you have started.
10. **STOPPING THE PROJECT**

The project director or your doctor can end your part in the research project if you are unable or unwilling to follow the instructions for each aspect of the study.

11. **COST TO THE SUBJECT**

You will not have any extra medical costs because you are in this study.

12. **PAYMENTS TO THE SUBJECT**

You will $5.00 an hour for your participation in the study.

13. **CONSENT**

This consent form has been reviewed with you. You have read this consent form or it has been read to you. All of the procedures have been explained to you. You understand what you are being asked to do. Your questions have been answered, and any technical terms you did not understand have been defined for you. You agree to be in this study. You will be given a copy of this consent form.

____________________________________
Print Name of Subject

____________________________________
Subject’s Signature  Date

____________________________________
Investigator’s Signature  Date
REFERENCES


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