

IN SEARCH OF AN ELECTROPHYSIOLOGICAL CORRELATE TO
BETWEEN-CHANNEL MODULATION GAP DETECTION

by

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DALHOUSIE UNIVERSITY
SCHOOL OF HUMAN COMMUNICATION DISORDERS

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Abstract

Auditory processing disorder (APD) is characterized by deficits in the auditory modality that are not due to a global processing problem or to deficiencies in the peripheral auditory system. Diagnosis of APD is time-consuming and could benefit from an objective test. Temporal processing ability is often impaired in cases of APD, which includes deficits on gap detection tasks. Previous attempts to correlate gap detection thresholds to electrophysiological responses have used the P1-N1-P2 response, mismatch negativity (MMN), and 40 Hz auditory steady-state response (ASSR), but these attempts have not been successful, especially using between-channel gap detection tasks. The current study used a modulation gap detection task and recorded the above responses to supra- and subthreshold gaps and stimuli with no gap. A significant P2 response and a later positive peak distinguished perception of a suprathreshold gap. Improvements over previous studies, the relation to auditory training, and limitations and directions for future research are discussed.

List Of Abbreviations Used

ADHD	Attention deficit hyperactivity disorder
AM	Amplitude modulation
APD	Auditory processing disorder
ASSR	Auditory steady state response
ERP	Event related potential
ISI	Interstimulus interval
GDT	Gap detection threshold
LD	Learning disability
MGD	Modulation gap detection
MMN	Mismatch negativity
NVLD	Nonverbal language disability
SLI	Specific language impairment
VOT	Voice onset time

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Chapter 1 Introduction

1.1 Introduction

It is well known that some individuals have deficits that affect auditory abilities but are not due to impairments within the peripheral auditory system. Normal pure-tone thresholds can accompany auditory complaints such as difficulty discriminating speech in background noise and for children, these deficits can impede language development (Sharma, Purdy & Kelly, 2009; Muluk, Yalçinkaya & Keith, 2011). Above the level of the cochlea, significant processing of auditory information occurs within the central auditory system. Deficits at this level are subtler and more diverse than pure-tone hearing loss and can include, for example, difficulty with sound localization, frequency discrimination, and with temporal processing. Auditory temporal processing refers to the ability to discriminate changes in auditory stimuli over time. Temporal processing is important for segmenting and processing speech at several levels. Distinguishing voice-onset timing cues (i.e., the difference between a voiced and unvoiced stop consonant) and determining the relative order of lexical segments (e.g., differentiating *pest* and *pets*) require encoding temporal information over short time windows (0 – 100 ms) (Hickok & Poeppel, 2007; Sharma & Dorman, 1999). Suprasegmental information is carried over the length of the syllable, and depends on temporal information occurring over a longer window (150 – 300 ms) (Hickok & Poeppel, 2007).

It has been shown that temporal processing deficits result in receptive and expressive speech impairments in children (Muluk, Yalçinkaya & Keith, 2011). Auditory temporal processing ability can be assessed behaviourally through a

number of tests, including gap detection (e.g., Gaps-in-Noise, Musiek, Shinn, Jirsa, Bamiou, Baran & Zaiden, 2005, Random Gap Detection Test, Keith, 2000a), amplitude modulation detection, or discrimination of voice-onset time in voiced and voiceless plosives (Liu & Whitesell, 2008). Assessment of these processing deficits can be difficult, especially in children, since behavioural measures require focused attention and cooperation. The purpose of this study is to investigate the usefulness of several auditory electrophysiological responses to assess temporal processing ability of the auditory system, as it relates to gap detection. In particular, the study will attempt to correlate behaviourally obtained gap detection thresholds with cortical-evoked responses to the same stimuli. This paper will review the need for an objective test of gap detection ability, followed by a detailed analysis of the evoked responses in question and previous attempts to correlate them to behavioural gap detection thresholds. Methodological considerations used in the design of the current study in order to overcome limitations of previous attempts will also be discussed.

1.2 Temporal Processing

Speech is fast-paced and rapidly changing. Speech intelligibility therefore requires that the human auditory system have high temporal resolution (i.e., the ability to detect change over time) in order to segment speech into meaningful units. Individuals with impaired temporal resolution, even if they have normal hearing, can be severely impaired in their ability to understand speech (Zeng, Oba, Garde, Sininger & Starr, 1999). Deficits in auditory temporal processing can also impede

development of expressive speech (Muluk et al., 2010). One measure of temporal resolution is gap detection. Normal conversational speech is suffused with short silent gaps which convey useful information (e.g., the distinction between voiced and unvoiced stop consonants, Lisker & Abramson, 1964); therefore, a decreased ability to detect these small gaps interferes with the ability to discriminate speech.

Gap detection thresholds can be tested using a psychophysical task. The test generally consists of presenting noise to a subject, which is then followed by a brief pause (gap) and another noise presentation. The blocks of noise on either side of the gap are referred to as “markers”. The subject is presented with random trials that either contain the gap (target stimuli) or are a continuous stream of noise (control stimuli). Gap thresholds are obtained when the gap is made progressively shorter in duration until the subject can no longer distinguish the target from the control stimulus; this gap duration is the subject’s “Gap Threshold” or “Gap Detection Threshold (GDT)”. Behaviourally determined gap detection thresholds are affected by several factors, including marker frequency (Shailer & Moore, 1983), spectral similarity of the markers (Phillips & Hall, 2000; Oxenham, 2000), marker bandwidth (Eddins, Hall & Grose, 1992), marker duration (He, Horwitz, Dubno & Mills, 1999), and monotic, diotic or dichotic presentation (Lister & Roberts, 2005).

Several gap detection paradigms have been studied. These paradigms differ in the relationship between the markers that delineate the gap. The markers may be the same or differ in terms of frequency, intensity and other factors. These paradigms have been termed within-, between-, and across-channel. Within-channel stimuli use the same marker to delineate the gap, and tend to have the smallest gap

detection thresholds (Phillips & Hall, 2000). Within-channel gap detection thresholds for normal hearing listeners have reliably been reported as short as 2 - 3 milliseconds for broadband noise markers (Phillips & Hall, 1998) and slightly longer (5 - 10 ms) for puretones or narrowband noise markers (Phillips & Smith, 2004; Lister, Maxfield & Pitt, 2007). Between-channel gap detection tasks are characterized by a gap that is bounded by stimuli that are separated in frequency, location in space, or test ear. Between-channel paradigms result in larger gap detection thresholds than within-channel tasks; thresholds for normal hearing listeners are typically in the range of 25 -100 ms, with greater intersubject variability (Grose, Hall, Buss & Hatch, 2001; Phillips & Smith, 2004; Lister, Maxfield & Pitt, 2007). Phillips and Hall (2000) relate this to the need for increased attentional resources to shift from one neural channel to another and recognize the temporal relationship between the offset of the first marker and onset of the second. Finally, for across-channel gap detection tasks, the gap is bounded by identical markers which consist of more than one spectral element (Phillips & Hall, 2000). The use of paired markers tends to decrease gap detection thresholds, which suggests the auditory system integrates information across two channels to improve temporal processing ability in this context (Hall, Grose & Joy, 1996; Phillips & Hall, 2000).

Gap detection tasks have long been used to assess temporal processing ability. However, the efficacy of such tests is contingent on the cooperation of the subject. Behavioural measures are only reliable if the subject is motivated and has focused attention. Unfortunately, this is not always the case, especially when testing

pediatric patients. Currently, there is no clinically used objective measure of gap detection ability. The usefulness of such a test would be prodigious, particularly as a diagnostic measure of auditory processing disorder (APD). Auditory processing is defined by *ASHA Technical Report on APD* as "the perceptual processing of auditory information in the CNS and the neurobiologic activity that underlies that processing and gives rise to electrophysiologic auditory potentials" (ASHA, 2005). APD affects auditory processing ability independent of other sensory modalities; this impairment is not due to a hearing loss nor to a higher level disorder of language or cognition (though it may co-exist with other conditions). APD patients have normal cochlear function and their impairment is at a level above the cochlea, within the auditory neural centres (ASHA, 2005). Some of the deficits of APD are difficulties with sound localization and lateralization, auditory discrimination, auditory temporal resolution, and dichotic listening (ASHA, 2005). These problems can cause difficulties understanding speech in background noise, understanding rapid speech, and speech sound discrimination. Children with APD often present with difficulties in reading, spelling, speech and language, attention or social functions (ASHA, 2005).

The classification of APD as a disorder strictly pertaining to the auditory modality has been controversial. The difficulty lies in separating auditory processing deficits from more global impairments, or deficits that cross modalities.

Furthermore, the validity of assuming that auditory deficits can occur in isolation is questioned. Tasks such as reading, writing, and language, which can be delayed in cases of APD, arguably required modality interaction (i.e., between visual and auditory systems). The results of Bellis, Billet & Ross (2011) indicate that children

with a diagnosis of APD are impaired on auditory processing tasks, and also show deficits on visual analogs to those tasks. The question remains whether deficits in one area affect abilities in another, or if both deficits in performance are due to a single overarching learning disability.

A great deal of research has related learning and language disorders (e.g., dyslexia, non-verbal learning disability (NVLD), specific language impairment (SLI)) to APD. There are marked similarities between groups of children with learning disorder and APD diagnoses, and there is concern that the diagnosis a child receives depends on the profession which provides it (i.e., the same symptoms are given different diagnoses by different professions). As discussed above, children with APD may have difficulties with reading, spelling, expressive and receptive language. Children with SLI also have reading, spelling, expressive and receptive language (Miller & Wagstaff, 2011). Keller, Tillery and McFadden (2006) also reported overlapping symptoms between children with NVLD and children with APD, especially with tolerance-fading memory profile (see Katz & Smith, 1991, or Bellis & Ferre, 1999, for a description of APD profiles). Pinheiro, Oliveira, Cardoso & Capellini (2010) report that children with learning disorders (LD) show deficits on tests of auditory processing, and children with APD have symptoms which reflect LD. Furthermore, Illiadou et al. (2009) report a high prevalence of APD in children referred for LD. Clearly, the distinction between learning and language disorders and APD is not distinct. But whether one is a subtype of the other, or they are merely overlapping entities requires a great deal more research.

Attention is often problematic in children who are referred for APD testing. It

has been reported that up to 84% of APD children have behaviours that are consistent with a diagnosis of Attention Deficit-Hyperactivity Disorder (AD/HD) (Geffner, 2007) and some researchers have suggested that most of the listening difficulties associated with APD may be due to attention or working memory deficits (Moore, 2011). Bellis, Billet and Ross (2011) tested normal children, children with APD, and children with ADHD on a variety of auditory processing tests and their visual analogs. Both the APD and ADHD children have significant impairments on these tests, and only close examination of particular patterns of responses were able to discriminate the two groups. Keller et al. (2006) also reported similarities between ADHD and APD children in terms auditory processing performance.

The interaction between auditory processing, learning and attention is evident from the literature. Furthermore, research suggests that APD is not a single diagnostic entity. The profiles developed by Katz and Smith (1991) and Bellis and Ferre (1999) compartmentalize the possible APD symptoms somewhat, but even within these more defined diagnostic labels, there is extensive variability between individuals. Determining the aetiologies of various APD profiles and disentangling their effects from learning and attention is a laborious task, but it is hoped that future research will be able to provide useful clues.

The criteria for APD diagnosis are not universally agreed upon, nor are the screening methods (ASHA, 2005), but typically, diagnosis of APD is done with a lengthy battery of tests and the patient must fail any two for a positive diagnosis (e.g., SCAN-C, Keith, 2000b). This is a time-consuming procedure and many of the tests are dependent on attention. Temporal acuity has been shown to be impaired in

APD patients, and, therefore, one of the psychophysical tests commonly used in the APD test battery is gap detection. Phillips, Comeau, and Andrus (2010) have reported that children with a diagnosis of APD perform significantly worse on between-channel auditory gap detection tasks compared with age-matched controls. As a behavioural measure, this has limited use because behaviourally obtained results are only reliable if the subject is motivated and has full attentional capacity. As discussed above, attention is often problematic in children with APD. An electrophysiological measure, however, would allow clinicians to test for gap detection ability (and therefore for temporal processing ability) in children with poor attentional skills or who are uncooperative. An electrophysiological correlate of gap detection would provide a useful, objective tool for APD screening.

1.3 Electrophysiology

Objective clinical tools, such as the ABR, have become a fundamental part of testing hearing abilities of difficult patients who cannot or will not respond behaviourally. So far, the stimuli used in objective clinical testing have been limited to tone bursts, clicks, and similarly simple sounds, but there has been increased interest in objective testing using more complex stimuli that may require more sophisticated auditory abilities, such as gap detection. Attempts at recording evoked potentials in response to gap detection have thus far utilized the P1-N1-P2, the mismatch negativity, and the 40-Hz auditory steady state response. Previous research in these areas will be discussed below, including analysis of their strengths and limitations.

1.3.1 P1-N1-P2

The P1-N1-P2 response consists of three peaks: a positive peak (P1), followed by a negative peak (N1), and another positive peak (P2), which occur at approximately 50, 100, and 180 ms, respectively, after onset of the auditory stimulus. P1 is likely involved in sensory gating, and the generators have been localized to the superior temporal gyrus (Key, Dove & Maguire, 2005). N1 is the easiest of the three peaks to identify, and reflects sensory detection of the physical properties of the stimulus (Näätänen & Picton, 1987). Its generators are located in the superior temporal plane, and perhaps additional areas of the frontal and temporal cortex (Key, Dove & Maguire, 2005). The last component, P2, is also related to the physical parameters of the auditory stimulus, and its generators are located in the primary and secondary auditory cortices (Key, Dove & Maguire, 2005).

Lister, Maxfield and Pitt (2007) measured P1-N1-P2 responses to within- and between-channel gap detection tasks. They first established behavioural gap detection thresholds (GDT) for each subject, and then, using these values, tested four gap duration conditions: stimuli with gaps near GDT, stimuli with subthreshold gaps, suprathreshold gaps, and a standard stimulus with a 1 ms gap (used as a control in the behavioural threshold search). The authors hypothesized that there would be a P1-N1-P2 response to the first marker in all conditions; a response to the second marker in the within-channel condition only if the gap was greater than the behavioural gap detection threshold; and that a response would occur to the second marker in the between-channel condition regardless of gap duration. Because the

preceding and succeeding markers differ in between-channel paradigms, it was expected that the activation of a new channel would produce a P1-N1-P2 response, reflecting activity in a previously silent group of neurons, not detection of a gap.

Their results supported the hypotheses. For the within-channel stimulus, P1-N1-P2 responses to the second marker were generated for the GDT and suprathreshold conditions, but not for subthreshold or control conditions. Furthermore, a larger response was observed in the suprathreshold condition than at GDT, which may have reflected a greater neural response to second marker onset following longer gap durations. The second marker in the between-channel stimulus generated a response in all conditions. The P1-N1-P2 response to the second marker was greater in the between-channel stimulus; this is to be expected, as a previously silent group of neurons are activated, compared to the re-activation of the same neurons in the within-channel design, which must necessarily undergo a refractory period. These results suggest that the response measured to the second marker in the between-channel task was not related to detection of the gap, but was instead due to activation of a novel population of neurons.

Lister, Maxfield and Pitt (2007)'s results are supportive of Michalewski, Starr, Nguyen, Kong and Zeng (2005) and Pratt, Bleich and Mittelman (2005), who also found significant correlations between measured auditory evoked potentials and behaviourally obtained gap thresholds for a within-channel stimulus. Therefore, it has been well established that within-channel gap detection tasks can be measured objectively in individuals. However, this does not extend to between-channel tasks, which may be the more informative task. Arguably, between-channel tasks are much

more relevant to real-life listening demands, as the phonemes bounding gaps in speech tend not to be identical. For example, Elangovan and Stuart (2008) examined the relationship between within- and between-channel gap detection thresholds and the categorical perception of stop consonants. They found a significant correlation between between-channel gap detection thresholds and voice-onset time (VOT) phonetic boundaries (i.e., the categorical perception of voiced and voiceless stop consonants). This correlation did not extend to within-channel gap detection tasks. Likewise, across-channel gap detection tasks may also bear more relevance to real-life listening demands, as they reflect temporal coincidence – i.e., important sounds (e.g., harmonics of speech) tend to coincide, while unimportant sound (e.g., background noise) tend to be less temporally related. Furthermore, the results of Phillips, Comeau and Andrus (2010), which support gap detection as a means of differentiating APD children from non-APD children, found a significant outcome for the between-channel condition only. Phillips and Smith (2004) tested subjects on two within-channel tasks and a between-channel task and measured the correlation between outcomes. They found a stronger correlation between the within-channel tasks than between the within- and between-channel results. Therefore, it seems there are two different mechanisms at work when detecting gaps between like and different markers, and ability with one type of stimulus does not relate to ability with the other. Testing within-channel paradigms does not give insight into the subject's ability to detect gaps between unlike markers, which may be more relevant to measuring temporal processing abilities that are relevant to real-life situations (e.g., speech perception).

Within-channel paradigms have been studied extensively, but more research is needed with between-channel stimuli in order to determine their clinical utility. There is an inherent mismatch between measuring P1-N1-P2 responses to between-channel tasks and behavioural performance. The P1-N1-P2 response to the second marker is larger if there is a change in frequency compared to the first marker. This is intuitive. A new frequency channel means a new population of neurons is activated; therefore there is less interference from refractoriness. Conversely, if the frequencies of the two markers are identical, there is a small P1-N1-P2 response to the second marker – which is due to the neurons being in refractory. If the P1-N1-P2 response were a meaningful cue to gap detection, it would be expected that increasing frequency separation would increase behavioural performance. However, in within-channel gap detection tasks, the gap is bordered by identical frequency markers and this type of task reliably produces the lowest thresholds and is described by subjects as the least difficult (Phillips & Hall, 2000). Between-channel gap detection tasks have higher thresholds and are subjectively described as more difficult than within-channel gap detection (Phillips & Hall, 2000), yet the P1-N1-P2 onset response suggests that there is a stronger cue to perception of the second marker onset (i.e., onset response to new energy, regardless of gap duration). Additionally, frequency separation of the two markers in between-channel gap detection tasks is inversely correlated with performance; greater separation results in higher thresholds (Grose et al., 2000). But this is not what is reflected in behavioural scores. The separation of frequency between the two markers does not aid gap detection and the P1-N1-P2 response does not indicate perception of a gap.

Therefore, P1-N1-P2 responses to the lagging marker in between-channel gap detection tasks do not provide an electrophysiological correlate to behaviourally determined gap detection thresholds, at least not in the paradigm that was used by Lister and her colleagues.

A potential explanation for the incompatible results from P1-N1-P2 responses and behavioural thresholds was proposed by Phillips and Hall (2000) and involves attentional resources. Phillips and Hall (2000) examined five gap detection conditions: between-channel, within-channel, two across-channel conditions with either a simultaneous or roving gap, and a simultaneously-gated noiseband. They found that between-channel tasks had the highest thresholds (worst performance). This task involves individually presented frequency-separated markers on either side of the gap, and would presumably have a strong onset response to both markers. There were no significant differences between within-channel, simultaneously-gated noiseband, or the stimuli with continuous distracter. Phillips and Hall propose that the elevation of threshold in the between-channel task is due to allocation of attentional resources. In order to successfully detect the gap, the subject must make a comparison between the offset of the first marker and the onset of the second marker, and make a judgment about their temporal relationship. A between-channel task requires activation of a new set of neurons after the gap, and thus requires a neural attention shift. Phillips and Hall (2000) propose that once attentional resources have been allocated to detection of the offset of the first marker, there is a certain amount of "dwell time" before these resources can be redirected to detection of the second marker onset. This necessitates that the

duration of the gap be longer than the "dwell time". When the markers are in the same channel, this attentional shift is not required, and thus gap thresholds can be significantly lower in within-channel tasks. The circumstances that require a large shift in attention are the same circumstances that produce a large P1-N1-P2 response in Lister et al.'s study.

1.3.2 Mismatch Negativity

Other studies have attempted to use the mismatch negativity response as an electrophysiological correlate of gap detection. The mismatch negativity (MMN) is a negative component with a peak latency of around 100-200 ms (Näätänen & Escera, 2000). It often overlaps with the N1 component of the slow auditory ERP, though methods can be employed to separate the two responses, and they have been shown to have different generators. A more anterior source has been located for the MMN, compared to N1, on the superior surface of the temporal lobe (Sams, Kaukoranta, Hämäläinen & Näätänen, 1991) with contributions from the frontal cortex (Rinne, Alho, Ilmoniemi, Virtanen & Näätänen, 2000).

The typical method for measuring MMN uses the "oddball paradigm". This entails presentation of a frequent *standard stimulus* and a less frequent *deviant stimulus*, which are perceptibly different stimuli. The difference can be in any number of characteristics including frequency, intensity, duration, learned constructs such as phonemes, and almost any other discriminable deviation. Typically, the ERP waveform generated by the standard stimulus is subtracted from that of the larger deviant response, providing a *deviant-standard difference*

waveform.

The memory-trace explanation of the oddball-paradigm, proposed by Näätänen (1992), contends that the standard stimuli are retained in auditory memory and used as a reference for succeeding stimuli; if a difference is perceived, an automatic neural response is generated – the MMN (Näätänen & Escera, 2000; Bishop & Hardiman, 2010). An alternative explanation, presented by Winkler (2007), suggests that the MMN is reliant on predictive models in the brain, which encode sensory information to generate predictions about likely auditory occurrences; the MMN is elicited when reality deviates from neural predictions.

There are many benefits to the MMN response as an auditory electrophysiological measure: MMN is easy and inexpensive; it can be elicited without active attention, which is particularly helpful for obtaining results from difficult groups; it develops early (can be elicited in newborns, though with less reliability [Cone-Wesson & Wunderlich, 2003; Trainor, Samuel, Desjardins & Sonnadara, 2001]); and the location and functional significance of its generators have been relatively well studied (Näätänen & Escera, 2000). The applications for MMN are numerous and diverse, including such varied fields as autism, alcoholism, Parkinson's, depression, hypnosis, and many others (see Näätänen & Escera, 2000, for an exhaustive list).

However, there are some limitations to the MMN. Firstly, there is disagreement about the independence of the MMN response from attention; some authors report attention increases the response, so that is more reliable and easier to obtain when the subject is paying attention (e.g., Paavilainen, Alho, Reinikainen,

Sams, & Näätänen, 1991). This, of course, does not preclude the usefulness of measuring the MMN in the absence of attention, but only serves to add an additional variable to be aware of during the measurement procedure.

Secondly, the MMN is difficult to measure reliably in individuals. Because it is a small response that requires a lot of averaging to rise above the background noise, the majority of studies using the MMN have used group averages. However, Bishop and Hardiman (2010) demonstrated that the MMN can be measured in individuals with some reliability. They used a novel method of analysis and a frequency discrimination task with normal adult listeners. Their results showed an 82% hit rate and 12% false positives. Though this paradigm did not completely differentiate discrimination of the stimulus from non-discrimination, it is encouraging evidence that MMN may be used to *suggest* auditory dysfunction. With particular regard to assessment and diagnosis of APD, the current procedure requires a battery of behavioural tests, none of which can fully diagnose APD independently. Therefore, an objective test that can offer only a strong indication of abnormality can be as useful as current behavioural tests, and significantly more desirable for its objectivity. Therefore, Bishop and Hardiman's results support the possibility of MMN for practical clinical use as a screener for auditory dysfunction, or as part of a larger battery of tests.

The mismatch negativity response has previously been correlated to temporal acuity in the auditory system. Desjardins, Trainor, Hevenor and Polak (1999) used MMN to measure gap detection thresholds. They examined 4, 5, and 7 ms gaps in within-channel gap detection tasks. MMN responses were significant for stimuli

with gap durations of 5 and 7 ms, but for only a part of the waveform in response to the 4 ms gap stimulus (Desjardins et al., 1999). This study did not obtain behavioural thresholds for comparison, but cited previous literature for a comparison of typical gap thresholds and found them to be similar to the obtained MMN results.

Uther, Jansen, Huotilainen, Ilmoniemi, and Näätänen (2003) found similar results. They presented a within-channel gap detection task to subjects with three gap lengths (3, 5, and 7 ms) and measured both MMN responses and behavioural detection responses. They reported that the MMN amplitude increased with gap length, which correlated well with the behavioural response. One incongruity is that the MMN response to a gap length of 3 ms was not significant, even though the subjects still had a high, though significantly different, hit-rate at this gap length (88-93% hit rate for 3 ms, versus 95-97% hit rate for 5 and 7 ms) (Uther et al, 2003). Therefore, from these results, one must question whether the MMN response is capable of “predicting” the subject’s ability to detect the gap. The limitation of this study is that the data were averaged across the subjects. The authors did not do a threshold search for each individual, which may have provided a better correlate for the MMN response.

There have also been a few studies examining the MMN response to between-channel tasks. Heinrich, Alain and Schneider (2004) and Takegata, Heikkila and Näätänen (2009) both recorded MMN response to both within-channel and between-channel gap detection tasks. The results of Heinrich, Alain and Schneider (2004) did not demonstrate a significant difference in amplitude or latency of the

MMN response when comparing within- and between-channel stimuli, even though the behavioural thresholds were substantially different. Takegata, Heikkila and Näätänen (2009) posit that the 1000 and 2000 Hz markers used by Heinrich, Alain and Schneider were not spectrally different enough to elicit a difference in the MMN response.

In their study, Takegata, Heikkila and Näätänen (2009) queried whether perceptual discontinuity is an important element for preattentive gap detection, and hypothesized that increased discontinuity would be associated with increased MMN amplitude and latency. To test this hypothesis, the authors used two between-channel tasks with markers that spectrally overlapped, but one stimulus was slightly discontinuous while the other was widely discontinuous. Behavioural results demonstrated an increase in GDT associated with perceptual discontinuity – i.e., the smallest GDT occurred in response to within-channel stimuli, followed by the slightly discontinuous between-channel stimuli and the largest GDT were in response to widely discontinuous between-channel stimuli. The results show a decrease in amplitude for both between-channel stimuli, compared to the within-channel stimuli, and a delay in latency for the widely discontinuous stimulus only. Takegata, Heikkila and Näätänen's results demonstrated that 1) MMN can be recorded to between-channel stimuli, 2) detection of a between-channel gap occurs preattentively, and 3) as perceptual discontinuity increases, there is an increased disruption to the MMN response.

Mismatch negativity responses have also been recorded in children in response to a gap detection task (Trainor et al., 2001). Trainor et al. (2001) used a

within-channel gap detection task, and obtained reliable threshold responses in 6-month-old children. Furthermore, they found that the thresholds obtained were similar to adults (~4ms), as measured in previous studies (Desjardins et al., 1999), contrary to behavioural tests of gap detection, in which infants performed significantly worse than adults (Werner & Marean, 1992; Trehub, Schneider & Henderson, 1995). The obvious explanation for the discrepancy is the need for focused attention and motivation to obtain reliable behavioural measures. These findings once again exemplify the need for an objective method to reliably test temporal processing abilities in children and infants.

1.3.3 40 Hz Auditory Steady State Response

In contrast to transient evoked responses, which are short responses that occur immediately following a stimulus and reoccur with repeating stimuli (within an appropriate time course that exceeds the refractory period), steady state responses follow a repeated stimulus over a longer time window and are monitored for slow changes in amplitude and phase. Auditory steady state responses (ASSR) are often elicited in response to Gaussian tone pulses, repeating series of clicks, or amplitude-modulated tones (Ross, Herdman & Pantev, 2005).

ASSR can be elicited using stimuli presented at a rate of 1-200 Hz, but 40 Hz is a particularly strong response (Galambos, Makeig & Talmachoff, 1981). Galambos et al.'s pioneering research suggested the 40 Hz ASSR was a composite response made up of many overlapping ABR wave V and MLR wave contributions; this has been supported by convolution studies (Bohórquez & Özdamar, 2008). Source analysis

(Herdman, Lins, van Roon, Stapells, Scherg & Picton, 2002) and hemodynamic studies (Reyes, Salvi, Burkard, Coad, Wack, Galantowicz & Lockwood, 2004) have suggested a cortical site of activation -- likely the primary auditory cortex (Rademacher, Morosan, Schormann, Schleider, Werner, Freund & Zilles, 2001; Ross, Herdman & Pantev, 2005; Ross, 2008; Picton, 2011). The 40 Hz ASSR is reduced but not eliminated by sleep (Lins & Picton, 1995; Picton, John, Purcell & Plourde, 2003) and passive listening (Ross, Picton, Herdman, Hillyard & Pantev, 2004), and dramatically attenuated by anesthesia (Plourde & Picton, 1990).

The 40 Hz ASSR has been studied less in response to gap detection tasks than the previously discussed evoked potentials, but it has been observed that changes occur in the 40 Hz response reflecting perceptual detection of an auditory event. Makeig and Galambos (1989, as cited in Ross & Pantev, 2004) noted a decrease in ASSR amplitude following the omission of a single click in a train (analogous to a gap detection task), as well as a deviation in the ASSR phase response. Similarly, Ross and colleagues have noted a reduction in ASSR amplitude and a phase lag in response to silent gaps bounding amplitude-modulated tone-bursts (Ross & Pantev, 2004), changes in inter-aural phase (Ross, 2008), and introduction of a concurrent stimulus (Ross, Herdman & Pantev, 2005). The results of these various studies suggest that there is a generalized response to perception of a change in the auditory signal. Ross and colleagues suggest the synchronized oscillations of the ASSR establish a network configuration in response to a repetitive auditory stimulus. When the stimulus changes, in any of a number of features, the system must rest and a new network configuration is established. Much like the oddball-

paradigm used in MMN, there must be a repeated stimulus in order to establish a configuration in order for a change to be recognized and represented in the evoked response.

Ross and colleagues have established that a desynchronization (which is demonstrated by a decrease in amplitude and, more reliably, phase delay) occurs in response to a number of different changes in stimulus – i.e., change in IPD, periodicity, and introduction of an interfering stimulus. More importantly, the desynchronization of the ASSR is related to *perception* of the stimulus change (e.g., an increase in carrier frequency in the IPD study diminishes and then eliminates the ASSR change response, paralleling behavioural performance). Therefore, it is reasonable to suppose that a similar desynchronization will occur with the current gap detection paradigm, and, furthermore, will reflect perception of the gap and denote gap detection thresholds in the individual subjects.

1.4 Modulation Gap Detection

Previous studies have primarily utilized a within-channel paradigm, and there has been limited success with between-channel paradigms (e.g., Lister, Maxfield & Pitt, 2007). As previously discussed, within-channel tasks do not mimic important real-life listening demands and performance on within-channel gap detection tasks do not differentiate APD and non-APD children effectively (Phillips, Comeau & Andrus, 2010). Thus, between-channel tasks are more clinically relevant. The inherent problem with between-channel gap detection tasks is the lack of spectral continuity, because it is difficult to separate responses that relate to detection of the

gap from responses that relate only to the onset of a previously inactive neural channel. This has been the primary limitation in many of the previous attempts at correlating behavioural gap detection thresholds to evoked potentials; therefore, a novel approach is necessary.

Modulation gap detection (MGD) has been a less used paradigm that offers some advantages over traditional gap detection tasks. The stimulus used in MGD tasks is an amplitude-modulated noiseband or pure tone. Therefore, it is characterized by both a carrier frequency and a modulation frequency. In lieu of a silent gap, subjects are required to detect a brief period in the stimulus that is unmodulated. Therefore, the carrier frequency is continuous, and the gap is in the modulation only.

Grose, Hall and Buss (1999) used MGD to assess the ability of the auditory system to make use of spectral continuity to aid wideband temporal analysis. Grose, Hall and Buss capitalized on the spectral characteristics of MGD by developing a between-channel stimulus which maintained activity in both channels. Two noisebands were presented synchronously (i.e., as in an across-channel paradigm) but the amplitude modulation “jumped” from one channel before the gap to the other channel after the gap. This characterizes a between-channel task, in the sense that the need to make a temporal judgment between the offset of the modulation in one channel and the onset of modulation in the second channel remains, but as both carrier frequencies are continuously active (i.e., as in a within-channel paradigm), an onset response to the second marker isn’t expected. The key difference between traditional gap detection stimuli and MGD stimuli is that the gap is in the

modulation, while the sound itself is continuous.

Grose, Hall and Buss (1999) used MGD to test whether spectral continuity is sufficient to facilitate wideband temporal analysis of stimuli which transverse frequency. They concluded that it was not – between channel stimuli in an MGD task resulted in poorer performance than isofrequency stimuli. Nevertheless, for the purpose of the current study, MGD will be useful to reduce the effects of onset/offset response that were problematic for Lister and colleagues. Furthermore, between-channel paradigms exploit the already poor ability of the auditory system to make temporal judgments about stimuli that transverse frequency. An additional advantage of the MGD stimulus is that the use of a modulation frequency overlapping the carrier frequencies allows measurement of the ASSR.

1.5 Current study and research questions

The current study will re-examine the efforts of previous researchers and attempt a new method of correlating behavioural gap detection thresholds with objective electrophysiological measurements. In order to maximize the likelihood of finding an evoked potential correlate to behavioural gap detection thresholds, three responses were examined – P1-N1-P2, mismatch negativity, and 40 Hz ASSR amplitude and phase response. The stimuli for the current experiment consisted of a two simultaneous and continuous channels overlaid with a 40 Hz modulation frequency.

We measured P1-N1-P2 onset responses to the leading and trailing (post-gap) markers. The first marker is characterized by the onset of energy, as well as the

onset in modulation, for which a strong onset response is expected and unremarkable. Activity following the second marker is more informative, but previous studies on between-channel gap detection tasks have been confounded by the activation of a novel population of neurons that occurs with the onset of the second marker. The continuity of the two channels in the current stimulus should reduce onset responses to the second marker, except as it relates to the onset of post-gap modulation. Because the onset of modulation is not associated with recruitment of a new population of neurons, as a new frequency channel would be, if there is a difference in the post-gap P1-N1-P2 response between gap conditions, it is more likely to be related to temporal characteristics associated with the gap itself.

In order to obtain a mismatch negativity response, we will present the gap and no-gap stimuli in blocks that create a standard or deviant, and each gap condition will have the opportunity to be the standard. Attempts using MMN to assess perception of a within-channel gap have been the most successful and reliable (e.g., Desjardins et al., 1999; Uther et al., 2003), while two studies using between-channel stimuli have had dissimilar results (i.e., Heinrich, Alain & Schneider, 2004; Takegata, Heikkila & Näätänen, 2009). The MMN is a useful objective tool, as it relates solely to discrimination of a difference. The current stimulus is complicated by multiple aspects (i.e., modulation frequency, carrier frequency), which may create a complicated pattern of responses for the P1-N2-P2 and 40 Hz ASSR. The MMN, however, is a simple response to complex stimuli and should be measurable as long as the subjects can psychophysically tell that the stimuli are different.

We opted to use a modulation frequency of 40 Hz, as this is the optimal rate to

measure the auditory steady-state response. The currently studied paradigm has not been used in conjunction with steady-state responses previously, but Grose, Hall and Buss (1999)'s amplitude modulated gap stimulus is perfectly suited to measurement of the ASSR. Furthermore, the research of Ross and colleagues, which has repeatedly reported a comparable effect on the 40 Hz ASSR using several different stimuli, is supportive of a generalized response to auditory change.

The hypotheses for the current study are as follows. For the P1-N1-P2 response, there will be a strong onset response to the first marker in all conditions. But, because the tones are continuous, response to the second marker should relate more to restart of modulation after the gap (i.e., detection of the gap). Therefore, there will be a stronger P1-N1-P2 response to suprathreshold conditions. For the mismatch negativity, three discriminations will be queried: *No Gap* versus *Sub Gap*, *No Gap* versus *Supra Gap*, and *Sub Gap* versus *Supra Gap*. It is hypothesized that a MMN will occur in response to the latter two discriminations, but *No Gap* and *Sub Gap* will be indiscriminable, and therefore will not produce a MMN. Finally, for the 40 Hz ASSR response, we predict that detection of the gap in modulation frequency (i.e., the suprathreshold) will result in a phase lag and amplitude decrease (similar to the Ross et al. studies), but no change in 40 Hz amplitude or phase will occur in response to the subthreshold or no gap conditions.

Chapter 2 Methods

2.1 Participants

Ten normal hearing right-handed adult participants (six female) were recruited from within the university. Each subject underwent audiometric screening to ensure normal thresholds (i.e, 25dB or less at 500, 1000, 2000 and 4000 Hz). Ethics approval for this study was obtained from the Dalhousie University Health Sciences Human Research Ethics Board for research involving human subjects.

2.2 Stimulus

The stimulus used in this study was modeled after the stimulus used by Grose, Hall and Buss (1999). The stimulus consists of two continuously and concurrently presented tones. An amplitude modulation frequency of 40 Hz (100% modulation depth) begins in one channel, and midway through the stimulus, switches to the second channel. Therefore, the modulation occurs in only one channel at any given time. When the modulation switches channel, there may be a brief period when neither channel is modulated – i.e., a gap in the modulation. This is the *Gap condition*. In some conditions, there is no gap; i.e., the modulation ends in channel one at the same instance that modulation begins in channel two. This is the *No Gap condition*.

Two gap detection paradigms were included in this study: within-channel and between-channel. In the within-channel condition, both channels consisted of a 2 kHz tone – therefore, the markers before and after the gap were exactly the same

(i.e., 2 kHz tone with 40 Hz AM). Additionally, there were two across-channel stimuli, which consisted of a 500 Hz tone and a 2 kHz tone presented concurrently. In the .5/2 kHz stimulus, the modulation began in the 500 Hz channel (while 2 kHz was unmodulated), and then, midway through the stimulus, the modulation jumps to the 2 kHz channel (while 500 Hz becomes unmodulated). The reverse is true in the 2/.5 kHz stimulus (i.e., modulation begins in the 2 kHz channel and jumps to the 500 Hz channel). It is important to note that in all three stimuli, the “gap” is in the modulation frequency only, and the tones themselves are continuous.

The levels of the modulated segments were manipulated to prevent intensity cues. The results of Moore, Vickers, Baer and Launer (1999) indicate that equal loudness occurs when the modulated and unmodulated segments of a stimulus have equal RMS energy. This was accomplished by scaling the modulated segment according to the scaling equation reported by Grose, Hall and Buss (1999) -- $1/\sqrt{(1+m^2)/2}$, where m is the modulation index ($m = 1$ in the present case). The modulation was ramped up and down by a 10 msec \cos^2 ramp in order to ensure a smooth transition between modulated and unmodulated segments of the stimulus (i.e., to eliminate clicks). The experimenters confirmed that there were no audible clicks in the stimulus and that the perceived loudness did not change throughout the stimulus. The VU meter of the audiometer (which was used to route the signals) visually confirmed that the energy in the signal did change during the transition between the gap and the modulated segments. See Figure 1 for an example image of the stimulus.

In order to reduce overall duration cues, five different marker lengths bounded the gap – 312.75, 412.75, 512.75, 612.75, and 712.75 ms. Depending on the length of the gap, the longest and shortest overall durations were excluded, so that stimuli with a gap could not be more than 25 ms longer than stimuli without a gap. Therefore, overall length of stimulus was an unreliable cue to presence or absence of a gap. The length of the leading and lagging markers varied randomly on each trial, within the above restrictions.

The inter-stimulus interval (ISI) varied randomly from 1 to 2 seconds. This ISI was sufficient to prevent overlap between the response to the offset of one stimulus and the response to the onset of the next.

The stimuli were presented at an overall level of 80 dB SPL through insert earphones.

2.3 Procedure

2.3.1 Behavioural

The first phase of the task was to determine the individual behavioural thresholds of the participants. The stimuli were presented binaurally via Etymotic ER-3 type insert earphones. Each participant was given instructions and an opportunity to practice with feedback, until they felt comfortable with the task. The task was presented as a computer program, programmed in LabVIEW (National Instruments). The screen displayed three buttons, corresponding to the presented stimuli, and a graph, displaying gap length on the y-axis and trial on the x-axis. When the correct stimulus was chosen, the gap length remained the same or decreased

(after three correct choices); this was visually displayed, so the participants had immediate feedback. When the incorrect stimulus was chosen, the gap length increased; again, this was displayed on the graph for immediate feedback. The stimuli were presented in a three-alternative forced-choice paradigm, with one *Gap* stimulus and two *No-Gap* controls in each trial. The task began with a gap duration of 512 ms. We employed a 3-down, 1-up adaptive stepping rule; i.e., after three correct choices at one level, the duration of the gap decreased to the next smallest interval, and if they chose incorrectly, gap duration increased to the previous level. A threshold search was performed twice for each stimulus type (i.e., 2/2kHz, .5/2kHz, 2/.5kHz). To determine threshold, the arithmetic mean of the last five reversals was calculated, and then the arithmetic mean of the result of the two runs. Subthreshold gaps were determined at 50% less than each individuals' thresholds, and suprathreshold gaps were determined at 50% above each individuals' threshold. This should clearly separate a perceivable versus imperceivable gap.

However, the step sizes of the gap durations decreased by a percentage amount, not by a fixed amount. Therefore, the geometric mean should have been calculated for the five reversals, followed by an arithmetic mean of the two runs. Calculating the thresholds in this way resulted in similar final results that fell well within the +/- 50% criteria for sub- and suprathreshold gaps. For the within-channel stimuli, the average difference between the original and corrected thresholds was 8.89% (range: 0.84-29.04%). For the between-channel stimuli, the average difference was 4.35% (range: 0.68-8.92%). Therefore, the correct thresholds were still within the +/- 50% cutoffs for every participant.

2.3.2 Evoked potentials

In the second phase, the participant watched a close-captioned movie of their choice in a sound-proof booth while the stimuli were presented binaurally via Etymotic ER-3 type insert earphones and evoked potentials were recorded. In this phase, there were only two gap duration options: a gap duration 50% above their threshold (*Suprathreshold*), and one at 50% below their threshold (*Subthreshold*). These two durations were selected to clearly separate detection of the gap. A stimulus without a gap in the modulation (*No Gap*) was included as a control.

The subjects were optically isolated as the stimuli were presented and electrophysiologic responses were recorded using a 128-electrode Biosemi cap and eight off-cap electrodes (TP 9/10, FT 9/10, F 9/10, one EOG electrode on the right infraorbital ridge, and one on the right outer canthi). Responses were acquired using a Biosemi Active Two multichannel biopotential system at a sampling rate of 2048 Hz. The system used active amplification of the responses at the electrodes, a 5th-order lowpass filter set to 1/5th of the sampling rate, and no high-pass filtering. Electrode offsets were maintained below 25 kOhm. The responses were digitized on a computer along with digital triggers which indicated stimulus timing (i.e., of the onset of the first marker and the second marker) and stimulus type (explained below). The stimulus and digital triggers were presented from a National Instruments PXI System. The sounds were generated by a 24-bit Dynamic Signal Acquisition card (PXI 4461) and the digital triggers were generated by a National Instruments M-series PXI card. The two cards were synchronized across the back plane of the PXI system. An oscilloscope was used to confirm that the triggers

occurred at the sound onset with a sub-millisecond precision, but no correction was made for the .9 ms latency introduced by the insert earphones.

The fifty-four triggers coded indicated whether the sound was the beginning of the first marker or the second marker; the type of gap condition (No Gap, Sub-Gap, Supra-Gap); frequency condition (2/2, .5/2, 2/.5); and the conditions were also coded separately depending on which gap condition was the standard in that particular block; i.e., 2 marker choices x 3 freq choices x 3 gap conditions x 3 standard choices.

We analyzed the following responses: mismatch negativity (MMN), P1-N1-P2 onset response, and 40 Hz ASSR phase and amplitude. To this end, presentation of the stimuli was organized to allow for occurrence of a mismatch response, while retaining enough trials for an adequate signal-to-noise ratio (see Table 1). By controlling the presentation of the target and foil conditions in each block, a “deviant” stimulus was created, which can generate a MMN response. The standard stimulus was presented on a randomized 80% of trials, while each of the two deviants were presented randomly on 10% of the trials, with the following constraint: one of each deviant occurred within each set of ten trials. Also, the same deviant stimulus was never presented more than once in any set of three trials (i.e., there were always at least two intervening stimuli between each deviant). The deviant and standard stimuli changed across blocks, so that each participant had the opportunity to respond to each gap choice presented as both a standard and deviant. E.g., For Block 1 (as presented in Table 1), *No Gap* is the standard stimulus, while *Sub* and *Supra* are the deviants.

We measured the P1-N1-P2 response to the onset of the leading marker and the onset of the lagging marker in each stimulus, coded separately for each frequency.

The 40 Hz ASSR was obtained using a Fourier analyzer coded in MATLAB (see Aiken & Picton, 2006) with a 40 Hz reference frequency and a 300 ms time window). The complex magnitude and phase angles of the response were obtained from the complex response.

2.4 Analysis

We estimated the cortical sources of the scalp activity using brain electrical source analysis (BESA) software from Megis Software GmbH. Source waveforms were used for further analysis. After recording, the data were decimated by a ratio of $\frac{1}{4}$ to a new sampling rate of 512 Hz. The data were visually inspected in BESA for bad channels, and noisy channels were interpolated or removed, as appropriate. An average reference was used for all subsequent analysis.

2.4.1 P1-N1-P2 response

For the purpose of analyzing P1-N1-P2 onset responses, the data were averaged over the epoch -100 to 1000 ms, bandpass filtered from 1-15 Hz, and artifact rejection was set to 100 μ V.

For the source analysis, the raw files were averaged across all participants, irrespective of frequency/gap paradigm. The data was analysed in the time window of 0 – 250 ms post-stimulus onset. Individual source models were initially calculated

for each gap and frequency condition, as well as to a grand average of all conditions, however. Two sources accounting for eye movements were clearer in the individual condition averages than in the grand average, because noise associated with eye movements tended to cancel-out more on the grand average, resulting in a more posterior location (i.e., behind the eyes) with higher residual variance. The ocular sources did not vary between conditions, so the two sources at the eyes were fixed based on a single condition average, and then two more symmetrical dipoles were fit based on the grand average of all onsets. These dipoles were placed at the location in the brain which could provide the best forward model of the grand average response recorded at all electrodes on the scalp, using an iterative algorithm to minimize residual variance between the model and the recorded response. The optimal sources localized to the vicinity of the auditory cortex. Source locations remained fixed across participants, but dipole orientations were allowed to vary for each participant's data, as there tends to be more individual variation in the anatomy that determines orientation (i.e., folds of gyri and sulci) than gross location. The average dipole source waveforms (both hemispheres) were then sent to MATLAB for analyses.

2.4.2 Mismatch Negativity

For the purpose of analyzing MMN responses, the data were measured over the epoch -100 to 1000 ms, bandpass filtered from 1-15 Hz, and artifact rejection was set to 100 μ V. As described above, the blocks were organized such that the one gap condition was presented on 80% of trials, and therefore constituted a

“standard” stimulus. The other two gap conditions were each presented on 10% of trials, and therefore are considered “deviant” stimuli.

There were three discriminations queried: 1) discrimination between *No Gap* and *Supra*, 2) discrimination between *No Gap* and *Sub*, and 3) discrimination between *Sub* and *Supra*. To this end, standard and deviant averages were created, and the MMN was calculated as the difference between the response to the deviant and the response to the standard. For each discrimination, the difference was calculated between responses to the same stimuli (to minimize differences in the N1-P2 response that could contaminate the MMN); the only difference was whether the stimuli had been standard or deviant during that block. For example, for the first discrimination (i.e., *No Gap* and *Supra*), the standard average consisted of all *No Gap* responses when the *No Gap* was standard and all *Supra* responses when *Supra* was standard. The deviant average consisted all the *No Gap* responses when *Supra* was standard, and all the *Supra* response when *No Gap* was standard. For the second discrimination (i.e., *No Gap* and *Sub*), the standard average consisted of all *No Gap* response when the *No Gap* was standard and all the *Sub* responses when *Sub* was standard. The deviant average consisted of all *No Gap* responses when *Sub* was standard and all *Sub* responses when *No Gap* was standard. For the final discrimination (i.e., *Sub* and *Supra*), the standard average consisted of all *Sub* response when *Sub* was standard and all *Supra* responses when *Supra* was standard. The deviant average consisted of all *Sub* responses when *Supra* was standard and all *Supra* responses when *Sub* was standard. A source model was attempted using the post-gap difference responses, but the MMN data were too noisy to find reliable

sources. In fact, the grand average onset model (described above) fit the MMN data better than the post-gap model (i.e., had the least residual variance). The average dipole source waveforms (both hemispheres) for the difference waves were therefore based on the all-onset source model.

2.4.3 40 Hz Auditory Steady State Response

The amplitude and phase response of the 40 Hz ASSR were examined. In order to determine sources of the 40 Hz response, the averaged data were first filtered from 20-40 Hz. Responses were averaged over an epoch of -100 to 1000 ms and artifact rejection was set to 50 μ V. Decimated data was not used for this analysis, because a (decimated) sampling rate of 512 Hz would be too low to properly represent the frequency characteristics of the 40 Hz responses. Visual inspection of the decimated data confirmed this by indicating response peak at 39 Hz, which would be highly unlikely with a stimulation rate of 40 Hz. In the non-decimated data (i.e., sampling rate of 2048 Hz), the response clearly peaked at 40 Hz.

Sources were fit twice. First, the sources were fit to the grand average within-channel post-gap response. Two symmetrical sources were fit and localized to approximately auditory cortex. Two more symmetrical sources were fit and localized to the eye region. The latter two sources were kept in place, and the first two re-fit. They moved slightly more anterior than the original source dipole positions. Second, the sources were found using the grand average of all between-channel post-gap conditions (all three gap conditions), in the same procedure as

above. The resulting sources were remarkably similar to those of the grand average onset model (as described in the previous section), and the two models had equivalent residual variance. The between-channel source model was therefore chosen for the analysis, and used to fit each individual subjects data. Dipole orientations were fit individually, as with P1-N1-P2 and MMN source analysis.

Source waveforms for each participant were sent to MATLAB and analyzed for the following factors: gap condition (*No Gap, Sub, Supra*), gap paradigm (within- or between-channel), hemisphere (left or right), dipole orientation at each source location (vertical, radial, horizontal) and time (50 and 250 ms). Visual inspection of the resultant waveforms suggested a possible latency factor; i.e., the three conditions appeared to be differentiated around 50 ms and again around 250 ms post-stimulus onset. Therefore, two time points were analyzed; the response was averaged over 200 ms, centered on 50 ms (i.e, -50 to 150 ms) and 250 ms (i.e., 150-350 ms).

For each data set, all of the 2/2kHz leading marker onsets were averaged together, and the lagging marker onsets were averaged separately for each condition (*No Gap, Sub, Supra*). The same was done for .5/2 kHz and 2/.5 kHz, except both between-channel data sets were collapsed together, to form one average between-channel condition. Therefore, for the 40 Hz phase and amplitude analysis, there were the following averages: Within-Onset, Within-No Gap, Within-Sub, Within-Supra, Between-Onset, Between-No Gap, Between-Sub, and Between-Supra.

2.5 Statistical analysis

2.5.1 P1-N1-P2

P1-N1-P2 data were analyzed over the time window for P1 (0-100 ms), N1 (70-150 ms), and P2 (150-250 ms), using a bootstrapping approach to determine the 95% confidence intervals for each response (based on 1000 random samples of the recorded data with replacement). The confidence intervals were used to determine whether the differences were significant. The following comparisons were made: 1) *No Gap* versus *Sub+Supra*, 2) *No Gap+Sub* versus *Supra*, 3) *No Gap* versus *Supra*, 4) *No Gap* versus *Sub*, and 5) *Sub* versus *Supra*. Additionally, visual inspection of the waveforms revealed a late positive peak which appeared to vary between conditions; therefore, analyses in the window of 300-400 ms were included as well.

2.5.2 Mismatch Negativity

MMN data were analyzed over the time window 100 – 250 ms post-stimulus onset using the same bootstrapping method in order to compare the 95% confidence intervals for the standard and deviant waveforms in each condition. A significant MMN was deemed to have occurred only when the confidence intervals did not overlap in the 100-250 ms time window.

2.5.3 40 Hz Auditory Steady State Response

Phase and amplitude of the 40 Hz ASSR were analyzed over the time window of 0 – 300 ms post-stimulus onset. The three gap durations and two paradigms were

analyzed separately. The results of the vertical dipole for the right and left hemisphere responses were graphed to visualize changes in amplitude and phase over time.

Chapter 3 Results

3.1 Behavioural Gap Detection Thresholds

The within-channel condition (2/2 kHz) resulted in the lowest thresholds for all participants, though there was large variability ($x = 39.6$ ms, $SD = 40.6$ ms). Similar to the within-channel task, there was high variability in performance for the .5/2 kHz ($x = 219.1$ ms, $SD = 73.8$ ms) and 2/.5 kHz between-channel tasks ($x = 233.8$ ms, $SD = 115.1$ ms). Both between-channel stimuli resulted in longer gap detection thresholds than the within-channel task. Participants' behavioural threshold scores and group mean and standard deviations are listed in Table 2.

3.2 P1-N1-P2

A clear P1-N1-P2 onset response was observed in response to the leading marker in all conditions. Figures 2 – 5 depict the analysis of the P1-N1-P2 responses using the bootstrapping method. The top two graphs in each figure plot the amplitude versus latency of the P1-N1-P2 response of the two conditions being compared. The bottom graph in each figure plots all the mean difference between the two conditions with respect to the amplitude and latency of the peak occurring within the selected time window, along with confidence intervals. The comparison can be considered significant if the confidence intervals do not include zero (i.e., cross the zero-axis). When the confidence intervals include zero, the null hypothesis (that there are no differences between the conditions with respect to that peak) cannot be rejected with an error rate below 5%.

Peak analysis of the post-gap P1-N1-P2 response to the three gap conditions revealed a significant difference in the amplitude of N1 (Figures 2 and 3) and P2 (Figures 4 and 5). Latency did not differ significantly for either N1 or P2. Amplitude and latency of the P1 peak did not differ significantly across gap conditions.

The N1 response was significantly larger (i.e., more negative) for the *Sub* condition ($x = -4.3$ nAm) compared to the *No Gap* ($x = -7.9$ nAm) (Figure 2) or the *Supra* ($x = -7.4$ nAm) (Figure 3) conditions. There were no significant differences in amplitude between the *No Gap* and *Supra* conditions. Latency did not differ significantly between any of the conditions.

The P2 response was significantly smaller in response to the *Supra* (mean = 5.2 nAm) condition compared to the *No Gap* (mean = 8.2 nAm) (Figure 4) and *Sub* (mean = 7.4 nAm) (Figure 5) conditions, though the latter two groups did not differ from each other. It is also noteworthy that the latency of the P2 peak varied dramatically in the *Supra* group compared to *No Gap* and *Sub*.

A later time window (i.e., 300-400 ms) was also analyzed for peak differences. Most subjects had a positive peak around 360 ms in the *No Gap* and *Sub* conditions, but not in the *Supra* condition (Figure 6).

3.3 Mismatch Negativity

The three MMN discriminations queried were 1) discrimination between *No Gap* and *Supra*, 2) discrimination between *No Gap* and *Sub*, and 3) discrimination between *Sub* and *Supra*. The waveforms were compared within the time window of

MMN, 100-250 ms post stimulus onset. None of the mismatch comparisons reached significance.

3.4 40 Hz Auditory Steady State Response

3.4.1 Amplitude

Within-subject repeated measures ANOVAs revealed significant main effects for dipole orientation ($F = 12.486$, $p < .01$), gap condition ($F = 4.100$, $p < .05$), and time window (50 or 250 ms) ($F = 5.129$, $p = .05$). The most important of these results relates to gap condition. There was a significant difference between the *Sub* ($x = 1.335$ nAm) and *Supra* ($x = 1.548$ nAm) conditions, but comparisons involving *No Gap* ($x = 1.254$ nAm) did not reach significance. However, there was a significant trend associated with gap duration; the amplitude of the 40 Hz response increased as the length of the gap increased.

There was a significant interaction between gap condition and gap detection paradigm (between-channel or within-channel) (Figure 7). For the within-channel paradigm, the amplitude of the 40 Hz response was clearly larger for the *Supra* gap condition ($x = 1.640$ nAm), while *Sub* ($x = 1.073$ nAm) and *No Gap* ($x = 1.264$ nAm) resulted in similar amplitudes. Conversely, the between-channel paradigm did not result in as large a separation between the three gap conditions (*No Gap*, $x = 1.243$ nAm; *Sub*, $x = 1.596$ nAm; *Supra*, $x = 1.457$ nAm).

The time window was an important factor as well. Visual inspection of the waveforms revealed a change in response characteristics around 250 ms post-stimulus onset, compared with the earlier time window. The response at these two

time points differed significantly. Additionally, there were significant interactions between time and gap condition ($F = 14.140$, $p < .01$) (Figure 8), and time and paradigm (i.e., between-channel or within-channel) ($F = 24.257$, $p < .01$). Analysis of the 40 Hz amplitude response at 50 ms revealed a significant difference between *No Gap* ($x = 1.094$ nAm) and *Supra* ($x = 1.575$ nAm). Like the overall analysis, the response to the *Supra* condition was the largest, but unlike the overall analysis, *Sub* ($x = 0.927$ nAm) was the smallest, though not significantly different from *No Gap*. Analysis of the 40 Hz amplitude response at 250 ms revealed an overall significant main effect of gap condition, but individual pairwise comparisons did not reach significance. A different trend was observed at this time point: the largest response was in response to *Sub* ($x = 1.743$ nAm), followed by *Supra* ($x = 1.522$ nAm) then *No Gap* ($x = 1.413$ nAm).

3.4.2 Phase

Within-subjects repeated measures ANOVAs revealed significant main effects of gap condition ($F = 9.000$, $p < .05$) and dipole orientation ($F = 13.719$, $p < .01$). The response to *No Gap* ($x = -13.298$ deg) had a smaller phase shift than *Sub* ($x = -114.225$ deg) and *Supra* ($x = -76.977$ deg). The phase shifts in response to *Sub* and *Supra* gap conditions did not differ significantly.

Chapter 4 Discussion

4.1 Behavioural Gap Detection Thresholds

Like previous studies (e.g., Grose, Hall & Buss, 1999; Phillips & Hall, 2000; Lister, Maxfield & Pitt, 2007; Grose et al., 2001), within-channel gap detection thresholds were substantially smaller than between-channel thresholds (compare within-channel mean threshold of 39.6 ms to between-channel mean threshold of 226.5 ms). These scores are significantly larger than previously reported for within- and between-channel gap detection thresholds (e.g., Lister, Maxfield & Pitt, 2007; Phillips & Hall, 2000); this is likely related to the complexity of the MGD stimulus. Grose, Hall and Buss (1999) used a between-channel paradigm with a modulation frequency of 8 Hz, and found gap detection thresholds as low as 50 ms, but also reported that some participants were unable to detect the gap using the longest duration measured (250 ms). The larger gap thresholds and greater intersubject variability reported by Grose, Hall and Buss (1999) is in concordance with the current results. It is interesting to note that for the two between-channel conditions, there was not a consistent pattern in performance. Half of the participants performed better with the .5/2 kHz between-channel stimulus compared to the 2/.5 kHz between-channel stimulus, while two participants showed the reverse pattern and the remaining three participants performed equally well on both tasks. Stimuli were presented in a pseudorandom order, and there was no correlation between pattern of thresholds and which stimulus was presented first. Therefore, the difference in performance suggests that there may be different strategies being used

when the modulated channel changes from a lower to higher frequency compared to the reverse, and there is individual variation in the employment of these strategies. It would be interesting to examine the auditory evoked potentials for differences related to the type of pattern a participant utilized; i.e., compare the .5/2 kHz condition to the 2/.5 kHz with preference as a dependent variable. However, responses were always recorded to stimuli that were a fixed percentage above and below gap threshold, so differences in behavioral performance should have been controlled for.

Average thresholds for MGD are not well established; larger studies with normal hearing listeners and controlled circumstances are needed to establish norms. A number of factors likely affect modulation GDTs. It is clear from the current results that, like conventional gap detection tasks, between-channel stimuli result in larger modulation gap thresholds. Furthermore, Grose, Hall and Buss (1999) showed a marked increase in GDTs as modulation frequency increased. The phase relationship between the modulation frequency preceding and following the gap is also an important determinant of gap detection performance (Sek & Moore, 2002).

4.2 Evoked Potentials

The hypotheses for this study were that 1) there would be a strong onset response to all leading markers; 2) there would be a stronger P1-N1-P2 response to the suprathreshold post-gap marker; 3) there would be MMN when comparing suprathreshold responses to either of the other two conditions, but not when

comparing the Sub condition with the No-Gap conditions; 4) and that the suprathreshold post-gap marker would result in an amplitude decrease and phase lag of the 40 Hz ASSR. The first hypothesis was supported by the data; though this is an unremarkable finding, as it has been well established in the literature. The latter three hypotheses were not supported by the data, though some potentially meaningful responses did occur.

The purpose of the evoked potential part of this study was to find a correlation between objective electrophysiological responses and behavioural threshold – i.e., to find a response which occurred in the suprathreshold condition but not the subthreshold or no gap conditions. This will be the focus of the following discussion.

The current results report significant differences between gap conditions for N1 and P2 only. Lister et al. (2007) reported significant differences for P1 and N1, though Michalewski et al. (2005) and Heinrich, Alain and Schneider (2004) also found that N1 and P2 differentiated the gap conditions in their respective studies. N1 and P2 have a stronger commonality; they have similar sources that aren't necessarily distinct (Knight, Scabini, Woods & Clayworth, 1988; Zouridakis, Simos & Papanicolaou, 1998) and they are both related to perception of a change in acoustic characteristics (Key, Dove & Maguire, 2005). It is therefore intuitive that there would be a correlation between the N1 and P2 responses, and that they may relate to perception of an acoustic change. Though N1 and P2 response were both significant in the current study, they did not demonstrate the same trend as Michalewski et al. (2005) and Heinrich, Alain and Schneider (2004).

The P2 response was the more informative response. Michaelewski et al. (2005) reported a P2 amplitude increase in response to a gap, using a traditional (i.e., not modulation gap detection) within-channel paradigm, wherein the gap was bounded by continuous broadband noise. The current study also reports a significant difference in P2 amplitude between gap conditions. However, contrary to the results of Michaelewski et al., P2 was significantly *smaller* for the suprathreshold condition than for the subthreshold and no gap conditions, not larger as was hypothesized. In order to detect the gap in the current stimulus, the participants were required to compare the timing of the offset of modulation (i.e., the first marker) to the onset of modulation (i.e., the second marker). As the participants have not had previous experience with this kind of stimulus, this could be considered a form of novel pattern analysis – i.e., learning to detect a new cross-frequency pattern. Intuitively, one would expect that the gap would be the object of detection in this learned cross-frequency pattern, but the current results show a larger P2 response for the subthreshold gap and no gap conditions. It is possible that the learned task is actually to detect the offset of the first marker and the onset of the second marker, without a gap, as a single continuous event.

The learning of novel acoustic patterns and discriminations has been studied in conjunction with the P1-N1-P2 response. Studies by Tremblay and colleagues (e.g., Tremblay, Kraus, McGee, Pontin and Otis, 2001; Tremblay, Shahin, Picton & Ross, 2009) examined changes in N1-P2 complex relating to learning a novel auditory discrimination – i.e., differentiation of a prevoiced bilabial stop (/mba/) from a voiced bilabial stop (/ba/) by native English speakers. The prevoiced /mba/

is not a phonemic combination which occurs in English, and so the participants required training to distinguish it from the more common /ba/. Tremblay et al. (2001) reported increases in N1-P2 complex following training to discriminate /mba/ (-10 ms VOT) from /ba/ (-20 ms VOT). Prior to training, there were no significant differences in the N1-P2 response between -10 ms VOT and -20 ms VOT. The increase in the N1-P2 amplitude was associated with increased performance (i.e., learning the novel discrimination is associated with a measurable change in the N1-P2 complex). Furthermore, Tremblay et al. (2009) showed that some learners demonstrated a strong pre-training N1 response, and these individuals showed greater gains in perceptual performance. This further established that the N1 response relates to auditory training and may even predict ability to improve behavioural performance.

Like Tremblay et al. (2001) the current study required participants to learn a novel discrimination related to timing between events occurring in different frequency bands: a pair of modulated tones with and without a gap in the modulation. Participants subjectively described the task as initially difficult, and expressed confusion about what the target discrimination was -- i.e., the majority of participants expressed that they could not initially perceive a difference between the stimuli with or without a gap, even with long (512 ms) gap durations. However, with practice, they quickly learned the discrimination, and all participants were able to obtain gap detection thresholds of significantly less than the starting point of 512 ms. Though the "training" session was neither formal nor extensive, the task was definitely novel to all participants initially, and previous literature has

demonstrated that formal training is not necessary to demonstrate a change in the P2 response (i.e., exposure to the stimulus accounts for some of the changes observed following training) (Sheehan, McArthur & Bishop, 2005), though training will likely effect a larger increase to P2 amplitude (Tremblay et al., 2009). For each participant in Tremblay et al. (2001)'s study, a change in the N1-P2 complex was noted before increases in behavioural performance were observed. This suggests, therefore, that the participants in the current study may have undergone a change in the N1-P2 complex over the course of their participation in the behavioural phase of the study.

In the study by Tremblay et al. (2001), the learned discrimination was reflected in the response to both stimuli – after training, there were still no significant differences between them, because both responses amplitudes had increased. The current study had no baseline to comment on whether the amplitude of the N1-P2 complex changed over the course of the study, but, after the discrimination was learned, there was a difference between the *No Gap/Sub* conditions and the *Supra* condition. It can be supposed that a learning effect occurred but applied to only one of the stimuli in the discrimination. Alternatively, learning effects may have occurred for all stimuli, but it may have been more pronounced for the *No Gap/Sub* condition; this could have been due to the number of repetitions (i.e., if sub and no gap are indiscriminable, then there are twice as many trials of “no gap” than “gap”). A difference related to exposure effects between “no gap” and “gap” stimuli seems particularly likely given the results of Sheenan, McArthur and Bishop (2005) – i.e., that some effects of training are due solely to

stimulus exposure. Furthermore, the degree of change in N1-P2 amplitude may be important and vary across individuals (Tremblay et al., 2009). In order to further analyze the effects of training and experience on the P1-N1-P2 response to between-channel modulation gap detection stimuli, it is necessary to have a baseline measure and objectively measure changes in the P1-N1-P2 complex before, during and after discrimination training.

Another element of auditory training is the time course over which training and neurophysiological changes occur. Several studies (Karni & Bertini, 1997; Alain, Campeanu & Tremblay, 2010; Tremblay et al., 2001) have compared the results of fast perceptual learning (occurring within the first hour post-training) to slow perceptual learning (occurring over days following training). Increases in the N1-P2 complex have been reported to both fast and slow perceptual training (Alain, Campeanu & Tremblay, 2010), though greater changes are observed with more extensive training (Tremblay et al., 2001). The current study potentially incorporates elements of fast perceptual training, as did the pioneering study by Grose, Hall and Buss (1999). The effects of slow perceptual training on MGD have yet to be examined.

Though these results are very preliminary, they encourage further investigation into the potential benefit to auditory processing disorder assessment and treatment. If the P2 response is a reliable indicator of detection of a gap, using a between-channel paradigm, it would be extremely useful as an objective tool to test for APD. Furthermore, if temporal patterns can be learned and a measurable change in the P2 response recorded, it could be used as a validation tool in APD therapy.

Future research direction should verify these results with a larger population of participants and more stringent control of training and experience with the stimuli (including baseline measurements). Furthermore, in order to have clinical utility, this response needs to be measurable in an individual. The research by Tremblay and colleagues into the effect of phonemic discrimination training on the P1-N1-P2 response has thus far not been encouraging for individual measurement (Kraus, McGee, Carroll, King, Tremblay & Nicol, 1995; Tremblay, Kraus, Carroll & McGee, 1997; Tremblay, Kraus & McGee, 1998).

In the current study, N1 did not differentiate the suprathreshold gap from the subthreshold and no gap conditions. The subthreshold condition resulted in the largest N1 amplitude with no significant differences between suprathreshold and no gap conditions. It is difficult to explain why the subthreshold condition would result in a larger amplitude, and that the suprathreshold and no gap conditions did not differ significantly from each other. It is possible that this is an accidental finding (i.e., a Type I error), and is not actually meaningful. However, stimulus characteristics may be an important criterion to eliciting changes in the N1 response. Alain, Snyder, He and Reinke (2007) reported changes in both the P2 and N1 in response to a vowel discrimination task. However, a later study (Alain, Campeanu & Tremblay, 2010), in which the task was to differentiate timing cues, no significant changes in the N1 response were observed. The two studies used similar procedures and the authors queried whether the type of stimulus (i.e., speech versus non-speech) was the source of the discrepancy in the N1 response. If so, the current study has a greater commonality with Alain, Campeanu and Tremblay

(2010) (i.e., non-speech, involving timing cues) and a change in N1 would not be expected.

The other significant result that showed promise in discriminating gap detection was the amplitude of the 40 Hz auditory steady state response. The 40 Hz ASSR amplitude increased with gap duration; i.e., the suprathreshold gaps resulted in the largest amplitude, followed by subthreshold gaps and finally, no gap (though the latter two were not significantly different from each other). The studies by Bernard Ross and colleagues (Ross, 2008; Ross & Pantev, 2004; Ross, Herdman & Pantev, 2005) consistently reported a desynchronization in the 40 Hz ASSR in response to a number of different perceptible acoustic changes. However, this desynchronization has presented as a *decrease* in 40 Hz ASSR amplitude. Like the P2 response discussed above, the current results stand in apparent contradiction to previous research. But also like the P2 response, the current results can be coalesced with Ross et al.'s findings if the opposing view is taken – i.e, that there is a decrease in 40 Hz ASSR amplitude in response to no gap (or subthreshold gap), rather than an increase in amplitude in response to the gap.

Phase shift of the 40 Hz ASSR did not distinguish suprathreshold gaps from the subthreshold and no gap conditions. Phase lag has been reported as a more reliable indicator of 40 Hz reset (Ross, 2008), but this was not observed in the current study.

There was a significant interaction between gap paradigm (within- or between-channel) and gap conditions. When the two types of paradigms are analyzed separately, the pattern of an amplitude increase in response to *Supra*

persists in the within-channel paradigm, but not for between-channel stimuli. There is no significant difference between any of the three gap conditions when the between-channel paradigm is analyzed independently. This suggests that, like many previous studies, the 40 Hz ASSR is able to differentiate gap detection in within-channel paradigms but is not successful when a between-channel paradigm is used. As discussed extensively in the introduction, the utility of within-channel gap detection tasks is limited. The current study was designed to be exploratory, using a comprehensive approach to analyze many different responses. A more focused approach to further investigate the potential of the 40 Hz ASSR using a between-channel paradigm is necessary.

Previous research has established that MMN can be reliably recorded in response to gap detection tasks. However, there were no significant findings involving the MMN in the current study. Previous studies have focused on within-channel gap detection tasks, with simple markers of noisebands or pure tones, though Takegata, Heikkila and Näätänen (2009) reported MMN response to between-channel gap detection tasks. MMN responses have not previously been recorded in response to MGD tasks, and the current MGD paradigm was apparently not effective for measuring MMN. The MMN is a small response which requires a lot of averaging to separate it from background noise. Additional participants or more trials may have resulted in a mismatch response. Furthermore, Tremblay, Kraus and McGee (1998) reported an increase in the MMN associated with learning the discrimination between /mba/ and /ba/. The current study involved a short practice period before the behavioural threshold search, which could be construed

as “training”. If a formal training period were extended, it may have a learning effect on the mismatch response, which may result in a measurable response. Conversely, McGee, King, Tremblay, Nicol, Cunningham and Kraus (2001) queried whether the MMN response remains stable over a testing period or if habituation to the stimulus occurs. Their results suggest that habituation of the MMN response can occur after as little as 11 minutes of testing – which confounds the popularly held belief that many stimulus samples increases the signal-to-noise ratio of the MMN response. The current testing occurred over a two-hour period. More focused research on the MMN over different time courses is needed to find an optimal MMN procedure for modulation gap detection.

The last potentially meaningful response observed was a positive peak that occurred at around 360 ms post-stimulus onset for subthreshold and no gap conditions. It occurred in the window of the P300 response, but as the participants were not actively paying attention to the stimulus and it is unlikely that anything about the stimulus would grab their attention, it is unlikely that this peak is related to the P300. This positive peak was not observed in response to the suprathreshold gap condition. Like the P2 response discussed above, there was a noticeable response to the *absence* of a gap. Though it is difficult to say what this positive peak relates to, it is a second opportunity to observe this interesting trend. Alain et al. (2007) reported a similar pattern (i.e., an enhancement which may relate to the P2 response, ~130 msec, and an enhancement in a later time window, ~340 msec) in response to a speech-sound differentiation task. In these studies that the enhancement only occurred when active training occurred (i.e., passive listening

was not sufficient), and the changes persevered only if practice continued. Other studies (Alain & Snyder, 2008; Ben-David, Campeanu, Tremblay & Alain, 2011) have reported a similar late wave positivity in response to learning acoustic patterns with active attention. The current study did not incorporate a stringent training program, but the behavioural threshold search required active participation in the task and this session preceded the evoked potential phase of the study. It can be reasoned that the AEPs recorded reflected changes that occurred over both the active and passive listening sessions. Furthermore, Carcagno and Plack (2011) also reported an increased positivity in a similar time window, and the participants in their study were *not* paying active attention to the stimulus; like the participants in the current study, they listened passively while watching a close-captioned movie. Therefore, there are now two instances of this late positivity associated with learning a novel acoustic pattern and passive listening, as well as several with active participation (Alain et al., 2007; Alain & Snyder, 2008; Ben-David, Campeanu, Tremblay & Alain, 2011).

As discussed in the introduction, the aetiology of APD is not clear, but the interaction between APD, learning and attention is apparent. The current results do not offer evidence towards an underlying effect of learning, attention or strictly auditory processing. However, the relationship to other research on training and learning auditory patterns is intriguing. If auditory learning, or more general learning abilities, are required to discriminate between a continuous and non-continuous stimuli, deficits in this ability would be detrimental to between-channel gap detection, as is observed in cases of APD. The within-channel task did not

demonstrate the same relationship to the results of Tremblay and colleagues; it is unclear if and how learning plays a role in these tasks, but the underlying demands on this task are clearly different than those of between-channel gap detection paradigms.

Attention is also implicated in APD and as a requirement for detection of a gap in a between-channel paradigm. Phillips and Hall (2000) have posited that detection of a between channel gap is limited by attentional resources. Between-channel GDTs are higher because of the shift in attention required to detect the offset of the leading gap and the onset of the lagging gap. Within-channel tasks are easier, and require less demand on attention; therefore, these tasks are preserved, but a higher demand on attentive capabilities demonstrates performance deficits. Reduced attentional capabilities would, presumably, also have detrimental effects on between-channel gap detection.

4.3 Limitations & Potential Conflicts

The benefit of the modulation gap stimulus is the spectral continuity of the carrier frequencies. This, in theory, would limit the onset response to the second marker. But, the salient features of sensory input are related to change – in this case, a constant carrier frequency persists for a period and then amplitude modulation begins. The change in amplitude would likely evoke some response from auditory neurons. It is hoped that the response to the modulation onset is smaller than the full onset. Furthermore, the results support that the P1 response can differentiate the subthreshold from the suprathreshold gap; some of the response is likely related

to the onset of modulation, but nevertheless, there is a measurably different response to the two durations of gaps.

Another potential confound in this experiment relates to the duration of the gaps. There was a great deal of variability between the individual participants, and the gap durations tested were dependent on each participants' individual gap threshold. Consequently, the test stimuli for each participant during the evoked responses phase of the study differed in terms of gap duration. This could have had effects on the responses measured, especially in terms of latency and the interaction between responses to offset (i.e., of the first marker) and onset (i.e., of the second marker). It is a difficult confound to address; to test consistent gap durations would be confounded by individual skill at gap detection. It is well established that individual gap detection ability varies, especially for between-channel stimuli (Grose, Hall & Buss, 1999). The purpose of the study was to correlate evoked responses to psychoacoustic gap thresholds, and for this purpose, it was necessary to have individually determined thresholds. An alternative approach, which would allow discrimination of perceivable versus imperceivable gaps while controlling for the durations across individuals, would be to test a series of discrete gap durations for all individuals, and analyze the results using psychoacoustic thresholds as a dependent variable. The downside of this approach is the increased time required, as many gap durations would must be tested to account for the broad range of psychoacoustic thresholds obtained.

The concern related to individualized gap durations is that there is overlap between the offset of the first marker and onset of the second marker, which would

differ across different gap durations. It is unclear to what extent the offset response will interfere with the subsequent onset. Including a control stimulus with no second marker would allow measurement of the offset response in isolation.

Another significant limitation is the lack of individual measurement. Though it is recognized that this is a very important element to developing a clinical test, at the current stage in the investigation of an evoked potential correlate to between-channel gap detection, the focus must start with group measurements, in order to find a promising direction for future research.

4.3 Summary & Conclusion

Several responses were found to potentially relate to the detection of a suprathreshold gap, compared to a subthreshold gap or the absence of a gap. These include the P2 peak of the P1-N1-P2 complex; changes in amplitude of the 40 Hz auditory steady state response; and a positive peak which occurred in the time window of 300-400 ms post-stimulus onset. The presence of these three characteristics (i.e., a stronger P2, larger 40 Hz ASSR amplitude, or a positive peak ~360 ms) related to the *detection of a non-gap*, while the absence of these characteristics was correlated with the presence of a suprathreshold gap. It is proposed that detection of the offset of modulation in the first marker and onset of modulation in the second marker as a continuous, unified event is the response trigger. This may be considered a type of novel pattern analysis, and may be associated with learning effects. The effects of training and stimulus exposure may offer an explanation as to why greater P2 amplitudes were observed for the *No Gap*

and *Sub* conditions. If these two conditions are indiscriminable, then they received twice the stimulus exposure than the *Supra* condition, and therefore, a greater learning effect.

The current study was designed to use a novel gap detection paradigm (i.e., based on the stimulus developed by Grose, Hall & Buss, 1999) to address limitations of many previous attempts to correlate gap detection to objective electrophysiological measures. As such, it was intended to be a “catch-all” – examining several responses to determine promising directions for future research. Consequently, though there are some encouraging results, they are not conclusive. Further research is needed to focus on each of the responses discussed here. In particular, the P2 response requires more stringent controls regarding the effects of learning and training. The current results suggest that P2 may be useful in determining detection of a gap in amplitude modulation. However, previous literature on auditory training (e.g., Tremblay, Kraus & McGee, 1998; Tremblay et al., 2001; Tremblay et al., 2009) illustrate that training and stimulus exposure play an important role in changes to evoked potential responses, and controlling for these factors is necessary in order to focus on the differential response to a gap versus a continuous stimulus. Baseline measures, individual response changes, and controlled training periods (for comparison of fast versus slow perceptual learning) are important elements that should be incorporated into future studies. Furthermore, a limitation of the current study is the small sample size; investigation with a greater number of participants would be more illuminating.

In order to have clinical utility, an objective response to gap detection must be measurable in the individual. This is a desirable end-goal, but first a reliable correlate that can be repeated in groups needs to be established. The P2 response and the 40 Hz ASSR are promising avenues for future research.

Furthermore, to be used clinically, we must be able to determine if the response is “normal” or “abnormal”. The stimulus used in the current study has been relatively unstudied (aside from the pioneering study by Grose, Hall & Buss, 1999). The behavioural thresholds obtained were higher for both within- and between-channel conditions compared to conventional gap detection stimuli (i.e., gaps bounded by pure tones or noisebands). Though the current gap thresholds are not largely different from those reported by Grose, Hall and Buss (1999), it is unclear if they are representative of normal hearing individuals. Factors that affect MGD thresholds include the phase relationship of the modulation before and after the gap (Sek & Moore, 2002) and frequency of modulation (Grose, Hall & Buss, 1999). Likely, the factors which affect conventional between-channel tasks (i.e., marker length and bandwidth, spectral similarity of markers, etc.) will also affect MGD thresholds. A study with a larger sample population of normal hearing listeners is required to determine gap detection norms for this type of stimulus and the factors that affect performance.

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Appendix A Tables & Figures

Table 1				
<i>Organization of stimuli presentation for mismatch negativity recording</i>				
Frequency	Block	Standard (160)	Deviant (20)	Deviant (20)
2/2 kHz	1	No Gap	Sub	Supra
	2	Sub	No Gap	Supra
	3	Supra	Sub	No Gap
2/.5 kHz	4	No Gap	Sub	Supra
	5	Sub	No Gap	Supra
	6	Supra	Sub	No Gap
.5/2 kHz	7	No Gap	Sub	Supra
	8	Sub	No Gap	Supra
	9	Supra	Sub	No Gap

Table 1. Nine blocks of the stimulus were presented (3 each of 2/2 kHz, 2/.5 kHz, .5/2 kHz). Within each block, one of the three gap conditions was *standard* (presented on 160/200 trials) and the other two conditions were *deviant* (presented on 20/200 trials each). Each gap condition was the standard once and the deviant twice for each type of stimulus.

Table 2									
<i>Behavioural thresholds and order of stimulus presentation for individual participants</i>									
Participant	2/2 kHz (ms)	.5/2 kHz (ms)	2/.5 kHz (ms)	Presentation Order					
				1	2	3	4	5	6
1	13.8	93.7	95.5	.5/2	2/2	2/.5	2/2	.5/2	2/.5
2	93.9	262.5	307.6	.5/2	2/.5	2/.5	2/2	.5/2	2/2
3	16.9	164.4	206.4	2/.5	.5/2	2/.5	2.2	2/2	.5/2
4	21.6	183.2	287.7	2/.5	2/2	.5/2	.5/2	2/2	2/.5
5	133.5	355.4	352.5	2/2	.5/2	.5/2	2/.5	2/2	2/.5
6	13.9	205.2	199.4	2/2	2/.5	2/2	.5/2	2/.5	.5/2
7	20.1	246.3	66.3	2/2	2/.5	2/2	.5/2	2/.5	.5/2
8	31.5	227.5	425.2	2/.5	2/.5	.5/2	.5/2	2/2	2/2
9	19.6	165.7	263.8	2/.5	.5/2	2/2	.5/2	2/2	2/.5
10	31.4	287.2	133.4	.5/2	2/2	2/.5	2/2	2/.5	.5/2
Mean	39.6	219.1	233.8						
Standard Deviation	40.6	73.8	115.1						

Table 2. Behaviourally determined gap detection thresholds for each participant and stimulus. Participants shaded in grey had similar .5/2 kHz and 2/.5 kHz thresholds (+/- 5 ms). Participants shaded in grey with diagonal lines performed significantly better in the 2/.5 kHz condition, compared to .5/2 kHz. The remaining participants performed significantly better in the .5/2 kHz condition, compared to 2/.5 kHz. All participants performed better in the within-channel task. Each stimulus was presented in two runs, in a random order. Presentation order did not correlate with performance.

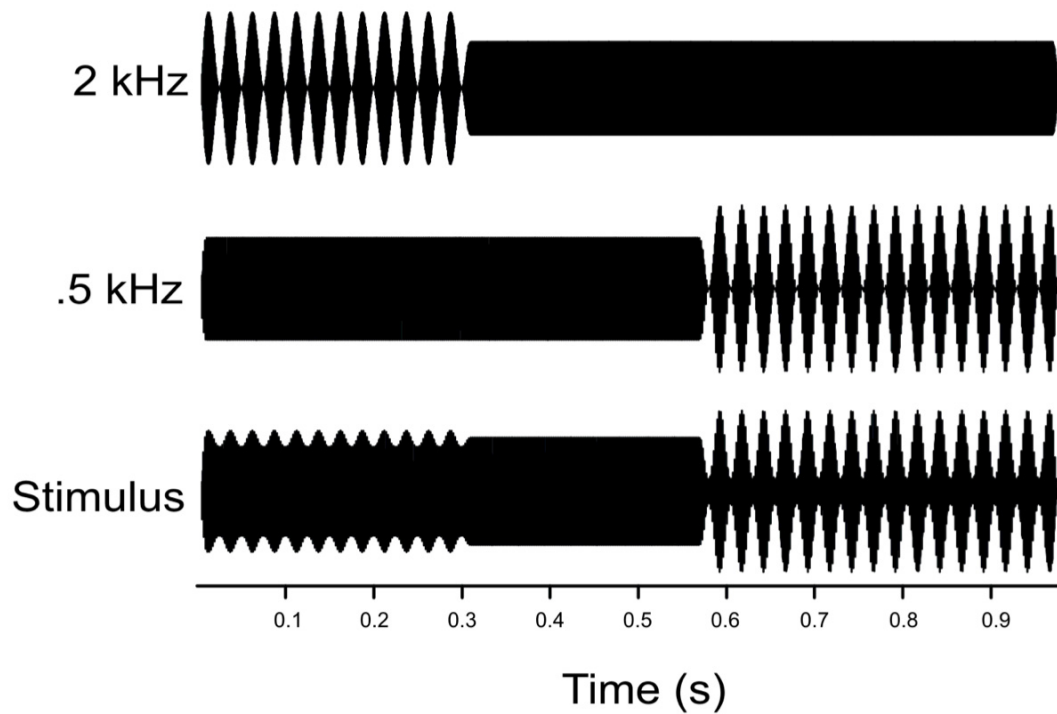


Figure 1. Example of the between-channel modulation stimulus with a gap. Two channels (2 and .5 kHz) are presented concurrently; the modulation frequency (40 Hz) “jumps” from one channel before the gap to the other channel after the gap. In no-gap stimuli, the modulation switches channel halfway through the stimulus with no pause between offset and onset.

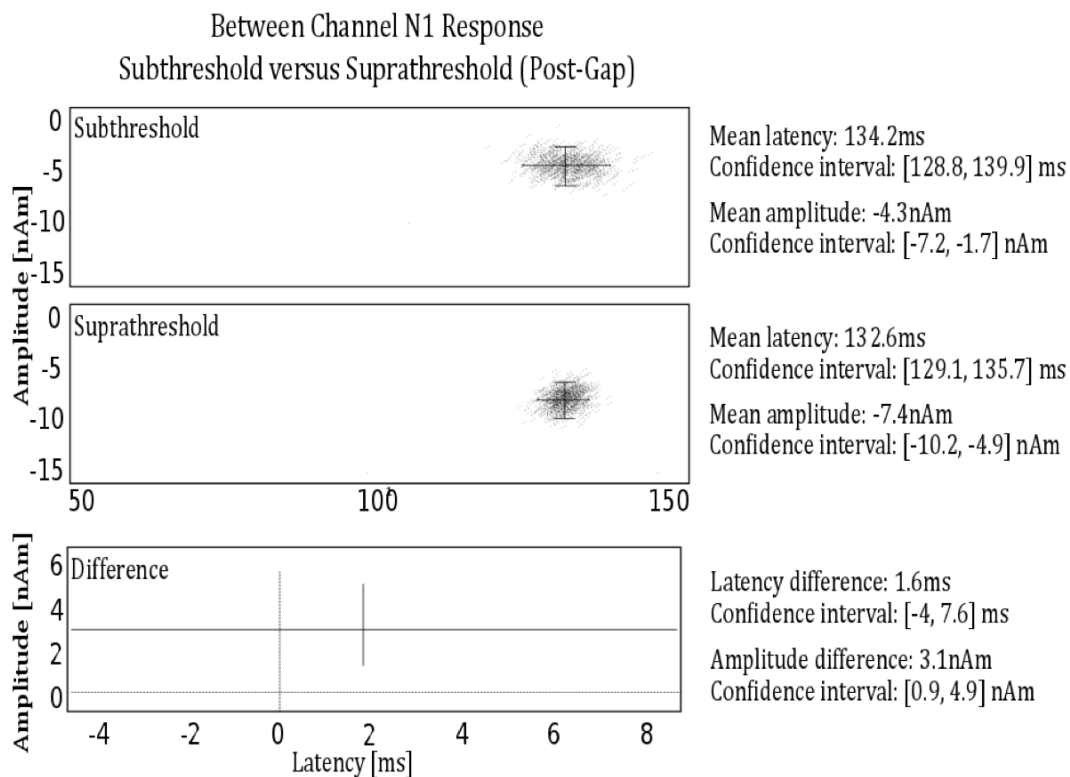


Figure 2. N1 peak amplitudes and latencies for between-channel *Sub* and *Supra* conditions. The top two graphs plot amplitude versus latency for each group, using a bootstrapping approach. The mean latencies and amplitudes are listed to the right of each graph. The bottom graph plots amplitude versus latency as a difference measure between the two groups, including variance intervals. Significant effects occur when the plotted lines do not include zero (i.e., cross the axes). N1 peak amplitude is significantly smaller (more positive) for *Sub* versus *Supra*.

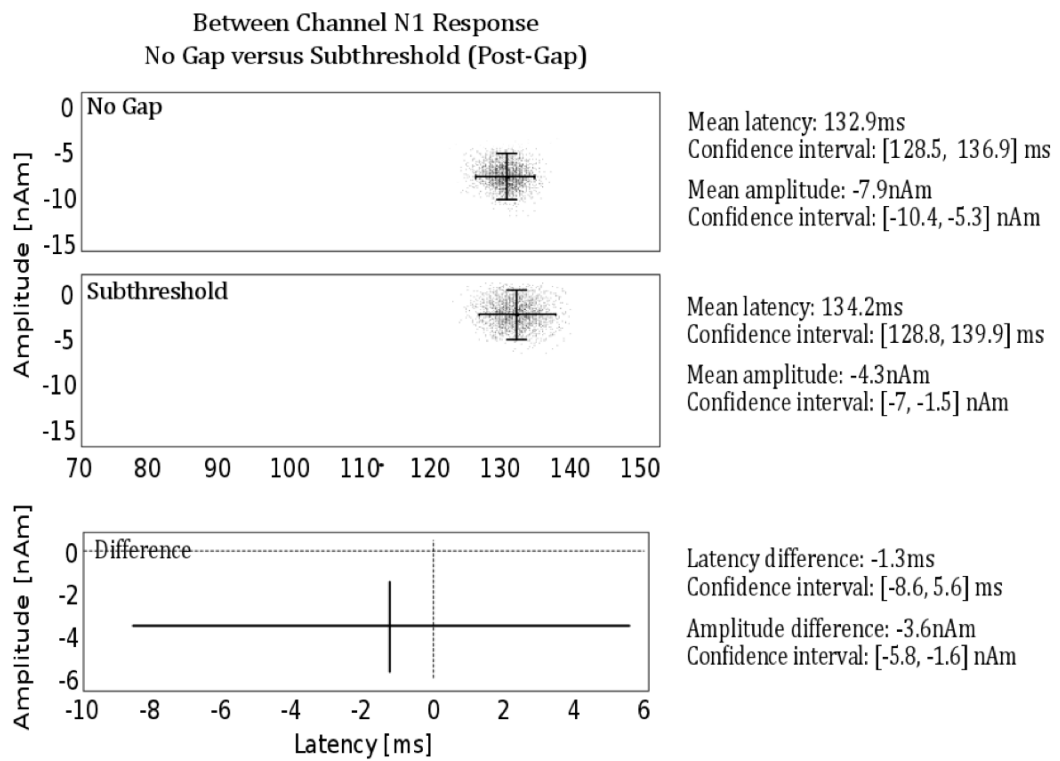


Figure 3. N1 peak amplitudes and latencies for between-channel *No Gap* and *Sub* conditions. N1 peak amplitude is significantly smaller (more positive) for *Sub* versus *No Gap*.

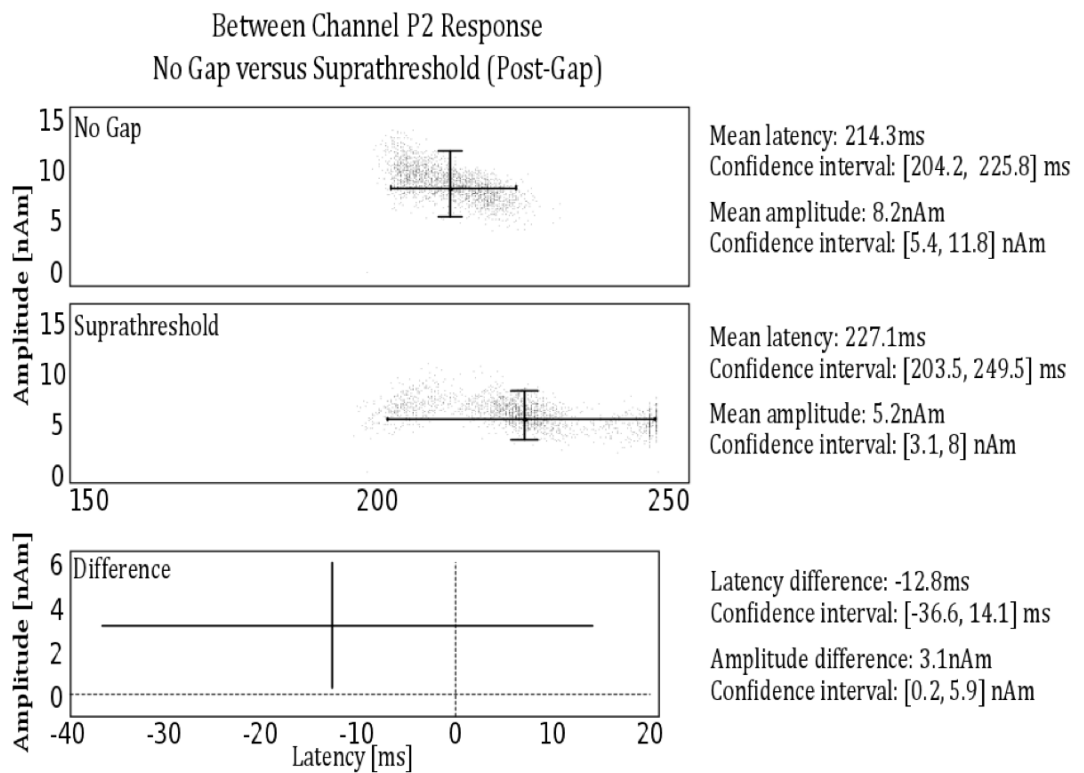


Figure 4. P2 peak amplitude and latencies for between-channel *No Gap* and *Supra* conditions. P2 peak amplitude in response to *No Gap* is significantly larger than *Supra*. Note the wide variability in peak latency in response to *Supra*.

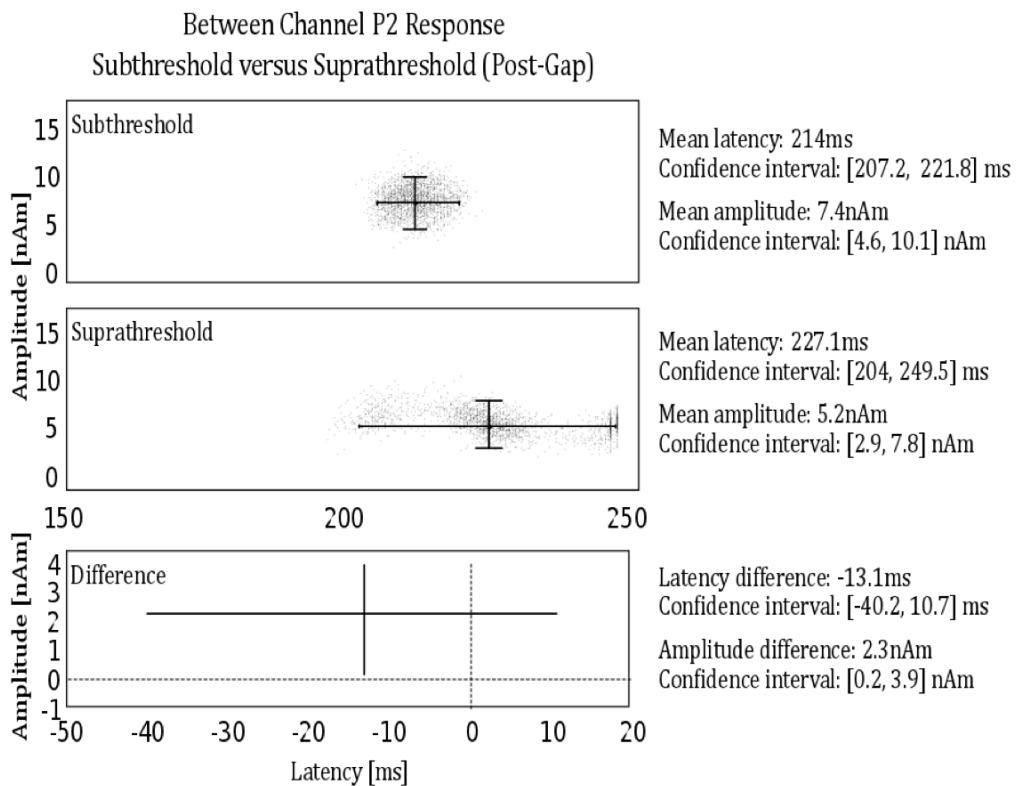


Figure 5. P2 peak amplitudes and latencies for between-channel *Sub* and *Supra* conditions. P2 peak amplitude in response to *Sub* is significantly larger than for *Supra*. Note the wide variability in peak latency in response to *Supra*.

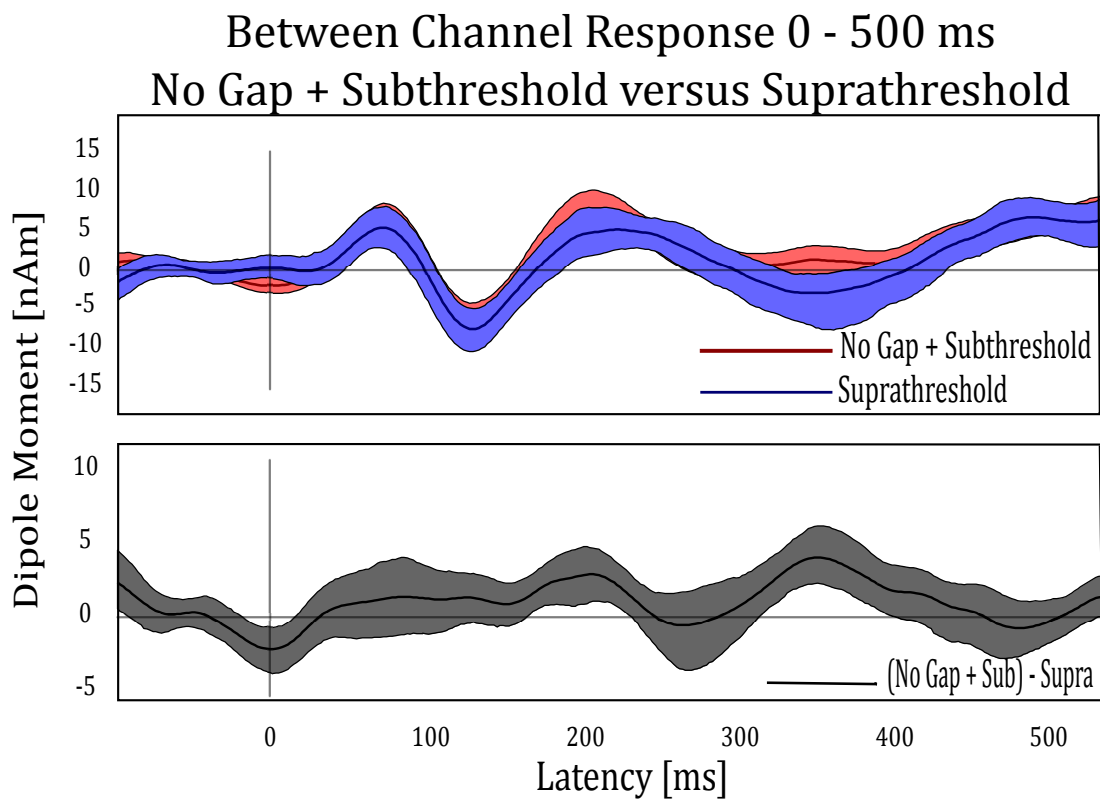


Figure 6. The top graph displays the amplitude changes over time for between-channel *No Gap + Sub* and *Supra*. The bottom graph shows the difference between the two groups. Significance occurs when the difference (black line) +/- error (shaded area) is not equal to zero. A positive peak occurs at approximately 360 ms post-stimulus onset for *No Gap + Sub* but not for *Supra* and this difference is significant.

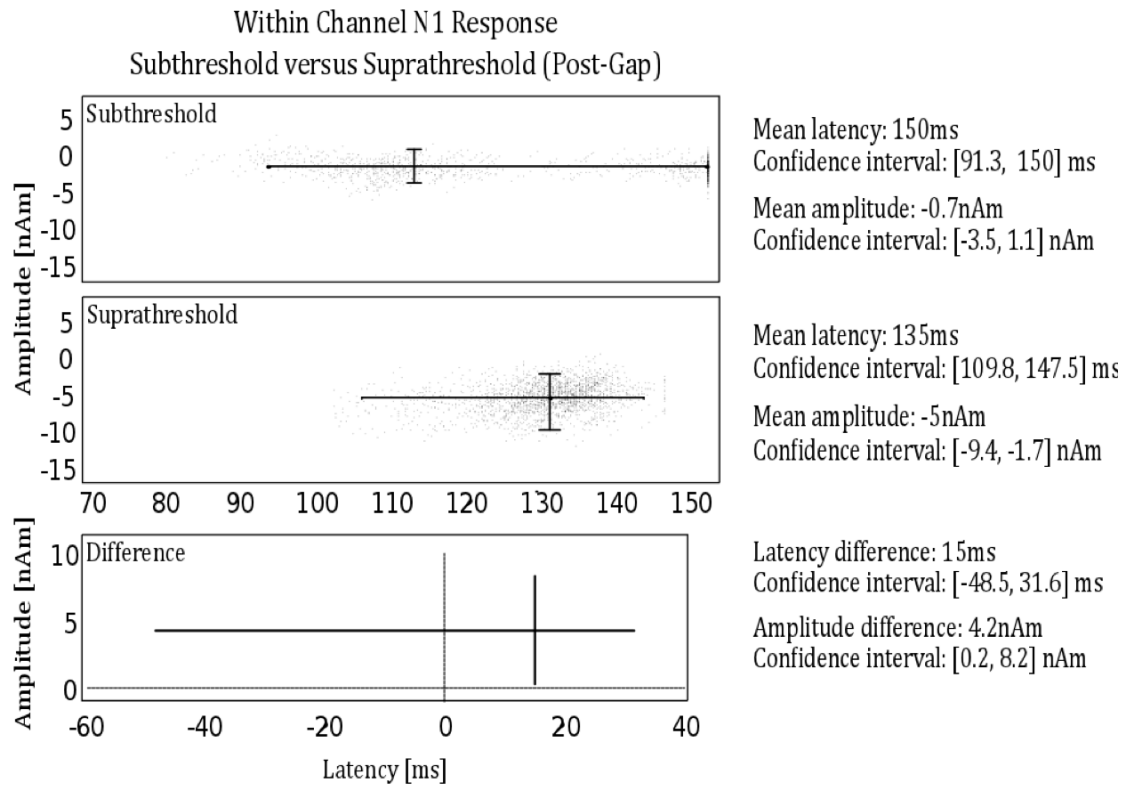


Figure 7. N1 peak amplitudes and latencies for within-channel *No Gap* and *Supra* conditions. N1 peak amplitude in response to *No Gap* is significantly larger than for *Supra*.

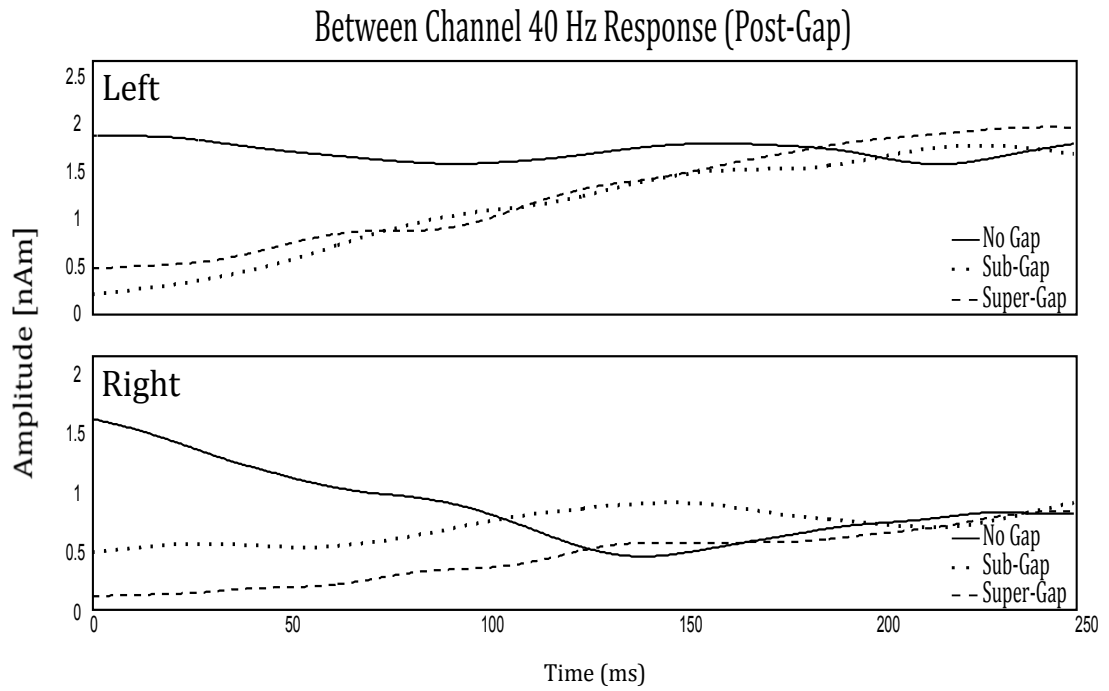


Figure 8. The 40-Hz ASSR amplitude changes for each between-channel gap condition, as measured from the right and left hemispheres.

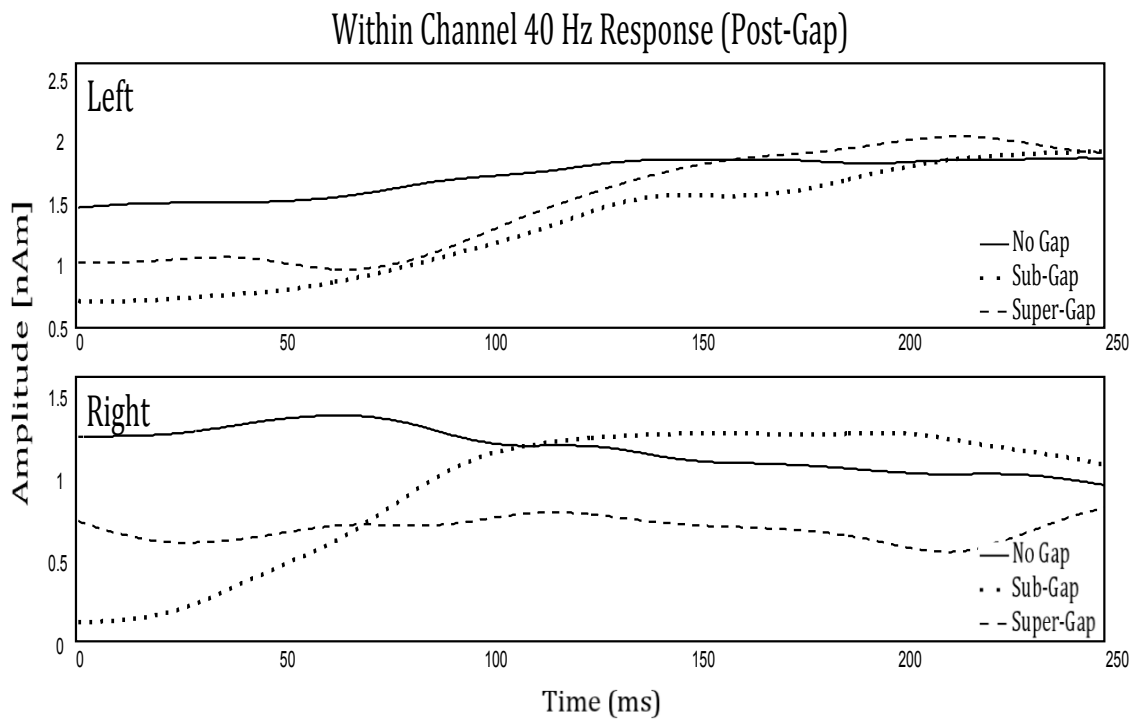


Figure 9. The 40 Hz ASSR amplitude changes for each of the within-channel gap conditions, as measured from the right and left hemispheres.