EFFICIENCY OF SINGLE VERSUS MULTIPLE STIMULI FOR 40-HZ AUDITORY STEADY-STATE RESPONSES

by

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Abstract

Auditory steady-state responses (ASSRs) were elicited in normal-hearing, awake adults to 500-, 1000-, 2000-, and 4000-Hz carrier frequencies amplitude-modulated in the 40-Hz range in three conditions: individually [monotic-single(MS) – one carrier], simultaneously in one ear [monotic-multiple(MM) – total four carriers], and simultaneously in both ears [dichotic-multiple(DM) – total eight carriers], at intensities of 30, 55, and 80 dBHL. In general, response amplitudes (collapsed across frequency and intensity) decreased with increasing number of simultaneous stimuli, and were 270, 155, and 107 nV for MS, MM and DM conditions, respectively. Amplitude decreases at 30 dBHL, however, were not significant. Relative efficiency (relative test efficiency of multiple versus single conditions) increased from single- to multiple-stimulus conditions, but there was no significant difference between MM and DM conditions. Mean relative efficiencies were 1.00, 1.38, and 1.39 for MS, MM and DM conditions, respectively. At 80 dBHL, there was no significant increase in relative efficiency with multiple stimuli. These results suggest that 40-Hz ASSRs to low and moderate intensities are most efficiently assessed using monotic-multiple stimuli, and that there may be little advantage to simultaneously stimulating both ears. High intensities might be more efficiently assessed using single stimuli.

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Literature Review: Auditory Steady-State Responses in Audiology

Audiological assessment, in particular the determination of auditory thresholds at various frequencies, usually requires behavioural responses from the individual being assessed. In the prevalent paradigm, the subject is asked to raise a hand or push a button in response to hearing a pure tone. The threshold is defined as the lowest level at which the subject will respond 50% of the time, and is determined using a bracketing procedure (Stach, 1998). When using this method, the accurate determination of the hearing threshold is dependent on the subject's ability and willingness to respond to the tones that are presented.

There are, however, a number of situations where behavioural responses are not possible, or their accuracy may be in question. Objective techniques for assessing hearing have therefore been developed, and are especially useful in the evaluation of infants, who are unable to respond behaviourally, and in the evaluation of adults in medical-legal and compensation cases, where subjects may choose not to cooperate and confirmation of behavioural results is required. Electrophysiological techniques involving the recording of brain waves in response to auditory stimuli, known as auditory evoked potentials (AEPs), are usually used for the objective determination of frequency-specific auditory thresholds. The current standard for the objective assessment of infants and children is the auditory brainstem response (ABR) recorded in response to brief-tone stimuli (Stapells, 2000). For the objective assessment of adults, current standard practice is the slow cortical potential (SCP) (Hyde, 1994; Stapells, 2002).

A significant disadvantage of both the ABR and SCP is the need for subjective interpretation of the recorded waveforms by an experienced clinician (John & Picton, 2000). Considerable research has therefore focused on developing an objective, frequency-specific, and time-efficient technique to evaluate auditory thresholds using auditory evoked potentials in both children and adults. The AEPs that have received the most attention in recent years are auditory steady-state responses (ASSRs).

This literature review provides an overview of ASSRs and their use in audiological assessment, developing the background and rationale for the study that was performed.

ASSRs Definition and History

Auditory steady-state responses are scalp-recorded electrophysiological potentials evoked by auditory stimuli presented periodically; these periodic stimuli may be amplitude modulated (AM), frequency modulated (FM), or a combination of both. ASSRs have frequency components that remain constant in amplitude and phase over a temporal window much longer than the length of a single stimulus cycle (Picton, John, Dimitrijevic, & Purcell, 2003). ASSRs are also known as the envelope-following response (Dolphin & Mountain,

1992) and the amplitude-modulation-following response (AMFR) (Griffiths & Chambers, 1991).

Steady-state responses may be elicited from the brain with stimuli in the visual, auditory, and somatosensory modalities (Regan, 1989), and were first recorded in response to visual stimuli (Regan, 1966). Steady-state responses to auditory stimuli may be evoked with modulation frequencies (MFs) between 1 and 200 Hz (Picton et al., 2003), although for audiological assessment MFs in the 40-Hz or 80-Hz ranges are usually used. It is possible to use a variety of auditory stimuli to elicit ASSRs, including periodically repeating or modulated pure tones or noise, click trains, and tonebursts (Picton et al., 2003). Early ASSR research focused on the largest of these responses, those to MFs in the 40-Hz range (Galambos, Makeig, & Talmachoff, 1981; Kuwada, Batra, & Maher, 1986; Stapells, Linden, Suffield, Hamel, & Picton, 1984; Stapells, Makeig, & Galambos, 1987). However, when it was discovered that ASSRs to MFs in the 40-Hz range could not be reliably recorded in infants, and decreased in amplitude during sleep (Aoyagi, Kiren, Kim, Suzuki, Fuse, & Koike, 1993; Levi, Folsom, & Dobie, 1993; Maurizi, Almadori, Paludetti, Ottaviani, Rosignoli, & Luciano, 1990; Stapells, Galambos, Costello, & Makeig, 1988; Suzuki & Kobayashi, 1984), the research focus shifted to ASSRs in the 80-Hz range for both children (Lins, Picton, Boucher, Durieux-Smith, Champagne, Moran, et al., 1996; Luts, Desloovere, & Wouters, 2006; Rickards, Tan, Cohen, Wilson, Drew, & Clark, 1994) and adults (Dimitrijevic, John, Van Roon, Purcell, Adamonis, Ostroff, et al., 2002; Herdman & Stapells, 2001; Lins, Picton, Picton, Champagne, & Durieux-Smith, 1995; Lins et al., 1996). Despite the current focus on 80-Hz ASSRs, it has been shown that for awake adult subjects, the response amplitude is largest at MFs in the 40-Hz range (Galambos et al., 1981; Stapells et al., 1984), and detection efficiency of low-intensity stimuli, which is important for assessment of adult auditory thresholds, has been shown to be best with ASSRs in the 40-Hz range (Cohen, Rickards, & Clark, 1991; Dobie & Wilson, 1998). More recently, Van Maanen and Stapells (2005) showed that the 40-Hz ASSRs may be faster and more accurate than 80-Hz ASSRs in predicting behavioural thresholds of awake, hearing-impaired adults. Similar findings were obtained by Petitot, Collet, and Durrant (2005), who found that thresholds measured using 40-Hz ASSRs were closer to behavioural thresholds than those measured using 80-Hz ASSRs.

It may also be possible to significantly increase the efficiency of ASSR-based objective audiometry by simultaneously presenting multiple stimuli to one or both ears, then analyzing the response to each stimulus based on the spectral components corresponding to each modulation frequency (Lins & Picton, 1995). Such a technique, if it does not substantially reduce the amplitudes of the responses in the multiple condition compared to the amplitude to each stimulus presented individually, could result in much greater efficiency because more information would be collected for a given period of time. The sections that follow provide details on ASSR generators, physiology, detection, stimuli and subject factors, as well as the results of previous ASSRs studies using both single- and multiple-stimuli paradigms.

Generators of the ASSR

Animal research has shown that neurons at all levels of the auditory system can temporally follow modulated auditory stimuli, and that these neurons preferentially encode lower modulation frequencies as one ascends in the auditory system from the brainstem to the cortex (for review, see Frisina, 2001). Neurons at all levels of the auditory system can therefore encode low (< 80 Hz) modulation rates, while high (> 80 Hz) modulations rates are preferentially encoded in lower levels (i.e., in the brainstem). It follows that generators of the ASSR to low modulation frequencies may originate from any level of the neural auditory system from the brainstem to the auditory cortex. On the other hand, generators of the ASSR to high modulation frequencies likely originate from lower brainstem structures in the auditory system.

Using rabbits as an animal model, Kuwada and colleagues found that ASSRs recorded locally in the brain using microelectrodes showed a decrease in the modulation frequencies that could be followed at progressively higher locations in the auditory pathway (Kuwada, Anderson, Batra, Fitzpatrick, Teissier, & D'Angelo, 2002). They also performed surface recordings of the ASSR and found that it had multiple generators, although different generators dominated the response depending on the modulation frequencies. Low modulation frequencies (< 80 Hz) seem to have mainly cortical generators while higher modulation frequencies appear to have two main sources with delays of 3 ms and 5 ms, which the authors speculate may correspond to the superior olivary complex or cochlear nucleus, and midbrain or pons, respectively. Szalda and Burkard (2005) recorded ASSRs in chinchillas from inferior colliculus and auditory cortex sites, both while the animals were unanesthetized and while they were anesthetized with nembutal. A 2000-Hz carrier was modulated using difference tones from 29 to 2249 Hz in approximately 20-Hz steps. Their results showed more robust responses to higher modulation frequencies (> 90 Hz) in the inferior colliculus (a midbrain structure) compared to the auditory cortex (higher up in the auditory pathway). When the modulation rate transfer functions (MRTF) were plotted, showing the ASSR amplitude as a function of modulation frequency, they found the peaks in the MRTF to be at lower frequencies in the auditory cortex compared to the inferior colliculus. The nembutal anasthesia decreased responses at both sites, but the magnitude of the decrease was much greater at the auditory cortex.

Few studies have investigated the generators of ASSRs with electrophysiological recordings in humans. Herdman and colleagues used brain electric source analysis to determine the generators of ASSRs with MFs of 12, 39, and 88 Hz (Herdman, Lins, Van Roon, Stapells, Scherg, & Picton, 2002). The 88-Hz responses primarily had brainstem activation, with minor activation of higher structures in the auditory pathway. The responses to 39 Hz also had a brainstem generator, but activation of cortical sources was much more significant. The responses at 12 Hz were small, but the source analysis showed activation of both brainstem and cortical sources.

The animal and human studies of ASSR generators support the general conclusion that ASSRs with low MFs (< 80 Hz) originate predominantly from cortical generators, whereas ASSRs with higher MFs originate predominantly from brainstem generators.

Measurement and Analysis of the ASSR

A number of commercial systems have recently become available to record and analyze ASSRs (Cone-Wesson & Dimitrijevic, in press; Stapells, Herdman, Small, Dimitrijevic, & Hatton, 2005). Although the concepts discussed below are applicable to the recording and analysis of ASSRs in general, the discussion will focus on the implementation of these concepts in the MultiMASTER system (John & Picton, 2000), which was used for this study.

ASSRs can be recorded in either the time or frequency domain (Picton et al., 2003). In the time domain, the peaks and troughs of a response can be selected along with latencies to measure the response. It can be difficult to distinguish individual responses in the time domain, for example the individual harmonics may be difficult to distinguish, and the peak measurements can be distorted by noise (Picton et al., 2003). For these reasons, ASSRs are usually transformed to the frequency domain using Fourier analysis (Stapells et al., 1984) or by fast Fourier tranform (FFT) (Rickards & Clark, 1984). In the MultiMASTER system, an FFT algorithm is digitally implemented, which allows the amplitude and phase to each stimulus to be measured at its modulation frequency. Because ASSRs have energy primarily at the modulation frequency and its harmonics, the FFT results in a spectrum with a vertical line representing amplitude of the response at each modulation frequency, as well as an associated phase measurement.

When potentials are recorded from the scalp, the resulting recording includes not only the EEG activity of interest, but also normal background EEG activity (e.g., alpha, beta, and gamma waves) as well as muscular activity and non-physiological electrical noise from the environment. One must be able to separate the response of interest (the signal) from this "background noise" to be able to determine if the response is indeed present (i.e., significantly different from the background noise). Assuming that the background noise is random, averaging the response to a repeated, unchanging signal will reduce the noise by the square root of the number of samples in the average (Picton, Linden, Hamel, & Maru, 1983). Averaging is the main method of increasing the signal-to-noise ratio (SNR) of ASSRs. The amount of time required to reach a particular SNR will depend on the amplitude of the response and the background EEG noise at frequencies surrounding the response.

To achieve the goal of objective response detection, statistical methods must be applied to determine the absence or presence of a response, and these are usually based on the SNR. There are a number of ways to increase the SNR in an ASSR recording. As mentioned above, averaging is the main method, and MultiMASTER averages together repeated recordings, known as "sweeps", which usually consists of 16 sequential epochs joined together. Given an analog-to-digital (A/D) conversion rate of the EEG signal of 800 Hz, with a buffer containing 1024 points, each epoch will last 1.28 seconds, with each recording sweep of 16 epochs lasting 20.48 seconds. The total sweep is what is submitted for FFT analysis, with the reciprocal of the length of the sweep determining the resolution of the FFT, in this case 0.05 Hz (John & Picton, 2000). The SNR can also be increased by eliminating recordings where transient electrical activity surpasses a pre-set limit (e.g., muscular activity due to subject movement). This is known as artifact rejection, and in the MultiMASTER system would result in the elimination of any epoch that surpassed the artifact rejecting limit, for example ±50 μV. In addition to artifact rejection, transient electrical noise can also be reduced with the implementation of weighted averaging (John, Dimitrijevic, & Picton, 2001), which assigns higher "weight" to recorded epochs that are quiet compared to sections that are noisy, based on the variance of amplitudes in the epoch.

<u>Objective methods for ASSR detection.</u>

The averaging, filtering, artifact rejection, and weighted averaging discussed above are all performed on-line before the FFT, ensuring the highest possible SNR before statistical analysis is performed to determine the absence or presence of a response. A number of methods to objectively differentiate a response from the background EEG noise have been developed over the years. These methods fall into two general approaches: those based on repeated measurements, and those based on measurements of the frequency spectrum (Picton et al., 2003). Approaches based on repeated measurements include phase coherence (Jerger, Chmiel, Frost, & Coker, 1986; Stapells et al., 1987) and magnitude-squared coherence (Dobie & Wilson, 1989, 1995). The most common approach based on measurements of the frequency spectrum is the F-test (Picton et al., 2003). As implemented in the MultiMASTER system, the F-ratio is computed between the response amplitude at the modulation frequency(ies) with the amplitudes in the 60 frequency bins above and below the modulation frequency (John & Picton, 2000). This test compares the power at the modulation frequency to the power at other frequencies in the spectrum. If no response is present, the power at the modulation frequency should be similar to the power at the adjacent frequency bins (i.e., not significantly different from the noise). The F-ratio therefore estimates the probability that the amplitude at the modulation frequency is within the distribution of amplitudes for frequency bins that are expected to contain background noise (John & Picton, 2000). If this probability is $< .05$, the response is considered to be significantly different from the noise, and MultiMASTER indicates that a response is present. The F-test is much more flexible than the other methods because the number of frequency bins that are evaluated may be changed, allowing easier exclusion of frequencies contaminated by line noise, or of other responses that are being recorded to simultaneous stimuli (Picton et al., 2003).

Stimulus Factors

Types of stimuli.

ASSRs may be elicited with a variety of stimuli, including periodically repeating brief tone-bursts or clicks, beats, sinusoidally amplitude-modulated tones, modulation based on the third power of the sinusoidal envelope, frequency modulation, mixed modulation consisting of both amplitude and frequency modulation, and modulated noise (Picton et al., 2003). Sinusoidal amplitude modulation has been the most common, and contains spectral energy at the carrier frequency as well as at sidebands above and below, separated from the carrier frequency by the modulation frequency. For example, a 1000-Hz carrier 100% amplitude modulated at 40 Hz would have energy at 1000 Hz as well as 960 and 1040 Hz.

Intensity.

The amplitude of the ASSR increases with increasing stimulus intensity. The increase in 40-Hz ASSR amplitude to a 500-Hz carrier has been shown to be essentially linear with increasing intensity from 20 dB nHL (near threshold) to 90 dB nHL, with a slope of 20 nV/dB (Stapells et al., 1984). Rodriguez, Picton, Linden, Hamen, & Laframboise (1986) obtained similar results at 500 Hz, with a slope of 17 nV/dB, but found that the decrease in amplitude is not as pronounced for higher carriers, obtaining a slope of 14 nV/dB at 2000 Hz. ASSRs in the 80-Hz range are smaller than those near 40 Hz, and the changes in amplitude with changing stimulus intensity are also much smaller, although the changes are more pronounced at high intensities. A 1000-Hz carrier modulated at 91 Hz has been shown to have a slope of 1.9 nV/dB below 70 dB SPL, and a much steeper slope of 7.8 nV/dB above 70 dB SPL (Lins et al., 1995).

Carrier frequency.

With MFs in the 40-Hz range, ASSR amplitude decreases significantly with increasing carrier frequency (Rodriguez et al., 1986; Stapells et al., 1984). Picton et al. (2003) suggest that this effect may be due to enhanced combination of brainstem and cortical generators of the ASSR for lower carrier frequencies, or to the broader cochlear activation resulting from low-frequency carriers resulting in more neural activation compared to high-frequency carriers. For MFs in the 80-Hz range, the responses have been shown to be largest from 1000-2000 Hz, and smaller at higher and lower frequencies (John, Dimitrijevic, van Roon, & Picton, 2001).

Rate.

In general, the response amplitudes decrease with increasing stimulus rate. Stapells et al. (1984) recorded ASSRs to rates from 10 to 60/s using a 500-Hz carrier, and found that the highest amplitudes occurred with rates from 40-45/s, with the lowest response amplitudes occurring at the slower and faster rates. Lins et al. (1995) recorded ASSRs at modulation rates from 67-111 Hz. They found that the response amplitude decreased from 67-71 Hz, then increased to a plateau from 83-91 Hz, and then decreased again from 91-111 Hz. Picton et al. (2003) combined the results of nine studies that manipulated either stimulus rate or modulation frequency, and found that in addition to the general decline in response amplitude with increasing stimulus rate, there are areas of enhanced response, most notably near 40 Hz, but also near 90 Hz.

Multiple Simultaneous Stimuli

A unique feature of ASSRs is the ability to present multiple carriers simultaneously to either one or both ears, and independently analyze the response to each carrier in the frequency domain by the spectral components corresponding to each modulation frequency. Given that the residual background EEG noise in an average will decrease at the rate of the root of the number of sweeps averaged (John, Purcell, Dimitrijevic & Picton, 2002; Picton et al., 1983), using multiple simultaneous stimuli rather than a single stimulus will increase the amount of available information for a given amount of recording time, while the noise will continue to decrease at the same rate as it would with only one stimulus. If the amplitudes of the responses when the stimuli are presented simultaneously are not significantly different from the amplitudes of the same stimuli presented individually, such a paradigm could theoretically increase the efficiency of ASSRs by a factor of the number of simultaneous stimuli. For example, presenting two simultaneous stimuli to one ear would be two times faster than presenting each stimulus individually. Similarly, presenting four stimuli simultaneously to each ear would be eight times faster. The stimuli could be different carrier frequencies modulated at different rates, or could be one carrier frequency at different intensities, modulated at different rates. However, presenting multiple stimuli often results in decreased response amplitudes (compared to amplitudes when stimuli are presented alone); nevertheless, the multiple-stimuli technique is more efficient than the single stimulus technique providing the amplitude decrease is not more than $1-1/\sqrt{N}$, where N is the number of stimuli (John, Lins, Boucher, & Picton, 1998). For example, for four simultaneous stimuli to be more efficient than the single stimulus technique, the amplitude of the four simultaneous stimuli cannot be less than one half the amplitude of the single stimulus.

ASSRs to multiple simultaneous stimuli with modulation rates in the 80-Hz range were first investigated by Lins and Picton (1995), who found that there was no significant decrease in response amplitude for four tones presented simultaneously in one ear (500, 1000, 2000, 4000 Hz) compared to each 60 dB SPL stimulus presented alone. They also found that overall there were no significant decreases in the responses for eight simultaneous stimuli (four in each ear) as long as the carrier frequencies were separated by at least an octave. However, they found significant decreases in the response when carriers of the same frequency (modulated at different rates) were presented simultaneously.

John et al. (1998) investigated the effect of multiple simultaneous stimuli on both 40-Hz and 80-Hz ASSRs. With 80-Hz ASSRs, they found no significant change in amplitude with four stimuli in one ear when the carriers were separated by at least one octave and intensities were no higher than 60 dB SPL. At higher intensities, there were interactions between responses to the stimuli, resulting in attenuated responses, opposite to what is seen when stimuli are presented individually (i.e., an increase in intensity usually results in an increase in response amplitude). Also, when two carriers within one-half octave of each other were presented simultaneously, there was a decrease in the response to the lowest carrier. For ASSRs to 40-Hz stimuli, their investigation was limited to comparing the amplitude of ASSRs to a single 1000-Hz carrier presented at 60 dB SPL to the amplitude of the same carrier in combination with three other carriers (500, 2000, and 4000 Hz) in one or both ears. Modulation rates were separated by 4 Hz within one ear, and by 2 Hz between the ears when stimuli were presented to both ears. A significant decrease in amplitude (34%) was found in the multiple condition (four stimuli in one ear), and a significant decrease (56%) was found in the dichotic condition (four stimuli to each ear for a total of eight carriers). Although these amplitude decreases are theoretically more efficient (when compared to the 50% and 65% criteria for four and eight stimuli, respectively), John and colleagues concluded that the multiple stimuli were not substantially more efficient than testing each carrier frequency individually when recording ASSRs in the 40-Hz range (John et al., 1998).

Herdman and Stapells (2001) determined the thresholds of adults using 80-Hz ASSRs in single- and multiple-stimulus conditions. Carriers were 100% amplitude-modulated and were presented individually (monotic single - MS), with four carriers (500, 1000, 2000, 4000 Hz) simultaneously in one ear (monotic multiple - MM), and with four carrier simultaneously in each ear (dichotic multiple - DM). For stimuli of 60 dB SPL or lower, there were no significant differences in ASSR amplitudes, phase delays, and thresholds between the modulated carriers presented individually, four in one ear, or four in each ear (eight total). Other studies have demonstrated the success of multiple ASSRs in the 80-Hz range (e.g., Dimitrijevic et al., 2002; Herdman & Stapells, 2003; Picton, Dimitrijevic, & John, 2002; Picton, Dimitrijevic, Perez-Abalo, & Van Roon, 2005; Vander Werff & Brown, 2005; Van Maanen & Stapells, 2005) Based on these data, it may be more efficient to record 80-Hz ASSRs with four carrier frequencies in each ear simultaneously.

Van Maanen & Stapells (2005) compared the thresholds of awake, hearing-impaired adults determined using multiple 40-Hz and 80-Hz ASSRs (four simultaneous stimuli in one ear - MM condition), as well as SCPs. They found the 40-Hz ASSRs and SCP to be faster than the 80-Hz ASSRs. Additionally, the 40-Hz ASSRs more accurately predicted behavioural thresholds compared to 80-Hz ASSRs and SCPs.

Physiology Underlying Interactions Between Stimuli

Under certain stimulus conditions the ASSRs to multiple simultaneous stimuli can be reduced or increased in amplitude compared to single stimuli. For example, John et al. (1998) found significant decreases in response amplitude when the carrier frequencies were separated by less than one octave and when the simultaneous stimuli were presented at intensities greater than 60 dB SPL. They also found a small enhancement of the response to a high carrier frequency by the presence of a lower-frequency stimulus. Although the mechanisms have not been thoroughly investigated, responses to multiple simultaneously-presented stimuli may interact with each other in the cochlea and/or in higher neural pathways.

It is well-known that the cochlea responds as a non-linear system (Rhode & Robles, 1974). Because of these non-linear responses, multiple simultaneously-presented stimuli can physically interact on the basilar membrane, resulting in suppression or enhancement of the response. Most of the research on stimulus interactions has been performed using the "two-tone suppression" paradigm, in which mutual suppression, low-side suppression, and high-side suppression may be observed in the cochlea using precise measurements of basilar membrane displacement in animals, although much of the early research measured suppression at the level of the auditory nerve (for review, see Ruggero, 1992). Mutual suppression is the result of two simultaneous tones (a probe tone and a suppressor tone) suppressing each other's response. Experimental results show that mutual suppression does not begin until the suppressor reaches a sufficient intensity (> 50 dB SPL), and the degree of suppression increases with suppressor intensity (Geisler, 1998). Low-side suppression results when displacement of the basilar membrane due to the probe tone is suppressed by a suppressor tone of lower frequency. High-side suppression results when a probe tone is suppressed by a higher-frequency suppressor. Suppressors close in frequency to the probe tone have a more pronounced effect, and low-side suppressors seem to have a broader frequency range of effectiveness compared to high-side suppressors, likely because of the upward spread of activation of low-frequency tones along the basilar membrane. The range of effective suppression frequencies also increases with increasing intensity. These cochlear suppressions can be accounted for by outer hair cell mechanisms, and it is now clear that suppressions measured in the auditory nerve arise from basilar membrane and outer hair cell mechanisms (Ruggero, Robles, & Rich, 1992).

Applying these findings to ASSRs, cochlear interactions would be expected at higher intensities (i.e., > 50 dB SPL) when multiple stimuli are simultaneously presented, and the effects of these interactions would be expected to increase with increasing intensity. This effect was demonstrated by John et al. (1998) for 80-Hz multiple ASSRs (see Multiple Simultaneous Stimuli above). Greater interactions between simultaneous stimuli would also be expected at high intensities due to the broadening of auditory filters with increasing intensity at frequencies greater than 1000 Hz (Pick, 1980).

In addition to cochlear interactions, there are neural interactions beyond the level of the auditory nerve between simultaneously-presented stimuli. John et al. (1998) showed that the decreases in ASSR amplitude from the simultaneous presentation of multiple stimuli could not completely be accounted for by cochlear mechanisms, and that there must be interactions at the level of the brainstem and/or auditory cortex. The response to a low-frequency AM tone was attenuated more than the response to a simultaneously-presented high-frequency AM tone, which is the opposite of what would be predicted from what is known about masking (for review, see Moore, 1995). Using 40-Hz ASSRs, they also measured a decrease in response amplitude when four tones were presented to one ear at 60 dB SPL, and a further decrease in response amplitude with four tones to two ears (binaural presentation - total of eight tones). Such decreases cannot be accounted for by cochlear processes, and result from binaural interactions at the level of the brainstem or higher in the auditory pathway. Recently, significant interactions were shown at 14, 40, and 80 Hz for four tones simultaneously presented to one ear at 80 dB SLP, and it was also shown there were greater interactions at 40 Hz compared to 14 and 80 Hz (Armstrong, 2006). For multiple ASSRs, the decrease in amplitude at intensities greater than 60 dB SPL is likely due to cochlear suppression mechanisms (John et al., 1998). However, because statistically significant decreases in amplitude have been found for multiple 40-Hz ASSRs (John et al., 1998) and not for 80-Hz ASSRs (Herdman & Stapells, 2001) presented at the same intensity (60 dB SPL), there are clearly neural interactions resulting in the suppression of multiple 40-Hz ASSRs. Interactions between simultaneously-presented stimuli have also been found using magnetoencephalograhy. Ross, Draganova, Picton, & Pantev (2003) found significant interactions between two simultaneously-presented tones modulated in the 40-Hz range. The decrease in ASSR amplitude was greatest when the interfering tone had a higher carrier frequency than the test tone. Cochlear interactions were also likely a factor in this study due to the high intensity used (70 dB SL, or approximately 80 dB SPL).

Frequency and Place Specificity

The frequency specificity of stimuli used to assess hearing is a consideration for any audiological application of ASSRs. Frequency specificity includes both acoustic specificity and cochlear place specificity (Herdman, Picton, & Stapells, 2002b). Behavioural hearing tests usually use pure-tone stimuli, which are the most acoustically frequency-specific stimuli available. A goal of stimulus selection for electrophysiological assessment of hearing is to replicate the acoustic and place specificity of a pure tone. The brief-tone and click stimuli often used in ABR testing have significant spectral spatter, resulting in poor acoustic specificity at high intensities (Stapells, Picton, Perez-Abalo, Read, & Smith, 1985). This can result in discrepancies between the behavioural audiogram and the electrophysiological technique due to spread of excitation on the basilar membrane. For example, poor acoustic specificity could result in a high-frequency tone-burst being heard by an individual with severe high-frequency hearing loss and near-normal hearing in the lower frequencies (Herdman et al., 2002b). Notched noise has been successfully used to limit the spectral splatter from these types of stimuli, thereby increasing frequency specificity (Picton, Ouellette, Hamel, & Smith, 1979; Stapells, Gravel, & Martin, 1995). Sinusoidally amplitude-modulated tones, in contrast, are very acoustically frequency-specific by their nature, having energy only at the carrier frequency and two sidebands separated by the modulation frequency above and below the carrier frequency (Regan, 1989).

Place specificity refers to the location of basilar membrane activation by a particular stimulus; good place specificity implies that the stimulus activates the region of the basilar membrane that would be maximally activated by a pure tone of the same frequency (Herdman et al., 2002b). Poor place specificity could result in a low-frequency stimulus being heard by an individual with no hair cells beyond the first turn of the cochlea (i.e., profound low-frequency hearing loss). In this case, the response is mediated by the cochlear regions that are most sensitive to high-frequency tones (Herdman et al., 2002b). Using a simultaneous-masking tuning-curve paradigm, Klein (1983b) showed that the responses to brief tones at frequencies of 500, 1000, 2000, and 4000 Hz, repeating at 40/s, were place-specific up to intensities of 80 dB SPL, and were similar to single-unit tuning curves. The response at 250 Hz did not have good frequency specificity, and was not recommended as a test frequency. Griffiths and Chambers (1991) demonstrated that the 40-Hz ASSR has good place specificity in both normal subjects using a high-pass masking paradigm in which a derived response was obtained from sinusoidally amplitude-modulated stimuli. They also tested a small number of hearing-impaired subjects and found that thresholds measured using 40-Hz ASSRs had good agreement with behavioural thresholds. Herdman et al. (2002b) performed a similar study for 80-Hz ASSRs, finding good place specificity for both single and multiple (500, 1000, 2000, and 4000 Hz simultaneously in one ear) ASSRs to 60 dB SPL stimuli. Stapells et al. (1985) demonstrated decreasing frequency specificity with increasing intensity for a 500-Hz tone at 40/s in high-pass noise.

Evidence for place specificity can also be obtained from studies that estimate behavioural thresholds in individuals with hearing loss. Herdman and Stapells (2003) found that multiple 80-Hz ASSRs accurately predicted the configuration of hearing loss in individuals with steeply-sloping hearing losses (slope $\geq$30 dB/octave), and did not underestimate behavioural thresholds, indicating good place specificity. Good place specificity has also been demonstrated for normal-hearing subjects (Herdman et al., 2002b; John et al., 1998).

Beyond the acoustic and place specificity discussed above, the frequency specificity (i.e., tuning curves) of the neurons generating the ASSR should be considered. Due to the narrow tuning of cochlear filters, the tuning curves of auditory-nerve fibres are essentially the same as the activation patterns of the basilar membrane (Pickles, 1988). Some of the frequency specificity of primary auditory neurons is maintained higher up in the auditory pathways, while other central auditory neurons have broader tuning curves (Pickles, 1988). Herdman et al. (2002b) suggest that for 80-Hz ASSRs, the neuronal specificity is less than that of primary auditory neurons, and that there is integration of frequency information from a range of cochlear filters surrounding the carrier frequency of the stimulus. Because sensorineural hearing loss causes broadening of auditory filters in the cochlea (Pickles, 1988; Tyler, 1986), it is possible that resulting decrease in neuronal specificity could lead to responses that are not very frequency-specific (Picton et al., 2003). Adding the complexity of multiple simultaneous stimuli could also result in decreased neuronal specificity due to suppression and lateral inhibition. Results from Herdman et al., (2002b) suggest that, at least for a moderate intensity (60 dB SPL), multiple stimuli have good neuronal specificity. This is supported by results showing that 80-Hz ASSRs accurately predict behavioural thresholds in individuals with steeply sloping hearing losses (Herdman & Stapells, 2003).

Subject Factors

Maturation.

Very few studies have investigated the maturation of ASSRs in infants and young children. Suzuki and Kobayashi (1984) found that the enhanced ASSR amplitude at rates from 35-40/s in adults was not found in infants and young children, and that for these children the amplitude of the response decreased with increasing modulation frequency. There must therefore be maturational changes that eventually result in the amplitude peak found near 40 Hz for adults. Stapells et al. (1988) also found maximal ASSR amplitude near 40 Hz for adults, but there was no corresponding maximal amplitude in children aged 3 weeks to 29 months. The 40-Hz ASSR could not be reliably recorded in these infants. Aoyagi et al. (1993) also reported that the 40-Hz ASSR was difficult to detect in sleeping children, and speculated that this response has not yet matured in children. Pethe, Mühler, Siewert, and von Specht (2004) found that for single near-threshold ASSRs, the 40-Hz response increased in amplitude with increasing age, and the 80-Hz response changed very little. The 40-Hz ASSRs was very low in amplitude (less than 50 nV) in children less than two years old, which they attributed to maturational or arousal factors. The 40-Hz ASSR was adult-like by

14 years of age. Using a measure of the signal-to-noise ratio, they also found that the optimal modulation frequency shifted from 80-Hz to 40-Hz at about 13 years of age.

Savio, Cárdenas, Pérez Abalo, González, & Valdés (2001) found significant age-related changes in thresholds, response amplitude, and response detectability from birth to 12 months of age for multiple 95- to 105-Hz ASSRs. Thresholds were found to decrease with age, and these changes were more pronounced for higher frequency carriers compared to lower ones, suggesting that ASSRs to high-frequency carriers mature sooner than for low-frequency carriers. Variability was higher at the younger ages. Overall, they concluded that the thresholds obtained were reasonably adult-like. A recent study by Rance and Tomlin (2006) also found high variability in 80-Hz ASSR thresholds during the neonatal period, with results spread over 35 dB. Developmental changes in the mean ASSR thresholds were observed, with thresholds improving an average of 10 dB over the six-week period of the study.

ASSRs have been found to be stable in adulthood, with no significant differences between young and aged adults reported for 40-Hz responses (Boettcher, Poth, Mills, & Dubno, 2001). Picton et al. (2003) reported no significant changes in the amplitude or phase of ASSRs modulated at 3, 43, and 95 Hz in adults ranging in age from 20 to 81 years.

Arousal state.

Sleep and arousal state can have an effect on many electrical responses measured from the brain, and these effects tend to be greater for responses that originate from sources in higher auditory pathways (i.e., greater effect of arousal on cortical versus brainstem sources) (Picton et al., 2003). Sleep has been shown to significantly decrease the amplitude of 40-Hz ASSRs (Cohen et al., 1991; Dobie and Wilson, 1998; Linden, Campbell, Hamel, & Picton, 1985; Pethe, von Specht, Mühler, & Hocke, 2001), but as discussed below, even during sleep the amplitudes of the adult responses are largest in the 40-Hz range.

Linden et al. (1985) investigated the effect of sleep on responses to 500-Hz tonebursts presented in the 40/s range. They found that the rate at which maximal ASSR amplitude was recorded was similar to that found during wakefulness (i.e., 30-50/s), but the magnitude of the response was significantly smaller during all stages of sleep, with no significant difference between different sleep stages. The response amplitudes were found to increase faster with increasing intensity in wakefulness compared to sleep, but there were no significant differences in thresholds obtained, which in both sleep and wakefulness were close to behavioural thresholds. There have, however, been studies that have shown a significant 10-20 dB increase in thresholds obtained with 40-Hz ASSRs during wakefulness and sleep (e.g., Klein, 1983a), but Picton et al. (2003) suggest that thresholds may not change, and the difference arises because the responses are more difficult to recognize during sleep. It is important to point out that 40-Hz ASSRs may still be used for adults during sleep.

The smaller amplitudes compared to wakefulness will likely result in a longer test time, but it has been shown that even with amplitude decreases during sleep, the response detectability is highest in the 40-Hz range (Dobie & Wilson, 1998). ASSRs to rates higher than 70 Hz are not significantly affected by sleep, shown by a number of studies (e.g., Cohen et al., 1991; Lins & Picton, 1995; Pethe et al., 2001)

Summary and Rationale for the Study

ASSRs are electrophysiological responses recorded from the scalp in response to auditory stimuli (carriers) periodically modulated between 1-200 Hz. Using averaging and statistical analysis techniques, very small responses can be differentiated from the background EEG noise, and the probability of a real response can be automatically calculated. ASSRs have therefore been found to be useful in the objective assessment of auditory thresholds. In addition to the benefits of automatic response detection, it is possible to increase the efficiency of the testing by simultaneously evaluating multiple carrier frequencies modulated at different rates, in either one or both ears.

The largest of the ASSRs occur in the 40-Hz range. However, response amplitudes at this modulation rate have been found to decrease significantly during sleep, and are not reliably recorded in infants. For this reason, much of the focus has been on multiple 80-Hz ASSRs, which have been shown to accurately predict behavioural thresholds in both adults and children. However, recent studies suggest that 40-Hz ASSRs may be the method of choice for the objective assessment of adults (Petitot et al., 2005; Van Maanen & Stapells, 2005). Multiple 40-Hz ASSRs have been shown to be faster than 80-Hz ASSR, and have also been found to be a better predictor of thresholds than either 80-Hz ASSRs or SCPs in adults with sensorineural hearing loss (Van Maanen & Stapells, 2005).

To date, the largest source of data on multiple 40-Hz ASSRs was collected by John et al. (1998), who investigated amplitude changes in the response to a 1000-Hz carrier presented alone, in 2-carrier combinations, with 4 carriers simultaneously in one ear, and with 4 carriers simultaneously in each ear. Their investigation of amplitude changes was limited to 1000 Hz, and was only performed at the single intensity of 60 dB SPL. Before conclusions can be made on the efficiency of multiple 40-Hz ASSRs, additional data are required at more frequencies and intensities. It is quite possible that the strong interactions found by John et al. (1998) will be substantially reduced at near-threshold intensities. It is also possible that results will vary depending on carrier frequency. Further, although response amplitude decreases are expected with the addition of simultaneously-presented stimuli, the efficiency of the multiple-stimulus technique may still be higher than the single-stimulus technique if these amplitude decreases are limited to a particular criterion, as discussed above. This has yet to be thoroughly investigated for multiple 40-Hz ASSRs.

The purpose of this study is therefore to record responses to single, multiple monotic (4 tones in one ear), and multiple dichotic (4 tones in each ear, for a total of 8 tones) conditions for the four most important audiometric frequencies (500, 1000, 2000, and 4000 Hz), and at three intensities (30, 55, and 80 dB HL) corresponding to near-threshold, moderate, and high intensities, respectively. The amplitude data will then be analyzed to determine the relative efficiency for each condition, at each frequency and intensity. This will allow for recommendations to be made on the most efficient paradigm for objective assessment of hearing thresholds using 40-Hz ASSRs in adults.

Introduction

Auditory steady-state responses (ASSRs) can be used to objectively assess audiological thresholds in individuals who are either unable to respond behaviourally, or who choose not to cooperate (for review, see Picton, John, Dimitrijevic, & Purcell, 2003). This electrophysiological technique can be especially useful in the assessment of infants and in compensation or medical-legal cases. One particularly significant advantage of ASSRs over other objective hearing assessment techniques is that statistical techniques may be used to objectively determine if a response is present from any of the combined multiple stimuli, rather than subjective waveform analysis by a clinician (John & Picton, 2000). A second advantage is the ability to test multiple frequencies simultaneously, known as multiple ASSRs, theoretically reducing the time required for assessment by the number of additional stimuli used (John, Lins, Boucher, & Picton, 1998; Lins & Picton, 1995).

However, interactions between simultaneously-presented stimuli can result in decreased response amplitudes compared to the response to single stimuli, especially at high intensities or when the stimuli are separated by less than one half-octave (John et al., 1998; Picton et al., 2003). Because of potential interactions, the efficiency of the single-stimulus versus multiple-stimulus technique must be determined by testing human subjects, using measurements such as response amplitude, audiometric thresholds, and/or time required for hearing assessment.

The efficiency of multiple simultaneous stimuli relative to the efficiency of a single stimulus, assuming background noise remains approximately constant, is a balance between: (1) the change in ASSR amplitude resulting from the increase in the number of stimuli, and (2) the increase in information collected due to the additional stimuli, which shortens the time required for assessment. The residual EEG background noise in an average is known to decrease by the rate of the square root of the number of sweeps averaged (Picton, Linden, Hamel, & Maru, 1983). Because of interactions, presenting multiple stimuli often results in decreased response amplitude (compared to amplitudes when stimuli are presented alone), which can require more EEG averaging to distinguish smaller ASSR amplitudes from the background noise; however, the multiple stimuli technique is more efficient than the single stimulus technique provided that the amplitude decrease is not more than $1 - 1/\sqrt{N}$, where N is the number of stimuli (John et al., 1998). Therefore, for the multiple technique to be more efficient, the response amplitude of any one carrier when presenting four simultaneous stimuli cannot decrease more than 50% compared to the response of its counterpart presented as a single stimulus. Similarly, the amplitude cannot decrease more than 65% for eight simultaneous stimuli. Based on this, a measure of "relative efficiency" for each condition can be calculated.

ASSRs may be evoked with modulation frequencies (MFs) between 1 and 200 Hz (Picton et al., 2003). Although initial research on the use of ASSRs for audiometric assessment used MFs in the 40-Hz range (e.g., Galambos, Makeig, & Talmachoff, 1981;

Griffiths & Chambers, 1991; Kuwada, Batra, & Maher, 1986; Stapells, Linden, Suffield, Hamel, & Picton, 1984), research on 40-Hz ASSRs for audiometric assessment has been limited likely because it cannot be reliably recorded in infants (Aoyagi, Kiren, Kim, Suzuki, Fuse, & Koike, 1993; Maurizi, Almadori, Paludetti, Ottaviani, Rossignoli, & Luciano, 1990; Stapells, Galambos, Costello, & Makeig, 1988; Suzuki & Kobayashi, 1984) and is affected by arousal state (Cohen, Rickards, & Clark, 1991; Galambos et al., 1981; Linden, Campbell, Hamel, & Picton, 1985; Pethe, von Specht, Mühler, & Hocke, 2001). It is important to note, however, that even during sleep, adult ASSRs have been shown to be largest (Linden et al., 1985) and most efficiently detected (Dobie & Wilson, 1998) in the 40-Hz range.

John et al. (1998) reported that interactions between simultaneous stimuli were greater for MFs in the 40-Hz range compared to those in the 80-Hz range. Strong interactions have also been found using magenetoencephalography by Ross, Draganova, Picton, & Pantev (2003), for two tones amplitude-modulated in the 40-Hz range at 70 dB SL. Recently, significant interactions were shown at 14, 40, and 80 Hz for four tones simultaneously presented to one ear at 80 dB SPL (Armstrong, 2006). On the other hand, Herdman and Stapells (2001) showed that there were no significant interactions for ASSRs to tones amplitude-modulated in the 80-Hz range, for intensities of 30 and 60 dB SPL. Research has therefore focused on ASSRs in the 80-Hz range for audiometric assessment (e.g., Dimitrijevic, John, Van Roon, Purcell, Adamonis, Ostroff, et al., 2002; Herdman & Stapells, 2001, 2003; Perez-Abalo, Savio, Torres, Martin, Rodriguez, & Galan, 2001; Picton, Dimitrijevic, Perez-Abalo, & Van Roon, 2005; Rance, Rickards, Cohen, De Vidi, & Clark, 1995). However, for awake adult subjects, the response amplitude is largest at MFs in the 40-Hz range, and detection efficiency of low-intensity stimuli has been shown to be highest with ASSRs in the 40-Hz range (Cohen et al., 1991; Dobie & Wilson, 1998). These results are consistent with recent research, which suggests that multiple stimuli in the 40-Hz range may be faster and more accurate than 80-Hz ASSRs in predicting behavioural thresholds of awake, hearing-impaired adults (Van Maanen & Stapells, 2005). These clinical results are promising, but more basic research of 40-Hz ASSR responses is required to further evaluate the efficiency of the single- versus multiple-stimulus techniques.

To date, the largest source of data for multiple simultaneous 40-Hz ASSRs is from John et al. (1998). Their investigation was limited to comparing the amplitude of ASSRs to a single 1000-Hz carrier presented at 60 dB SPL to the amplitude of the same carrier in combination with three other carriers (500, 2000, and 4000 Hz) in one or both ears. Modulation rates were separated by 4 Hz within one ear, and by 2 Hz between the ears when stimuli were presented to both ears. A significant decrease in amplitude of 34% was found in the multiple condition (four stimuli in one ear), and a significant decrease of 56% was found in the dichotic condition (four stimuli to each ear for a total of eight carriers). Although these amplitude decreases are less than the theoretical criteria of 50% for four stimuli and 65% for eight stimuli, John and colleagues concluded that the multiple stimuli were not substantially more efficient than testing each carrier frequency individually when recording ASSRs in the

40-Hz range. This conclusion was perhaps premature because their data actually suggest that the multiple stimulus technique for 40-Hz ASSRs may be more efficient than the single-stimulus technique. Moreover, their conclusion was based on results for only one carrier frequency (1000 Hz) at only one intensity (60 dB SPL); results may be different at lower or higher intensities, and for different carrier frequencies. Thus, more data are required to determine the efficiency of single versus multiple stimuli for ASSRs in the 40-Hz range, including an investigation of the effects of intensity and carrier frequency.

The present study measured the amplitudes of ASSRs in the 40-Hz range to single and multiple stimuli in one or both ears, for four carrier frequencies, and for near-threshold, moderate, and high intensities. The hypothesis was that for most intensities, response amplitudes would not decrease enough with an increase in number of stimuli (i.e., from 1 to 4 to 8 stimuli) to make it more efficient to use single stimuli rather than multiple stimuli. If this hypothesis is proven, the results of this study will lead to recommendations on the development of more efficient protocols to objectively test hearing thresholds for awake adults.

Methods

Subjects

Twelve subjects (7 females) between the ages of 23 to 35 years (mean 30.4 years) participated in this study. All subjects had behavioural hearing thresholds equal to or better than 15 dB HL (re: ANSI S3.6-1996) at 500, 1000, 2000, and 4000 Hz for both ears. One additional subject was excluded from participation because of occluding cerumen.

Stimuli and Conditions

Stimuli.

Stimuli were 100% sinusoidally amplitude-modulated (AM) tones with carrier frequencies of 500, 1000, 2000, and 4000 Hz generated by the Rotman MultiMASTER research system (John & Picton, 2000), attenuated through Tucker-Davis Technologies (TDT) PA4 attenuators, then routed to a TDT HB6 module. All stimuli were presented via air conduction through EAR-3A insert earphones and were calibrated in dB HL (re: ANSI S3.6-1996) using a Quest Model 1800 sound level meter and a Brüel and Kjaer DB0138 2-cc coupler. The tones were calibrated to within ±0.5 dB individually for each carrier frequency.

Modulation frequencies in the 36-47 Hz range were selected to achieve approximately 3 Hz of separation between the modulation frequency of individual carriers within one ear, and approximately 1.5 Hz between the ears for the dichotic multiple condition (see below). In the test ear, the 500-, 1000-, 2000-, and 4000-Hz carriers were modulated at 35.937, 39.062, 42.187, and 45.312 Hz, respectively. For the conditions that involved stimuli to the non-test ear, the 500-, 1000-, 2000-, and 4000-Hz carriers were modulated at 37.5, 40.625, 43.75, and 46.875 Hz, respectively . These specific modulation frequencies were used to ensure an integer number of modulation and carrier frequency cycles in each EEG recording sweep (see below).

Conditions and intensities.

Three stimulus conditions were used: (1) Monotic Single (MS), in which each AM tone of 500, 1000, 2000, and 4000 Hz was presented individually to one ear; (2) Monotic Multiple (MM), in which all four AM tones were presented simultaneously to one ear; and (3) Dichotic Multiple (DM), in which four AM tones were presented to each ear simultaneously (for a total of eight AM tones). Each condition was tested at three intensities: 30, 55, and 80 dB HL corresponding to near-threshold, moderate, and high intensities, respectively. Each subject was therefore tested for a total of 18 blocks.

EEG Recordings

ASSRs were recorded using three gold-cup electrodes placed on the scalp. The non-inverting electrode was placed at Fz (based on the International 10-20 system for EEG electrode placement). The inverting electrode was placed midline at the nape of the neck, just below the hairline, and the ground was placed on the forehead. All electrode impedances were kept below 3 kΩ at 10 Hz. The EEG signal was band-pass filtered from 5 to 100 Hz (12 dB/octave slope) and amplified with a gain of 80,000. The EEG signal was monitored during recording to ensure the subject was relaxed, and an artifact rejection limit of ± 60 μV for 10 of the 12 subjects was set to minimize the effect of muscle artifacts due to movement. For two of the subjects, the artifact rejection limit had to be increased due to electro-cardiogram activity that exceeded ± 60 μV; the artifact rejection limit was therefore increased to ± 70 μV for one subject and ± 80 μV for the other. The analog-to-digital (A/D) conversion rate of the EEG signal was 800 Hz, with each recording sweep consisting of 16 epochs of 1024 data points joined together and lasting 20.48 seconds. Any recording epoch where the signal exceeded the artifact rejection limits was eliminated. Weighted averaging (27-55 Hz) of the signal was used in the MultiMASTER system (John, Dimitrijevic & Picton, 2001). Responses were averaged in the time domain and converted on-line to the frequency domain for analysis by the MultiMASTER system using a Fast Fourier Transform (FFT).

Response significance was determined using the MultiMASTER system's online F-ratio computations (with 2 and 240 degrees of freedom), which compare the response amplitude at the modulation frequency with the amplitudes in the 60 frequency bins above and below the modulation frequency (considered to be representative of the EEG noise) (John & Picton, 2000). EEG recording continued until a significant response was present with a maximum noise level of ≤80 nV. If no significant response was present, recording continued until the noise was ≤60 nV (Van Maanen & Stapells, 2005). In addition to the significance and noise stopping rules, a minimum of 10 and a maximum of 48 sweeps were recorded for each condition. A response amplitude was considered significant from the background EEG noise at the $p < .05$ level.

Procedure

This research was approved by the University of British Columbia Behavioural Research Ethics Board. Written informed consent was obtained from subjects prior to testing, and subjects were free to withdraw from the study at any time. A subject's ears were examined with otoscopy to ensure they were clear, and a hearing threshold test was administered at 500, 1000, 2000, and 4000 Hz to confirm normal hearing at those frequencies. Subjects relaxed in a recliner placed in a double-walled soundproof room, and watched a closed-captioned video of their choice during the ASSR testing. Subjects were asked not to sleep during the testing, and compliance was verified using video monitoring. The total testing time was approximately three hours and subjects were paid an honorarium for their participation. The order of test blocks as well as the test ear were randomized across subjects; the choice of test ear was also counterbalanced so that an equal number of right and left ears were tested.

Data Analyses

Response amplitudes were averaged across subjects for each test block. For any non-significant responses, the actual amplitude measured was used in the average. A 3-way repeated-measures analysis of variance (ANOVA) was performed on ASSR amplitudes.

Factors were: Condition (3 levels), Frequency (4 levels), and Intensity (3 levels). Huynh-Feldt epsilon correction factors for degrees of freedom were used where appropriate. Differences in the amplitudes were considered to be significant at the $p < .05$ level. Newman-Keuls post-hoc analyses with a significance level of $p < .05$ were performed for significant main effects and interactions.

In general, residual background EEG noise in an average will decrease at the rate of the square root of the number of sweeps averaged (John, Purcell, Dimitrijevic & Picton, 2002; Picton et al., 1983). Using multiple simultaneous stimuli rather than a single stimulus will increase the amount of available information for a given amount of recording time, while the noise will decrease at the same rate. Presenting multiple stimuli often results in decreased response amplitudes (compared to amplitude when stimuli are presented alone); however the multiple stimuli technique is more efficient than the single stimulus technique providing that the amplitude decrease is not more than $1 - 1/\sqrt{N}$, where N is the number of stimuli (John et al., 1998). For example, for four simultaneous stimuli to be more efficient than the single stimulus technique, the amplitudes in response to the four simultaneous stimuli cannot be less than one half the amplitude of the single stimulus. To allow statistical comparisons of the different conditions, the relative efficiency of each subject's amplitudes were calculated in the following way: Each subject's response amplitude for a particular condition, frequency, and intensity was divided by the mean all subjects' responses to the corresponding frequency and intensity in the MS condition. This normalized the MM and DM responses to the MS condition. The normalized MM condition values were then multiplied by two ($\sqrt{4}$, representing four times more information being recorded compared to the single condition) and the DM condition values were multiplied by 2.828 ($\sqrt{8}$, representing eight times more information being recorded compared to the single condition). Thus, if the amplitude for four stimuli was half that of the one stimulus condition, this calculation would result in a relative efficiency of one, or equal efficiency. These relative efficiency values were then averaged across subjects. To examine differences in relative efficiency with condition, frequency, and intensity a 3-way repeated-measures ANOVA was performed on the relative efficiency values using the same factors and alpha criteria as the amplitude analysis.

Results

ASSR Amplitudes

A representative subject's responses are shown in Figure 1, which illustrates typical ASSR amplitude measurements in the frequency domain at intensities of 30, 55, and 80 dB HL for the MS condition at 2000 Hz as well as the MM and DM conditions (which both include all carrier frequencies). Filled arrows and triangles indicate responses that were significantly different from the background noise ($p < .05$); for this subject all responses were significant. The filled arrows differentiate the responses at 2000 Hz from the other carrier frequencies, which are labelled with filled triangles. The figure clearly illustrates the decrease in response amplitude with decreasing intensity. The decrease in 2000-Hz ASSR amplitude resulting from additional simultaneous stimuli can also be seen by comparing the MS, MM, and DM conditions for a specific intensity.

The mean amplitudes for all subjects are shown grouped by carrier frequency in Figure 2. The results of a repeated-measures ANOVA carried out on these data are summarized in Table 1. Overall, response amplitudes decreased as the number of simultaneous stimuli was increased (significant main effect of Condition) and as the intensity was decreased (significant main effect of Intensity). There were also differences in the amplitude of the response depending on the carrier frequency (significant main effect of Frequency). The overall amplitudes (collapsed over condition and intensity) were largest at 500 Hz (232 nV), followed by 4000 Hz (174 nV), 1000 Hz (167 nV), and smallest at 2000

Hz (137 nV). Post-hoc analyses also showed that the amplitudes at 500 Hz were significantly larger than all the other carrier frequencies, but there were no significant differences between the amplitudes for carriers of 1000, 2000, and 4000 Hz. In addition to the significant main effects of Condition, Frequency, and Intensity, all the interactions between these factors were significant.

Newman-Keuls post-hoc analyses of the interactions between the factors showed that although the general trend was for amplitudes to decrease from the MS to MM condition, and to further decrease from the MM to DM condition, the lowest intensity does not follow the trend. At 30 dB HL there were no significant changes in response amplitude when the number of simultaneous stimuli was increased for all carriers except 500 Hz, where a significant decrease was found only when the number of simultaneous stimuli was increased from the MM to the DM condition ($p < .01$). At the higher intensities, there were exceptions to the general trend of amplitude decreases with increasing number of simultaneous stimuli. At 55 dB HL, there were no significant changes in amplitudes from the MM to DM conditions for 1000, 2000, and 4000 Hz; there was also no significant change from the MS to MM conditions at 4000 Hz. At 80 dB HL there were no significant changes in amplitudes from the MM to DM conditions at 1000 and 2000 Hz.

Relative Efficiency

Although amplitudes may decrease with increasing number of stimuli, it may still be more efficient to use multiple stimuli. If amplitudes are greater than 50% (MM) or 35% (DM) of the single-stimulus condition, the multiple-stimulus condition is more efficient. In the present study, pooled across carrier frequencies, the MM condition was more efficient for 100% of subjects at 30 dB HL, 100% of subjects at 55 dB HL, but only 17% of subjects at 80 dB HL. Similarly, the DM condition was more efficient for 100% of subjects at 30 dB HL, 83% of subjects at 55 dB HL, and only 33% of subjects at 80 dB HL.

The above calculations, which indicate the percent of subjects where multiple conditions were more efficient, do not quantify the extent of the change in efficiency. Relative efficiency was therefore calculated, the results of which are presented in Figure 3, with results of a 3-way repeated-measures ANOVA for these calculations summarized in Table 2. Only main effects and interactions that involve condition are of interest, as the study investigated the changes in ASSR amplitude when the number of simultaneous stimuli was changed. Multiple-stimulus conditions (MM and DM) results are all relative to the single-stimulus condition (MS), and the mean relative efficiency of the MS condition is always 1. If the relative efficiency is greater than 1 for a MM or DM condition, the multiple-stimulus technique is more efficient than the single-stimulus technique. Figure 3 shows that, in general, relative efficiency increases in the MM and DM conditions at 30 dB HL. At 55 dB HL, the increases in relative efficiency are present but less pronounced, and at 80 dB HL the trend is for a decrease in relative efficiency with increasing number of stimuli. Overall, there was a significant main effect of condition, with post-hoc tests showing that the multiple conditions (MM and DM) were significantly more efficient than the MS condition ($p < .001$), but not significantly different from each other ($p = .88$).

Post-hoc analysis of the significant condition x intensity interaction showed a significant increase in relative efficiency from the MS to MM condition and from the MS to DM condition at 30 dB HL ($p < .001$) and 55 dB HL ($p < .001$). At 80 dB HL, relative efficiency decreased in all conditions, but the changes were not statistically significant ($p = .35$ from MS to MM; $p = .31$ from MS to DM; and $p = .73$ from MM to DM). For all intensities, there was no significant change in relative efficiency from the MM to DM conditions.

Post-hoc analysis of the condition x frequency interaction showed more increase in relative efficiency for higher frequencies. Also important to note is that when pooled across intensity, the relative efficiency for the MM and DM conditions was always higher than that of the MS condition, although in some cases the increase in relative efficiency was not statistically significant. At 500 Hz, there was a significant increase from MS to MM ($p < .001$) and from MS to DM ($p = .01$). There was a small but significant decrease in relative efficiency from MM to DM ($p = .03$); nevertheless the relative efficiency did not decrease to worse than the MS level. At 1000 Hz, there was no significant change in relative efficiency from MS to MM ($p = .82$), although there was a significant increase from the MS to DM condition ($p < .01$), and a non-significant trend toward an increase from MM to DM ($p = .05$). At 2000 Hz, there was a non-significant trend for the relative efficiency to increase from the MS to MM condition ($p = .06$) and a significant increase from the MS to DM condition ($p < .01$). There was no change from MM to DM ($p = .74$). At 4000 Hz, relative efficiency increased from MS to MM ($p < .001$) and MS to DM ($p < .001$), but there was no significant change from MM to DM ($p = .73$).

In summary, the relative efficiency generally increased significantly from the MS to MM conditions for low (30 dB HL) and moderate intensities (55 dB HL). At higher intensities (80 dB HL) the relative efficiency did not change significantly from the MS condition to either the MM or DM condition. For all intensities, there was little or no further increase in relative efficiency from the MM to the DM condition. There was no significant difference in the relative efficiency of the different conditions for different carrier frequencies.

Discussion

ASSR Amplitudes

Overall, the present study's results follow the expected decrease in ASSR amplitude due to the addition of simultaneously-presented stimuli. Amplitudes collapsed over frequency and intensity were 270, 155, and 107 nV for the MS, MM and DM conditions, respectively. Very few studies have investigated multiple simultaneous stimuli for ASSRs in the 40-Hz range. The response amplitude results of this study expand on data reported by John et al. (1998): the range of frequencies and intensities measured in this study was expanded to include the four most important audiometric frequencies (500, 1000, 2000, and 4000 Hz), as well as intensities that would correspond to near-threshold (30 dB HL), moderate (55 dB HL), and high (80 dB HL) intensities in adults with normal hearing, enabling the investigation of the effects of multiple stimuli on other carrier frequencies and intensities.

John et al. (1998) had concluded that for 40-Hz ASSRs, multiple stimuli were less efficient than single stimuli, but their conclusion was based only on the limited results from a 1000-Hz carrier at 60 dB SPL. Although they recorded this carrier in two-tone, MM, and DM multiple-stimulus combinations with carriers at other frequencies, they only baselined the 1000-Hz carrier in the MS condition, therefore they could not evaluate the amplitude changes at other frequencies. In the present study, a decrease in ASSR amplitude for the 1000-Hz carrier at 55 dB HL was found from the MS condition to the MM condition, and from the MM condition to the DM condition, which is consistent with the the results from John and colleagues for 1000 Hz at 60 dB SPL. The decrease in amplitude from the MM condition to the DM condition was not statistically significant at 1000 Hz. The present study, however, significantly expanded on the number of frequencies and intensities tested.

The results at 80 dB HL showed the greatest interactions between responses, and were consistent with published literature showing that there are cochlear and neural interactions resulting in significant ASSR amplitude decreases with the addition of multiple stimuli above 60 dB SPL (John et al., 1998). These interactions have also recently been shown for multiple ASSRs in the MM condition modulated near 14, 40, and 80 Hz at 80 dB SPL (Armstrong, 2006). At 55 dB HL, there are significant interactions when increasing from one to four stimuli, except for 4000 Hz. The addition of four additional stimuli in the contralateral ear (the DM condition) did not result in further interactions compared to the MM condition, except at 500 Hz. The present study's results are especially interesting at the lowest intensity measured. No significant decrease was found for ASSR amplitudes at 30 dB HL between the MS, MM, and DM conditions, except between the MM and DM condition only at 500 Hz. This suggests that there are very few cochlear or neural interactions between stimuli presented simultaneously at low intensities, and that for low intensities, the multiple-stimuli 40-Hz ASSR technique may be more efficient than testing only one stimulus at a time.

Overall results for frequency (collapsed over condition and intensity) show that the largest ASSR amplitudes occur at 500 Hz, followed by 4000 Hz, 1000 Hz, and 2000 Hz.

Single ASSRs have been shown in previous studies to decrease in amplitude with increasing carrier frequency (e.g., Galambos et al., 1981; Rodriguez, Picton, Linden, Hamel, & Laframboise, 1986; Stapells et al., 1984). The results of this study also showed decreasing ASSR amplitude with increasing carrier frequency in the MS condition, but this did not hold when multiple simultaneous stimuli were used in the MM and DM conditions, which accounts for the overall result of 4000 Hz responses being larger than 1000 and 2000 Hz. This could be due to an enhancement of responses to high-frequency carriers by the addition of a low-frequency simultaneously-presented stimulus, previously reported by John et al. (1998).

The present study's results confirm that there are indeed significant decreases in amplitude at moderate and high intensities with the addition of simultaneous stimuli, consistent with John et al.'s (1998) results for 1000 Hz. However, this does not hold for the near-threshold intensity of 30 dB HL, which did not have significant changes in amplitude at any frequency with multiple stimuli, except for 500 Hz from MM to DM conditions. It also does not hold for 4000 Hz at 55 dB HL, which had no significant change in amplitude with the addition of simultaneous stimuli. Overall, even at the moderate and high intensities, there were few significant changes in amplitude when increasing from four stimuli in one ear to four stimuli in each ear, except at 500 Hz.

Relative Efficiency

An important objective of this study was to determine not only if ASSR amplitudes would decrease significantly with increasing number of simultaneous stimuli, but also to quantify the relative efficiency of the different conditions. Because more information is being collected when a higher number of stimuli is used, recording responses to multiple simultaneous stimuli (either monotically or dichotically) may be more efficient even when there is a significant decrease in ASSR amplitude compared to the single-stimulus technique. The relative efficiency calculations incorporate the theoretical criteria for increased efficiency due to the time saved by simultaneously assessing multiple stimuli. The results of the relative efficiency calculations, collapsed over frequency and intensity, were 1.00, 1.38, and 1.39 for MS, MM and DM conditions, respectively.

Overall, the results indicate that there is a significant efficiency advantage to simultaneously testing four carrier frequencies in one ear (MM condition) compared to testing each one individually (MS condition) at 30 and 55 dB HL. Doubling the number of multiple simultaneous stimuli from one ear in the MM condition to two ears in the DM condition seems to result in little change in efficiency overall, but it is important to note that, in general, testing two ears simultaneously does not reduce the efficiency. Given that there is no increase in relative efficiency from the MM to the DM condition (i.e., no advantage in increasing the number of simultaneous stimuli from 4 to 8), it may be more simple to use the MM technique. At the higher intensity of 80 dB HL, decreases in relative efficiency were measured in most cases when multiple simultaneous stimuli were used, but again, these decreases were not statistically significant.

Relative efficiency calculations allow the comparison of different conditions based on the theoretical maximum gain in information collected when increasing the number of simultaneous stimuli. The increase in efficiency should theoretically be reflected clinically in the actual test time, but this has been shown to not always be the case. For example, Herdman & Stapells (2001) found that the recording times for 80-Hz ASSRs in the MM and DM conditions were approximately half of their theoretical efficiency. The present study did not investigate the time required to obtain significant responses from each carrier frequency, nor were threshold searches performed. Relative efficiency represents the best-case scenario, and there are situations where the time required to obtain an audiogram using multiple ASSRs would be expected to be considerably more than the theoretical minimum. In the case of a steeply sloping hearing loss, the thresholds would be higher with increasing frequency. If multiple ASSRs are used with the carrier frequencies all at the same intensity for each trial, the time savings from multiple stimuli may be negated by the number of trials/intensities required to bracket the threshold for each frequency (Herdman & Stapells, 2003; John et al., 2002). If both ears are to be tested simultaneously (i.e., using the DM condition), a similar decrease in the theoretical efficiency may arise if the thresholds are asymmetrical between the ears. For example, many intensities would be required if the DM condition was used to test someone with normal hearing in one ear and a steeply sloping mild to severe hearing loss in the other. There are no studies to date that have used 40-Hz ASSRs to compare the time needed to obtain thresholds using the MS, MM, and DM conditions. Van Maanen and Stapells (2005) found that the 40-Hz MM technique is faster than the 80-Hz MM technique to assess thresholds in adults with noise-induced hearing loss, but future research might indicate that the 40-Hz MS (single) technique is the fastest method clinically for non-flat and asymmetrical hearing losses. The results of the present study, however, would predict that multiple simultaneous stimuli will be more efficient than single stimuli. Future studies could shed some light on these questions.

Interactions

Previous studies have shown that there is no significant decrease in ASSR amplitude between MS, MM, and DM conditions in the 80-Hz range up to moderate intensities (Herdman & Stapells, 2001; Lins & Picton, 1995). The significant decreases in amplitude found in this study for low and moderate intensities using similar stimuli (e.g., 500 Hz) can therefore be assumed to be due to neural rather than cochlear interactions. The decrease in ASSR amplitude at high intensities is likely due to a combination of cochlear and neural interactions. Also of note is the fact that any difference between the MM and DM conditions for a particular intensity and frequency must be due to neural binaural interactions (i.e., beyond the cochlear nucleus). The results at high intensities are of great importance if multiple 40-Hz ASSRs are to be used in the assessment of severe or profound hearing losses. Based on the results of the present study, it would probably be more efficient to use single stimuli for such assessments, although this should be investigated.

Future Research

Although the results of this study show promise for the use of multiple 40-Hz ASSRs in the audiometric assessment of adults, more research is required before this technique can be recommended for widespread clinical implementation. Specifically, more information is required to determine the efficiency of multiple 40-Hz ASSRs in hearing-impaired subjects, and particular those with varying degrees and configurations of sensorineural hearing loss. One interesting question, especially for the low and moderate intensities, is whether the response is related to the sensation level of the stimulus at a particular frequency, or if it is simply dependent on the sound pressure level being used. Also of note is the fact that sensorineural loss causes a broadening of the auditory filters in the cochlea (Pickles, 1988; Tyler, 1986). This may have an effect, as yet unknown, on cochlear interactions between multiple simultaneous stimuli, and should be further investigated. As mentioned above, no studies have investigated the time required to obtain thresholds comparing 40-Hz ASSRs in MS, MM, and DM conditions. This should be investigated in both normal-hearing and hearing-impaired adults.

The modulation frequencies used were chosen to be similar to those used in previous studies (e.g., Van Maanen & Stapells, 2005), and also to satisfy the Multi-

MASTER system's requirement for an integer number of cycles in each sweep. These may not be the most optimal modulation frequencies to maximize efficiency, and future work could result in different recommendations for the MFs. It may also be possible to use a combination of modulation frequencies (i.e., the same carrier frequency simultaneously modulated at rates in the 40-Hz and 80-Hz range). This could take advantage of the large responses in the 40-Hz range as well as the resiliency to arousal state of responses in the 80-Hz range (Lins & Picton, 1995).

Clinical Implications

Of the currently available steady-steady responses techniques, it is clear that 40-Hz ASSRs are not appropriate for use in children due to their lack of presence in young children and large fluctuations in the responses with varying arousal states (Aoyagi et al., 1993; Maurizi et al., 1990; Stapells, et al., 1988; Suzuki & Kobayashi, 1984). However, the limitations of 40-Hz ASSRs in the pediatric population do not preclude their use for adult hearing threshold assessment. Although the need for electrophysiological assessment techniques in audiology is largely driven by the need to assess young children who are incapable of responding behaviourally, there are situations in audiology where objective assessment of adults is desirable, and even necessary. Such cases include medical-legal and compensation cases, and, potentially, elderly or disabled patients. Audiometric assessment for these cases is currently performed by either tone ABR or slow cortical potentials (Hyde, 1994; Stapells, 2002). Both these techniques require subjective analysis of waves by a highly-trained operator, and are both limited to testing one frequency at a time (Stapells, 2000).

Considering the amplitude and relative efficiency results at various intensities and frequencies from the present study, as well as the findings from Van Maanen and Stapells (2005) showing that 40-Hz ASSR thresholds using the monotic-multiple technique are closer to behavioural thresholds in adults than 80-Hz ASSRs and SCPs, 40-Hz ASSRs may be the technique of choice for adults. Van Maanen and Stapells (2005) also found that SCPs were faster than the ASSR methods (although not significantly faster than 40-Hz ASSRs), but the SCP requires analysis of waveforms by a clinician, which would likely negate and time savings (Van Maanen & Stapells, 2005). Until further research is performed, the most efficient protocol may be to use the monotic-multiple technique for low and moderate intensities, and switch to the monotic-single technique when high intensities are required.

Table 1. Summary of three-way repeated-measures ANOVA for amplitude measurements comparing effects of Condition, Frequency, and Intensity.

Effect	df	F	ϵ^a	p^b
CONDITION	2, 22	56.20	0.53	< .001*
FREQUENCY	3, 33	4.49	0.398	.048*
INTENSITY	2, 22	83.7	0.607	< .001*
CONDITION x FREQUENCY	6, 66	12.43	0.338	< .001*
CONDITION x INTENSITY	4, 44	65.4	0.376	< .001*
FREQUENCY x INTENSITY	6, 66	8.44	0.754	< .001*
CONDITION x FREQUENCY x INTENSITY	12, 132	7.67	0.512	< .001*

df = degree of freedom; [a] Huyn-Feldt epsilon (ϵ) correction factor for degrees of freedom; [b] Probability reflects corrected degrees of freedom; * significant ($p < .05$).

Table 2. Summary of three-way repeated-measures ANOVA for relative efficiency calculations comparing effects of Condition, Frequency, and Intensity.

Effect	df	F	ϵ^a	p^b
CONDITION	2, 22	26.13	1	< .001*
FREQUENCY	3, 33	2.77	0.482	0.105
INTENSITY	2, 22	28.26	0.561	< .001*
CONDITION x FREQUENCY	6, 66	12.64	0.895	< .001*
CONDITION x INTENSITY	4, 44	28.64	0.718	< .001*
FREQUENCY x INTENSITY	6, 66	1.2	0.708	0.325
CONDITION x FREQUENCY x INTENSITY	12, 132	1.38	0.615	0.22

df = degree of freedom; [a] Huyn-Feldt epsilon (ϵ) correction factor for degrees of freedom; [b] Probability reflects corrected degrees of freedom; * significant ($p < .05$).

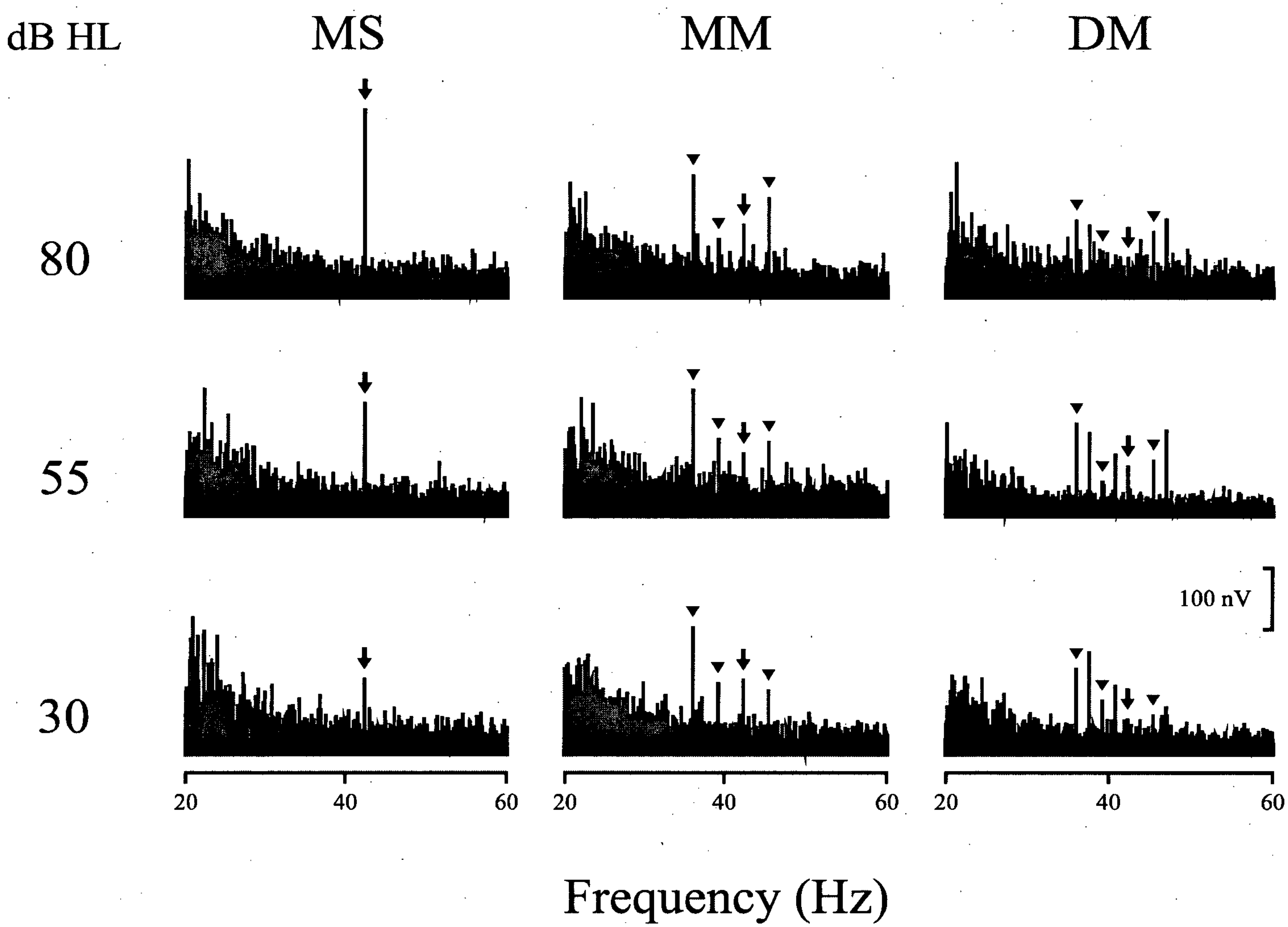

Figure 1: One subject's ASSR for 2000 Hz in the MS condition, as well as the MM and DM conditions at 30, 55 and 80 dB HL. Filled arrows indicate significant responses at 2000 Hz and filled triangles indicate significant responses at the other modulation frequencies for the carrier(s) in the test ear.

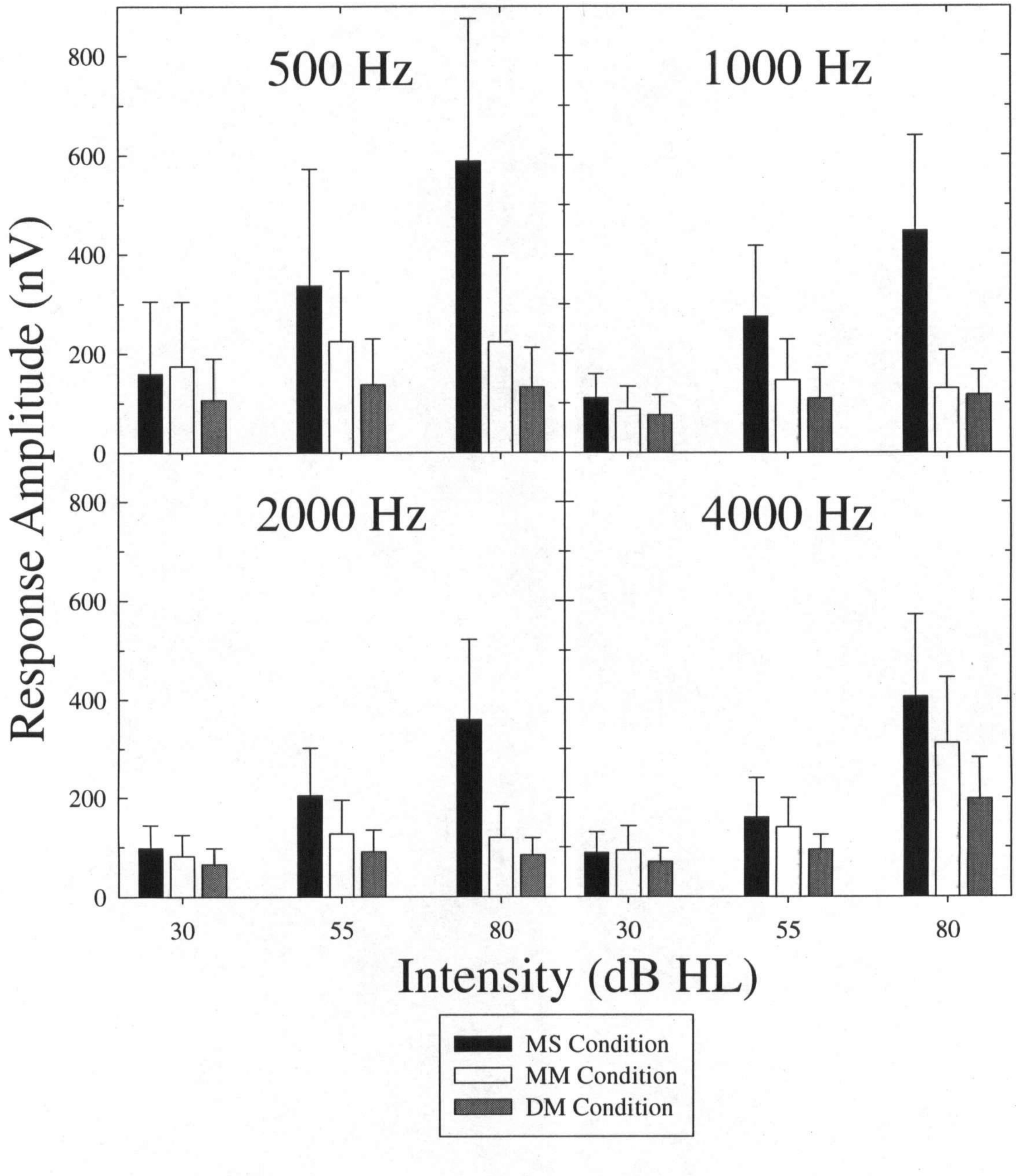

Figure 2. Mean ASSR amplitudes for carrier frequencies of 500, 1000, 2000, and 4000 Hz in condition MS, MM, and DM at intensities of 30, 55, and 80 dB HL. Error bars represent one standard deviation.

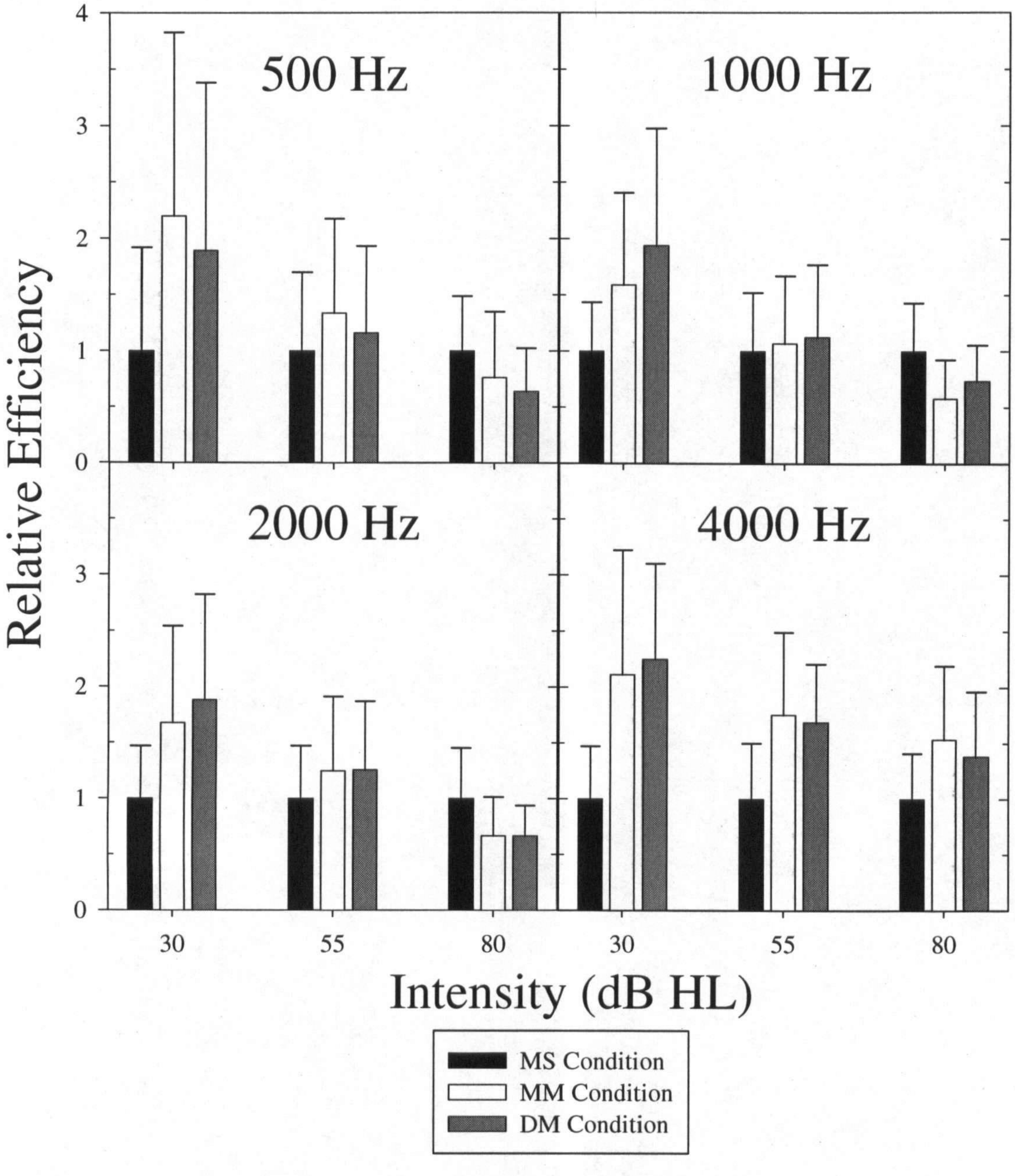

Figure 3. Mean relative efficiency for carrier frequencies of 500, 1000, 2000, and 4000 Hz in condition MS, MM, and DM at intensities of 30, 55, and 80 dB HL. Relative efficiencies in the MM and DM conditions are relative to the MS condition. Error bars represent one standard deviation.

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Appendix I: Amplitude Data by Subject

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Notes: Under each frequency the numbers 30, 55, 80 are in dB HL. All amplitude measurements are in nanovolts (nV). Shading in a cell indicates a non-significant response for which the amplitude measured was used.

				Monotic Single (MS) Condition											
				500 Hz			1000 Hz			2000 Hz			4000 Hz		
Subject	Gender	Test Ear	Age	30	55	80	30	55	80	30	55	80	30	55	80
1	M	R	31	62	170	380	132	290	370	87	193	388	107	246	495
2	F	R	31	122	280	573	114	343	587	108	350	488	127	111	481
3	M	R	35	545	925	1249	174	534	654	126	264	217	104	156	415
4	F	R	32	65	175	416	45	101	264	61	82	270	56	132	299
5	F	R	29	314	683	923	175	457	795	177	373	721	153	296	776
6	F	L	23	161	215	897	88	418	663	172	256	482	141	251	493
7	M	L	32	68	188	397	61	93	275	46	147	273	46	52	192
8	M	L	30	54	187	297	83	107	155	32	72	113	14	69	253
9	M	L	32	224	341	453	80	212	394	124	179	305	93	170	346
10	F	L	27	157	208	388	128	232	313	90	244	434	104	234	573
11	F	L	30	108	266	535	66	269	475	94	186	404	69	143	292
12	F	R	33	31	407	548	184	243	423	61	112	220	53	70	259
		Mean	30.4	159	337	588	111	275	447	98	205	360	89	161	406
	Standard Deviation		3	146	235	286	48	143	192	46	97	162	42	80	166

	Monotic Multiple (MM) Condition											
	500 Hz			1000 Hz			2000 Hz			4000 Hz		
Subject	30	55	80	30	55	80	30	55	80	30	55	80
1	70	76	56	81	116	52	69	111	111	107	175	418
2	171	261	113	97	94	194	83	266	190	139	142	434
3	518	604	695	158	217	222	42	91	189	82	184	257
4	110	144	133	8	99	52	43	72	90	55	93	235
5	299	369	311	133	259	261	137	223	172	150	231	552
6	200	205	328	73	320	238	154	171	223	174	207	448
7	76	136	73	48	66	73	42	97	47	16	42	164
8	31	112	101	44	71	65	30	34	20	34	51	174
9	210	207	201	121	122	98	125	104	121	108	116	166
10	118	196	213	112	155	112	116	158	115	134	188	418
11	140	162	224	47	60	84	51	144	79	53	142	254
12	156	226	237	134	180	102	94	59	80	75	120	215
Mean	175	225	224	88	147	129	82	128	120	94	141	311
Standard Deviation	130	142	173	45	83	77	43	68	62	49	60	134

Amplitude Data by Subject (continued)

	Dichotic Multiple (DM) Condition											
	500 Hz			1000 Hz			2000 Hz			4000 Hz		
Subject	30	55	80	30	55	80	30	55	80	30	55	80
1	33	38	47	43	30	30	46	29	55	77	105	229
2	104	189	91	104	182	182	91	154	106	59	73	268
3	329	363	338	161	205	213	86	124	121	101	136	167
4	65	43	92	38	66	100	8	55	106	46	59	191
5	181	204	163	118	179	137	137	122	85	97	123	332
6	112	82	160	102	178	154	79	149	152	113	122	285
7	76	77	61	54	65	107	53	74	64	32	72	95
8	25	71	82	21	42	86	42	12	39	68	54	107
9	139	155	135	91	56	71	60	78	64	66	91	109
10	80	121	85	74	110	115	83	107	109	100	127	306
11	104	116	125	38	76	76	56	103	42	46	120	139
12	30	199	210	68	125	126	43	84	72	44	70	158
Mean	107	138	132	76	110	116	65	91	85	71	96	199
Standard Deviation	84	92	80	41	62	50	33	44	35	27	29	83

Appendix II: Relative Efficiency Data by Subject

Appendix II: Relative Efficiency Data by Subject

Notes: Under each frequency the numbers 30, 55, 80 are in dB HL.

	Monotic Single (MS) Condition											
	500 Hz			1000 Hz			2000 Hz			4000 Hz		
Subject	30	55	80	30	55	80	30	55	80	30	55	80
1	0.39	0.50	0.65	1.19	1.05	0.83	0.89	0.94	1.08	1.20	1.53	1.22
2	0.77	0.83	0.97	1.03	1.25	1.31	1.10	1.71	1.36	1.43	0.69	1.18
3	3.42	2.74	2.12	1.57	1.94	1.46	1.28	1.29	0.60	1.17	0.97	1.02
4	0.41	0.52	0.71	0.41	0.37	0.59	0.62	0.40	0.75	0.63	0.82	0.74
5	1.97	2.03	1.57	1.58	1.66	1.78	1.80	1.82	2.01	1.72	1.84	1.91
6	1.01	0.64	1.53	0.79	1.52	1.48	1.75	1.25	1.34	1.59	1.56	1.21
7	0.43	0.56	0.68	0.55	0.34	0.61	0.47	0.72	0.76	0.52	0.32	0.47
8	0.34	0.55	0.51	0.75	0.39	0.35	0.33	0.35	0.31	0.16	0.43	0.62
9	1.41	1.01	0.77	0.72	0.77	0.88	1.26	0.87	0.85	1.05	1.06	0.85
10	0.99	0.62	0.66	1.15	0.84	0.70	0.92	1.19	1.21	1.17	1.45	1.41
11	0.68	0.79	0.91	0.60	0.98	1.06	0.96	0.91	1.12	0.78	0.89	0.72
12	0.19	1.21	0.93	1.66	0.88	0.95	0.62	0.55	0.61	0.60	0.44	0.64
Mean	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Standard Deviation	0.92	0.70	0.49	0.43	0.52	0.43	0.47	0.47	0.45	0.47	0.50	0.41

	Monotic Multiple (MM) Condition											
	500 Hz			1000 Hz			2000 Hz			4000 Hz		
Subject	30	55	80	30	55	80	30	55	80	30	55	80
1	0.88	0.45	0.19	1.46	0.84	0.23	1.41	1.08	0.62	2.41	2.18	2.06
2	2.15	1.55	0.38	1.75	0.68	0.87	1.69	2.60	1.06	3.13	1.77	2.14
3	6.51	3.58	2.36	2.85	1.58	0.99	0.86	0.89	1.05	1.84	2.29	1.27
4	1.38	0.85	0.45	0.14	0.72	0.23	0.88	0.70	0.50	1.24	1.16	1.16
5	3.76	2.19	1.06	2.40	1.88	1.17	2.79	2.18	0.96	3.37	2.87	2.72
6	2.51	1.22	1.12	1.32	2.33	1.06	3.14	1.67	1.24	3.91	2.57	2.21
7	0.95	0.81	0.25	0.87	0.48	0.33	0.86	0.95	0.26	0.36	0.52	0.81
8	0.39	0.66	0.34	0.79	0.52	0.29	0.61	0.33	0.11	0.76	0.63	0.86
9	2.64	1.23	0.68	2.18	0.89	0.44	2.55	1.02	0.67	2.43	1.44	0.82
10	1.48	1.16	0.72	2.02	1.13	0.50	2.36	1.54	0.64	3.01	2.34	2.06
11	1.76	0.96	0.76	0.85	0.44	0.38	1.04	1.41	0.44	1.19	1.77	1.25
12	1.96	1.34	0.81	2.42	1.31	0.46	1.92	0.58	0.44	1.69	1.49	1.06
Mean	2.20	1.33	0.76	1.59	1.07	0.58	1.67	1.24	0.67	2.11	1.75	1.53
Standard Deviation	1.63	0.84	0.59	0.82	0.60	0.34	0.87	0.66	0.35	1.11	0.74	0.66

Relative Efficiency Data by Subject (continued)

	Dichotic Multiple (DM) Condition											
	500 Hz			1000 Hz			2000 Hz			4000 Hz		
Subject	30	55	80	30	55	80	30	55	80	30	55	80
1	0.59	0.32	0.23	1.10	0.31	0.19	1.33	0.40	0.43	2.45	1.85	1.59
2	1.85	1.59	0.44	2.65	1.87	1.15	2.62	2.13	0.83	1.88	1.28	1.87
3	5.84	3.05	1.63	4.11	2.11	1.35	2.48	1.71	0.95	3.21	2.39	1.16
4	1.15	0.36	0.44	0.97	0.68	0.63	0.23	0.76	0.83	1.46	1.04	1.33
5	3.21	1.71	0.78	3.01	1.84	0.87	3.95	1.68	0.67	3.09	2.16	2.31
6	1.99	0.69	0.77	2.60	1.83	0.97	2.28	2.06	1.20	3.59	2.15	1.98
7	1.35	0.65	0.29	1.38	0.67	0.68	1.53	1.02	0.50	1.02	1.27	0.66
8	0.44	0.60	0.39	0.54	0.43	0.54	1.21	0.17	0.31	2.16	0.95	0.75
9	2.47	1.30	0.65	2.32	0.58	0.45	1.73	1.08	0.50	2.10	1.60	0.76
10	1.42	1.02	0.41	1.89	1.13	0.73	2.39	1.48	0.86	3.18	2.23	2.13
11	1.85	0.97	0.60	0.97	0.78	0.48	1.61	1.42	0.33	1.46	2.11	0.97
12	0.53	1.67	1.01	1.74	1.29	0.80	1.24	1.16	0.57	1.40	1.23	1.10
Mean	1.89	1.16	0.64	1.94	1.13	0.74	1.88	1.26	0.67	2.25	1.69	1.38
Standard Deviation	1.49	0.77	0.39	1.04	0.64	0.32	0.94	0.61	0.27	0.85	0.52	0.58

Appendix III: Pilot Study

Appendix III: Pilot Study

A total of 4 subjects (2 female) were tested as part of a pilot study in September and October 2004. Methods were similar to those in the study above, except for the following:

1. Intensities were 20, 50, and 80 dB HL rather than 30, 55, and 80 dB HL. The lowest intensity was increased for the study because a response was not present in some of the subjects at 20 dB HL, despite having normal hearing.

2. The non-inverting electrode was placed at the high forehead (below the hairline) rather than at Fz. There was variability in the hairline of the pilot subjects, and large inter-subject differences in the response amplitude were measured (e.g., 865 nV versus 232 nV in two subjects for single 500 Hz carrier). To help reduce inter-subject variability, the non-inverting electrode was consistently placed at Fz in the study..

3. The separation between the modulation frequencies was found to be uneven when using 1000 Hz A/D rate in the pilot study. The modulation rates were likely too close together between ears in the dichotic condition (as close as 0.9 Hz), which could have reduced the amplitude of the responses (John et al., 1998). Changing the A/D rate to 800 Hz with a DA factor of 40 in MultiMASTER enables the even separation between modulation rates.

Appendix IV: UBC Behavioural Research Ethics Board Certificate of Approval