Evaluating the Modulation Transfer Function of Auditory Steady State Responses in the 65 Hz to 120 Hz Range

David W. Purcell¹ and M. Sasha John^{2,3}

Objective: Auditory steady state response (ASSR) tests allow frequencyspecific assessment of the auditory system. The responses can be elicited with long-duration tones that are modulated at particular rates. The literature has reported that some rates may evoke larger responses than others. Modulation transfer functions (MTFs), which show ASSR response as a function of modulation rate, can be created by presenting a fixed carrier with a modulation rate that is swept over time. Here, we explore the profiles of MTFs with particular effort made toward examining (1) the rates in the MTF that provided the maximum and minimum values, (2) the means and ranges of ASSRs within each MTF, and (3) MTF test-retest repeatability. Because recording ASSRs to a 500-Hz carrier frequency is often difficult at 60 dB SPL or less, we focused our efforts on this frequency. The main objective of this study was to evaluate the possibility of using MTFs for the purpose of identifying both optimal and unfavorable modulation rates.

Design: Fifty-four normal hearing adult subjects were allocated to one of four experimental conditions. The first two conditions used a 500-Hz carrier and generated MTFs where modulation rate was varied continuously across a low (66 to 102 Hz) or high (86 to 121 Hz) range. In two additional conditions, a 500-Hz carrier having a modulation rate fixed at 82 Hz and a 2000-Hz carrier having a swept modulation rate (66- to 102-Hz range) were also obtained for comparison. Stimuli were presented at 60 dB SPL. The two ranges of modulation were used because these have implications for the generators and characteristics of the evoked responses. Responses were analyzed for each condition using a Fourier analyzer. To assess the stability of the MTF, two recordings, of 25 mins each, were obtained for each subject.

Results: MTF profiles and modulation rates associated with maximum and minimum amplitudes clearly demonstrated repeatability between the two recordings. More specifically, modulation rates for the maximum and minimum amplitudes showed correlations above 0.92 between the two recordings. Using combined data from the two replications, we found that differences between maximum and minimum amplitudes were between 34 and 51 nV when modulation rate was varied. For the fixed modulation rate condition, the difference was only 22 nV, which was due to fluctuations in noise. Response amplitude and noise estimates obtained in this study suggest that \sim 30% of individuals would require at least 10 mins more recording time if an actual hearing test was performed using the modulation rate associated with the ASSR amplitude minimum rather than the maximum. For some individuals, the ASSR would not be detected in a practical amount of time if the wrong modulation rate were relied upon during a clinical test.

Conclusions: In research applications requiring repeated measurements, or clinical contexts such as intraoperative monitoring or assessment of aided hearing, setting stimulus modulation rate parameters based on a previous analysis of an individual's MTF could be extremely beneficial. Sufficient time must be spent in recording the MTF to adequately attenuate the contribution of noise to the ASSR amplitude estimates.

(Ear & Hearing 2010;31;667-678)

¹National Centre for Audiology, School of Communication Sciences and Disorders, University of Western Ontario, London; ²The Rotman Research Institute, Baycrest, Toronto; and ³Institute of Biomaterials and Biomedical Engineering, University of Toronto, Toronto, Ontario, Canada.

INTRODUCTION

Infant hearing screening programs worldwide have enjoyed tremendous success in identifying hearing impairment using objective measurements within the first months of life, before it would be possible to perform reliable behavioral tests (e.g., Norton et al. 2000). This success presents the opportunity for interventions that can prevent delays in speech and language development (Joint Committee on Infant Hearing 2007). When hearing loss is detected, it is necessary to then learn more through a diagnostic assessment to appropriately tailor interventions. Although the tone-burst auditory brain stem response (ABR) is currently in widespread use for estimating behavioral pure-tone thresholds, there is excitement and interest about favorable properties offered by the auditory steady state response (ASSR; Cone-Wesson et al. 2002; Picton et al. 2003a; Ahn et al. 2007; Rance 2008; Van Maanen & Stapells 2009; Lin et al. 2009; Swanepoel & Ebrahim 2009). The ASSR is most commonly elicited with long-duration stimuli that are amplitude and (sometimes) frequency modulated. The acoustic specificity of the stimulus and place specificity of ASSR initiation in the cochlea are good, even with steeply sloping hearing loss (Herdman & Stapells 2003). The response occurs at the modulation rate and is often analyzed in the frequency domain. This facilitates the use of objective statistical methods in the detection of the response (e.g., Picton et al. 2003a), thus reducing the burden on the operator to make a subjective decision about the presence of an evoked waveform. It is possible to simultaneously test multiple carrier frequencies in both ears when each carrier is modulated at a unique rate (Lins & Picton 1995; John et al. 1998; John & Picton 2000). With the right implementation, this may allow reduced testing time relative to the tone burst ABR (e.g., John et al. 2002a; Van Maanen & Stapells 2005).

Two ranges of modulation rates have primarily been considered in ASSR testing: near 40 Hz and above \sim 70 Hz. Rates near 40 Hz elicit ASSRs that contain a large contribution from cortical sources in addition to brain stem sources. As modulation rate is increased above \sim 70 Hz, the response becomes increasingly dominated by brain stem sources (Plourde et al. 1991; Herdman et al. 2002). Testing in the 40-Hz range is most efficient for awake adults (Van Maanen & Stapells 2005), but this range is not appropriate for infants. Immaturity of the cortical generators and the necessity of sleep during the recording (to reduce myogenic noise) make the 40-Hz response difficult to detect in infants (Suzuki & Kobayashi 1984; Stapells et al. 1988; Aoyagi et al. 1993; Levi et al. 1993; Rickards et al. 1994). Therefore, modulation rates above 70 Hz have been adopted for testing infants and children, and these measurements are referred to generally as the 80-Hz ASSR.

0196/0202/10/3105-0667/0 • Ear & Hearing • Copyright © 2010 by Lippincott Williams & Wilkins • Printed in the U.S.A.

Despite the favorable characteristics of the ASSR, there are challenges that must be met to exploit its full potential and allow widespread clinical adoption. Immaturity of the auditory brain stem has a large effect on ASSR amplitude in the first 6 wks of life (e.g., Savio et al. 2001; Rance & Rickards 2002; John et al. 2004; Luts et al. 2004; Rance et al. 2005; Luts et al. 2006; Rance & Tomlin 2006), and maturation of the response likely continues until ~ 3 yrs (when the ABR is treated as adult-like). In addition, in both infants and adults, many studies have found that ASSR thresholds determined using a 500-Hz carrier are relatively increased above the behavioral threshold than carrier frequencies such as 1000 and 2000 Hz (e.g., Rickards et al. 1994; Aoyagi et al. 1999; Dimitrijevic et al. 2002; also see meta analysis in Table 4 of Herdman & Stapells 2003; Van Maanen & Stapells 2007). In-the-ear calibration data (versus adult coupler calibration) suggest that 4 kHz may also be increased for infants (Rance & Tomlin 2006). The tone-burst ABR also produces increased thresholds at 500 Hz (Gorga et al. 1988).

The special difficulty of the ASSR 500-Hz carrier has been addressed by methods that generally seek to increase ASSR amplitude by initiating a larger response beginning at the level of the cochlea (e.g., John et al. 2003). Assuming no change in background noise levels, an increase in the response amplitude means that the ASSR will be detectable to lower stimulus levels that are closer to the behavioral threshold (Cohen et al. 1991). Exponentially amplitude modulated tones have been investigated as a way to elicit more synchronous and therefore larger responses (John et al. 2002b). Stürzebecher et al. (2001) designed a stimulus to stimulate a slightly broader region of the cochlea by summing multiple tones amplitude modulated at the same rate. Mixed modulation stimuli seek to increase the recorded ASSR by the constructive addition of responses from somewhat independent neural circuits responsible for detection of amplitude modulation and frequency modulation (John et al. 2001a).

In addition to adjusting stimulus parameters to evoke larger responses, studies have highlighted the possibility that modulation rates may have an appreciable effect on response amplitude even within the 70 to 100-Hz range that is currently used in ASSR research and clinical instruments intended for infant testing. Most commonly, these studies have made multiple sequential measurements using fixed modulation rates spaced at fixed intervals. Three modulation rates spanning this range were used by Rees et al. (1986), but the spacing was too coarse to evaluate the detailed effect of modulation rate. Cohen et al. (1991) measured binaurally at 5-Hz intervals in this modulation range and reported a tendency for a response minimum ${\sim}70~\text{Hz}$ with a peak in the 80- to 100-Hz range (see their Figs. 7 and 8). However, for a 500-Hz carrier, this amplitude-by-rate profile did not extend to every individual. Lins et al. (1995) reported a similar minimum and maximum in their group result for a 1000-Hz carrier frequency (see their Fig. 2). Aoyagi et al. (1993) identified the 80- to 100-Hz range as better than 40 Hz for young children, but their modulation rates were too coarsely spaced to consider the former range in much detail. The population average data of Rickards et al. (1994) suggest that the best modulation rate may vary for different carrier frequencies (see their Fig. 2). Dobie and Wilson (1998) reported data across the 20- to 160-Hz modulation range at 10-Hz intervals for a 640-Hz carrier. Their data provided further evidence that some rates produce more robust ASSRs than others. In a conference presentation, Brennan and Stevens (2007) recently reported that *infant* ASSR amplitude varied with modulation rate (using a step size of 5 Hz) on an individual basis for carrier frequencies of 1000 and 2000 Hz. They noted that implications of this modulation rate effect are that testing time could be significantly affected as well as the accuracy of the estimated thresholds. Purcell et al. (2004) recently reported that the amplitude modulation transfer function (MTF) showed detailed rate-related profiles between 60 and 130 Hz when using broadband noise as the carrier. A null in response amplitude was reported near 71 Hz, although the exact modulation rate varied from one individual to the next.

Individual results are not emphasized in these previous studies, and it is noteworthy that repeated measurements are not reported to assess the reliability or replicability of individual patient's MTF profiles. This study investigates the monaural MTF in individuals with a particular emphasize on the 500-Hz carrier frequency. Our specific goals were to determine whether there were significant differences between worst and best modulation rates, identified as those with the lowest and highest ASSR amplitude, respectively and to evaluate the repeatability of the MTF in individuals with special emphasis on the characteristics of the maxima and minima. Our approach used long-duration recordings to minimize the contribution of noise and evaluated monaural stimuli whose modulation rate was continuously varied (swept) across time. Our working hypothesis was that modulation rate has a reliable effect on the amplitudes of ASSRs elicited by a 500-Hz carrier for modulation rates in the range from 65 to 120 Hz.

MATERIALS AND METHODS

Subjects

A total of 54 adults (27 females) participated in the study with ages varying from 17 to 33 yrs (mean 25 yrs). All individuals had normal pure-tone audiometric thresholds measured at 250, 500, 750, 1000, 2000, and 4000 Hz using TDH39 headphones and a Madsen Itera audiometer with a 10 dB down/5 dB up bracketing procedure. Subjects were recruited primarily from the University of Western Ontario community. The experiments were approved by the Health Sciences Research Ethics Board of the University of Western Ontario, and written informed consent was obtained from each subject after the nature of the study was explained.

Stimuli

To obtain an MTF, the ASSR stimulus modulation frequency must be varied. One approach is to sequentially conduct independent recordings of ASSRs using fixed modulation rates across the modulation range of interest. The approach used here is to continuously "sweep" the rate of modulation over the range of interest. A stimulus sweep consisted of thirty 1.024-sec epochs. The modulation rate was ramped linearly upward over 35.15625 Hz during the first 15 epochs and linearly downward over the same range during the second 15 epochs. Sweeps were constructed so that they could be concatenated and repeated without acoustic transients (Purcell et al. 2004). Each stimulus condition comprised two replications of 50 sweeps each, and each replication lasted for 25 mins 36 secs. Sounds were presented at 60 dB SPL, as

Experimental condition	Carrier frequency (Hz)	Modulation frequency range (Hz)	Rate of change of modulation frequency (Hz/sec)
500-fixed	500	82.03	0
500-low	500	66.41 to 101.56	2.29
500-high	500	85.94 to 121.09	2.29
2k-low	2000	66.41 to 101.56	2.29

TABLE 1. Stimulus parameters

Stimulus parameters are shown for each experimental condition (rounded to two significant digits).

calibrated using a Brüel & Kjær Type 2250 sound level meter with a Brüel & Kjær Type 4157 ear simulator coupled to a Etymotic ER2 earphone acoustic transducer.

There were four experimental conditions used in a betweensubjects design. Each subject was tested on one of the four conditions, and each condition comprised the presentation of a sinusoidal amplitude modulated tone to one ear. Subjects were pseudorandomly assigned to conditions so that the total number of subjects within each condition was well balanced. Stimuli used in each of the experimental conditions are shown in Table 1. Each condition contained 50 sweeps of 30.74 secs each and was repeated twice for a total recording time of 51 mins 12 secs. As will be discussed, the slow (i.e., 2.29 Hz/sec) change of modulation frequency allowed the modulation rate transfer function to be obtained with reasonably high resolution using a Fourier analyzer (FA).

If there was no measurement "noise" from the background EEG and myogenic sources, it is reasonable to assume that the amplitude of an ASSR dominated by the brain stem should remain relatively constant over time. Real-world brain stem ASSRs will show variability over time because of several factors. At the lowest modulation rates explored in this study, a small cortical contribution to the measured ASSR will affect its amplitude and may vary slowly over time. In addition, our ASSR estimates are always contaminated by "noise" because the EEG will endogenously produce energy at the frequency of the ASSR, which may add constructively or destructively with the actual response. Therefore, even for a fixed modulation rate, the measured response (i.e., the output of the FA) will not show completely steady amplitude when measured at different moments in time across the mean response sweep. Rather, the FA estimate of ASSR amplitude varies from moment to moment because of the influence of background noise. By including a condition in which modulation rate was fixed (500-fixed), the range of ASSR amplitudes obtained can be used to assess the effect of noise versus the effect of modulation rate. The 500-low and 500-high conditions were both included because the 500-low condition might have shown more variance because of larger cortical components. The 2k-low condition was included to compare the MTF profile of the 500-low condition to that seen by a carrier frequency, which generally provides more robust ASSRs. Including two repetitions in each stimulus condition allows evaluation of the hypothesis that, within the modulation ranges tested, modulation rate has a reliable effect on the measured amplitude of the ASSR and produces a repeatable MTF profile within a subject.

Stimulus Presentation and Response Recording

The experiment was controlled by software developed using LabVIEW (Version 8.2, National Instruments). A National Instruments PCI-6289 M-series acquisition card provided digital-to-analog conversion of the stimulus with 16-bit resolution at a rate of 32,000 samples/sec. Stimulus level was set using a Tucker-Davis Technologies PA4 attenuator, and power amplification was applied by one channel of an Amcron D-75 amplifier. The stimulus was transduced using an Etymotic ER2 earphone whose sound tube was sealed in the ear-canal using a disposable foam insert. The EEG was recorded from three disposable MEDI-TRACE Ag/AgCl electrodes using GRASS Technologies EC2 electrode cream. Electrodes were located at the vertex (Cz; noninverting) and just below the hairline at the posterior midline of the neck (inverting) with a ground (or common) on the collarbone. Electrode impedances were assessed using an F-EZM5 GRASS impedance meter and were <5000 ohm at 10 Hz. Interelectrode differences were <2000 ohm. The three electrode leads were braided and then connected to a GRASS LP511 amplifier that applied a gain of 50,000, and a filter having a passband of 3 to 1000 Hz. The PCI-6289 card applied a further gain of two (for a total gain of 100k) before digitizing the output signal of the GRASS amplifier at 4000 samples/sec using 18-bit resolution.

Data were collected with subjects residing in a sound-insulated and electromagnetically shielded booth (ECKOUSTIC model C-26 R.F.). Subjects reclined in a comfortable chair with a rolled towel under their neck to help support their head, and a blanket was provided to ensure comfort. The lights were turned off, and sleep was encouraged for the duration of the ASSR recording. Two ASSR recordings were made requiring \sim 51 mins for both.

Response Analysis

Real-time MTF results and indices of EEG signal quality were displayed during data collection to ensure quality recordings. A more extensive MTF analysis was then performed off-line using a custom LabVIEW program derived with improvements from previous studies (Purcell et al. 2004; Purcell et al. 2006). Individual 1.024-sec epochs were automatically rejected from a synchronous sweep average by the software if they did not meet the following criteria: First, a noise metric was calculated for every epoch of a stimulus condition by determining the average amplitude of frequencies across the modulation range being evaluated (i.e., low or high). The mean and SD of this noise metric was calculated across all epochs. A rejection criterion was then set using the mean + 2SD, and all epochs that exceeded this criterion were rejected from the mean response sweep. Second, epochs were also rejected automatically by the software if any saturation of the amplifier occurred (for example, due to a large myogenic artifact from subject movement) as reflected by points of the recorded EEG waveform having either the maximum or minimum value of the analog to digital converter.

This rejection procedure can lead to a different number of epochs contributing to each of the 30 mean epochs that comprise the averaged sweep. If many epochs were rejected, then this might be a cause for concern due to different signal-to-noise ratios (SNRs) for different portions of the averaged sweep. In practice, only $\sim 2.5\%$ of epochs were typically rejected, and these were randomly distributed across the averaged sweep. Nonrejected data from each of the 50

sweeps (30.74 secs each) were synchronously averaged in the time domain using weighted averaging to create a mean response sweep (similar to John et al. 2001b) such that epochs with a low-noise metric were weighted relatively heavily in the mean response sweep and vice versa.

The MTF data were extracted from the mean response sweep using a software implemented FA (Regan 1989; Purcell et al. 2004; Purcell et al. 2006). In this method, orthogonal reference sinusoids are matched in frequency to the instantaneous stimulus modulation rate. An estimated physiological delay of 8.5 msecs was used to improve the alignment between the reference and response waveforms during the analysis (Aiken & Picton 2006). This single delay is an estimate of a brain stem dominated ASSR for the tested modulation ranges (Purcell et al. 2004). The slow sweeping of modulation rate used here (i.e., 2.9 Hz/sec), likely caused the effect of using this delay on the estimated response to be very small, but it is wise to use such a delay nonetheless. Two 2.048 secs rectangular window filters were applied in series to each of the complex outputs of the FA. Because the mean response sweep had symmetrical increasing and decreasing modulation rates in each half, the second half of the FA output was folded over and vector averaged with the first half. This was done to improve the SNR of the measured MTFs. A final 2.048 secs smoothing filter was applied to the amplitude values calculated from the complex FA outputs. To provide a cross-check for the FA results, a discrete Fourier transform (DFT) was also used to estimate the ASSR in the 500-fixed condition. For this comparison, the unfolded mean response sweep was submitted to the DFT and the FA.

The probability that the estimated ASSR amplitude was drawn from the distribution of the background noise was determined using an F-ratio (Zurek 1992). The characteristics of the background noise were estimated using a DFT calculated from the mean response sweep folded and averaged in the time domain. The average noise levels in ± 60 DFT frequency bins (having 0.065 Hz frequency resolution for a total range of \pm 3.91 Hz) were multiplied by a scaling factor of 2.365222 (determined using simulated noise) to compensate for the narrower effective bandwidth of the DFT compared with that of the FA. The ASSRs were considered significantly different from the background noise estimates when the SNR was ~5 dB. In other words, to reach a p < 0.05 level of statistical significance, the amplitude F-ratio evaluated using 2 and 240 degrees of freedom must be above 1.75 (John & Picton 2000).

RESULTS

Seven of the 54 participants were removed from the data that were analyzed in this study. Three of the seven were removed for having excessive noise estimates that were above 18 nV, whereas average noise levels for the other participants were 12 nV (SD = 3 nV). In a clinical situation, these subjects would have been re-tested or would have required that the testing session duration be increased (to allow sufficient time to improve SNR levels through extended averaging). This was not done in this study because of time constraints of our subjects. The remaining four of the seven removed subjects were rejected because 25% or less of their MTF data were significant across corresponding portions of the original recording and its replication. In contrast, in the subjects who were retained for

analysis, an average of 83.3% (SD 18.3%) of significant ASSRs occurred across both recordings. Therefore, these four individuals produced data that were more than three SDs below the average number of significant responses, which were normally found across both recordings. These four individuals had particularly low-amplitude ASSR estimates. Three were from the 500-high condition and had their largest ASSRs near the lowest rates used (e.g., 86 to 87 Hz in the 500-high modulation range from 86 to 121 Hz). Although these cases are important and show that the MTF can be used to determine modulation rates which will be more likely to produce valid ASSRs in subjects with difficult to detect responses, these four subjects were clearly different from the other subjects assessed in this study and deserved separate mention. In the main analyses of this study, the final number of subjects in each of the four conditions was slightly different in part because of the removal of these seven subjects. There were 12, 11, 11, and 13 subjects in the 500-low, 500-high, 2k-low, and 500-fixed conditions, respectively.

Measurement Repeatability Across Experimental Condition

In general, the ASSR MTFs were repeatable. Figure 1 shows example ASSR amplitude and noise estimate data from two subjects for each of the four experimental conditions. For each subject, the difference between measurements was calculated at each modulation frequency (or corresponding point in time for the 500-fixed condition) in which the ASSR was statistically significant in both measurements. These values were then averaged with the sign of the difference ignored to obtain the "mean absolute change" between the two MTFs. The absolute change was used so that the variation observed between the two MTFs would not be hidden by positive and negative differences that average to near zero. Mean absolute changes between the amplitudes, phases (unwrapped for each ASSR), and MTF-noise estimates of the two MTF curves were determined for each subject. MTF noise estimates were only included for frequencies of the MTF in which the ASSR reached statistical significance in both replications. In Figure 1, the individual average absolute changes between the two MTF replications are given for each subject shown. The group averages and medians of these absolute changes for each condition are reported in Table 2. The table also reports the percentage of points that reached statistical significance in both MTFs. In the case of the 500-fixed condition, the modulation rate stayed the same during the entire sweep. The word "point" refers to either a given instant in time for the 500-fixed condition or a given modulation rate for the other three experimental conditions.

Statistical tests were performed to verify that all four experimental conditions showed similar variability between the two replications. Across individuals in an experimental condition, the distribution of values for the percentage of points where the ASSR reached statistical significance in both MTFs was left skewed with many subjects close to the maximum of 100%. Only three individuals had <50% of their MTFs statistically significant, whereas 23 subjects had >90% of their MTFs statistically significant. Because nonnormal distributions were found, to be appropriately conservative, a nonparametric framework was adopted to detect differences between experimental conditions. Nonparametric techniques do not assume homogeneity of variance or normality. A Kruskal-Wallis test demonstrated no overall



Fig. 1. Modulation transfer functions. Each row of the figure shows modulation transfer functions (MTFs) from two subjects selected for each experimental condition. Condition labels are shown to the right of each row. Each panel displays the two MTFs obtained from each subject. The thicker lines denote auditory steady state response (ASSR) amplitude with the solid line showing the first recording and the broken line showing the second. The thinner lines show the estimated noise amplitude for each recording, again using solid and broken lines. Near the ASSR response curves, the percentage of points where the ASSR was statistically different from the noise for the two recordings is given (e.g., percent significant [ps] = 100%). The mean absolute changes between corresponding points of each MTF (Δ MTF) and noise estimate (Anoise) are also shown. These were calculated by determining the absolute difference at each frequency in which the ASSR was valid in both measurements and then taking the average (for both ASSR amplitude and the estimated noise amplitude). The "*" symbols in the left panel of the second row highlight local maxima as discussed in the text.

effect of experimental condition for the percentage of points significant between the first and second replication (χ^2 [3] = 2.38; p = 0.50). Univariate analysis of variance was used to evaluate the effect of experimental condition on changes of the MTF measures between the two replications. There was no effect of experimental condition on the change of amplitude or phase for the points in the MTF between the two replications (F[3,43] = 0.28; p = 0.84 for amplitude; F[3,43] = 1.78; p = 0.16 for phase). Similarly, there was no effect of experimental condition on the change in noise estimates between the two replications (F[3,43] = 0.27; p = 0.85). In summary, there was no statistically significant differences

TABLE 2. MTF repeatability

found across experimental conditions with respect to MTF repeatability and noise levels within each replication.

Repeatability of MTF Extrema

The repeatability of the MTF between replications was evaluated by calculating the correlation of ASSR amplitudes for the two resulting MTFs. The group results for each experimental condition are given in Table 3 in which the mean and median correlation coefficients are listed. The percentage of individuals with a statistically significant correlation is also

		Mean absolute change		
Experimental condition	% valid	MTF amplitude (nV)	MTF phase (°)	MTF-noise estimate (nV)
500-fixed	86.7 (21.8), 100.0	12.6 (8.4), 10.0	18.2 (7.4), 17.6	2.6 (2.7), 1.5
500-low	83.5 (17.4), 85.0	11.0 (7.8), 7.8	19.7 (9.9), 19.9	2.3 (2.6), 1.5
500-high	77.1 (19.0), 75.0	10.6 (3.8), 11.2	15.5 (6.2), 11.7	3.1 (2.2), 2.8
2k-low	85.9 (14.5), 83.3	10.5 (3.3), 10.4	13.1 (5.0), 14.0	2.4 (1.8), 2.4

The first value of each cell is the population average with SD reported in parentheses. This is followed, after the comma, by the median. The column entitled "% Valid" is the percentage of points in the MTF where the ASSR amplitude was statistically different from the noise, as calculated across both replications. The average change between replications is given for ASSR amplitude, phase (unwrapped), and the noise estimate. Change values were calculated only at MTF values where the ASSR amplitude was statistically different from the noise in both replications. The average absolute changes were computed for each subject, and then the population summary statistics shown here were calculated.

Experimental condition	Correlation of ASSR amplitude between replications	% subjects with significant correlation
500-fixed 500-low 500-high	0.12 (0.34), 0.06 0.51 (0.37), 0.46 0.74 (0.25), 0.77 0.63 (0.46), 0.86	69.2% 91.7% 90.9%

TABLE 3. MTF test-retest correlations

This table shows the population average correlations of ASSR amplitudes between the two MTFs obtained for each subject. SD (in parentheses) across subjects is also reported, followed by median values. The reported values include correlation values that were not statistically significant at p < 0.05, because including these low correlations provides a more accurate summary of correlation. This occurred mostly in the 500-fixed condition where correlation was expected to be weaker. The third column gives the percentage of subjects in each experimental condition who had a significant correlation between measurements at p < 0.05.

given for each experimental condition. To evaluate potential differences between experimental conditions, a Kruskal-Wallis test was again used because the distribution of correlation values tended to be left skewed with most individuals falling near the maximum correlation value of +1. There was an overall main effect of experimental condition on the correlation between MTFs from the two recordings (χ^2 [3] = 15.8; p < 0.01). Pairwise comparisons were conducted within this omnibus effect using Mann-Whitney tests. The correlations found in the 500-fixed condition were smaller than those for the 500-low (U = 32.0, Z = -2.5; p < 0.05), the 500-high (U = 10.0, Z = -3.6; p < 0.001) and the 2k-low (U = 24.0, Z = -2.8; p < 0.01) conditions. There were no other statistically significant differences between conditions.

Figure 2 graphically shows the repeatability of the maximum (squares) and minimum (circles) ASSR amplitude for the replications of each subject's MTF. To obtain the maxima for this plot, the modulation rate of the maximum ASSR amplitude for each subject's second MTF was determined (the second MTF was chosen because it was assumed that subjects would be most relaxed at that point in the measurements; however, noise estimates were not statistically different between the two recordings). Some MTFs have multiple local maxima and/or minima (i.e., MTF extrema), as demonstrated with the two asterisk symbols in the left panel of the 500-low condition in Figure 1. Because MTFs from the two recordings have differences, a set of candidate local maxima were found for each subject's first MTF. The candidate maxima closest in modulation rate to that determined for the second MTF was then selected for Figure 2. This procedure was repeated to find a minimum for each recording. In the case of selecting a minimum, this approach prevented the selection of a minimum at a much different modulation rate in the first recording simply because it was slightly lower in amplitude than a local minimum, which occurred near the modulation rate found in the second recording. In Figure 2, most symbols fall close to the diagonal 1:1 line representing perfect repetition. The correlation between MTF extrema in replications one and two is given in the lower right of each panel.

Combined MTF Results

To obtain the best MTF estimates (i.e., best SNR levels) for the different conditions and to examine the effects of experimental condition (i.e., modulation rate and carrier frequency),



Fig. 2. Maxima and minima repeatability. This figure shows the modulation rates that elicited the maximum and minimum auditory steady state response (ASSR) amplitude in each of the modulation transfer functions (MTFs) obtained for each subject. Experimental conditions are indicated in the upper left corner of each panel. The horizontal axes indicate modulation rates selected for the maximum (squares) and minimum (circles) of the MTF recorded first and vertical axes show corresponding rates selected for the MTF recorded second. The diagonal dotted line indicates where points would fall if replication were perfect between measurements. The correlation calculated for the extrema measured from the first and second MTFs is given in the lower right corner of each panel.

the data from the two replications for each subject were concatenated into one dataset. Therefore, the "combined MTF" results reported in this section contain \sim 51 mins of data. Table 4

TABLE 4. Combined MTF results

		Only valid ASSR points	
Experimental condition	Range of ASSR	Mean ASSR	Mean noise
	amplitudes (nV)	amplitude (nV)	estimate (nV)
500-fixed	22.0 (10.2), 19.5	54.4 (28.4), 47.0	8.8 (2.6), 8.3
500-low	33.6 (18.9), 30.7	53.7 (30.5), 41.4	8.8 (2.0), 8.5
500-high	50.8 (35.7), 36.6	43.4 (19.1), 40.9	7.4 (1.9), 7.7
2k-low	45.8 (19.1), 47.7	54.3 (15.3), 54.0	8.6 (2.1), 9.1

Each cell contains the population mean and SD (in parentheses) followed by the median for the combined MTF dataset from both recordings. "Range of ASSR Amplitudes" was calculated as the mean of differences found between the largest and smallest ASSR amplitude estimated for each subject. The mean ASSR amplitude and noise estimates were calculated across the full MTF using only the ASSR amplitudes which were statistically different from the corresponding noise estimates.

shows within-condition population averages for the ASSR and noise estimates obtained from the combined MTFs. The range of ASSR amplitudes was calculated as the difference between the largest and smallest amplitudes within the combined MTF. Even though the SNR was increased in the combined MTF, the smallest values of the MTF still may have not have been statistically different from the corresponding MTF noise estimate. However, the complete range of MTF values was included in the range estimates of Table 4 so that the nulls in the MTF could be reflected by this metric. Table 4 also provides values for average ASSR amplitude and the average noise estimate. These were calculated across modulation frequency (or time for the 500-fixed condition) at points of the combined MTF where the amplitude was statistically different from the corresponding noise estimate. Figure 3 graphically



Fig. 3. Individual subject modulation transfer function (MTF) ranges. The range of auditory steady state response (ASSR) amplitudes observed in each subject's MTF (computed from data combined across both recordings) is plotted. Experimental condition is labeled in the top left corner of each panel. The horizontal axes indicate subject number, where subjects were ordered (moving to the right along the x axis) according to increasing range of ASSR amplitudes within their MTFs. The vertical axes show ASSR amplitudes across the measured modulation range. Diamonds indicate the mean ASSR amplitude computed across all significant values within each MTF. The vertical black lines running through the diamonds show the range of observed ASSR amplitudes. The bottom end of each line indicates the minimum and the top end indicates the maximum observed amplitude. For each subject, short gray horizontal lines show the minimum ASSR amplitude required for the response to be significantly different from the noise at p < 0.05.



Fig. 4. Arithmetic average responses across subjects. The population average auditory steady state response (ASSR) amplitude vs. modulation rate for each sample of subjects is shown. Curves show the averages for experimental conditions in which modulation rate was varied. The 500-fixed condition is a very short vertical line at 82.0 Hz because modulation rate was fixed. The top panel labeled "modulation transfer function" shows ASSR amplitude estimated at each modulation rate. The middle panel labeled "noise" gives the estimated noise amplitude calculated for each modulation rate. The bottom panel labeled "signal-to-noise ratio" is the ratio of these two values vs. modulation rate.

shows the mean and range of ASSR amplitude for each subject in the four conditions. The short horizontal gray lines indicate the minimum amplitude required for statistical significance of the ASSR at p < 0.05 based on an average of the individual's noise estimates across the entire MTF.

Statistical tests were performed to identify differences between experimental conditions for the combined MTF measures presented in Table 4. It was anticipated that the variance of the MTF amplitudes in the control condition, 500-fixed, would be significantly smaller than the other three experimental conditions in which modulation frequency was varied (as can be seen clearly in the grand arithmetic average plots of Fig. 4). Again to be conservative, a nonparametric framework was used to evaluate the range of ASSR amplitudes. A Kruskal-Wallis test demonstrated an overall effect of experimental condition (χ^2 [3] = 15.0; p < 0.01). Pairwise Mann-Whitney comparisons detected no statistically significant differences among the 500-low, 500-high, and 2k-low conditions. The range of ASSR amplitudes in the 500-fixed condition was



Fig. 5. Best and worst modulation rates. The maximum (squares) and minimum (circles) ASSR amplitude for each subject is shown. These were obtained for each subject by combining data from both recordings to compute one modulation transfer function. The top row shows ASSR amplitude maximums, and the bottom row shows amplitude minimums. Experimental condition is labeled at the top of each column.

significantly smaller than the 500-low (U = 40.0, Z = -2.1; p < 0.05), 500-high (U = 17.0, Z = -3.2; p < 0.01), and 2k-low (U = 19.0, Z = -3.0; p < 0.01) conditions.

The effects of the four stimulus conditions on individuals' average ASSR amplitude and average noise estimate across modulation rates were evaluated using univariate analyses of variance. The averages from each individual included only frequencies (or times in the case of the 500-fixed condition) where the point in the MTF was significantly different from the corresponding noise estimate. There was no effect of experimental condition on average ASSR amplitude (F[3,43] = 0.54; p = 0.66). Similarly, there was no effect of experimental condition on the average noise estimate (F[3,43] = 1.12; p = 0.35). Therefore, SNR was roughly similar across the four conditions.

The top panel of Figure 4 shows population average MTFs for the four experimental conditions. Some points of these MTFs, where ASSR amplitude is low, may include individual data where the corresponding points were not statistically different from noise. The data for the 500-fixed condition are shown as a vertical line at the fixed modulation rate of 82.0 Hz, which extends from the maximum to the minimum amplitude found. The middle panel shows the arithmetic average of the noise estimates from each subject at every modulation rate. The bottom panel gives the ratio (i.e., the SNR) of these two values: the ASSR signal amplitude over the estimated noise amplitude.

The combined MTF data were also used to obtain the best estimates of ASSR amplitude extrema across individuals. Figure 5 shows the amplitudes and modulation rates corresponding to each subject's MTF amplitude maximum and minimum.

Comparing the FA and DFT

As a cross-check between the FA and a more standard DFT analysis method, ASSR amplitude estimates from the two analysis techniques were compared in the 500-fixed condition. An average sweep was first calculated for each recording. From this average sweep, the DFT produces a single ASSR amplitude estimate. The FA yields many amplitude estimates during the time course of this average sweep. Therefore, the FA amplitude estimates were averaged together to obtain a single estimate for comparison with the DFT. In all cases, the average FA estimate was slightly but statistically larger than the DFT estimate using a sign test (p < 0.001). Across all individuals, and both replications, the mean value from the FA for the 500-fixed condition was 54.3 nV. The largest single difference between the FA and DFT estimates was 4.9 nV (i.e., 9%), but the mean and median differences were only 1.9 nV (SD = 1.3 nV) and 1.5 nV (i.e., 3%), respectively. The difference between the two replications from a given individual was essentially the same, across all subjects, whether the 500-fixed data were analyzed using the FA or the DFT approach.

DISCUSSION

MTF Test–Retest Reliability

The MTFs obtained here were functionally consistent between replications from a clinical context: modulation rates associated with maxima and minima as well as other MTF characteristics were repeatable and showed strong correlations. All experimental conditions demonstrated similar absolute changes in MTF amplitude between replications as given in Table 2. In addition, the linear correlations between replications, as given in Table 3, were stronger for the 500-low, 2k-low, and 500-high conditions than for the 500-fixed condition. This was because, in addition to amplitude fluctuations caused by noise that undoubtedly existed, there was also repeatable MTF morphology because of the effect of modulation rate. For the 500-fixed condition, the correlations of the two replications were close to zero in the group average. Although each pair of recordings in this experimental condition had similar average amplitude, each replication had randomly distributed peaks and valleys (examples are shown in the top row of Fig. 1) that led to weak positive or negative correlations between replications and averaged to near zero across the group of subjects. In the population average plots of Figure 4, which were computed on the combined MTF data where the influence of noise will be most attenuated, the 500-fixed condition can be observed to have a range of ASSR amplitudes substantially smaller than the experimental conditions in which modulation rate was varied.

Within each individual, the modulation rates at which the maximum and minimum MTF amplitude occurred were largely consistent between the two replications as demonstrated in Figure 2. Importantly, this figure shows that it is not only the population average MTF that has a reproducible signature but also individual MTFs are useful for determining good and bad modulation frequencies for an individual. The correlations of at least 0.92 suggest that if an individual's MTF were known, it would be possible to minimize ASSR testing durations by choosing modulation rates in which the MTF amplitude was at a maximum (assuming no substantial difference in noise level compared with other portions of the modulation range being considered). Although there are some individuals with relatively flat MTFs, when all subjects were considered, the ASSR amplitude estimates at the amplitude minima were statistically smaller than at the maxima. Of 23 MTFs in the 500-low and 2k-low conditions, only four fluctuated as a function of modulation rate by <50% of the mean ASSR amplitude and

 TABLE 5. Modulation rate and test times

	Difference in m	Difference in measurement time	
Experimental condition	Extra sweeps	Extra seconds	
500-low	8, 0 to 432	131, 0 to 7078	
500-high	8, 1 to 64	131, 16 to 1049	
2k-low	7, 1 to 522	115, 16 to 8552	

This table shows the additional measurement time that would be required to detect an ASSR (at p < 0.05) using the modulation rates that elicited a subject's minimum rather than maximum amplitude. The median and range (values after the comma) are shown. Extending test time reduces the noise sufficiently at the response minimum to achieve p < 0.05 in the *F* test. Sweeps were converted to seconds using the 16.384-sec sweep of the MASTER system (John & Picton 2000).

could be considered "relatively flat." Accordingly, for the majority (83%) of our adult sample in the 65- to 100-Hz modulation range, MTFs provide information that can likely be used to alter ASSR testing duration. In the 500-high condition, the smallest observed MTF fluctuation was 65% of the mean ASSR amplitude. These MTFs were not flat because amplitude consistently declined for the 500-Hz carrier as modulation rate was increased above 100 Hz toward 121 Hz.

Modulation rate selection is beneficial for individuals with differences between their minimum and maximum ASSR amplitudes. However, consideration of these differences is most important when the lower portion of the amplitude range is close to the noise floor. Figure 3 shows some individuals for whom the range of ASSR amplitudes is quite substantial, including those whose MTF was not always significantly larger than the estimated noise level. These cases are indicated by MTF minimum amplitudes that dip below the horizontal gray lines, which represent the criteria for detection at p < 0.05(e.g., subject 11 in the 500-high condition). Subjects 5 to 10 in the 500-low condition all have similar differences between maximum and minimum amplitudes. However, the MTF is especially relevant for subjects 5, 6, 8, and 10 because their MTFs intersect the detection threshold. Not only would test time be prolonged but also false negatives (saying a subject can't hear a tone when in fact they can) are more likely to result from using the "wrong" modulation rate during the test. Table 5 estimates the difference in measurement time that would be required if the modulation rate of the ASSR amplitude minimum were (unfortuitously) used instead of that for the amplitude maximum. Measurement time is given both as the number of extra sweeps in the recording and the time in seconds required to obtain extra sweeps of 16.384 secs that are used by the MASTER system (John & Picton 2000) as well as the commercially available Natus/Bio-Logic MASTER system. Each individual's ASSR amplitude and noise estimate values were used to calculate the difference in measurement time to achieve detection at p < 0.05 using the F test, assuming that noise decreases by $1/\sqrt{N}$ (where N is the number of sweeps in the average; see Eq. (1) on p34 of John & Purcell 2008). Some individuals with a deep response minimum would require many extra sweeps so the table gives the median and range of values across the group in each experimental condition. Although Table 5 shows that typically ~ 2 mins of measurement time could be saved, a poor choice of modulation rate could extend recording time by >10 mins for about a third of individuals in the 65- to 100-Hz modulation range. For some individuals, a poor choice of modulation rate could cause a response to fail to be detected in a practical amount of time (i.e., >1 hr of recording time would be required to reduce the background noise to small enough values in some cases). Failure to detect the ASSR would lead to a false negative due to a bad choice of stimulus characteristics rather than due to hearing loss. This is obviously even more relevant in the testing of infants where the infant can awake mid-test or where other factors may not permit sufficient testing time when extended time periods are needed to detect a response.

MTF Morphology

Table 4 shows that across the experimental conditions, ASSR response amplitude varied \sim 30 to 50 nV when modulation rate was changed, whereas the MTF of the control condition (500-fixed) showed smaller changes. This supports the position that characteristics shown in an individual's MTF profile are largely due to variations in modulation rate rather than noise in the recording. This range is evident in the population average curves of Figure 4. The figure also shows that both 500 Hz and 2 kHz MTFs demonstrate a lowfrequency minimum in amplitude near 70 to 75 Hz. Figure 1 shows examples of individual MTFs with 70 to 75 Hz nulls deep enough that the ASSR would not be statistically different from the noise estimate (i.e., both subjects in the 2k-low condition and the left panel for the 500-low condition). Approximately between 80 and 100 Hz, the amplitude of the average responses shown in Figure 4 is robust, with the 2-kHz carrier possibly showing a trend for larger amplitudes at the higher modulation rates in this range. Approximately above 100 Hz, as modulation rates increase, the response for the 500-Hz carrier decreases.

The vertical line for the 500-fixed data might be expected to overlap with the 500-low result at 82.0 Hz. However, the 500-low curve is $\sim 6 \text{ nV}$ higher than the middle of the 500-fixed line. This small offset can be attributed to the different groups of subjects used in the different conditions of this study. The 500-low and 500-high conditions share a modulation range in which the response amplitudes might also be expected to be similar. The curves are near coincident from ~ 95 to 101 Hz, but they deviate below that frequency range. Again, this lack of correspondence is at least partially attributable to the fact that the two curves are from two different groups of subjects.

In the middle panel of Figure 4, the noise estimate is shown to decline a few nanovolts across the two modulation ranges. This is substantially smaller than the range of ASSR amplitudes observed in the MTFs of the top panel (note the difference in vertical scales). The MTF, rather than the noise profile, therefore is the main factor driving the SNR curves shown in the bottom panel. The MTF is the greatest contributing factor in ASSR detection for these modulation ranges. Both the broad peak in the MTFs and the subsequent decline as modulation rate is increased are the reason why clinical instruments favor the modulation range between 80 and 100 Hz. Group data in Figures 4 and 5 suggest that a modulation rate near 82 Hz would typically be optimal for a 500-Hz carrier frequency. The minimums shown in Figure 5 for the 500-low condition demonstrate that some individuals have lower ASSR amplitudes toward 100 Hz. This is reflected in the decline of the 500-Hz MTF in Figure 4 after ~82 Hz. For a 2-kHz carrier, rates near 90 to 100 Hz may generally be best. The data suggest that somewhat higher modulation rates may also be efficient

for a 2-kHz carrier, but these were not measured here. Most individuals in the 2k-low condition have maximums shown in Figure 5 between 90 and 100 Hz; however, three individuals were at the ceiling for the modulation rate of 102 Hz. Although none of the subjects showed a null at 82 Hz for the 500-Hz carrier and only two had one near 95 Hz for the 2-kHz carrier (see Fig. 5 bottom right panel), a much larger sample would need to be collected in infants and adults to determine that this profile is applicable across the larger population. Still, our group results are similar to those found previously by others as discussed below.

The modulation rate chosen for each carrier frequency in multiple simultaneous ASSR testing has often been made to simplify visual inspection of the response spectrum. The modulation rates are usually arranged in ascending order with increasing carrier frequency. In other words, in a given test ear, the 500-Hz carrier will typically have the lowest modulation rate in the chosen range, and the 4000-Hz carrier will have the highest. Although visually pleasing, this paradigm is largely dissociated from actual clinical utility and may be detrimental when using a 500-Hz carrier frequency. The ASSR in response to a 500-Hz carrier is often harder to illicit at lower intensities than responses to other carriers and is typically presented with modulation in the 70- to 80-Hz range, in which amplitude nulls are more likely to appear. In a clinical instrument, the "wrong choice" of rate for an individual may occasionally be made because the response rates are not modified during clinical testing.

Analysis Method

Seven individuals were removed from further analysis in this study either because of excessive noise in their recordings which was above a rejection level or because they did not have >25% of their ASSRs statistically different from the background noise in both recordings. Presumably with more recording time, the background noise could have been attenuated sufficiently to improve the SNR and reveal the ASSR in these normal-hearing individuals. The lack of robust ASSRs in three individuals from the 500-high group is consistent with the adoption of modulation rates <100 Hz by clinical instruments, when testing frequency specific ASSR stimuli. As the modulation frequency increases above 100 Hz, measurement of the smaller 500-Hz ASSR at these rates becomes quite challenging in a reasonable amount of time. However, it should be noted that in the case of nontonal click stimuli in infants, rates above 100 Hz may offer advantages (Stürzebecher et al. 2003).

In the 500-fixed condition, the average FA estimate of ASSR amplitude was slightly larger than the DFT estimate, but functionally they were the same as has been found previously (Purcell et al. 2004). The FA allows more noise contamination of the ASSR amplitude estimate, which leads to a slightly larger overestimation of response amplitude than for the DFT. Both techniques will over estimate ASSR amplitude a small amount due to the presence of noise (Picton et al. 2005; Ménard et al. 2008).

Relationship of MTF Results to Previous Findings With ASSR

With a slow change of modulation rate, relative to the capabilities of the auditory system, the response at any given rate can be treated like a standard ASSR measurement in which

modulation rate is fixed (Purcell et al. 2004). The method used in this study employed a continuous change of modulation rate to obtain the MTF. Previous reports (e.g., Cohen et al. 1991; Dobie & Wilson 1998) have typically used a set of discrete measurements with fixed modulation rates in which the step size is usually 5 to 10 Hz or more. Individual ASSR estimates are typically completed in 3 to 4 mins, and there may be the potential for a time confound between the first and last measurements. For example, the subject may change arousal state, which could alter the contribution of small cortical components such that they contribute more to one response than another. If the noise sources change over time, the accuracy of response estimation may be altered. In this study, \sim 26 mins recording time was used to obtain single estimates of the MTF, and any potential time confound should be shared across modulation rates. The MTFs obtained here still contain noise, but Figure 2 demonstrated the repeatability of each person's MTF extrema. Further, across our conditions the SNR levels did not statistically differ, suggesting our results were largely due to experimental manipulations as intended. Dobie and Wilson (1998) could not conclude with their measurement technique that it would be worth seeking an individual's optimal rate in a clinical setting. Certainly, the time spent here was long by clinical standards, but this study was successful in consistently identifying best and worst rates. This was possible because noise contamination of the ASSR estimates was sufficiently attenuated and some individuals had MTFs with a large range of ASSR amplitudes.

It is difficult to numerically compare the range of ASSR amplitudes found here with those in Cohen et al. (1991) or Lins et al. (1995) due to small figure scales and in Dobie and Wilson (1998) because of the use of magnitude-squared coherence instead of response amplitude. However, despite the lower frequency resolution of the measurements in those reports, the general shape of the MTF reported here is similar. As mentioned in the Introduction section, a null near 70 Hz has been reported previously (e.g., Cohen et al. 1991; Dobie & Wilson 1998). For a noise carrier, Purcell et al. (2004) proposed a model in which this 70 Hz null might be created by the destructive interference of cortical and brain stem sources. Dobie and Wilson (1998) reported a decline in the magnitudesquared coherence (used as a statistic for response detection) above 100 Hz for modulated tonal stimuli, which is similar to the falling amplitudes observed here.

There is some evidence in the literature suggesting that MTFs may vary with carrier frequency. Cohen et al. (1991) reported that for a 2-kHz carrier, most subjects show a 70 Hz minimum and a broad MTF maximum somewhere between 80 to 100 Hz. Some individuals also showed this MTF pattern for a 500-Hz carrier, whereas others did not (see their Fig. 8). Cohen et al. (1991) briefly noted less prevalence of the 70 Hz minimum and broad peak between 80 to 100 Hz for carrier frequencies of 250 and 500 Hz compared with higher carrier frequencies. These differences in MTF morphology between low- and high-frequency carriers were also suggested in the detection efficiency function plotted by Rickards et al. (1994; their Fig. 2). In the present study, a significant difference was not found between the 500 Hz and 2 kHz carriers. The range of ASSR amplitudes for the 500-low and 2k-low conditions given in our Table 4 was not statistically different (medians 30.7 nV and 47.7 nV, respectively). However, the population average

plots in Figure 4 and the distribution of individual maximums in Figure 5 suggest that there may be subtle effects of carrier frequency. In Figure 4, the MTF for the 500-low condition seems to peak at a lower modulation rate than for the 2k-low MTF. Similarly, in the top row of Figure 5, the individual MTF maximums tend to be clustered at a lower modulation rate for 500-low compared with 2k-low. More within-subject data at different carrier frequencies would be required to thoroughly investigate a possible effect of carrier frequency on MTF morphology (e.g., rates at which the maximum and minimum occur).

To be of use in estimating hearing thresholds, the optimal modulation rate would need to be independent of stimulus level. This study was not designed to investigate this possibility and did not vary stimulus level. There are contradictory findings in the literature on this point. Dobie and Wilson (1998) concluded that the 80- to 90-Hz modulation range was not as favorable as stimulus level was decreased toward threshold (see their Fig. 5b). However, detection rates given in their Figure 6b suggest that the 80- to 90-Hz range remains better than higher rates, even at low-stimulus levels. Cohen et al. (1991) concluded that the overall morphology of the MTF was maintained as stimulus level was decreased toward threshold (visible in their Figs. 6-8). Further investigation would be required using long-duration measurements (i.e., low noise contamination) and a within-subjects design to clarify the potential effect of stimulus level on the MTF.

Utility of MTF Results and Future Studies

If the MTF is available for an individual then modulation rates can be selected to produce larger responses and modulation ranges that elicit poor responses can be avoided. In the context of a single diagnostic assessment, the method used here would likely consume too much time in usual clinical settings. There may be individuals with robust maximum responses in which the suprathreshold MTF could be estimated in 10 to 15 min. In addition, obtaining MTFs using a stimulus level that was raised to 70 dB SPL might decrease the time needed to obtain the MTF substantially. Further, the depths of the minima do not need to be probed; only the response maxima and the presence of likely minima need be estimated. Although obtaining MTF information could occur more quickly in the future, there are clinical contexts in which using 30 mins to obtain the MTF would currently be acceptable. For example, in a hearing health care model in which individuals are monitored longitudinally, knowing the best measurement rates could save clinical time when testing occurs periodically. In addition, intraoperative monitoring during surgical procedures which may damage the auditory system requires multiple sequential measurements using the same stimuli to assess the integrity of the auditory system (e.g., Picton et al. 2003b). In this context, obtaining a preoperative MTF could then enable monitoring to occur at short intervals to detect changes in auditory system integrity with less delay, more accurately, and possibly with increased sensitivity. Further, MTFs can improve scientific or clinical studies in which some variable other than modulation rate is to be manipulated so that a well-chosen modulation rate can be used to minimize recording time and allow more robust examination of the studied parameter. In infants, the ASSRs are smaller and so the effects seen here may be greater in that population and using the correct modulation frequency may even more significantly reduce test time and improve detection rates.

Additional research is needed to investigate MTFs in adult and infant populations including individuals with hearing loss. These studies should compare ASSR thresholds determined using instrument-fixed versus individually selected modulation rates. These ASSR thresholds should then be compared with behavioral thresholds to evaluate whether the choice of an individual's best modulation rates improves objective threshold estimation. Evaluations of carrier frequency and stimulus level effects should use within-subjects designs. Replicability of the MTFs should be evaluated both in an infant population and also using longer time intervals, such as 6 mos apart, to assess whether the long-term repeatability mirrors that found in the relatively short window used by this study.

Concluding Remarks

The MTF was measured twice in each subject, and its morphology and extrema were reasonably well repeated despite the ever-present contribution of noise to the ASSR estimates. The use of medium duration recording times (~ 25 mins each) generally allowed acceptable estimation of an individual's MTF. There were individuals for whom the MTF included a sufficiently broad range of ASSR amplitudes that selection of a modulation rate near the response minimum would require a significant increase in recording time relative to the response maximum. An individual's best rates might be exploited for auditory assessment contexts in which repeated measurements over time could justify the time required to estimate the MTF. Further data collected using a withinsubjects and repeated-measures design is required to clarify potential effects of stimulus level and carrier frequency on the MTF. MTFs should be replicated with a longer interval (1 to 6 mos) between test-retest. Infant MTFs will likely be subject to maturational changes, and it would be useful to document how orderly the MTF changes are as the infant ages.

ACKNOWLEDGMENTS

The authors thank the Hearing Foundation of Canada, the Canada Foundation for Innovation, the Canadian Institutes of Health Research, and the (Canadian) Natural Sciences and Engineering Research Council for their support of this research. They also thank Lindsay Gibson for her assistance in data collection and Bonnie Lampe for her work on data analysis.

Address for correspondence: David W. Purcell, National Centre for Audiology, School of Communication Sciences and Disorders, 1201 Western Road, Elborn College, University of Western Ontario, London, Ontario, Canada N6G 1H1. E-mail: purcelld@nca.uwo.ca.

Received December 4, 2009; accepted March 15, 2010.

REFERENCES

- Ahn, J. H., Lee, H. S., Kim, Y. J., et al. (2007). Comparing pure-tone audiometry and auditory steady state response for the measurement of hearing loss. *Otolaryngol Head Neck Surg*, 136, 966–971.
- Aiken, S. J., & Picton, T. W. (2006). Envelope following responses to natural vowels. *Audiol Neurootol*, 11, 213–232.
- Aoyagi, M., Kiren, T., Kim, Y., et al. (1993). Optimal modulation frequency for amplitude-modulation following response in young children during sleep. *Hear Res*, 65, 253–261.
- Aoyagi, M., Suzuki, Y., Yokota, M., et al. (1999). Reliability of 80-Hz amplitude-modulation-following response detected by phase coherence. *Audiol Neurootol*, 4, 28–37.

677

- Brennan, S., & Stevens, J. (2007). How does the ASSR response amplitude vary with modulation rate for individual babies? In *Proc XX Int Evoked Response Audiometry Study Group*, Bled, Slovenia.
- Cohen, L. T., Rickards, F. W., Clark, G. M. (1991). A comparison of steady-state evoked potentials to modulated tones in awake and sleeping humans. J Acoust Soc Am, 90, 2467–2479.
- Cone-Wesson, B., Dowell, R. C., Tomlin, D., et al. (2002). The auditory steady-state response: Comparisons with the auditory brainstem response. J Am Acad Audiol, 13, 173–187.
- Dimitrijevic, A., John, M. S., Van Roon, P., et al. (2002). Estimating the audiogram using multiple auditory steady-state responses. J Am Acad Audiol, 13, 205–224.
- Dobie, R. A., & Wilson, M. J. (1998). Low-level steady-state auditory evoked potentials: Effects of rate and sedation on detectability. J Acoust Soc Am, 104, 3482–3488.
- Gorga, M. P., Kaminski, J. R., Beauchaine, K. A., et al. (1988). Auditory brainstem responses to tone bursts in normally hearing subjects. *J Speech Hear Res*, 31, 87–97.
- Joint Committee on Infant Hearing. (2007). Year 2007 position statement: Principles and guidelines for early hearing detection and intervention programs. *Pediatrics*, 120, 898–921.
- Herdman, A. T., Lins, O., Van Roon, P., et al. (2002). Intracerebral sources of human auditory steady-state responses. *Brain Topogr*, 15, 69–86.
- Herdman, A. T., & Stapells, D. K. (2003). Auditory steady-state response thresholds of adults with sensorineural hearing impairments. *Int J Audiol*, 42, 237–248.
- John, M. S., Brown, D. K., Muir, P. J., et al. (2004). Recording auditory steady-state responses in young infants. *Ear Hear*, 25, 539–553.
- John, M. S., Dimitrijevic, A., Picton, T. W. (2001b). Weighted averaging of steady-state responses. *Clin Neurophysiol*, 112, 555–562.
- John, M. S., Dimitrijevic, A., Picton, T. W. (2002b). Auditory steady-state responses to exponential modulation envelopes. *Ear Hear*, 23, 106–117.
- John, M. S., Dimitrijevic, A., Picton, T. W. (2003). Efficient stimuli for evoking auditory steady-state responses. *Ear Hear*, 24, 406–423.
- John, M. S., Dimitrijevic, A., van Roon, P., et al. (2001a). Multiple auditory steady-state responses to AM and FM stimuli. *Audiol Neu*rootol, 6, 12–27.
- John, M. S., Lins, O. G., Boucher, B. L., et al. (1998). Multiple auditory steady-state responses (MASTER): Stimulus and recording parameters. *Audiology*, 37, 59–82.
- John, M. S., & Picton, T. W. (2000). MASTER: A Windows program for recording multiple auditory steady-state responses. *Comput Methods Programs Biomed*, 61, 125–150.
- John, M. S., & Purcell, D. W. (2008). Chapter Two: Introduction to Technical Principles of Auditory Steady-State Response Testing. In G. Rance (Ed). Auditory Steady-State Response: Generation, Recording and Clinical Applications (pp, 11–53). San Diego: Plural Publishing Inc.
- John, M. S., Purcell, D. W., Dimitrijevic, A., et al. (2002a). Advantages and caveats when recording steady-state responses to multiple simultaneous stimuli. J Am Acad Audiol, 13, 246–259.
- Levi, E. C., Folsom, R. C., Dobie, R. A. (1993). Amplitude-modulation following response (AMFR): Effects of modulation rate, carrier frequency, age, and state. *Hear Res*, 68, 42–52.
- Lin, Y. H., Ho, H. C., Wu, H. P. (2009). Comparison of auditory steady-state responses and auditory brainstem responses in audiometric assessment of adults with sensorineural hearing loss. *Auris Nasus Larynx*, 36, 140–145.
- Lins, O. G., Picton, P. E., Picton, T. W., et al. (1995). Auditory steady-state responses to tones amplitude-modulated at 80–110 Hz. J Acoust Soc Am, 97, 3051–3063.
- Lins, O. G., & Picton, T. W. (1995). Auditory steady-state responses to multiple simultaneous stimuli. *Electroencephalogr Clin Neurophysiol*, 96, 420–432.
- Luts, H., Desloovere, C., Kumar, A., et al. (2004). Objective assessment of frequency-specific hearing thresholds in babies. *Int J Pediatr Otorhinolaryngol*, 68, 915–926.
- Luts, H., Desloovere, C., Wouters, J. (2006). Clinical application of dichotic multiple-stimulus auditory steady-state responses in high-risk newborns and young children. *Audiol Neurootol*, 11, 24–37.

- Ménard, M., Gallego, S., Berger-Vachon, C., et al. (2008). Relationship between loudness growth function and auditory steady-state response in normal-hearing subjects. *Hear Res*, 235, 105–113.
- Norton, S. J., Gorga, M. P., Widen, J. E., et al. (2000). Identification of neonatal hearing impairment: Summary and recommendations. *Ear Hear*, 21, 529–535.
- Picton, T. W., Dimitrijevic, A., Perez-Abalo, M. C., et al. (2005). Estimating audiometric thresholds using auditory steady-state responses. J Am Acad Audiol, 16, 140–156.
- Picton, T. W., John, M. S., Dimitrijevic, A., et al. (2003a). Human auditory steady-state responses. *Int J Audiol*, 42, 177–219.
- Picton, T. W., John, M. S., Purcell, D. W., et al. (2003b). Human auditory steady-state responses: The effects of recording technique and state of arousal. *Anesth Analg*, 97, 1396–1402.
- Plourde, G., Stapells, D. R., Picton, T. W. (1991). The human auditory steady-state evoked potentials. *Acta Otolaryngol Suppl*, 491, 153–159.
- Purcell, D. W., John, S. M., Schneider, B. A., et al. (2004). Human temporal auditory acuity as assessed by envelope following responses. *J Acoust Soc Am*, 116, 3581–3593.
- Purcell, D. W., Van Roon, P., John, M. S., et al. (2006). Simultaneous latency estimations for distortion product otoacoustic emissions and envelope following responses. J Acoust Soc Am, 119, 2869–2880.
- Rance, G. (2008). Auditory steady-state response: Generation, recording and clinical applications. San Diego: Plural Publishing Inc.
- Rance, G., & Rickards, F. (2002). Prediction of hearing threshold in infants using auditory steady-state evoked potentials. J Am Acad Audiol, 13, 236–245.
- Rance, G., Roper, R., Symons, L., et al. (2005). Hearing threshold estimation in infants using auditory steady-state responses. J Am Acad Audiol, 16, 291–300.
- Rance, G., & Tomlin, D. (2006). Maturation of auditory steady-state responses in normal babies. *Ear Hear*, 27, 20–29.
- Rees, A., Green, G. G., Kay, R. H. (1986). Steady-state evoked responses to sinusoidally amplitude-modulated sounds recorded in man. *Hear Res*, 23, 123–133.
- Regan, D. (1989). Human Brain Electrophysiology: Evoked Potentials and Evoked Magnetic Fields in Science and Medicine. New York: Elsevier Science Publishing Co., Inc.
- Rickards, F. W., Tan, L. E., Cohen, L. T., et al. (1994). Auditory steady-state evoked potential in newborns. Br J Audiol, 28, 327–337.
- Savio, G., Cardenas, J., Perez Abalo, M., et al. (2001). The low and high frequency auditory steady state responses mature at different rates. *Audiol Neurootol*, 6, 279–287.
- Stapells, D. R., Galambos, R., Costello, J. A., et al. (1988). Inconsistency of auditory middle latency and steady-state responses in infants. *Electroencephalogr Clin Neurophysiol*, 71, 289–295.
- Stürzebecher, E., Cebulla, M., Neumann, K. (2003). Click-evoked ABR at high stimulus repetition rates for neonatal hearing screening. *Int J Audiol*, 42, 59–70.
- Stürzebecher, E., Cebulla, M., Pschirrer, U. (2001). Efficient stimuli for recording of the amplitude modulation following response. *Audiology*, 40, 63–68.
- Suzuki, T., & Kobayashi, K. (1984). An evaluation of 0.040 kHz event-related potentials in young children. Audiology, 23, 599–604.
- Swanepoel, D., & Ebrahim, S. (2009). Auditory steady-state response and auditory brainstem response thresholds in children. *Eur Arch Otorhinolaryngol*, 266, 213–219.
- Van Maanen, A., & Stapells, D.K. (2007). ASSRs to multiple simultaneous air-conducted stimuli: Criteria for normal hearing in infants. In Proc XX Int Evoked Response Audiometry Study Group, Bled, Slovenia.
- Van Maanen, A., & Stapells, D. R. (2005). Comparison of multiple auditory steady-state responses (80 versus 40 Hz) and slow cortical potentials for threshold estimation in hearing-impaired adults. *Int J Audiol*, 44, 613–624.
- Van Maanen, A., & Stapells, D. R. (2009). Normal multiple auditory steady-state response thresholds to air-conducted stimuli in infants. *J Am Acad Audiol*, 20, 196–207.
- Zurek, P. M. (1992). Detectability of transient and sinusoidal otoacoustic emissions. *Ear Hear*, *13*, 307–310.