Simultaneous multiple stimulation of the auditory steady-state response (ASSR)

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The present study evaluates some characteristics of the ASSR related to the use of multiple, simultaneous, band-limited chirp-stimuli. In a diagnostic study four one-octave-band chirp-stimuli (500, 1,000, 2,000 and 4,000 Hz) were used to measure the ASSR-threshold in 10 normal-hearing adults. The four stimuli were presented simultaneously to both ears (eight stimuli) with rates at about 90/s. The ASSRs were detected automatically (error rate 5%), and the thresholds evaluated with a resolution of 5 dB. The ASSR thresholds were compared to the audiometric thresholds for all 20 ears and the deviations evaluated by the group means and standard deviations. These data compare favorably well with similar data reported by others. In a screening study a low-frequency chirp, (Lo: 180 – 1,500 Hz) and a high-frequency chirp (Hi: 1,500 – 8,000 Hz), was used to record the ASSR in 72 newborns. The two stimuli were presented both sequentially and simultaneously using a rate at about 90/s and a level of 35 dBnHL. The ASSRs were detected automatically (error rate 0.1%), and evaluated by the detection time. The results from both studies demonstrate that simultaneous application of multiple, frequency-specific stimuli can effectively be applied without sacrificing response detection accuracy. However, in the screening study stimulus interactions were observed.

INTRODUCTION

ASSR (auditory steady-state response) is an electrophysiological response that is evoked by a periodically repeated auditory stimulus. The response is stable over time for as long as the stimulation is turned on. If the recording continues for a long time, then the response will consist of a series of discrete frequency components that are constant in both amplitude and phase. The ASSR is to be distinguished from the ABR (auditory brain stem response) because the ASSR is evoked by a series of sound stimuli that are presented at a high repetition rate, whereas the ABR is evoked by an individual, brief sound stimulus or a series of brief sound stimuli that are presented at a low repetition rate. At medium repetition rates there is a grey zone where the differentiation between the two response types is difficult to make. However, if the stimulus repetition rate is so high that the electrophysiological response to one stimulus overlaps with the response to the next stimulus, then the recorded activity can be meaningfully classified as an ASSR. At repetition rates higher than 60-70 stimuli per second, components of the ABR begin to overlap. This ASSR is dominated by early evoked activity from the brain stem and is therefore not influenced by test subject conditions

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such as attention, arousal and sleep (anesthesia and sedation). A review of ASSR techniques can be found in Picton *et al.* (2003).

The ASSR is most often analyzed in the spectral domain, because the response consists of specific components at frequencies that correspond to multiples (harmonics) of the stimulus repetition rate whereas the background noise has components at all frequencies (e.g. Cebulla *et al.* 2006). Simultaneous stimulation of the right and left ear is possible by presenting the stimuli to each ear with different repetition rates (e.g. Stürzebecher *et al.* 2003). Similarly, simultaneous stimulation to one ear can be applied by allowing different repetitions rates for two or more frequency-specific stimuli. The application of multiple, simultaneous stimuli may significantly reduce test time when the ASSR is used for audiometric evaluation (e.g. John *et al.* 2002).

The detection of an ASSR in the frequency domain will optimally utilize the amplitude and phase information from the first six to eight response harmonics (e.g. Cebulla *et al.* 2006). The accumulated amplitude and phase values (or spectral vectors) will demonstrate a small variance for each of the harmonic frequencies. However, for all other frequencies, which contain noise only, a random distribution is present corresponding to a large variance of the spectral values. These differences between the harmonic frequencies and all other frequencies can be used to detect the presence of the ASSR by means of a detection algorithm.

The ASSR has provided some new possibilities for hearing diagnostics and hearing screening. For hearing diagnostics narrow band (frequency-specific) stimuli must be applied. These can for example be filtered clicks, tone bursts or amplitude and/or frequency modulated pure tones. The most important audiological application is audiometry, where the observed ASSR thresholds provide an estimate of the pure-tone audiogram. The ASSR can also be used for hearing screening and for this purpose broad band stimuli are applied. These may for example consist of repeated clicks or other brief stimuli. For hearing screening a fixed stimulus level at 35 dBnHL is often preferred. The hearing screening gives only two possible outcomes: (1) either an ASSR is detected (false or true negative) or (2) an ASSR is not detected (false or true positive).

NEW STIMULI

Chirp stimuli

In order to increase the temporal synchrony of neural excitation in the cochlea, compensation for the cochlear traveling wave delay can be applied. This results in the design of chirp-stimuli, which can be used for the recording of broad-band ABR and ASSR. Chirp-stimuli are based on models of the cochlear traveling time and it has been shown that compared to click-stimuli, chirps result in higher amplitudes of the evoked response (e.g. Dau *et al.* 2000; Fobel and Dau 2004; Stürzebecher *et al.* 2005; Elberling *et al.* 2007). Recently we have used a model of the traveling time based on derived band click ABRs (Don *et al.* 2005). From this model a chirp (called CEChirp) was designed and used to record the ASSR in 49 normal-hearing adults (Elberling *et* *al.* 2007). The CEChirp with a flat amplitude spectrum in the frequency range from 200 to 8,000 Hz is shown in Fig. 1.

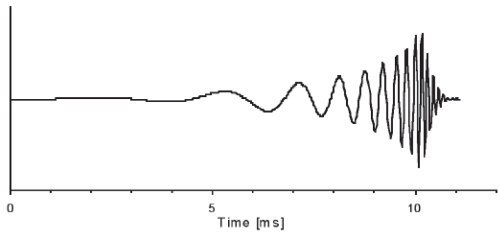

Fig. 1: CEChirp-stimulus having a flat amplitude spectrum (200 – 8,000 Hz).

Frequency-specific chirp stimuli

In order to enhance the efficiency of frequency-specific stimuli, delay-compensation can be applied within a pass-band using the cochlear delay model described above for the CEChirp. Stürzebecher *et al.* (2005) demonstrated that the ASSR recorded in normal-hearing adults to delay-compensated stimuli resulted in higher signal-to-noise ratios than the corresponding uncompensated stimuli.

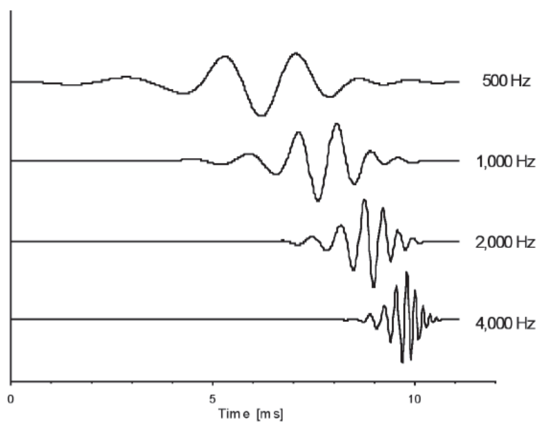

Fig. 2: One-octave-band delay-compensated stimuli.

One-octave-band stimuli

One-octave wide stimuli with the center frequencies 500, 1,000, 2,000 and 4,000 Hz have been constructed using the cochlear delay model. The temporal waveforms of these delay-compensated, frequency-specific stimuli are shown in Fig. 2, and the stimuli have been applied for ASSR hearing diagnostics in normal-hearing adults as described below.

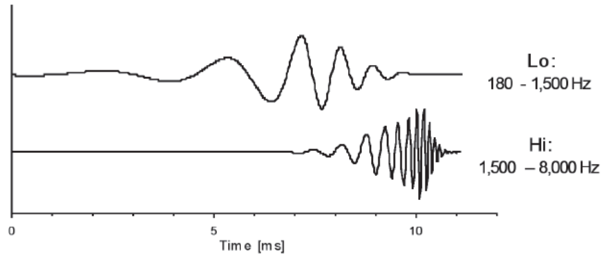

Fig. 3: Low-frequency (Lo) and high-frequency (Hi) delay-compensated stimuli.

Low-frequency and high-frequency stimuli

Delay-compensated low-frequency (Lo) and high-frequency (Hi) stimuli have also been constructed using the cochlear delay model. The Lo-stimulus covers the frequency range 180 Hz -1,500 Hz while the Hi-stimulus covers the range 1,500 Hz – 8,000 Hz. The temporal waveforms of these stimuli are shown in Fig. 3, and the two stimuli have been applied for ASSR hearing screening in newborns as described below.

HEARING DIAGNOSTICS WITH FREQUENCY-SPECIFIC ASSR

Introduction

Clinical methods to record ASSRs to multiple, simultaneous, frequency-specific stimuli presented at relatively high repetition rates (> 60-70/s) have since the 1990s gradually been developed and introduced into the audiological armamentarium as reviewed recently by D'haenens *et al.* (2007). The application of multiple, simultaneous stimulation (e.g. Lins *et al.* 1996), more effective stimuli (e.g. John *et al.* 2001) and efficient response detection algorithms (e.g. Cebulla *et al.* 2006) have contributed to this development. In the clinic, the ASSR can be used to test auditory sensitivity and to produce estimates of the pure-tone audiogram. The ASSR can be applied to groups of difficult-to-test patients (adults, children and very young children). Especially for the diagnostic follow-up of newborns that do not pass hearing screening, ASSR testing using multiple, simultaneous, frequency-specific stimuli has drawn much clinical attention. Most reports in the literature of ASSR-results to multiple, simultaneous, frequency-specific stimulation are obtained with non-commercial set-ups whereas results obtained using commercial clinical systems appear more sparsely. In the present report preliminary reference threshold data are presented from normal-hearing adults using delay-compensated frequency-specific stimuli combined with an efficient response detection algorithm implemented on a commercial electrophysiological platform.

Material and method

The test group consisted of N = 10 young, normal-hearing adults (20-40 y). The pure tone thresholds were 10 dB HL or better at the frequencies of 500, 1,000, 2,000 and 4,000 Hz. The test subjects were placed on a comfortable couch in a sound treated room and were instructed to relax and, if possible, to sleep during the ASSR-testing. Three active electrodes were placed - one at the Vertex (Cz) and two others at the Mastoids – whereas a ground electrode was placed at the Forehead. All recordings were made with the Eclipse platform with the ASSR-software (Interacoustics), using a two-channel preamplifier and ER-3A earphones. The EEG was band-pass filtered from 33 Hz to 8,000 Hz. An artifact rejection level of ± 40 μV was applied. The ASSR was automatically detected using a modified Mardia's q-sample test as described by Cebulla *et al.* (2006). This test was applied to the first six response harmonics using a sequential test strategy and an error probability of = 5 %, controlled for the effect of repeated testing (Stürzebecher *et al.*, 2005). The response to each stimulus was followed until the response was detected but not for longer than 360 s.

The four one-octave-band delay-compensated stimuli at 500, 1,000, 2,000 and 4,000 Hz were presented to both ears simultaneously (eight stimuli) at individual rates in the range 86 - 94/s. The level of each stimulus was calibrated in dBnHL. The ASSR threshold to each of the eight stimuli was found by the following procedure: An initial level of 60 dBnHL was chosen for all stimuli, followed by a lowering by 10 dB until no response could be detected before time-out; finally the level was raised by 5 dB. The lowest level where a response was detected was taken as the response threshold.

Results

The ASSR threshold minus the pure-tone threshold (the audiogram) was calculated for each of the 20 ears and the means and standard deviations are shown in Table 1. The average test time across the 10 test subjects was close to 30 minutes. Comparative literature data obtained with a test protocol similar to the one used herein are also given in Table 1. The average values (means and standard deviations) are calculated by weighting the contribution from each study in accordance with the number of test subjects used.

ASSR-thresholds minus Pure-tone thresholds (N = 20 ears)				
	Test frequency [Hz]			
	500	1,000	2,000	4,000
Mean	11.0	10.3	6.0	12.8
Stdev	7.3	7.1	4.8	4.1

Reference values (N = 131 ears) D'haenens *et al.* (2007) Dimitrijevic *et al.* (2002) Kaf *et al.* (2006) Werff and Brown (2005)			
19.5	12.7	9.4	11.9
11.5	9.1	7.5	7.9

Table 1: Means and Standard deviations of ASSR thresholds minus Pure-tone thresholds in N = 20 normal-hearing ears. Comparative reference values obtained from the literature are indicated to the right.

Discussion

The results from the present study compares favorably well with the values obtained in other studies. However, in two ways the one-octave-band delay-compensated stimuli are more efficient than the stimuli in the referenced studies: (1) the one-octave bandwidth is broader than the bandwidth of the frequency-specific stimuli used by others; therefore the present stimuli excite a relative large area of the cochlea, and (2) the delay-compensation increases the efficiency of the stimuli.

The present experiment has only evaluated the ASSR-threshold in normal-hearing subjects. This test group is not the target population for which the ASSR is designed and developed and therefore, the method needs to be evaluated systematically in hearing-impaired adults and small children. However, the findings in normal-hearing subjects by others (e.g. Rance *et al.* 2005, Dimitrijevic *et al.* 2002, Werf and Brown, 2005) seem to be related to the efficiency of the test paradigm also in hearing-impaired adults and children.

Multiple, simultaneous stimulation is a time-effective stimulus paradigm, which in the present study, leads to an average test-time of about 30 minutes in normal-hearing adults. This average test-time appears to be much shorter than reported by others using a similar stimulus paradigm.

When frequency-specific stimuli are presented simultaneously to the same ear stimulus interaction and masking will take place. This was studied systematically by John *et al.* (2002), and it was found that the presence of high-frequency stimuli attenuated the ASSR to low-frequency stimuli, and the presence of low-frequency stimuli enhanced the ASSR to high-frequency stimuli. However the authors concluded that while the interactions were interesting from a physiological point of view they were of a small size and didn't lessen the advantage of the multiple, simultaneous stimulus approach. John *et al.* (2002) found that the use of simultaneous stimulation in one ear reduced the total test-time by a factor 2-3 compared to applying the four stimuli sequentially.

HEARING SCREENING WITH FREQUENCY-SPECIFIC ASSR

Introduction

Over the last couple of years we have carried out a series of studies with the aim of improving response detection and stimulus condition for the recording of the ASSR for hearing screening in newborns (Stürzebecher *et al.*, 2005, Cebulla *et al.*, 2006 and Stürzebecher *et al.*, 2006). In newborn hearing screening both preparation time and test time is at a premium and should be kept low. Hearing screening is normally carried out with a broad-band stimulus (e.g. a click or a chirp) and will therefore not give specific information about the hearing loss when the newborn fails the screening. In an attempt to provide frequency-specific information a method based on multiple, simultaneous, frequency-specific stimulation was therefore devised and evaluated in a group of newborns. The method was based on the results we recently obtained using a chirp for the recording of ASSR in newborns and adults.

Material and method

The test group consisted of N = 72 newborns with a mean age of two days. The newborns were tested in the maternity ward lying comfortably in their cots. On each newborn one ear was tested corresponding to the ear most easily accessible for testing. Two active electrodes were placed – one close to the Vertex (Cz) and the other at the ipsi-lateral Mastoid – whereas the ground electrode was located just above the external ear. All recordings were made with the MB11 platform (Maico) using the hand-held BERAphone® which integrates the earphone and the three electrodes. The EEG was band-pass filtered from 25 Hz to 1,500 Hz. An artifact rejection level of ± 20 µV was applied. The ASSR was automatically detected using a modified Mardia's q-sample test as described by Cebulla *et al.* (2006). This test was applied to the first eight response harmonics using a sequential test strategy and an error probability of = 0.1 %, controlled for the effect of repeated testing (Stürzebecher *et al.*, 2005). The response to each stimulus was followed until the response was detected but not for longer than 180 s.

Three stimuli were used: the broadband CEChirp and the low-frequency (Lo) and the high-frequency (Hi) compensated stimuli described above. The chirp was presented alone and used as a reference, whereas the two band-limited stimuli were presented both sequentially and simultaneously. A 'spectral gap' of 250 Hz was introduced between the two band-limited stimuli (by raising the lower limiting frequency of the Hi-stimulus from 1,500 Hz to 1,750 Hz). This condition was tested in the simultaneous condition. The presentation level of all stimuli was 35 dBnHL, and the presentation rates close to 92/s.

Results

The main results (median detection time) for all test conditions are shown graphically in Fig. 4, where the chirp-data (17 s) serve as a reference. The chirp-ASSR was detected in all newborns for all stimulus conditions before time-out (180 s) corresponding to a detection rate of 100%. The median time to detect responses to both stimuli was 40 s for sequential stimulation, 30 s for simultaneous stimulation without the spectral gap and 28 s with the gap.

The response detection time for the Lo-stimulus was longer than the detection time for the Hi-stimulus for both sequential and for simultaneous stimulation and as well without as with insertion of the gap between the two stimuli ($p<0.05$).

The response detection time to the Lo-stimulus was significantly longer for the simultaneous than for the sequential stimulation, and the response detection time to the Hi-stimulus was significantly shorter for the simultaneous than for the sequential stimulation ($p<0.05$). These results indicate the presence of stimulus interactions, which were significantly reduced by insertion of the spectral gap between the two stimuli ($p<0.05$).

Discussion

The results clearly demonstrate that low-frequency and high-frequency delay-compensated stimuli applied simultaneously at rates around 90/s can be used for frequency-specific screening in newborns: the median test time of 30 s (28 s) was obtained with an error rate of 0.1% (a probability of only 0.1% that an ASSR is falsely detected). Thus compared to sequential stimulation the application of the two stimuli simultaneously reduced the test time about 25% without the gap and about 30% with the gap inserted.

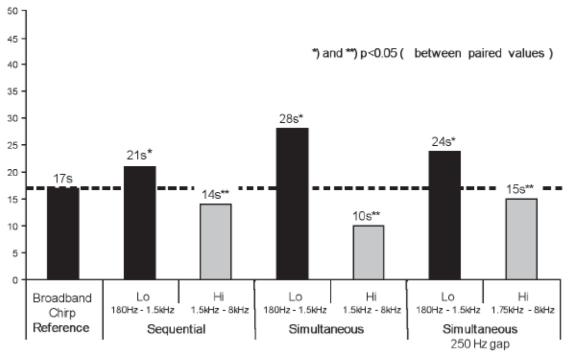

Fig 4: Median detection times obtained in the different test-conditions.

The results also demonstrate that stimulus interactions take place during simultaneous stimulation. The reduction of the response to the Lo-stimulus in the presence of the high-frequency stimulus may be related to masking or two-tone suppression, whereas the enhancement of the response to the Hi-stimulus in the presence of the low-frequency stimulus is surprising and can not readily be explained from the present data. Both interactions, however, are in accordance with the findings in normal-hearing adults by John *et al.* (2002).

SUMMARY AND CONCLUSION

ASSR to high stimulus repetition rates (e.g. around 90/s) can be obtained with the multiple, simultaneous stimulation technique. Combined with frequency-specific stimuli, which attempt to compensate for the cochlear traveling wave delay, this technique seems to provide an effective test method for hearing diagnostics and screening. The stimulus interactions that take place when two or more stimuli are presented simultaneously to the same ear, do not seem to seriously affect the test-time advantage of multiple, simultaneous stimulation.

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