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CHAPTER 4

AUDITORY STEADY STATE RESPONSES (ASSR) AND PSEUDOHYPACUSIS

AIM
To critically evaluate and describe a specific, auditory evoked potential, the auditory steady state response, as a frequency-specific threshold estimation procedure for use in certain difficult-to-test-populations. A motivation for the use particularly in pseudohypacusic populations with suspected noise-induced hearing loss is also given.

4.1 INTRODUCTION

In seeking a truly objective hearing threshold estimation technique for difficult-to-test populations, the emphasis worldwide has been on auditory evoked potentials. Hence, this was the main focus in the previous chapter.

The ultimate goal of an objective threshold estimation technique is to establish an audiogram in a frequency-specific manner without any need for voluntary responses from the subject (Picton, 1991; Aoyagi *et al.,* 1994). One aspect of objectivity that is not addressed in this criterion is that of the clinician's perception, experience and skill in detecting the appropriate wave form during AEP tests. This suggests that subjectivity persists in the decision of whether or not an evoked potential is present.

Rance *et al.* (1995) point out that ASSRs can be detected automatically, excluding the subjective evaluation, through real-time statistical analysis of samples from the response phase using a digital computer. This statement needs to be qualified somewhat, in that real-time statistical analysis has to be directed by research in that an appropriate clinical test set-up, noise floor determinants, number of averages and sweeps need to be standardised (especially to make comparisons between research studies more meaningful). Provided that this final component of objectivity is addressed, it is possible to use electrophysiological measures to assess patients who cannot or will not co-operate with conventional hearing test procedures (Sininger & Cone-Wesson, 2002).

Auditory steady state responses are discussed in this present chapter as a possible means to determine frequency-specific hearing thresholds estimates for pseudohypacusic patients, without any need for the subjective detection of responses on the part of a clinician. The discussion below defines and contextualises ASSRs. The stimulus parameters used to elicit responses are addressed. The chapter concludes with the limitations and advantages of this technique with specific reference to its application to pseudohypacusic workers. This theoretical study of ASSRs has formed the basis for a research programme (see Chapter 5) to evaluate their clinical value in a population of South African mine workers with noise-induced hearing loss and possible pseudohypacusis.

4.2 THE DEVELOPMENT OF AUDITORY STEADY STATE RESPONSES

Auditory steady state responses and steady state evoked potentials (SSEPs) are the two most frequently used labels found in a survey of relevant literature to describe this "new" type of AEP. Other, less frequently used, terms are "steady state fields" (Pantev *et al.,* 1996), "frequency following response" (Kuwada *et al.,* 1986) and "envelope following response" (Dolphin & Mountain, 1993). Although there are some differences in their applications, the definitions of these terms boil down to more or less the same concept. The term ASSR and SSEP are commonly used interchangeably, but, Sininger and Cone-Wesson (2002) have concluded that ASSR has become the term of choice in recent years. This assessment can, however, not be accepted without a critical analysis of the uses and implications of the term ASSR as the name for a new auditory evoked potential. Such an analysis is provided below.

Critics of the term "response" argue that in conventional audiometry, this term is applied to instances where the patient reacts to a stimulus that is presented in the form of a sound. Schmulian (2002) also questions the use of the term "response" in relation to evoked potential methods, since electrical waves are measured without any regard to a conscious or voluntary response on the part of the subject (Goldstein & Aldrich, 1999). Notwithstanding this discrepancy, it seems that the use of the term ASSR has gained wide acceptance and it is therefore used in the rest of this study. In a clinical context, the term "response" would certainly be acceptable, as protocols are designed and recorded to establish a response, for example, at the threshold level.

The AEP technique known as ASSR was discovered and developed at the University of Melbourne during the 1980s (ERA Systems Pty Ltd, 2000). This clinical test system was preceded by research on human steady-state evoked potentials in the visual field (Picton *et al.*, 2003). Galambos, Makerg and Talmachoff's (1981) research provided the main impetus for extensive research into auditory steady state responses (Picton *et al.*, 2003). Rance *et. al.* (1995) and Rance *et al.,* (1998) indicate that ASSRs address the main shortcomings of ABR testing, in that ASSR is an alternative frequency-specific approach which does not suffer the spectral distortion problems associated with short-duration stimuli. ASSRs are periodic scalp potentials arising in response to regularly varying stimuli, such as a sinusoidal amplitude- and/or frequency-modulated tones (Rance *et. al.,* 1998).

ASSRs could be conceptualised as follows:

> Imagine the waveform for an evoked response which is displayed as a waveform in the time domain. Imagine the waveform for an evoked response if two tone burst stimuli were presented within an averaging epoch. Each tone burst would be expected to produce a response, and

> so the response waveform would be repeated twice, within the averaged epoch. Now imagine a 200 ms train of 2-1-2 cycle tone bursts, say at 1000 Hz, with an inter stimulus interval between each burst of 20 ms. Imagine that the signal-averaging epoch is also 200 ms in duration. One thousand 200-ms trains are presented and the response to each train is averaged. There are 10 responses in the time-averaged waveform for the 200-ms sample. Since the recorded response is periodic it can be analysed using frequency domain methods. To summarise: steady state responses are recorded when stimuli are presented periodically and they demonstrate how the brain reacts to a stimulus (Picton *et al.*, 2003)

From this description it can be seen that ASSRs are evoked by stimuli in the form of rapidly changing auditory signals, presented at such a high rate as to cause overlapping of responses. This yields what is effectively a steady state response to a sustained sound or continuous stimuli, as opposed to a transient response to changing auditory stimuli (Stapells, *et al.,* 1984).

ASSR techniques also use various protocols to evaluate the presence of a response. Transient responses like ABRs are usually described in terms of the latencies and the amplitude of specific waves. Latency can be explained as the time interval between the stimulus onset and the peak of a waveform. In the case of an ABR, the latency of wave I is for instance, 1,6 ms after stimulus onset (Hood, 1998). ASSRs by contrast, are not measured in the time domain (between the stimulus and the response), but in the frequency domain. Lins *et al*. (1996) explain that the compound electrical activity recordings contain the spectral component for the rate of modulation at which the tone is presented. Thus the stimulus drives the response to reflect the same amplitude and frequency modulation with which the stimulus was presented (Picton *et al.*, 2003).

Human steady state responses were initially studied in the field of visual modality (Stapells *et al*., 1984; Picton & Scherg, 1990). A description of the auditory steady state response by Galambos *et al.* (1981) reawakened interest in the phenomenon and its possible use in objective threshold estimation (Picton *et al.,* 1987). It was shown that when stimuli are presented at a rate of 40 per second, the middle latency responses have an amplitude some two to three times greater than when stimuli are presented at the conventional rate of 10 per second. (Stapells *et al.*, 1984). Unfortunately, the 40 Hz response has proved to be unreliable for young infants, so clinicians turned to stimulation rates of 80 to 100 Hz, as they are less affected by sleep, maturation and sedation (Rance *et al.,* 1995; Herdman & Stapells, 2001; John, Dimitrijevic & Picton, 2002).

A recent ASSR development is the multiple-frequency technique, where several carrier frequencies are presented to both ears simultaneously (Lins & Picton, 1995; John, Dimitrijevic & Picton, 2001b). The purpose of this procedure is to shorten test time, which is a critical requirement in clinical practice, particularly in the case of difficult-to-test patients and infants, who often do not remain asleep long enough for the test to be completed.

In recent years, the stimuli used in ASSR testing have also been manipulated. Initially, the pure-tone was only amplitude modulated (John & Picton, 2000; Cohen, Rickards & Clark, 1991), but later developments showed that tones modulated in terms of both frequency and amplitude (mixed modulation) give improved threshold estimates (Dimitrijevic *et al*., 2001).

From the above it is clear that the ASSR technique has virtually exploded in the last five years within the AEP context. The initial findings were promising, but limited due to maturational and wakefulness effects, it was relegated to more of a research endeavour (Schmulian, 2002). Thus far, ASSRs have been tested mainly on normal hearing subjects and on very small samples. Difficult-to-test populations examined have included mainly babies and young children (Sininger & Cone-Wesson, 1994; Savio *et al.,* 2001; Aoyagi *et al*., 1996; Rance *et al.* 1998). No studies on adult pseudohypacusic populations could be found.

The fact that the technique has been used in babies (always a difficult-to-test population) and since "automated response detection" brings an extra dimension of objectivity to the evaluation of difficult-to-test populations motivated an attempt to evaluate this technique for use in an adult pseudohypacusic population.

Relevant testing parameters and previous research findings related to ASSRs were evaluated in Section 4.3 to obtain guidelines for an experimental design.

4.3 RESEARCH FINDINGS WITH ASSRs

4.3.1 TYPES OF STIMULI

One of the key differences between ASSR techniques and other AEP methods are in the stimuli used, as discussed below.

Rob *et al.* (2000) list the various stimuli used in ASSR testing as click trains, trains of short tone-bursts and modulated tones. Modulated tones are the most widely used stimuli for eliciting steady state responses, because tones are continuous and, hence, are not affected by the spectral distortion problems associated with brief tone bursts or clicks (Rance *et al*., 1995). As has been demonstrated in the previous chapter, tone bursts and clicks have been used in ABR testing with pseudohypacusic patients, but these stimuli have not been frequency-specific enough. In medico-legal evaluations (such as mine workers with noise-induced hearing loss) the availability of frequency-specific threshold estimates at all the legally specified frequencies are of the utmost importance and thus the use of tones with longer rise and fall times is promising with regard to achieving frequency-specificity with pseudohypacusic adults.

4.3.2 STIMULUS INTENSITY

The speed at which thresholds can be determined with this technique depends in part on the amplitude of the ASSR, as the response must be distinguished from background noise. The greater the response's amplitude, the more rapid detection is. Nevertheless, research has shown that ASSRs can be recorded at low sensation levels (Dobie & Wilson, 1998). Rance *et al.* (1995) have found that ASSRs could be recorded at low sensation levels even with patients who are sleeping or sedated, provided that the modulation frequency is greater than 70 Hz.

Schmulian (2002) has also discussed the influence of intensity on multiple frequency (MF)-ASSR techniques, saying that at low-to-moderate intensity levels, the responses elicited with different carrier frequencies (CFs) show little overlap, provided CFs are one octave apart to ensure that effects on the basilar membrane occur at different locations. At higher intensities, the basal end of the cochlea tends to dominate, causing significant overlap to occur- hence, frequency-specific responses are more difficult to detect.

Low intensity MF-stimulation is particularly important in a population of mine workers, since noise-induced hearing loss is usually a sloping hearing loss with thresholds at 500 and 1000 Hz, near normal levels (Dobie, 2001).

4.3.3 CARRIER FREQUENCY

The effects of carrier frequency are quite different for stimuli modulated at rates of 40 to 80 Hz (Picton *et al.*, 2003). The 40 Hz responses significantly decrease in amplitude with increasing carrier frequency (Galambos *et al.,* 1981). For the 80 to 100 Hz responses, the amplitude is larger for the middle frequencies (1000 to 2000 Hz) than for either higher or lower frequencies (Picton *et al.*, 2003). Some of this effect at 80 Hz MF-techniques might be due to the fact that the stimuli at different CFs are presented at the same sound pressure level (normal hearing thresholds are found at lower frequencies).

It has been proven that the higher the carrier frequency and the greater the hearing loss, the better the correlation between ASSR and pure-tone thresholds is (Sininger & Cone-Wesson, 1994; Rance *et al*., 1995). This fact could be due to recruitment when monotic procedures are used.

John and Picton (2000) found that the latency of human ASSRs to amplitude modulated (AM) tones changes significantly and consistently with the carrier frequency in a MF-stimulation procedure. Latency periods are shorter for higher frequencies (for example, latency reduced from 6,0 to 5,5 ms when the CF was increased from 500 to 6 000 Hz). Such changes in the latency period appear to result from two cochlear processes: the filter build-up time of the hair cell transduction process and the transport time for acoustic energy to reach the responsive region of the basilar membrane, which is at the apex of the cochlea for low-frequency stimuli.

Schmulian (2002) explains that the lower amplitude of responses observed when a low CF is used is due to the fact that the activation pattern on the basilar membrane extends over a greater area than is the case with higher carrier frequencies. This causes a “jitter”, which could attenuate the amplitude of the response. The intrinsic jitter at 500 Hz has also been attributed to neural asynchrony (Lins *et al*., 1996). Other researchers have also discussed diminished responses at 500 Hz (John & Picton, 2000; Perez-Abalo *et al.,* 2001; Lins *et al.,* 1996; Aoyagi *et al*., 1994). One explanation attributed this lower amplitude of responses at lower CFs to a possible effect of ambient noise on stimuli at these frequencies (Lins *et al.,* 1996).

In the evaluation of this technique in a population of mine workers, it is important to note that 500 Hz is a frequency that must be tested by law (RMA guidelines, 2003) and thus it is important that accurate threshold estimates should be obtained at 500 Hz. One way of addressing the problems that various researchers have experienced in testing at 500 Hz is to limit the masking effect of ambient noise, in other words, to test in a sound-proof booth (Herdman & Stapells, 2001). In the clinical situation this should not imply any extra cost, since an acoustic booth is already used for conventional audiometry.

4.3.4 MODULATION FREQUENCY

With AEP methods, such as tone burst ABR, stimuli can evoke a response, but the latency, amplitude and threshold of the ABR are all affected by the stimulus level, rise-time and rate of presentation. Conventional signal averaging is used to detect the response, which is displayed as a wave form in the time-domain (Sininger & Cone-Wesson, 1994). This wave form needs to be identified by the clinician.

By contrast, ASSRs are periodic and can therefore be analysed by means of frequency domain methods. The spectrum of the response shows a major component at the rate at which the tone or stimulus is repeated or modulated and at the second harmonic of that frequency. It is thus clear that a response follows the same modulation rate as the stimulus and therefore the response detection is much more objective. It should be noted that with high modulation frequencies (for example, 100 Hz), each modulation has a 10 ms duration, with a 5 ms sinusoidally ramped rise-fall time and no plateau. The spectrum of the response peaks at the modulation frequency, thus determining the response's amplitude and phase characteristics, with no contamination of the response spectrum by the stimulus (Sininger & Cone-Wesson, 1994; John *et al*., 2002).

Not only is the frequency of the stimulus modulated, but the CF amplitude modulation introduces a replicable stimulus parameter, allowing a reliable estimation of hearing thresholds across the normal audiological test range, based on research on a wide range of modulation frequencies (4 to 450 Hz) (Cohen *et al.,* 1991). The success of amplitude modulation can be attributed to spectral power being present only at the CF and at two side bands (John *et al.,* 2002). This fact that it is possible to estimate behavioural thresholds across the audiological test range opens up the possibility that the degree and nature of hearing loss can now be determined in difficult-to-test populations. In fact, it has made this research possible.

Galambos *et al. (*1981) has described the initially popular modulation rate of 40 Hz, for which large and defined response amplitudes have been observed. One disadvantage of using the 40 Hz response is that at lower modulation frequencies such as 40Hz, responses have proven to be problematic, in that threshold estimation is affected by state of consciousness and sleep (Herdman & Stapells, 2001; Maiste & Picton, 1989; Lins et. al., 1995), maturation (Lins *et al.,* 1995) and anaesthesia (Plourde & Picton, 1990). As the modulation frequency is reduced, the principal site of evoked potential responses is likely to move up the auditory pathway, thereby increasing the latency period. Such effects were to be expected, given the sensitivity of response generators in the auditory cortical and lemniscal brainstem to a person's state of consciousness. Nevertheless, some researchers have proven that the 40 Hz response is a very effective means of threshold estimation, including John and Picton (2000), who maintain that 40 and 80 Hz are the most suitable modulation frequencies for threshold estimation. Unfortunately, the 40 Hz response is not reliable in young infants and children, due to maturation effects and the effect of state of consciousness, as mentioned above.

Dobie and Wilson (1998) state that ASSRs for adult patients are best recorded at low intensities in the alert/awake state, based on reduced 40 Hz responses among sleeping or sedated adults. They conclude that the 40 Hz response at low intensity levels is optimal for both alert and sedated adults. In sedated subjects, the reduced background noise made responses more detectable.

Due to the above difficulties with the 40 Hz response, a greater interest in the use of high repetition rates arose after it was found that they increased the amplitude of responses (Rickards & Clark, 1984). Modulation rates of 75 to 110 Hz were seen to be the most suitable for threshold estimation (Cohen *et al.*, 1991; Lins & Picton, 1995; Lins *et. al*., 1996). Lins *et al.* (1996) have demonstrated that modulation rates of 75 to 110 Hz can be used to estimate pure-tone thresholds to within 10 to 20 dB in sleeping babies and in normal and hearing-impaired adults. Lins and Picton (1995) have reported that a modulation frequency of 80 Hz gives response latencies that are similar during sleep and wakefulness. A rate of 80 Hz has also been regarded as an effective modulation frequency for sedated adults (Dobie & Wilson, 1998). Higher modulation rates (770 Hz) have also proven to be effective in estimating hearing thresholds when they are used at low intensities (Clark *et al.,* 1991). In terms of the available equipment, the 40 Hz and 80 to 110 Hz are the most popular modulation frequencies at this stage.

The focus of the preceding discussion is amplitude modulation. However, Cohen *et al.* (1991) have found that frequency- and amplitude-modulated tones (AM/FM) yield larger response amplitudes that amplitude modulated tones alone, because additional processing channels are associated with frequency modulation and AM/FM tones excite a larger portion of the basilar membrane. This combined amplitude and frequency modulation is also called multiple modulation (MM) (Schmulian, 2002), and produces tones that sound similar to the warble tone used in paediatric audiology. John and Picton (2000) have found that responses elicited using both amplitude and frequency modulation reaches significance at twice the speed of tones that are only amplitude modulated.

Since different modulation frequencies have been shown to be successful in different populations, one can conclude that it is important to evaluate both a lower (40 Hz) and a higher modulation frequency (80 to 110 Hz) in an untested pseudohypacusic adult population, and to use mixed modulation in an experimental design, since it has already been proven to be more accurate in threshold estimation than amplitude or frequency modulation alone.

4.3.5 DICHOTIC STIMULATION

The above discussion of ASSR stimulus parameters has focused on monotic stimulus presentation, in which each frequency is assessed separately for each ear. Monotic presentation techniques were developed for hearing assessments in cochlear implant programmes, because dichotic presentation limits the separation of responses at high intensities, which are quickly reached during evaluations of cochlear implant candidates with limited residual hearing (Rickards *et al.,* 1994).

An optimised variant of ASSRs called multiple simultaneous amplitude modulation has been described by Lins and Picton (1995). Distinct modulation rates (separated by more than one octave) are used for eight carrier tones (four per ear), and the modulated tones are combined to produce an acoustic stimulus capable of simultaneously activating different regions of the cochlea (Perez-Abalo *et al*., 2001). Herdman and Stapells (2001) have found that MF-ASSR testing of both ears produces responses comparable to the use of only one carrier frequency or four carrier frequencies to a single ear. It is claimed that the technique can predict eight thresholds in the time it takes to observe one single threshold (Lins *et al.,* 1996; Perez-Abalo *et al.,* 2001).

The MF-ASSR technique is also a variant of the 75 to 110 Hz ASSR that Perez-Abalo *et al. (*2001) have found to be reliable in predicting behavioural thresholds, with 80,9 per cent of ASSR and behavioural thresholds within 20 dB of each other. Similar results were reported by Herdman and Stapells (2001) with 87 per cent of ASSR and behavioural thresholds within 20 dB of each other.

There is an urgent need for techniques that will enable audiologists to determine behavioural thresholds in a time-efficient manner. An ASSR test time of 164 minutes for eight separately determined frequencies and a corresponding time of 83 minutes for multiple dichotic ASSR testing have been reported (Herdman & Stapells, 2001). Although 83 minutes is shorter, this is still impractical for clinical applications, especially for difficult-to-test patients. This is true even for a test time of 21 minutes, as reported for normal hearing subjects (Perez-Abalo *et al.,* 2001).

Swanepoel (2001) maintains that MF-ASSR techniques show great promise as a threshold estimation technique for patients of all ages, but, clinical validation is limited (see Section 4.3.6). It has thus been postulated that the technique cannot be considered for clinical use until additional studies have optimised parameters (John *et al.,* 2001b). Furthermore, Schmulian (2002) has pointed out that studies thus far have only used normal adults, well infants and a very limited (small) number of hearing-impaired subjects.

An exciting topic for future study is indicated by John *et al*. (1998) , who point out that everyday sounds contain multiple frequencies and, that therefore, the results of MF-ASSR methods may be more representative of actual hearing than those of tests using discrete stimuli.

Finally, the mere fact that simultaneous testing of eight frequencies is possible is an important advantage in a difficult-to-test population and in an industry (mining) that produces very high case loads. This is another (important) motivation for validating the technique in a mining environment.

4.3.6 LIMITED CLINICAL VALIDATION

In 2001, Swanepoel commented that ASSRs had not been studied very extensively. This is still the case, as no literature could be obtained pertaining to ASSRs and to noise-induced hearing loss and pseudohypacusis, which constitute the focus of the present study. When experimental testing began in September 2002, only one ASSR system was available at the University of Pretoria. As indicated before, clinical applications of ASSRs are in their infancy , and relevant research findings are limited (Schmulian, 2002).

The above debate will be illuminated further because the clinical validation of MF-ASSR is particularly limited for hearing-impaired subjects (Perez-Abalo *et al.,* 2001). Schmulian (2002) quotes six MF-ASSR studies in which no findings are reported regarding the possible impact of ASSR on an impaired auditory system. The present author would add that ASSR research is characterised thus far by very small experimental groups. Johnson and Brown (2001) used only ten subjects, and Valdez *et al.* (1997) used only 16. The limited clinical validation and research is a confounding factor to the present research, since there are no similar studies available to which results can be compared to. In that sense then, this study is exploratory in nature.

4.3.7 LENGTH OF PROCEDURES

One disadvantage of AEP techniques, mentioned before, is the length of test procedures. ABR, the most popular AEP method, also presents this limitation in evaluating difficult-to-test patients (Stach, 1998). John *et al.* (2001a+b) report that, particularly with children, the examiner must obtain as much information as possible in the shortest possible time.

A positive factor is that continuing research has led to newer developments that reduce the time required for threshold determinations. The amplitude of the response limits the speed of threshold determination, as responses must be distinguished from background noise, indicating that it would be advantageous to increase response amplitude (John *et al*., 2002). Techniques that have already increased the speed of determination include the following:

- the use of multiple modulated (amplitude and frequency) stimuli for more rapid determination of thresholds than with simple amplitude modulation or frequency modulation of stimuli (John *et al.,* 2001b);
- amplitude modulation of stimuli using exponential envelopes can reduce the average test time by up to 21 minutes (Perez-Abalo *et al.,* 2001). This was achieved by increasing ASSR amplitude and latency, to reduce the time needed for responses to become significant (John *et al.,* 2002);
- evaluation of responses to several (eight) simultaneously presented amplitude-modulated (at different rates) stimuli (Lins & Picton , 1995) can reduce test time by allowing eight frequencies to be assessed

simultaneously. (This is in contrast with the more time-consuming separate assessment of individual frequencies in single carrier frequency tests (Herdman & Stapells, 2001; Perez-Abalo *et al.,* 2001). However, John *et al. (*2001b) postulate that MF-ASSR testing is not yet suitable for clinical applications, saying that more trials are needed to optimise stimulus and recording parameters before this procedure can be validated); and

- the use of analysis algorithms to automatically conclude stimulation and sampling once a predetermined probability value (for example P<0, 3) is achieved, thereby minimising test time for any given trial (ERA systems Pty Ltd, 2000).

Lengthy testing time can be seen as a negative factor when testing pseudohypacusic mine workers with ASSRs, since the mining industry produces very large case loads. A further negative influence of testing time is the impossibility of evaluating different test protocols with the same subject (De Koker, 2003).

4.3.8 SUBJECT-RELATED FACTORS

In recording AEPs and ASSRs, it is important to consider that a subject may induce inaccurate recordings by interfering with procedures or the test environment (Aoyagi *et al*., 1994; Schmulian, 2002). Body movement, tenseness and an inability to follow instructions or remain still create excessive background noise and have a negative effect on the quality of data collected (Sininger & Cone-Wesson, 1994). The same authors have recommended that the clinician optimises the amplitude of the response and minimises background noise to ensure quality recordings:

- a correct placement of electrodes improves recordings;
- adequate epoch duration is important;
- a suitable filter bandwidth should be selected;
- minimal electrical noise should be present;

- a sufficient number of sweeps is needed to yield reliable averages; and
- accommodation for the patient's age and state of consciousness should be made.

Because factors such as filter bandwidth, epoch duration and the number of sweeps averaged are controlled by computer software using algorithms developed during research, the clinicians main concern should be to control artefacts and background noise. Clinician's should also be aware of the need for a quiet test environment during ASSR threshold estimates, according to Herdman & Stapells (2001), who have found that the accuracy of threshold estimates improved by 5 to 10 dB when tests were conducted in an acoustically treated test booth. Subjects should be relaxed to minimise artefacts (John & Picton, 2000), and the head should be positioned for a relaxed posture to reduce peri-auricular and muscle potentials (Halliday, 1993). Dobie and Wilson (1998) recommend that patients be tested in a supine position, and in a darkened room.

Sedation is sometimes administered to ensure low noise levels, but this practice has medico-legal and ethical implications. Furthermore, patients must give informed consent before such a procedure is performed and medical support must be available. The latter aspect has financial implications. This statement paints a negative picture but, on the positive side**,** John and Picton (2000) observe that it is possible that, as researchers' experience with ASSR methods increased, inter-subject variance may diminish.

Since there are no previous data available on the adult difficult-to-test population of pseudohypacusic mine workers, it is important to verify if sedation will influence the accuracy of threshold estimates and to control the factors that have already been proven to reduce the quality of threshold estimation. Lack of co-operation and tenseness has led to routine sedation of pseudohypacusic mine workers during ABR testing (De Koker, 2003).

Sedation might thus be needed if pseudohypacusic patients withhold co-operation.

4.3.9 APPLICATIONS OF ASSR IN CLINICAL AUDIOLOGY

Various applications for ASSR testing have been proposed in the literature:

- probing the ongoing state of a subject during operations (Sininger & Cone-Wesson, 1994);
- neonatal screening (Rickards *et al*., 1994);
- neuro-otological diagnosis of retro-cochlear abnormalities (Sininger & Cone-Wesson, 1994);
- as an electrophysiological technique analogous to speech discrimination tests (Picton *et al.* (1987) state that the ability to discriminate changes in a sound's frequency and intensity is essential to auditory perception, and Dimitrijevic *et al.* (2001) have followed the same line of thought in proposing ASSRs as an objective test for supra-threshold hearing); and
- estimating pure-tone behavioural thresholds (clearly the most important clinical application for ASSRs , particularly in difficult-to-test patients).

Pseudohypacusic patients certainly fall into the difficult-to-test category, and discussions of AEP and ASSR testing in the last two chapters raises the question whether **ASSR testing is an accurate, feasible and time-efficient way to evaluate pseudohypacusic mine workers with noise-induced hearing loss, or, more to the point, whether ASSR-based threshold estimates for this group (who are difficult-to-test and have true sensory-neural hearing loss) are accurate enough to finalise compensation and fitness-for-work assessments.**

4.3.10 APPARATUS

MF-ASSR methods use the same recording montage as ABR tests. Rance *et al.* (1995) advise the use of silver-silver chloride disk electrodes on the forehead and earlobe/mastoid, with a third electrode on the contra-lateral mastoid or cheek to serve as an earth. ASSR test systems and software require a personal computer running Windows, as well as an electroencephalogram amplifier. Earphones are inserted in addition to the electrodes.

The fact that the same electrode montage is used as for the ABR enables the clinician to perform an ABR, when needed, as well.

4.3.11 THRESHOLD DETERMINATION TECHNIQUE

Attention has been drawn to the fact that different threshold-seeking procedures may account for differences between ASSR and behavioural thresholds, where 10 dB steps have mainly been used in AEP procedures and 5 dB steps in behavioural testing.

A concern in experimental work is the lengthy procedure involved for all AEPs. Is it practicable to test at 5 dB intervals when using ASSR-methods when a clinician has a large case load as is typical in the mining industry?

4.3.12 RESPONSE GENERATORS

There has been very little research on neural generators of ASSR as a function of the modulation rate (Sininger & Cone-Wesson, 1994). The physio-logical interpretation of scalp-recorded ASSR latencies remains difficult. The main problem is that responses may be derived from more than one generator in the auditory pathway (John & Picton, 2000). Sininger and Cone-Wesson (1994) cite studies of ASSR neural generators in relation to modulation rate, which found that the VIII cranial nerve, cochlear nucleus, inferior colliculus and primary auditory cortex are all responsive to amplitude and frequency modulated signals.

The literature clearly indicates that, for the purpose of threshold estimation, the presence or absence of an ASSR is mainly determined by the integrity of the cochlea and the VIII cranial nerve (Dimitrijevic *et al.,* 2001). The cochlea is the area of concern in noise-induced hearing loss, at it is thus relevant to use this technique on a population with noise-induced hearing loss.

4.3.13 FREQUENCY-SPECIFICITY

As for the clinical determination of hearing thresholds, AEP threshold estimates should be provided for each ear at frequencies corresponding with the range of human speech communication (Sininger & Cone-Wesson, 1994). The reason for this is that once a person develops a hearing loss, a clinician needs to characterise its degree, type and configuration. Relevant frequency-specific information enables a clinician to apply appropriate amplification and, in the mining sector, to evaluate compensability and fitness for work. In South Africa, compensation assessments must consider hearing at 500, 1 000, 2 000, 3 000 and 4 000 Hz (Workmen's Compensation Commissioner, 1995). According to ERA Systems Pty Ltd (2000) and John and Picton (2000), ASSRs can be elicited in the frequency range between 250 and 8 000 Hz, thereby meeting the need for specificity across the range of frequencies for conventional audiometry and satisfying legal requirements.

The excellent frequency specificity of ASSRs is based on the frequency content of an amplitude-modulated stimulus that is concentrated where there is no spectral splatter (Lins *et al*., *1996).* Rance *et al.* (1995) and Lins *et al*. (1996) have shown that the configuration of hearing loss does not influence the accuracy of ASSR results.

4.3.14 RESISTANCE TO STATE OF CONSCIOUSNESS

A clinician must be aware of factors like the patient's state of consciousness, which can affect the quality of AEP measurements. ABR testing has proven to be effective, particularly for infants, since it is not affected by the infant's state of consciousness or sleep, in contrast to the 40 Hz responses, which are considerably affected by sleep and sedation (Cohen *et al.,* 1991).

It is of the utmost importance that the testing procedures used for difficult-to-test patients are not affected by sleep or sedation, as such cases are characterised by a lack of co-operation. Testing under sedation often becomes a necessity. Cohen *et al.* (1991) and Rance *et al.* (1995) have found that ASSR techniques give reliable results for sleeping adults and children, while Hood (1998) also concludes that ASSRs evoked by tones with a modulation rate of 75 to 110 Hz are not significantly affected by sleep or sedation.

4.3.15 ABSENCE OF GENDER BIAS

During ASSR research, no evidence of gender bias has been found (Stapells *et al.,* 1984). This is not only an important clinical characteristic of a specific research technique, but it is also of specific importance in the present study, since mine workers are traditionally male and thus it is highly unlikely that a comparison between male and females in this population would be possible. Results of research using male mine workers can therefore quite possible be generalised to females as well.

4.3.16 ACCURACY OF THRESHOLD ESTIMATES

The main problem clinicians have with pseudohypacusic patients is great difficulty in obtaining the accurate, reliable and objective hearing thresholds which are imperative to meaningful assessments. This problem can possibly be overcome by using ASSRs, but clinicians must take into account that ASSR thresholds are not hearing thresholds *per se*, but physiological thresholds used to predict auditory thresholds (Sininger & Cone-Wesson, 1994).

Furthermore, it is important to acknowledge that, when one compares pure-tone and physiological thresholds, pure-tone thresholds are *influenced* by factors such as:

- instructions given to patients;
- the size of the dB step or increment used in tests;
- the earphone fit;
- background noise in the test environment; or
- the threshold determination criterion used by the audiologist, for example, a 50 per cent or a 75 per cent detection rate (Sininger & Cone-Wesson, 1994).

The above issues are not relevant to ASSRs. Electrophysiological thresholds, by contrast, are detected when they are distinct from random neural and muscle potentials, and from random airborne activity. Any factors that influence the amplitude of the response or the amplitude of the noise affect detection. Nevertheless, several researchers have found a high correlation between ASSR and pure-tone thresholds.

Lins *et al.* (1996) have found ASSR thresholds to be approximately 10 dB higher than conventional pure-tone hearing thresholds among adults with normal hearing. They have also found that threshold estimation in a group of infants was slightly worse than reported by Rickards *et al.* (1994), who found differences of 41, 24 and 35 dB hearing level at frequencies of 500, 1 500 Hz and 4 000 Hz respectively, among well babies. Lins *et al.* (1996) have tested adolescents with quantified hearing losses, and have found that ASSR measures provide reliable frequency specific information for this population.

Due to the excellent correlation found between behavioural and ASSR thresholds (an overall coefficient of 0,97 for all the frequencies tested) (Rance *et al., 1995),* a linear regression analysis has been developed to translate electrophysiological thresholds into a conventional audiogram. Use of the regression line enables predictions of behavioural thresholds across a range of carrier frequencies to within 10 dB in 96 per cent of cases.

The accuracy of the estimation of behavioural thresholds by ASSRs is the one very important factor that will decide whether this technique will be acceptable in medico-legal investigations in general and in the mining industry in particular.

4.3.17 DETECTION OF THRESHOLDS THROUGH THE SEVERITY RANGE

The validity of ASSR thresholds in normal hearing populations has so far been the most extensively researched. Rickards *et al.* (1994), Swanepoel (2001) Schmulian (2002), Rance *et al.* (1995) and Lins *et al.* (1996) have studied the threshold estimation accuracy of ASSRs in normal hearing people, and they all conclude that ASSR is a suitable procedure for this application.

Although it has not been as extensively studied (Schmulian, 2002), threshold estimation in people with hearing loss, has also shown ASSR testing to be a suitable substitute for pure-tone testing. Lins *et al.* (1996) found the prediction of pure-tone thresholds from ASSR thresholds to be in the order of r = 82, with differences averaging between 9 and 14 dB. Rance *et al*. (1998) have tested infants and children who were candidates for cochlear implants to assess the ASSRs ability to predict severe hearing loss and establish the presence of residual hearing. ASSR thresholds were within 20 dB of pure-tone thresholds for 99 per cent of these cases, and within 10 dB for 82 per cent of them.

It can therefore be concluded that ASSR methods of threshold estimation are suited for normal and impaired hearing cases, but that estimates of hearing thresholds are better in pathological ears, due to the effects of recruitment (Rance *et al.,* 1995). This again motivates the drive to test this method in a mine worker population that is known to have a high incidence of hearing loss.

4.3.18 LACK OF AGE-RELATED INFLUENCES

The use of ASSRs has been studied for a wide range of age groups, including neonates, children, adolescents and adults. In all these groups, it has been found that ASSR testing provides a reliable and objective measure of hearing thresholds. Stapells *et al.* (1984), Sininger & Cone-Wesson (1994) and Rance *et al.* (1995) have found no age effects during ASSR testing.

It has also been proven that ASSRs are appropriate for screening neonates during the first four days after birth (Rickards *et al.,* 1994). Savio *et al.* (2001) have shown that ASSR techniques are valid, but they are the only researchers who have demonstrated changes in threshold amplitude and detectability during the first year of life. They have found that thresholds at 4 000 Hz decrease by 14 dB between birth and 12 months of age, and that such changes occurred more slowly for ASSR thresholds at lower frequencies.

Age effects are not relevant to this study, since the difficult-to-test population are all adults.

4.3.19 THRESHOLD DETECTION IN THE FREQUENCY DOMAIN

As stated previously, a critical requirement that has to be met by AEP testing is an objective detection of responses. Although no voluntary responses are needed from the patient (Lins *et al*., 1995), it is preferable that clinicians also play no role in determining or assessing the presence of a response.

When an ASSR stimulus is presented at or above a threshold, hair cells in the cochlea are activated in a locus corresponding with the carrier frequency. An analysis of the response in the cochlea and subsequent parts of the auditory pathway requires no visual detection of wave forms, nor any measurement of peak latency or amplitude. ASSRs are detected by applying computer algorithms to the recorded elctroencephologram. The algorithms analyse the magnitude and phase of the electrical activity corresponding with the modulation frequency. Lins and Picton (1995) explain that the complex wave forms in the time-domain are transformed to the frequency-domain by means of Fast-Fourier processing. In the frequency-domain, the analysis is done using spectral analysis techniques.

ERA Systems Pty Ltd (2000), the manufacturers of the Audera ASSR system, state that 64 samples are analysed in each trial, which comprises a tone of a specific frequency-amplitude combination, for example, 1000 Hz at a 30 dB hearing level. In each electroencephalogram sample, the magnitude and phase of the electrical activity corresponding with the modulation frequency are quantified and shown as a vector in a polar plot. The vector's length represents amplitude, and its angle reflects the phase or time delay between tone modulation and the brain's response (ERA Systems Pty Ltd, 2000).

When vectors are clustered, this indicates a phase-locked brain response; in other words, the electroencephalogram samples are synchronised with the tone modulation frequency, which can only occur if the ear and brain have responded to a sound. Vectors distributed randomly around the polar plot indicate a lack of phase relationship between the electroencephologram and tone modulation (no response).

Statistical analyses are done in real-time as samples are collected, and the analysis algorithms (Sininger & Cone-Wesson, 1994) halt stimulation and data sampling when certain probability values have been obtained, for example, p (probability value)<0, 3.

The statistical analysis of vector phases uses a measure known as phase coherence squared (PC^2), calculated as each new vector is obtained for an electroencephalogram sample. The resulting PC^2 values can range from 0 to 1, with values approaching 0 indicating low phase coherence between the sample and tone, and those approaching 1 indicating high phase coherence.

The PC^2 value is evaluated using statistical tables of circular variance to obtain a probability value, "p". This level of significance is thus determined by a statistical test and gives an indication of whether a response is present. A probability value of $p<0{,}03$ sets the false positive rate for ASSR detection at 3 per cent (there is a less than 3 per cent chance that results are due to noise alone). A trial contaminated by excessive noise is automatically terminated, labelled as such and excluded from further evaluations. The lowest level at which a phase-locked response is obtained is taken as the electrophysiological threshold, which is used to estimate pure-tone behavioural thresholds by means of an algorithm based on the research of Rance *et al*. (1995) (see Figures 5.14 to 5.18).

Picton *et al.* (2001) has found that detection protocols based on both phase and amplitude (the f-test and the phase-weighted t-test) are more effective than those using phase alone (phase coherence and phase-weighted coherence) (Stapells *et al*., 1984; Aoyagi *et al.,* 1994). The f-test evaluates whether a response to the stimulus differs from noise in the recording at adjacent frequencies (Lins *et al.*, 1996; Perez-Abalo *et al*., 2001), and the T2 statistic determines whether a response is replicable across a number of averaged responses (Valdez *et al.,* 1997; Picton *et al.,* 1987). Lins *et al.,* (1996) have found the f-test to be slightly more effective than the T2 test. Picton *et al.* (2001) have found that using both the phase and the amplitude data in detection protocols identified more ASSRs than phase data alone.

The above detection of responses and thus threshold estimation objectively done by means of computer algorithms is the most important reason for evaluating this technique in an adult population with pseudohypacusis, since this objectivity has been lacking in traditional AEP testing.

4.3.20 ASSESSMENT OF SOUND PROCESSING

ASSR testing has created the possibility of evaluating sound processing by means of binaural stimulation, rather than traditional monaural stimulation. Multi-sensory processing and interactions between the visual and auditory systems have not yet been researched (Schmulian, 2002), but a possibility may exist that one could use ASSRs in the evaluation of reading difficulties where auditory and visual processing abnormalities coincide. The possible advantages of evaluating a patient's hearing using this technique would be the fact that binaural multiple-frequency stimulation can approximate human hearing to a much greater degree than monaural pure-tone testing does.

4.4 SUMMARY

In this chapter, auditory steady state responses have been defined and put into a historical perspective. The relevant testing parameters have been discussed with reference to their importance for a pseudohypacusic adult population. Advantages and disadvantages of this AEP have been evaluated in order to decide on the possibility of using this method as a threshold estimation technique in adults with noise-induced hearing loss.

A summary of the current research findings related to the rationale for the clinical and research use of ASSRs is set out in Table 4.1 below.

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TABLE 4.1: RATIONALE FOR THE SELECTION OF ASSR IN EXPERIMENTAL RESEARCH WITH MINE WORKERS

ADVANTAGE OF ASSRs	REFERENCES
Objective threshold estimation	Sininger and Cone-Wesson (1994) ERA Systems Pty Ltd (2000) Rance *et al. (1995)*
Frequency-specificity	Sininger and Cone-Wesson (1994) ERA Systems Pty Ltd (2000) John and Picton (2000) Lins *et al*. (1996) Rance *et al*. (1995)
Resistance to state of consciousness	Cohen *et al*. (1991) Rance *et al. (*1995) Hood (1998)
Absence of gender bias	Stapells *et al.* (1984)
No amplitude deterioration with pathology	Schmulian (2002)
Correlation with behavioural thresholds	Sininger and Cone-Wesson (1994) Lins *et al*. (1994) Rance *et al.* (1995)
Response generators: cochlea and VIII nerve	Dimitrijevic *et al*. (2001)
Application in threshold estimation	Rance *et al.* (1995) Rickards *et al.* (1994)
Age unimportant	Stapells *et al*. (1984) Rance *et al*. (1995) Rickards *et al*. (1994)
Tonal stimuli	Rob *et al*. (2000) Rance *et al*. (1995)
Stimulation of eight simultaneous frequencies	Perez-Abalo *et al*. (2001) Herdman and Stapells (2001)
Accurate throughout severity range	Rickards *et al*. (1994) Rance *et al*. (1995) Lins *et al*. (1996) Rance *et al*. (1998)

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The above theoretical advantages indicated in Table 4.1 motivated the application of ASSRs in an empirical clinical study as is discussed in Chapter 5.