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AUDITORY EVOKED POTENTIALS (AEPS): UNDERLYING PRINCIPLES

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Auditory evoked potentials (AEPs) is the collective term for electrical potentials evoked by externally presented auditory stimuli from any part of the auditory system, from the cochlea to the cerebral cortex [1]. Evoked responses represent electrical potentials as a manifestation of the brain's response to sound.

AEPs infer a summation of electrical potentials generated along the auditory pathway. Summation or averaging of the response is necessary due to the size of the auditory response in relation to the body's ongoing neurophysiological activity. A typical human adult EEG (electro-encephalogram) signal is about 10µV to 100 µV in amplitude when measured from the scalp, while auditory brainstem response (ABR) waves, which are the most widely used AEPs, have an amplitude of <0.5 µV. So, for one to see this small response to sound amongst all the other millions of neural processes going on, one needs to gather and average as many of these electrical potentials as possible.

What happens when sound activates the auditory nervous system is that the activation is detected as a change in neuroelectrical energy in the auditory nerve, the auditory centres of the lower part of the brain (brainstem), as well as from higher up in the auditory pathways, at the midbrain, thalamus and cortex. The notion of *change*, and of *synchronous neural firing* (co-ordinated, simultaneous triggering of compound action potentials along the auditory neural pathway) is key as there is always some ongoing spontaneous electrical activity within the auditory pathway. However, when activation by sound occurs, the neurons fire more synchronously and neuronal activity increases or decreases in response depending on the source, frequency or volume of the sound stimulus [2]. One can objectively, and for the most part non-invasively, measure this response, by attaching a few electrodes to the head and with earphones in the ear canals.

There are several AEP classification systems [3–6]. One of the earliest and most widely accepted is that of Davis [4], who proposed that AEPs be classified by latency, i.e. the time at which they typically occur after stimulus presentation. Four components are recognized, namely early, middle, slow and late AEPs. The latency also represents how long the auditory stimulus takes to reach various neural generators along the auditory pathway. The identification of a particular neural centre as the neural generator of a response at a particular time is, however, an over-simplification. The ascending auditory pathway is complex and incoming auditory stimuli may be processed both along the ipsilateral pathway (on the same side as the ear the sound was presented to), or the signal may cross over to the opposite or contralateral pathway on its way up to the cortex. Most of the processing does seem to generally occur in the contralateral pathway. Consequently, the different neural structures may contribute to the AEP at the same latency [7].

Early AEPs occur at a latency of 0 to 20 ms and comprise of the ABR and electro-cochleography (eCochG). Middle AEPs occur at 10 - 100 ms and refer to the middle latency AEP (MLAEP). Although the slow and late AEP categories are often considered together as 'late' AEPs, the author prefers using the original 'slow' and 'late' classifications as described by Davis [4] and recommended by Stapells [6]. The slow cortical auditory evoked potential (CAEP)

occurs at 50 - 300 ms latency following onset of the stimulus, while late AEPs refer to AEPs occurring at 150 - 1000 ms. Late cortical AEPs include the mismatch negativity (MMN), P300, N400 and P600 responses [4,6]. The auditory steady-state response (ASSR) spans both middle and slow latency categories as different stimulus rates result in different neural generators.

Early AEPs can be thought of as non-voluntary, automatic *hearing* functions – the ones we cannot switch off. These tests that can therefore be done with the adult or child asleep, or even under general anaesthesia. In contrast, slow and late AEPs require the patient to be *listening* and for their cortex to be very much awake. CAEPs provide information about detection of sound, whilst tests like P300 and MMN are related to auditory discrimination and identification of change. So, when one is asleep, one is still able to hear, but, as I always tell my students, "if you are asleep in class, I'm pretty sure you are no longer able to listen".

AEPs are capable of accurate behavioural pure tone threshold estimation. AEPs are not measures of hearing as such but are highly correlated with hearing thresholds [4,7–9]. It is for this reason that the phrase 'estimation of behavioural pure tone auditory thresholds' is used. What one dos is to identify a pattern of waves, and then to turn down the volume of the sound stimulus to find a threshold response, which is the lowest intensity at which a small response is present. This threshold, minus a small correction value, correlates with an individual's hearing threshold [1]. However, this is true for all but a small handful of individuals with Auditory Neuropathy Spectrum Disorder (ANSD). Accuracy of estimation of the AEP threshold is dependent on neural synchrony. In ANSD, and in cases of lack of evidence of neural synchrony, AEP will not provide an accurate estimation of true behavioural hearing threshold. A discrepancy between behavioural pure tone thresholds and AEP threshold intensity (AEP indicating better hearing sensitivity) in a population suspected of nonorganic (exaggerated) hearing loss is strong evidence that behavioural pure tone threshold findings are inaccurate [7]. The clinical use of AEP for this purpose has been reported on extensively [4,7,8,10–17]. As such, AEPs play a critical role in the assessment of hearing in individuals who cannot or will not participate actively in standard hearing assessment procedures (mentally retarded or malingering patients), as well as in infants and young children [9].

Early AEPs include the ABR and eCochG. The ABR is the most widely used AEP.

AUDITORY BRAINSTEM RESPONSE (ABR) TESTING

The ABR is defined as a far-field recording of neuroelectric activity of the eighth nerve and brainstem auditory pathways that occurs over the first 10 - 15 ms after an abrupt click stimulus [18]. It is characterised by five to seven vertex-positive peaks representing synchronous neural discharge from generators located along the auditory pathway to the inferior colliculus of the midbrain [8,18]. Each peak is labelled by consecutive Roman numerals [19].

A participant's attention to stimuli, or the lack thereof, has little or no effect on these short latency responses [20,21], resulting in robust, repeatable recordings despite differences in a participant's state of consciousness. ABRs do require that individuals lie still with minimal movement to reduce artefacts; sedation is sometimes required for children or even adults who do not comply. A two-year-old can barely sit still for two minutes let alone for the hour

and half to two hours that is needed to complete a neurological evaluation and threshold determination. Despite this, the stability of these potentials over participant state, the relative ease with which they may be recorded, and their sensitivity to dysfunctions of the peripheral and brain-stem auditory systems make them ideal for clinical use. This has led to the almost universal application of ABR for behavioural pure tone threshold estimation for children and infants too young to be tested using standard behavioural measures [22]. In addition to estimating hearing sensitivity, ABR is used as an objective tool to assess auditory-neural integrity and synchrony. If one knows that there is synchrony in the way in which the auditory nerve fires, then one knows that AEPs can be used to estimate hearing thresholds. That is the core reason why every AEP assessment needs to begin with a neurological, click-evoked ABR.

A click is an abrupt onset stimulus with a broad frequency spectrum. Synchronous firing of multiple neurons, which is the general physiological foundation of the ABR, is dependent on an abrupt stimulus onset [8]. It is for this reason that the click stimulus is routinely used in clinical ABR recordings. A typical 100 μs square wave click has a broad frequency spectrum with equal energy from 0.1 - 6 kHz [7]. The click stimulus therefore activates a wide area of the basilar membrane. However, the click-evoked ABR is not frequency specific and provides little information regarding audiometric configuration or sensitivity at a particular frequency [18]. There is widespread belief that the greatest agreement between the click-evoked ABR and behavioural pure tone thresholds is in the 2 - 4 kHz frequency range [4,7,8,18,23,24]. This is generally true and across a large group of individuals with hearing loss, but untrue for some individuals, especially those with hearing loss restricted to certain frequencies [6]. The click-evoked ABR is virtually independent of low frequency hearing sensitivity [7]. A normal ABR may therefore be recorded in individuals with hearing loss with only isolated regions of residual normal hearing sensitivity in the 2 to 4 kHz region [7,25].

The click-evoked ABR is an important indicator of integrity of the auditory nerve and the brainstem auditory pathways and is a tool to screen for hearing loss in infants [6]. A new broadband stimulus, the chirp stimulus, has also been used for hearing screening in automated ABR software. The chirp was developed to counterbalance the delay of the sound wave on its journey through the cochlea. Although the click stimulus is broadband, due to the tonotopic arrangement of the cochlea, the high frequencies at the base of the cochlea are activated first, followed by the mid-, then low frequencies, as the travelling wave moves along the spiral basilar membrane to the apex of the cochlea. This is part of the reason why the click stimulus correlates better with high frequency thresholds. With regard to neural synchrony, the best would be for the hair cells along the cochlea to depolarise at the same time. The broadband chirp stimulus does this by sending the low frequency sound first, followed by the mid- and finally the high frequencies. The timing is based on various formulae accounting for the timing of the basilar membrane travelling wave [26]. The result is simultaneous stimulation of hair cells at all frequencies, providing better neural synchrony and consequently, recording of responses with larger amplitudes. There are several types of chirps but the one most people have in their commercial equipment is the CE Chirp (CE after Claus Elberling who developed this chirp) [27–29]. One can also use a chirp stimulus for a neurological ABR although there are different opinions regarding whether chirps or clicks are the better option [30,31].

For threshold determination, one needs a stimulus that still provides some neural synchrony but is more frequency specific that clicks or chirps. Pure tones are in theory the most frequency specific but do not get enough cochlear hair cell nerve fibres to fire for the response to generate AEPs. A tone burst and narrow band chirp is a compromise between neural synchrony and frequency specificity. It is not as frequency specific as a pure tone and not as abrupt as a click, nor does it result in as much neural synchrony as a click or chirp, but one can use these stimuli to build an estimated audiogram.

By using a combination of neurological ABRs, and air and bone conduction ABRs for threshold estimation, one is able to differentiate between conductive, sensorineural and retrocochlear disorders. Although inferences can be made from an ABR about hearing, these are not tests of hearing as such, but rather tests of synchronous neural function; the ability of the central nervous system to respond to external stimulation in a synchronous manner [8]. Even though there is a correlation between neural synchrony and auditory perceptual thresholds, it is possible to have good neural synchrony and poor auditory perception. This is especially true if there is dysfunction at neural centres higher than the neural generators of the particular AEP test used.

In addition to the ABR, eCochG is classified as an early latency AEP.

ELECTROCOCHLEOGRAPHY (ECochG)

ECochG is essentially a zoomed in Wave I of the ABR. The eCochG zooms in on the cochlear hair cells, the cochlear nerve, and the synapse between the two. The eCochG is a near-field recording, recorded using either an electrode in the ear canal, an electrode on the tympanic membrane, or an electrode passed through the tympanic membrane to contact the promontory or round window.

The eCochG is characterised by a summating potential (SP) before 0.9 ms, which is generated predominantly by the inner hair cells [32]. This is followed by a (compound) action potential (AP) which is the same as Wave I of the ABR and is generated by the peripheral cochlear nerve [32]. The relative amplitude of the SP and the AP is often used to determine the presence of endolymphatic hydrops.

In addition to evaluating endolymphatic hydrops, ECochG is clinically used to identify the ABR Wave I, and for intra-operative monitoring [33]. The eCochG is also useful to determine the site-of-lesion in children with auditory neuropathy spectrum disorders (ANSD – see discussion later). The application of eCochG for the estimation of behavioural pure tone hearing thresholds has been reported [16]. Ferraro and Ferguson [34] found no significant differences between the thresholds obtained with eCochG using a transtympanic electrode and conventionally recorded ABR thresholds in individuals with normal hearing. ECochG with an extratympanic electrode does not require sedation or general anaesthesia and causes minimal discomfort, but behavioural pure tone threshold estimations are not as reliable as those obtained using the transtympanic technique [35].

MIDDLE LATENCY AEP (MLAEP)

The middle latency AEP is an electrophysiological recording of the electrical activity of the auditory thalamus and early auditory cortex [18]. It occurs 10 - 80 ms after the onset of a click or tone burst stimulus. The waveform consists of four

positive waves (Po, Pa, Pb, Pc) and three negative waves (Na, Nb, Nc) [36]. Wave Pa is the most prominent and most robust component of the middle latency responses. Generators in the auditory thalamus and early primary auditory cortex contribute to the Pa component of the response [7]. Middle latency AEP, therefore, evaluates the auditory pathway in practically its entirety. With behavioural pure tone audiometry as the gold standard and most comprehensive audiometric procedure, the extent of the auditory pathway evaluated by the middle latency response constitutes an advantage over earlier latency AEP such as the ABR and eCochG. In addition, several authors report agreement between middle latency AEP and behavioural pure tone responses [7,37,38]. However, because of the central anatomic origins of the middle latency AEP response, sleep and sedation affect the response by reducing the amplitude of the Pa [36]. This is a disadvantage when assessing infants and children.

The middle latency AEP is advocated due to its good frequency specificity [7,36,37]. However, Cacace and McFarland [3] caution against the use of middle latency AEP for behavioural pure tone threshold estimation in patients with steeply sloping, high frequency hearing loss. Middle latency AEP may underestimate the magnitude of high frequency hearing loss due to the spread of excitation to lower stimulus frequencies as intensity is increased [3]. The middle latency AEP may therefore not be the ideal AEP tool to use in a population typically at risk of a high frequency hearing loss, as is the case with individuals exposed to occupational noise.

This review of the theoretical and clinical knowledge of AEP used for behavioural pure tone threshold estimation has identified certain limitations of the ABR, eCochG and middle latency AEP that may affect the accuracy of estimation of behavioural pure tone thresholds in individuals who present with a steeply sloping high frequency hearing loss. Several authors have, however, named CAEP (a transient scalp potential complex – see below) as the measure of choice for individuals exposed to occupational noise and at risk of developing a high frequency hearing loss [6,39,40]. Stapells [6] states that the CAEP is ideal to use when an objective estimate of behavioural pure tone hearing thresholds is required for a patient who is likely to be passively co-operative or non-alert.

CORTICAL AUDITORY EVOKED POTENTIALS (CAEP)

The CAEP is a transient scalp potential complex evoked by changes in the perceived auditory environment that are sufficiently abrupt [39]. This AEP occurs at 50 - 300 ms following onset of the stimulus, and follows the cochlear and eighth cranial nerve responses, the ABR and the middle latency AEP in the time domain [6]. The CAEP is characterized by a P1-N1-P2 sequence of waveforms. Hall [7] states that CAEP is the ideal response for frequency specific electrophysiological auditory assessment from a stimulus perspective due to the reduced spectral splatter and increased frequency specificity. This frequency specificity is achieved because the CAEP can be evoked by tone bursts of relatively long rise-fall times and duration in comparison with the abrupt rise-fall times required to elicit ABR using tone burst stimuli [41]. Better frequency specificity results in AEP thresholds that are closer to behavioural pure tone thresholds in a variety of audiometric configurations. The susceptibility of this response to state of arousal renders CAEP unsuitable for infants and young children [8]. Reading or mental alerting tasks are sufficient to ensure that adults remain alert without a decrease in

response amplitude and increase in threshold intensity associated with sleep and drowsiness [6,39].

Hone et al. [15] listed the advantages of CAEP, stating that CAEP is non-invasive, and recorded from a higher auditory level than eCochG or ABR, and therefore less likely to be affected by neurological disorders. An important advantage of CAEP over earlier AEPs is that it represents the complete auditory system. The presence of N1 to a stimulus provides physiologic evidence of the arrival of the stimulus at the auditory cortex The N1 therefore reflects the presence of the audible stimulus i.e. detection of sound [6]. The N1 is the vertex negative peak with a latency of approximately 100 ms, which, together with the P2 positive peak, comprises the most prominent component of the CAEP.

Middle ear pathology affects the latency of the components of the CAEP. Yet increased response latency is likely to have a minimal effect on response amplitude and threshold intensity [39]. Therefore, middle ear pathology has no real effect on CAEP thresholds and estimation of behavioural pure tone threshold using CAEP thresholds.

Numerous studies have demonstrated that CAEP thresholds and behavioural pure tone thresholds are typically within 10 dB HL of each other [6,11,39,42]. It has been reported that CAEP thresholds can provide a closer estimate of behavioural pure tone thresholds than ABR thresholds [39]. Tsui et al. [43] pointed out that a greater CAEP response amplitude results in fewer averages being needed to yield a "noise" free repeatable waveform than ABR.

Over the past two decades, a new clinically available AEP technique, the ASSR has been proposed as an alternative AEP for behavioural pure tone threshold estimation [17,22,44,45].

AUDITORY STEADY STATE RESPONSE (ASSR)

The ASSR is a brain potential evoked by continuous stimuli characterized by periodic modulations in amplitude of a carrier frequency [22,46]. It yields a waveform closely following the time course of the stimulus modulation and a response specific to the frequency of the carrier [46,47]. The response is generated when the stimulus tones are presented at a rate that is sufficient to cause an overlapping of transient potentials [2]. By varying the intensity of the eliciting stimulus, one can seek the threshold response [46].

ASSR testing, using continuous modulated tones, offers significant advantages over techniques that require transient stimuli [2]. As the tones are continuous, they do not suffer the spectral distortion problems associated with brief tone bursts or clicks. As such, they are comparatively more frequency specific than responses to transient stimuli [48]. This specificity permits testing across the audiometric frequency range, including sloping high frequency hearing losses, reducing the possibility of underestimation of high frequency behavioural pure tone thresholds due to poor frequency specificity for this audiometric configuration [17,44,49,50]. Assessment at high intensity levels (i.e. up to 120 dB HL) is possible, due to the continuous nature of the ASSR stimuli and, hence the absence of calibration corrections to account for temporal summation differences between short and long duration signals associated with stimuli such as tone bursts and clicks [2,51].

Initially, the most widely studied ASSR was evoked by stimuli presented at rates

close to 40 Hz [52–54]. In sleeping or sedated adults, 40 Hz ASSR amplitudes are smaller than in the awake state [52,55,56]. ASSR to tones modulated at frequencies between 80 and 100 Hz, however, are minimally affected by sleep or maturation [17,47,49,57] and can therefore be recorded in children and infants [48]. Another advantage of the ASSR is that multiple frequencies can be evaluated simultaneously, in one or both ears, without significant loss in the amplitude of any of the responses, provided each stimulus has a different modulating rate and that the carrier frequencies differ by one octave or more [44,58,59]. This may reduce the testing time required to obtain behavioural pure tone threshold estimation.

Clinical use of the ASSR is greatly facilitated by objective response detection, which is measured in the frequency domain using various statistical methods [59]. Errors that result from observer bias or from poor interobserver and intra-observer reliability, are therefore eliminated by objective response detection [60,61]. In addition, an experienced tester is not required to report ASSR threshold findings, as subjective interpretation of waveforms is not required. Objective response detection of an ASSR response can control bias, perform with stable and known sensitivity, and can "outperform" human observers [62–65].

Several characteristics of the ASSR suggest that this AEP may also be applicable to clinical practice to estimate behavioural pure tone thresholds in individuals exposed to occupational noise and at risk for noise induced hearing loss. The ASSR may be an appropriate tool to estimate behavioural pure tone thresholds [22] because of the potentially better frequency specificity of continuous rather than transient tonal stimuli, independence of participant attention or states of arousal, and the ability to obtain higher output levels . In addition, the objective nature of response determination makes ASSR attractive in a clinical setting.

P300 RESPONSE

The final AEP that is commonly used clinically is the P300. If the CAEP represents detection of sound, the P300 represents discrimination of auditory change [66] - something that is critical for auditory processing of speech. The P300 is a late latency auditory response, which is most frequently recorded with the "odd ball" measurement paradigm that typically involves two different acoustic signals. The frequent signals in the "oddball" stimulus paradigm are predictable, accounting for 80% of presented stimuli [67]. The infrequent, unpredictable, and rare stimulus is presented in a pseudo-random fashion, accounting for about 20% of stimuli presented. Diverse regions of the brain contribute to generation of the P300 response, including subcortical structures, auditory regions in the cortex, parietal lobe and frontal lobe [32]. With regard to the clinical implication of the P300, the P300 latency is directly related to the speed with which an individual classifies auditory signals, updates memory, and allocates attention [32].

PRINCIPLES OF AEPS

Four core principles underpin measurement of auditory evoked responses:

1. Evoked vs. non-evoked responses
2. Near-field vs. far-field recording
3. Neural synchrony
4. Signal averaging

1. Evoked vs. non-evoked responses

Evoked responses are elicited by specific external stimuli, and are therefore caused by

specific external, controllable events that are locked in time to the recording of the response presented through earphones or loud-speakers. Non-evoked responses are recordings of ongoing electrical potentials without the presence of external stimuli, for example an EEG.

2. Near-field vs. far-field recording

These are distinguished by the proximity of the recording electrodes to the actual generators or sources of the neural response of interest.

Near-field recording refers to when responses are recorded at or near source and is often used in animal research and during intra-operative monitoring. The recording electrodes are often placed on or very close to the neural generator. This results in a strong response with large amplitude that is easily identifiable above the unrelated, non-evoked responses. The drawback is that such a recording is very invasive and requires some sort of surgical intervention in order to place electrodes close to the AEP generator, for instance on the auditory nerve or cochlea.

Far-field recording is far more practical and refers to when electrodes are placed at a distance from the source. The surface electrodes often used for AEPs is an example thereof and represents activity from all generators between and around the recording electrodes, so there are multiple potential neural sources of response. If the potentials of interest have very low amplitude, such as with ABR, and far-field recording is used, on is left with a poor signal to noise ratio (SNR). In such cases, signal averaging is very important to reduce the unrelated responses and to enhance the target response. The low amplitude ABR responses are easily masked by background electrical or neurogenic "noise".

3. Neural synchrony

The simultaneous recording of discharges of many neural units, or *synchronous discharge*, is known as *neural synchrony*.

When using far-field recordings, background electrophysiological "noise" masks low amplitude responses. However, if we one can persuade more neurons to fire simultaneously within a very brief period, this will lead to an increase in response amplitude. The greater the amplitude, and the more abrupt the stimulus onset, the easier it is to identify the AEP response from far-field recorded response. Synchronous neural firing is best elicited by an electrical pulse, a click, or a chirp. A pulse, or click, is characterised by an abrupt or rapid onset, and a broad frequency bandwidth containing all frequencies. The broader the frequency response of the stimulus and the greater the portion of the cochlea that is activated, the greater the number of nerve fibres that are stimulated simultaneously. A chirp is also a broadband stimulus but does not start abruptly like a click. Instead, by delaying the start of the high and mid frequencies, and by matching the timing to that of the basilar membrane travelling wave, a chirp activates the low, mid- and high frequency nerve fibres at the same time. Neural synchrony is therefore really a principle of "the more the merrier".

4. Signal averaging

Signal averaging involves averaging a great number of responses together. As was previously discussed, one needs to distinguish a low-amplitude response from higher amplitude background "noise" with AEPs. The onset of computer sweep averaging must be time-locked to onset of the stimulus. This allows for the target AEP response to be summed, while the background, non-evoked "noise" of random nature averages toward zero and is

attenuated. The longer the signal averaging, the more responses are added together and the more the residual "noise" is reduced. The SNR is therefore a function of the number of computer sweeps that are averaged together.

It should now be clear how the four cornerstones of AEP recordings can help improve SNR of small AEP responses.

ADDITIONAL STEPS TO ACHIEVE ACCURATE AEPs

There are a few additional steps to achieve accurate AEP results:

- Environmental considerations
- Patient considerations
- Instrumentation
- Recording parameters.

Environmental considerations

You don't need to test in a soundproof booth – a quiet room is sufficient. The room should be relatively quiet – especially when one has a child with normal hearing and one turns down the volume to minimum levels. What causes more issues however, is electrical interference in the room, as electrical artefacts are a source of "noise" and frustration. Testing in an electrically shielded room is ideal but not easily available. Ensure that unnecessary equipment, appliances and power plugs are switched off and cables unplugged. Avoided multi-plug adapters. If wires are sticking out of a power cable plug they must be concealed, as they will definitely cause interference with the readings. Rather switch the lights off than employ a dimmer switch, as it will cause electrical artefacts. Always earth your equipment well. My earth cable has a loop at one end so it fits securely over the screw at the back of my equipment, and a small clamp on the other end (Figure 1). This works especially well in surgical theatres and when testing a baby in a neonatal ICU while asleep.

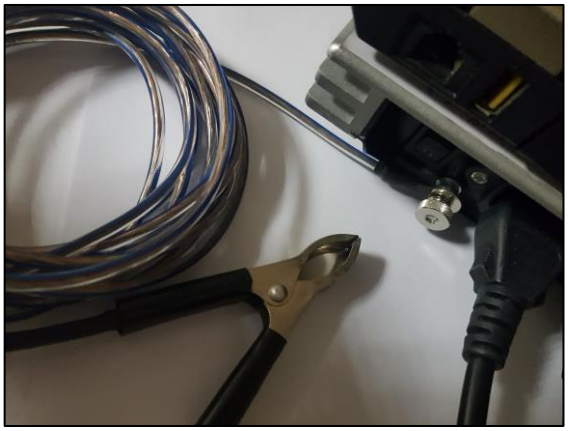

Figure 1: An earth cable attached to the back of the AEP device with a small clamp on the other end for ease of attachment to e.g. a metal bed

Patient considerations

A patient's muscle contractions generate the largest source of disturbance. The patient therefore needs to lie still with eyes closed during registration of early and middle latency AEPs and ASSR. Lying perfectly still but with eyes open introduces large artefacts, which is very detrimental to the SNR. An eye mask is useful to encourage older children to keep their eyes closed. You need about 90min for testing and even two minutes of sitting still could be impossible for a small child. With children aged six months to five years, and who no longer sleep for long periods during the day, sedation or general anaesthesia may be required. I start with a low dose oral antihistamine with strict instructions to parents about sleep deprivation the evening and morning before examination. I discourage parents from giving the child too much sugar or caffeine on the day of testing. This includes sweets, sugary carbonated drinks (e.g. Coca Cola), fruit juice and tea. Certain medications contain preservatives that may have a contrary effect on a young patient. I've often seen children initially

become irritated and frustrated with strong sedatives like chloral hydrate before finally, (after two hours of screaming) falling asleep. Consult the child's paediatrician to prescribe the sedative. Irrespective of the choice of sedative, it should be administered under medical supervision with monitoring and resuscitation equipment and oxygen at hand.

Some comments about testing under general anaesthesia: Even though some of the older anaesthetic gases could negatively influence ABR and other AEP testing, I have never experienced problems with modern gases or medications. This holds true irrespective of whether the child is only in theatre for AEP testing or whether testing is done repeatedly during a 10-hour neurosurgery procedure. Anaesthetists like keeping a patient's body temperature stable, and this should help to avoid changes in the AEPs.

Hydrocephalus and other causes of raised intracranial pressure can influence AEP waves, and by obliterating ABR waves, create an inaccurate estimation of the true hearing thresholds.

Instrumentation

Before placing the surface electrodes for AEP testing, and before sedation takes effect, use an abrasive scrub like "neoprep" to prepare the skin of the contact site to reduce contact impedance (resistance). The lower the electrode contact impedance, the less "noise" and the better the SNR. A small area of good contact is all you need to yield low impedance values of ≤ 5 kOhms. Also ensure that each electrode impedance does not differ by more than 2 kOhms. For a single-channel recording, 3 electrodes are required *(Figure 2).*

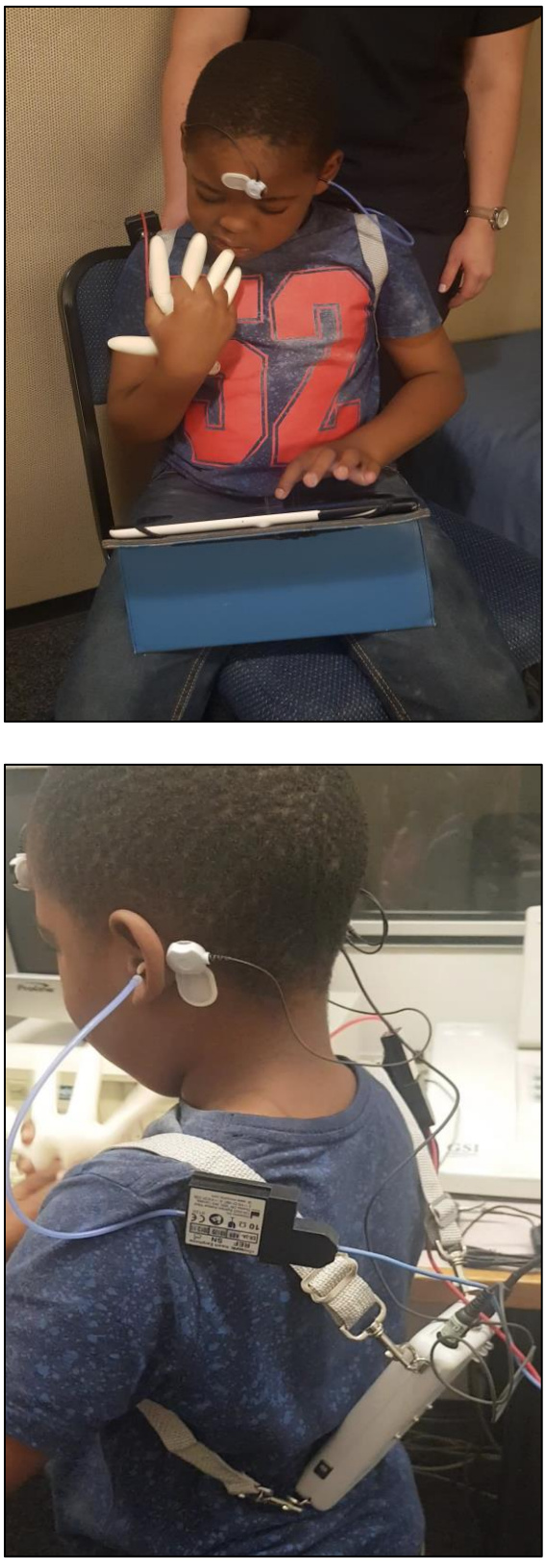

Figure 2: A 10-year old being tested using a single channel electrode montage with electrodes on the high forehead and on each mastoid

For a two-channel recording, 4 electrodes (with non-inverting, high forehead electrode functioning for both left and right-sided recordings) are used *(Figure 3)*.

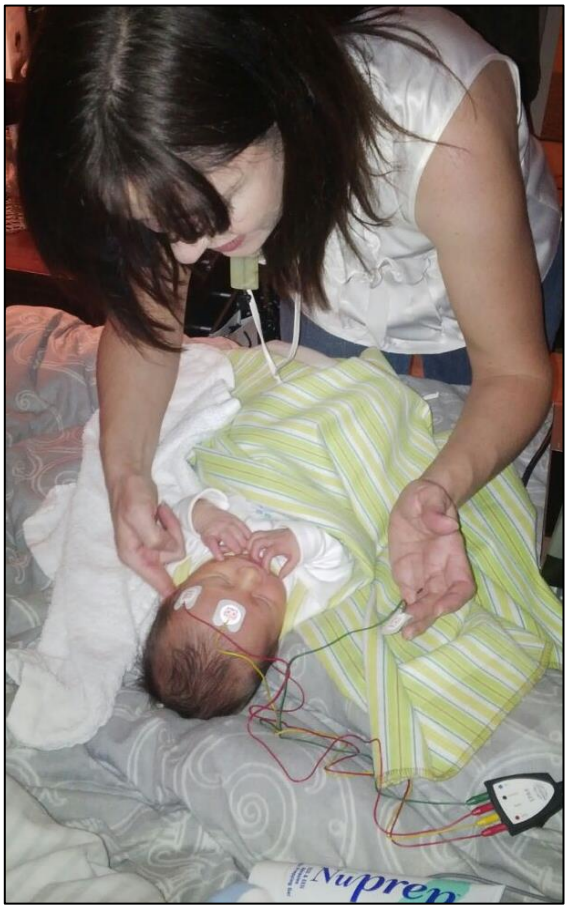

Figure 3: Two-channel electrode placement with electrodes on forehead and mastoids with ground on the temple

Consult the equipment manual to see what electrode montage is advocated. I prefer using a two-channel recording for ABR, ASSR, CAEPs and P300. The inverting electrodes are placed on the ipsilateral mastoid, the non-inverting electrode on high on the forehead and the ground on the side of the forehead / temple. One can also place the ground electrode on the lower forehead between the eyebrows; but with small heads, there simply is not enough space for this placement.

I place the inverting electrode on the mastoid rather than the earlobe with small head sizes as it is simpler to do. However, a strong postauricular muscle (PAM) response (characterised by a large peak and trough around 10 ms) may occur with mastoid placement *(Figure 4)*. Yet I don't find that the PAM interferes in a standard battery of AEPs as my preference is not to do MLAEPs, which is an AEP that would be influenced by large PAMs.

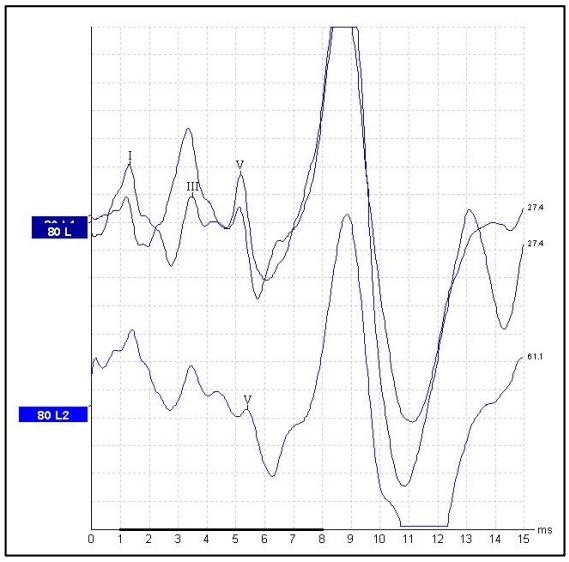

Figure 4: Neurological ABR followed by a strong postauricular muscle (PAM) response characterised by a large peak and trough around 10ms

In addition to electrode paste in the cup surface electrodes, I put a dot of electrode gel on the skin before sticking the electrode in place with hypoallergenic tape to further reduce impedance. Others use a drop of saline for the same reason. I avoid using alcohol swabs as this can increase impedance by dehydrating the skin.

If one can do a near-field recording, do so. By placing the electrodes closer to the source of the response, the SNR will increase significantly, with larger response amplitudes and less non-evoked "noise". A tip-trode electrode *(contact with ear canal; Figure 5)*, or a tympanic membrane contact

electrode during standard testing will increase the amplitude of Wave I which is generated by the first portion of the auditory nerve closest to the cochlea *(Figure 6)*.

Figure 5: Example of tip-trode electrode

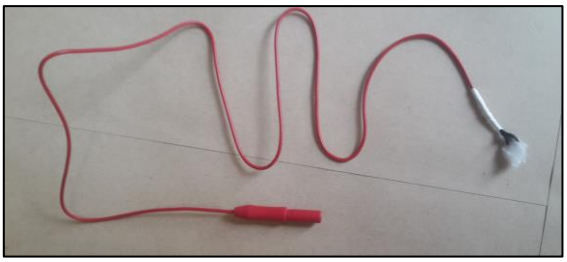

Figure 6: Example of 'homemade' tympanic membrane electrode I use for intra-operative monitoring using eCochG/ABR combination assessment

AEP equipment is sold with insert earphones as the standard transducers *(Figure 7)*. Not only are insert earphones more comfortable and easier to use with babies and young children than supra-aural headphones, but they also improve SNR by reducing interference from ambient noise in the room. In addition, using insert earphones leads to larger interaural attenuation, meaning that there is less cross-hearing of sounds between the ears, meaning that one does not have to worry about masking as often as one would if one was using headphones.

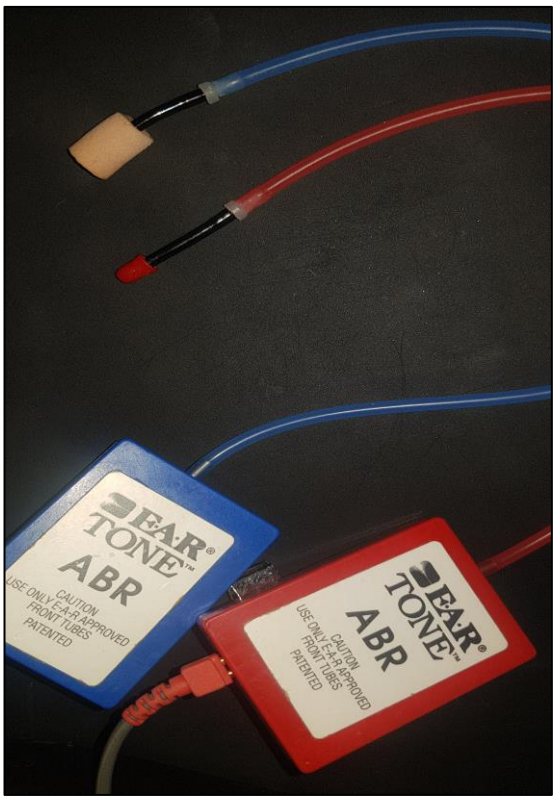

Figure 7: Insert earphones with a foam ear tip and neonatal ear tip

The AEP system has a few built-in ways to improve the SNR. Common mode rejection eliminates any EEG information that is identical at all the electrodes as this is then obviously not a target response. If the equipment has a notch filter or feature such as 'minimize interference,' switch it on. These features try to minimise artefacts caused by the electrical current of the mains electricity. Some equipment also makes use of a weighting algorithm like Bayesian weighting; when signal averaging occurs, more weight is given to quieter responses than "noisier" waves. If your equipment has these software features, make sure that they are activated – every little bit of help you can get to improving the SNR is important.

Recording parameters

Your patient is now asleep or lying quietly, and the electrodes and earphones are in place. The electrode impedances are low

and there is no electrical interference. While you are testing, there are ***a few parameters you can adjust to further improve the SNR.***

In this section, the parameters that one can change during ABR testing are discussed. Each AEP one performs has its own recipe for stimuli, ***artefact rejection, filters, stimulus rate, response averaging and repetition***.

Artefact rejection

The artefact rejection value represents the maximum response amplitude that the software will accept and include during signal averaging. For ABR, this is typically 25 - 40 uV. Any response that is larger in amplitude than that value is discarded and not averaged.

This will be evident from the number of accepted versus rejected sweeps in your AEP software. This is really helpful if your patient suddenly coughs or moves unexpectedly – the large myogenic responses from muscle contractions that are consequently generated mask the low amplitude target AEP response. The "artefact rejection" setting will reject these unwanted, "noisy" responses. Conversely, if you want to be stricter, and only accept really small amplitude responses, which are likely to include your target response, and reject other non-evoked or myogenic responses, then make the artefact rejection value smaller. A reduction of the artefact rejection value from the default setting is something you will be able to do if your EEG is "super-calm" and beautiful, with no artefacts – you can then afford to be even more strict. This will improve (increase) the SNR. If you find that a large percentage of the sweeps are being rejected and the number of collected sweeps is increasing very slowly or not at all, you may need to increase the artefact rejection value to avoid a long wait for a single trace to be completed. Be warned though – by reducing the artefact rejection you are allowing more "noise" to be averaged with the response. But this is sometimes necessary, e.g. with CAEPs and P300, where firstly, the patient must be awake with the eyes open, and, secondly, the lowest filter setting is really low (to capture the response for these late AEPs). I also adjust artefact rejection when monitoring hearing during neurosurgery, and when, for example, the noise from the internal auditory meatus being drilled open is interfering with the responses. The surgeon requires accurate, prompt feedback which cannot be achieved if all the responses are being rejected. In such a situation, it does help to test at supra-threshold levels of 90 dB nHL (decibel normal hearing level).

Filters

Filters can help one increase the SNR and give clearer waves. AEP filter settings are largely determined by the AEP one is performing. Generally, the higher up the neural generator of the AEP (the more central the source of the AEP), the lower the filters are. Think about filters in terms of the frequency response of a microphone or receiver. The broader the filter, the more detail, but also the more "noise" is allow in. If one narrows the stimulus filters, one reduces some unwanted, non-evoked "noise", increasing SNR, but at the same time, reducing the detail in the response. For example, if one performs a neurological ABR, one wants a lot of detail so that one can mark each wave and look at absolute and interpeak latencies. One will then need broad filter settings of 30 - 3000 Hz. If there is a lot of "noise" with these settings, and one is unable to reduce the "noise" by rescrubbing the skin, or reinstructing the patient to lie perfectly still, then one may increase the low filter (some refer to this as a high pass filter, which is confusing). Elevating the low filter to 100 Hz or at the

very most to 150 Hz, cancels out quite a bit of the myogenic "noise" in an awake patient. To round the waves a little one may also drop the high filter (or low pass filter) to 2000 Hz. When one gets to frequency threshold determination, one is no longer interested in exact latencies and interpeak latencies. One is really only looking for a clear Wave V. In such a case, one can afford to reduce the filters to 100 - 1500 Hz without affecting quality or responses. If one reduces the filters anymore, one is in fact reducing energy and amplitude of the response and the responses deteriorate and will no longer be close to true behavioural hearing thresholds.

Stimulus rate

By reducing the stimulus rate, one obtains more detail in response and increases early wave amplitude (response amplitude), thereby increasing SNR. This is particularly good for the neurological ABR. If one is simply looking for a single wave V, one can afford to increase the rate, as this also speeds up the testing time. For threshold determination, it doesn't matter whether wave V is measured at 7.1 ms or 7.5 ms – provided one sees a repeatable wave V. The detailed determination of latency is then no longer important.

Generally, the higher up one goes in terms of neural generators, the slower the stimulation rate should be. Think about it as follows: to hear, which is what the early latency AEPs evaluate, the auditory stimulus rate can be fast – namely 25 Hz or faster. But to evaluate listening, which we do using late latency AEPs, we need to slow the stimulus rate.

Response averaging

We've already discussed under *section averaging* how the longer one averages, the more one reduces background "noise", and the more target response increases. In other words, the longer one averages, the better the SNR. If one sees a good strong response during ABR testing, continue for at least 700 - 800 sweeps, then stop and repeat. Stop and repeat to see if the response is repeatable. If repeatable, then turn the volume down – way down. No need to go down in 10 dB steps – use your intuition and go down to minimum or where you are expecting to find a threshold response. You can always turn the volume up if necessary. Time is of the essence. You need to get answers as quickly as possible. When dealing with a very small threshold response, you need to average for a really long time to ensure that you are cancelling out the maximum amount of "noise" in order to see the small amplitude threshold response. Then you need to average 2000 to 4000 sweeps together before repeating. If your AEP software tells you what your residual "noise" is for each trace, ensure it is below 40 nV for adults and 30 - 20 nV for children and babies before concluding that you have determined threshold of hearing.

Repetition

Because ***response detection is subjective*** for all AEPs except automated ABR and ASSR, repeatability of the response is a key way to judge whether a response is present or absent. If it can't be repeated, it was never there to begin with. This means that the tester needs to determine whether the response is present or absent.

I say to parents that are sitting watching and looking for repeatable waves with me: if I show the waves to someone completely independent, they should agree with how I have marked the waves. If I think they will argue with me, then I will not mark that particular wave.

This raises the question what can be considered a minimum acceptable response? In

addition to repeating the response, continue signal averaging until the residual "noise" readings are as low as possible. This is especially important with small threshold responses, which are "no response" waves. That way you know you are not missing a small response that is masked by non-evoked "noise". The British Society of Audiology has some guidelines for determining residual "noise" if the AEP software does not provide one with a measure of this [68]. Importantly though, what is key when determining minimal response levels, is the ***display gain.***

Display gain

The display gain is how much one zooms in or out of the display of the waves. Zoom in too much and one can create waves that aren't really there. The opposite is true if one zooms out too much. For ABR, I use 0.6 uV / division the Biological Navigator Pro and for the GSI Audera. The display is in nV for the Interacoustics Eclipse and the default is 200 nV / division. I always stick to the default display gain for mid- and high frequency threshold estimations. It is advisable to do the same for your AEP system. I only ever make an exception for 500 Hz threshold estimations. If one can't see a repeatable wave having zoomed in by a maximum of one increment on the display gain for low frequency threshold estimation, it is not there. Also, remember, one can only compare apples with apples – meaning keeping the display gain of the waves for each frequency or for the neurological ABR all the same. Never try to compare waves that have different display gains.

Each AEP has its own recipe for stimulus and acquisition parameters. In the chapter entitled 'Auditory Brainstem Response in Clinical Practice', I describe the recipes for the neurological ABR, and ABR for threshold determination and bone conduction ABR.

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