Auditory evoked potentials (AEP) represent the response of the auditory pathway to an auditory stimulus, typically a click presented through headphones. The electroencephalogram (EEG) is recorded using surface electrodes placed on the scalp and the response of the auditory pathway is derived by computer averaging. The AEP is categorized on the basis of the latency of the response following the auditory stimulus. For example, the auditory brainstem response (ABR) occurs in the first 20 ms after the stimulus, the middle latency response (MLR) from 20 to 70 ms, and the slow vertex response (SVR) up to 500 ms after stimulation (Fig. 1).

The MLR has been suggested as a possible indicator of depth of anaesthesia, although it is not known whether the click stimulus itself affects the level of arousal of the patient. Several studies have reported changes in the response with anaesthesia. However, the response is very small (typically 1 μV). It can therefore be difficult to measure in the clinical environment and there are a number of potential pitfalls that can prevent acquisition of a good quality MLR. This note is intended as a guide for clinicians and researchers who wish to measure the MLR as an indicator of depth of anaesthesia but who may not have a background in hearing science.

We have recently conducted research into new stimulation methods to improve acquisition of the MLR with a view to using the response as an indicator of depth of anaesthesia. Several of these difficulties were encountered during the course of the research.

Effects of hearing loss

The MLR is thought to represent the synchronous firing of neurones in the primary auditory cortex to an acoustic stimulus. As it is an auditory response, it cannot be evoked from subjects who are profoundly deaf (indeed one use of the AEPs is to detect hearing loss in children). Furthermore, if a subject has a mild or moderate hearing loss, then a given auditory stimulus will generally sound quieter to that subject. This is particularly the case for conductive hearing losses, where sound is attenuated in the outer or middle ear before reaching the cochlea. Hearing loss will therefore result in a reduction in the amplitude of the AEP. Consequently, the signal-to-noise ratio (SNR) of the MLR, and hence the signal quality, will be reduced. Despite this, several studies investigating the use of the MLR as a measure of depth of anaesthesia have not measured hearing thresholds in their subjects before using the technique.

Lightfoot suggested that, in order to record the ABR, it must be possible to achieve a sound sensation level of at least 20 dB above the hearing threshold. It is likely that the same is true for the MLR. Use of the MLR as a measure of depth of anaesthesia is therefore probably not appropriate for patients with severe or profound hearing loss, which affects around 2% of the younger adult population, rising to 4% in the age group 61–70 yr and 10% in the age group 71–80 yr. Severe hearing loss is defined as average hearing thresholds in the range 71–95 dB hearing level (HL).
between 0.25 and 4 kHz, and profound hearing loss as average hearing thresholds above 95 dB HL.

We therefore recommend that a hearing test be performed before MLR recording, in order to identify subjects from whom either the MLR cannot be recorded, or who have some degree of hearing loss that will reduce the quality of the MLR.

**Electrode placement and the postauricular muscle response**

Placement of the EEG electrodes is critical to obtaining good quality AEP recordings. The active electrode is typically placed on either the high forehead (Fz) or the vertex of the head (Cz) and the ground electrode on the low forehead (Fig. 2). When recording the ABR, the reference electrode can be placed over the mastoid process behind the ear. However, this is not recommended when recording the MLR because of interference from the electromyogram of the postauricular muscle (PAM). The PAM lies behind the ear and can be triggered by loud sounds. PAM interference is seen as a large dip in the AEP trace at around 15 ms (i.e. it occurs after the ABR but overlaps with the MLR). It has a magnitude of approximately 5 μV, which is too large to be neural in origin. It also causes an apparent change in the morphology of the whole MLR, with the Nb wave of the MLR appearing to be at approximately 45 ms instead of 35 ms (Fig. 3). (The large magnitude PAM overlays the smaller MLR and has a large negative trough at 45 ms which can be confused with the MLR.)

The PAM response can easily be confused with the MLR and is not abolished by averaging, as it is triggered by the same evoking stimulus as the MLR. It is obtained with a small number of averages as it is so much larger in amplitude than the MLR. However, the PAM response is abolished by muscle relaxants and is also reduced when the subject relaxes under anaesthesia.

In order to avoid recording the PAM response, the reference electrode should be moved away from the mastoid process to a non-encephalographic position. We recommend the nape of the neck as a reference position, although this may be difficult to access if the subject is lying on their back. A sternal reference position is a possible alternative, although this may result in interference from the ECG signal, reducing the quality of the MLR signal.

**Filter settings**

Analogue filters are used when recording the MLR to exclude unwanted high and low frequencies from the EEG data to improve the SNR (see ref. 5 for a thorough discussion). The high-pass filter setting is critical when recording the MLR because significant EEG activity occurs at quite low frequencies. Making the high-pass filter cut-off frequency too low will reduce the SNR by allowing unwanted low frequency noise into the recording system. Conversely, making the cut-off frequency too high will exclude important AEP information. Additionally, making the slope, or roll-off, of the filter too steep can result in phase distortion of the MLR. We recommend a band-pass setting of 15–250 Hz when recording the MLR, with a gradual roll-off of around 12 dB per octave.

**Power main interference**

The power main frequency (50 Hz in the UK) lies within the typical band-pass filter range used for recording the MLR, and therefore will still be present on the data after filtering. Mains interference levels can be high, particularly in rooms where strip lighting and mains-powered monitoring...
equipment is used; we have found mains-powered infusion pumps to be a particular problem. Mains frequency interference is reduced by averaging so long as the mains frequency, or its harmonics, are not an integer multiple of the AEP stimulus frequency. For example, multiples of 10 Hz should be avoided as the stimulus frequency. Nonetheless, mains interference levels may still be high after averaging.

If mains frequency interference is so great that the input stage of the recording amplifier becomes overloaded (saturated), the EEG signal will be clipped (distorted) and it will not be possible to apply filtering to remove the interference from the data. Care must be taken to keep the gain of the amplifier low enough to avoid saturation. The practical step of keeping the leads from the electrodes to the amplifier as short as possible and all the same length will reduce mains interference. Placing the EEG pre-amplifier near the patient’s head will enable the leads to be kept short.

Analogue filtering of the EEG to remove 50 Hz interference can introduce phase distortion of the MLR waveform, so filtering to remove mains frequency interference is best done digitally. Digital filters can have a very sharp roll-off, allowing accurate removal of specific frequencies. If a signal is passed both forwards and backwards through a filter, any phase distortion introduced in the forward direction is cancelled in the reverse direction, so the MLR will not be distorted by the filtering. This is generally easier to implement with digital than with analogue filters. This can be done very quickly with modern computers, so the resulting AEP can still be seen in real time.

**Signal quality**

When recording the AEP, poor signal quality will result in unreliable or unrepeatable results. Despite this, most studies of the MLR as an indicator of depth of anaesthesia have not quoted the SNR. An on-line display of SNR when recording the MLR helps to assess the quality of the data as it is being recorded. Problems such as myogenic or mains frequency interference result in a poor SNR. Although there is no fixed criterion for what constitutes ‘good quality’, a signal twice as large as the noise probably indicates that the MLR is of acceptable quality.

Two statistics routinely used to estimate the signal quality of the AEP are the plus–minus (±) difference and the $F$-value at a single point ($F_{sp}$). The ± difference estimates AEP quality based on a comparison of two sub-averages of the AEP.7 The $F_{sp}$ estimates the quality of the evoked responses based on the $F$-test. The variance across time of the averaged AEP (a measure of signal magnitude) is compared with the variance across epochs of a single point, a fixed-delay post-stimulus (a measure of noise magnitude), using an $F$-test.8 An estimate of the SNR can be derived from both measures. However, the ± difference is unstable when low frequencies are present in the signal. As the MLR contains low-frequency energy (below 100 Hz), we recommend the $F_{sp}$ statistic for use with the MLR.

**Conclusions**

The MLR is an AEP occurring 20–70 ms after an auditory stimulus. It is approximately 1 µV in amplitude and is therefore difficult to record in the electrically noisy environment of the operating theatre suite. It is possible that several published studies of the MLR as a measure of depth of anaesthesia have not recorded a good quality MLR. We have highlighted some steps that can help to obtain a good quality MLR. These include screening subjects for hearing loss, moving the reference electrode away from the mastoid to avoid interference form the PAM response, optimizing the filter settings to record the MLR, taking steps to minimize mains frequency interference, and assessing the quality of the MLR as it is recorded. Following these steps will help to avoid poor quality recordings and reduce the potential for misleading results from studies using the MLR.

**References**

