MONITORING DEPTH OF ANAESTHESIA

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One of the objectives of modern anaesthesia is to ensure adequate depth of anaesthesia to prevent awareness without inadvertently overloading the patients with potent drugs. One of the achievements of modern anaesthesia is the ability to monitor depth of anaesthesia.

The overall incidence of intraoperative awareness with recall is about 0.2–3%,[1] but it may be > 40% in certain high risk patients, like, those with multiple trauma, caesarean section, cardiac surgery and haemodynamically unstable patients.[2] Intraoperative awareness is a major medico-legal liability to the anaesthesiologists and can lead to postoperative psychosomatic dysfunction in the patient, and therefore should be avoided at all costs.[3]

Various methods have been described to measure the depth of anaesthesia from time to time. John Snow in 1847, described five degrees of narcotism for ether anaesthesia.[4] These were later refined by Guedel[5] into four stages on the basis of somatic muscle tone, respiratory parameters and ocular signs.

In 1954, Artusio[6] divided Guedel's stage I into 3 planes. In 1957, Woodbridge[7] defined anaesthesia as having four components; sensory blockade, motor blockade, blockade of autonomic reflexes and loss of consciousness. According to Prys-Roberts,[8] common feature of general anaesthesia is suppression of conscious perception of noxious stimuli. Analgesia, autonomic stability and muscle relaxation are desirable but not actual components of anaesthesia. Prys-Roberts divided the noxious stimuli into somatic and autonomic components, which were further, divided into sensory, motor and respiratory, haemodynamic, pseudomotor and hormonal (Fig. 1).

The afferent fibers from the nociceptors reach in the dorsal root ganglion of spinal cord and terminate within the grey matter of dorsal horn, from where crossed

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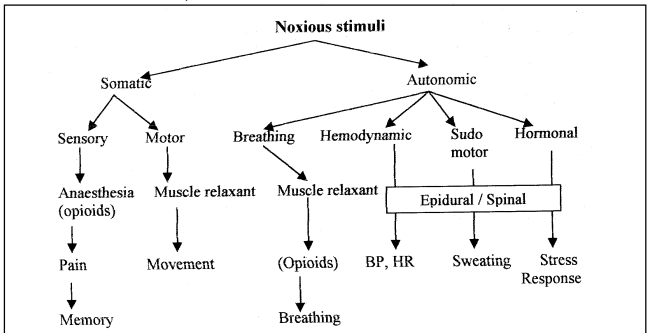

Figure 1 : Various noxious stimuli and their effects

anterolateral pathways originate. These pathways project into reticular formation and reach the primary somatosensory cortex, secondary somatosensory cortex and posterior parietal cortex[9] (Fig. 2). General anaesthetics can suppress the response to these noxious stimuli by interrupting their transmission at various levels of CNS, the most common being ascending reticular system.

A gradually increasing concentration of general anaesthetic agent produces a progressive decline in the ability of the brain to carry out tasks and to remember these afterwards. The effect of anaesthesia on cognition and memory occurs before noticeable autonomic effects.

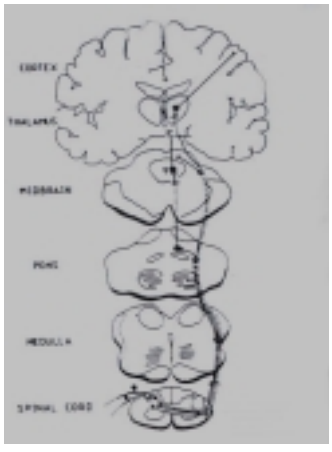

Figure 2 : Nerve pathways representing injury-related information to primary and secondary somatosensory cortex and posterior parietal cortex

Cognition is described in the terms of short-term and long-term memory. Short-term memory is concerned with learning, decision-making and retrieving information from very large, long-term memory. It is associated with conscious awareness. The long-term memory can be divided into procedural memory-knowing how to do things and, the declarative memory. The declarative memory is further divided into somatic memory-simply remembering the facts without knowing how to learn them and, episodic memory-remembering both the facts and how they were learnt. (Table 1)

Table 1 : Types of memory and stages of awareness during anaesthesia

Types of memory
1. Short term memory
2. Long term memory
a. Procedural memory (implicit memory)
b. Declarative memory
- Somatic memory (implicit memory)
- Episodic memory (explicit memory)
Stages of awareness
1. Conscious awareness with explicit recall
2. Conscious awareness with no explicit recall
3. Subconscious awareness with implicit recall
4. No awareness or recall.

The somatic and procedural memories, which require effortless retrieval, are referred to as implicit memory. Episodic memory requires effort for recall and is often referred to as explicit memory.[10] Explicit memory systems are more sensitive than implicit memory systems to the effects of general anaesthetic. With very low concentration of anaesthetic there is little effect on conscious awareness and explicit memory. With increasing anaesthetic concentration there is little effect on conscious awareness but explicit memory is lost. Further increase in anaesthetic concentration abolishes conscious awareness but there may be perception of events without consciousness, which can be demonstrated, with tests of implicit memory.

Griffith and Jones[11] recognize four stages of awareness (Table 1). The 4th stage is of conventional deep anaesthesia with no awareness or recall.

White[12] has suggested that anaesthesia is a continuum, but there is no absolute unit of anaesthetic depth with which to mark progress along the continuum, making cross-patient comparisons of absolute depth impossible. In view of all this, it is desirable to have a safe, non-invasive and reliable anaesthetic depth indicator that could be easily quantified, readily interpreted and be independent of anaesthetic technique and surgical stimulus.

Pharmacological Principles Of Measuring Depth Of Anaesthesia

Depth of anaesthesia is a pharmacodynamic measurement. Measurement of the effect of an anaesthetic drug which is the essence of measurement of depth of anaesthesia, depends primarily on the following factors:

1) The equilibration of the drug's concentration in plasma with the concentration of the drug at its site of action and with the measured drug effect. 2) The relationship between drug concentration and drug effect 3) The influence of noxious stimuli.

Specific Drugs And Clinical Situations

Inhalational agents

The purposeful movement of any part of the body in response to noxious perioperative stimuli is one of the most useful clinical sign of depth of anaesthesia. On the basis of this, Eger et al[13] defined the minimum alveolar concentration (MAC) of inhaled anaesthetics as the concentration required to prevent 50% of subjects from responding to painful stimuli. Later on, MAC has been expanded by evaluating other clinical end-points or stimuli.[14-16]

MAC-intubation[14] the minimum alveolar concentration of inhalational anesthetic that would inhibit movement and coughing during endotracheal intubation.

MAC-incision the minimum alveolar concentration of inhalational anaesthetics that would prevent movement during initial surgical incision.

MAC-BAR[15] the minimum alveolar concentration of inhalational agents necessary to prevent adrenergic response to skin incision, as measured by the venous concentration of catecholamine.

MAC-awake[16] the minimum alveolar concentration of inhalational anaesthetics that would allow opening of the eyes on verbal command during emergence from anaesthesia.

The MAC curves (representing the relationship between the concentration of anaesthetic agent and the probability of response) are located from left to right in the order: MAC-awake < MAC-incision < MAC-intubation < MAC-BAR[17] (Fig. 3). Tracheal intubation represents stronger noxious stimuli than all surgical stimuli,

therefore, MAC curves for various intraoperative stimuli falls between MAC-incision and MAC-intubation. In unstimulated patients both explicit and implicit memory may be absent at end-tidal concentration of inhalational agents equal to MAC-awake.[18]

The MAC-awake and MAC-incision curves are so steep that the difference between MAC 5% and MAC 95% is approximately 0.2% for halothane.[19] The MAC-bar curve is much less steep, which means that very high concentrations are needed to eliminate the catecholamine response[15] (Fig. 3).

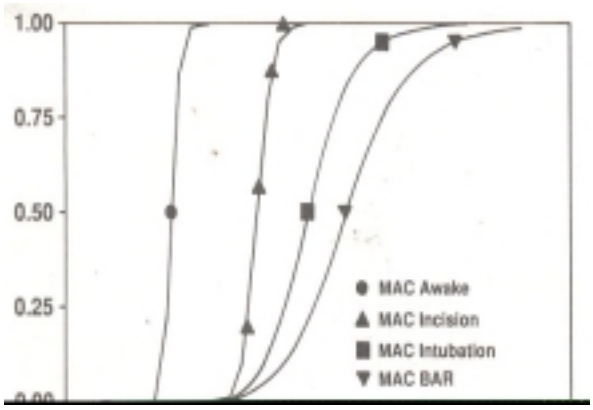

Figure 3 : Mac Curves of Halothane

In contrast to somatic reflexes, haemodynamic responses to noxious stimuli do not correlate well with end-tidal drug concentration. Consequently the relationship between somatic (movement) and autonomic (haemodynamic) responses is poor during inhalational anaesthesia.[20] During first hour of halothane anaesthesia, decreasing mean arterial pressure (MAP) was the only useful clinical sign of depth of anaesthesia whereas heart rate remains constant. Also pupils were constricted and non-reactive, there was no eye movement or tearing. However after 5 hour of halothane anaesthesia, further increase in concentration no longer causes a decrease in MAP.

Cullen et al[20] found that skin incision modified most clinical signs of drug effect e.g. during halothane and oxygen anaesthesia, heart rate, respiratory rate, tidal volume and pupil diameter increase after skin incision and return to normal after about 12 minutes. The systolic and diastolic blood pressure may not change.

Numerous altered physiological states (aging, alcoholism, pregnancy, hypoxaemia, hypo or hyperthermia, anaemia) may change the requirement of inhaled anaesthetics. MAC can also be changed with the use of nitrous oxide, other anaesthetics and CNS drugs.[21]

Intravenous agents

Hypnotics

These are commonly used for induction of anaesthesia. The depth of anaesthesia increases rapidly (causing loss of consciousness), peaks and then decreases as plasma concentration declines due to rapid redistribution of the drug. The CNS depression lags behind the plasma concentration manifesting as hysteresis on curves plotting against plasma concentration. Clinical end points that are useful in assessing depth of anaesthesia during induction include-

1. loss of verbal responsiveness
2. loss of eye lash reflex
3. loss of corneal reflex and
4. absence of movement in response to squeezing the trapezious muscle.

Maximum stimulation occurs during laryngoscopy and intubation, which cannot be eliminated completely with only the intravenous hypnotic agent. Because they do not provide sufficient analgesia, the haemodynamic response to major noxious stimuli is great even when large doses are given. Therefore, assessment of depth of anaesthesia using clinically relevant noxious stimuli (laryngoscopy/intubation) requires the concurrent administration of other analgesic and adjuvant drugs (opioids/nitrous oxide, muscle relaxants) to provide haemodynamic control.

For total intravenous anaesthesia (TIVA), Sear et al[22] proposed the concept of minimum infusion rate (MIR) to compare the anaesthetic requirements for intravenous anaesthetics. They calculated the 50% effective dose (ED_{50}) and 95% effective dose (ED_{95}) infusion rates using the movement response to skin incision, which were analogous to MAC. An IV bolus injection of an anaesthetic combined with a maintenance infusion can produce a steady state plasma concentration of the drug. Unfortunately, the MIR is also affected by pharmacokinetic properties of the drug, age and physical status of the patient and the use of other drugs (opioids, N_2O) in addition to the anaesthetic requirement or responsiveness of the CNS.

Narcotics (opioids)

Various narcotics like morphine, fentanyl, alfentanil, remifentanil have been used in higher dosage to produce anaesthesia in patients with severe valvular or

congenital heart disease because of their ability to maintain cardiovascular stability.[23,24] However, in a study, using high dose fentanyl induction in patients for cardiac anaesthesia, Stanley et al[24] found that even increasingly large doses of fentanyl could not always produce a complete anaesthetic state in all subjects. Murphy and Hug[25] found that even high plasma concentration of fentanyl (> 20 $ngml^{-1}$) did not decrease enflurane MAC beyond 60-70% of its initial value. In current clinical practice, high-dose opioids are supplemented with amnesic drugs (benzodiazepines) or low concentrations of potent inhalational anaesthetics.

The Cp_{50} values (Steady-state plasma concentration of the drug which will prevent purposeful movement to noxious stimuli in 50% population) were calculated for three clinical events: intubation, skin incision and skin closure. The relationship curves of alfentanil show that intubation requires significantly higher concentration of alfentanil than skin incision and skin closure.[26] Drugs having a slower rate of blood-brain equilibration (fentanyl, sufentanil, and morphine) would be less amenable to the kind of pharmacodynamic analysis of plasma concentration versus clinical effect relationship.[27] The minimum infusion rate of opioids during surgery has titrated to the following end points:

i. An increase in SBP >15 mmHg above normal value.

ii. HR > 90 beats/min in absence of hypovolemia.

iii. Somatic response, such as body movements, swallowing, coughing, grimacing or opening of eyes, and

iv. Autonomic signs of inadequate anaesthesia (lacrimation, flushing, sweating).

If any clinical sign occurred, the infusion rate has increased 20-30% and a small bolus doses was given.

Techniques for monitoring depth of anaesthesia (Table 2)

Depth of anaesthesia is a clinical term that accounts for both diverse drug effects and diverse clinical needs. Adequate depth of anaesthesia occurs when the concentrations of the agents are sufficient to produce the effects needed for the comfort of the patient and the conduct of surgery. There are both subjective and objective methods of assessing depth of anaesthesia. Subjective methods rely on the movement and autonomic response to stimuli and depend on the opinion and experience of an anaesthesiologist. The objective methods rely on the sensitivity of the monitor.

Table 2 : Methods of assessing depth of anaesthesia

A.	**Subjective methods**
	1. Autonomic response
	• Hemodynamic changes
	• Lacrimation
	• Sweating
	• Pupilary dilatation
	2. Isolated forearm technique
B.	**Objective methods**
	1. Spontaneous surface electromyogram (SEMG)
	2. Lower oesophageal contractility (LOC)
	3. Heart rate variability (HRV)
	4. Electroencephalogram and derived indices
	• Spectrual edge frequency
	• Median frequency
	• Bispectral index
	5. Evoked potentials
	• Auditory evoked potentials
	• Visual evoked potentials
	• Somatosensory evoked potentials
	• Auditory evoked potential index

Subjective methods

Autonomic response

These are commonly used in day to day practice as clinical indicators of depth of anaesthesia. Sudden hypertension and/or tachycardia, sweating, tearing or mydriasis may indicate lightening of anaesthesia. However, a wide range of other events like, hypotension, dehydration, hypoxia, hypo or hyperthermia, sudden massive blood loss etc may also lead to such haemodynamic changes. Factors like, built of the patient, baseline tone, cardiac drugs; e.g. beta-blockers, other anti-hypertensive drugs, inotropes and vasodilators may also affect blood pressure and heart rate. Beside this various drugs used in anaesthesia like muscle relaxants and opioids may suppress these responses but not produce hypnosis.

Patient response to surgical stimulus (PRST) score, based on autonomic changes in response to surgical stimulus is a poor indicator of depth of anaesthesia[28] (Table 3). It has been proven that haemodynamic responsiveness to noxious stimuli does not necessarily signify awareness, nor does lack of haemodynamic changes guarantee unconsciousness.[29] In most of the cases of ASA closed claim for recall during anaesthesia, there was no concomitant autonomic sign.[30] Among the patients with

recall during anaesthesia, 15% showed hypertension, 7% showed tachycardia and only 2% showed movement.[30] In a study conducted by Vernon et al,[31] it has been shown that pre-incision haemodynamic variables did not predict patient response to skin incision.

Table 3 : Patient Response to Surgical Stimulus (PSRT) Scoring system (29)

Index	Condition	Score
Systolic blood pressure	< control + 15 < control + 30 > control + 30	0 1 2
Heart rate	< control + 15 < control + 30 > control + 30	0 1 2
Sweating	Nil Skin moist Visible beads of sweat	0 1 2
Tears	No excess tears in open eyes Excess tears in open eyes Tears over flowing	0 1 2

Isolated forearm technique (IFT)

A purposeful movement in response to verbal command indicates light anaesthesia. In this method a tourniquet is placed on an arm of the patient before administration of a muscle relaxant and inflated above systolic pressure to exclude its effect. The arm is therefore free to move during anaesthesia. Ischaemia has to be prevented by periodically releasing the tourniquet, usually before topping up the muscle relaxant. Patient may then be asked to move his fingers to check adequacy of depth of anaesthesia.[32]

Despite a simple technique, IFT has some limitations as a monitor of depth of anaesthesia, like -

1) non specific startle response may be interpreted as consciousness. 2) the levels of anaesthesia needed to prevent movements in patients using IFT are significantly higher than those routinely used, since the advent of muscle relaxant. 3) patients have reported that they heard commands to move the isolated arm, but were unable to do so, even though nerve stimulator suggested that the arm was not paralyzed.[33]

Objective methods

Spontaneous surface electromyogram (SEMG)

In patients who are not completely paralysed spontaneous surface electromyogram (SEMG) can be recorded from various muscle groups, especially facial, abdomial and neck muscles. Frontalis muscle is innervated by a branch of the facial nerve and is less affected by the neuromuscular blockade. A stick on electrode positioned over the frontalis muscle can record the frontalis electromyogram (FEMG). The level of FEMG has been observed to fall during anaesthesia and to rise to pre-anaesthetic levels just before awakening.[34] During deliberate lightning from enflurane – nitrous oxide anaesthesia, a 30 % increase in neck muscle EMG activity preceded movement responses in 28 of 30 patients.[35] However, the scales were not absolute and there may be variability in response. The FEMG together with EEG provide better results. The ABM monitor system (Datex) records both EEG indices and FEMG via the same electrodes.[36]

Lower oesophageal contractility (LOC)

The non-striated muscles in the lower half of oesophagus retain their potential activity even after full skeletal muscle paralysis by neuromuscular blocking agents. Measurements of LOC therefore, provide two prime derivatives.

i. Spontaneous lower oesophageal contractions (SLOC)

These are non-propulsive spontaneous contractions mediated via vagal motor nuclei and reticular activating system in the brain stem. The frequency of these movements is increased as the dose of the anaesthetic is reduced.

ii. Provoked lower oesophageal contractions

These are obtained by inflation of a small balloon in the lower oesophagus. The brief inflation of small balloon provokes a secondary pulsatile response, which increases in amplitude as anaesthetic depth decreases.

Evans and colleagues[37,38] were the first to propose that depth of anaesthesia might be measured by the degree of spontaneous contractions of lower oesophagus. Sessler et al[39] demonstrated that the frequency of such contractions can predict movement on response to skin incision during potent inhaled anaesthetics like halothane but not with N_2O/opioid anaesthesia. The absence of spontaneous contractions of the lower oesophageal sphincter 6 min before skin incision correlated well with no movement on incision in subjects given halothane anaesthesia. By contrast, no correlation existing in spontaneous contraction of the lower oesophageal sphincter and movement in patients given alfentanil and nitrous oxide.[39]

Heart rate variability (HRV)

Recent research using animal models have shown that the anaesthetic agents either directly or indirectly first act on the brain stem and then probably inhibit the cerebral cortex via ascending efferent projections from the midbrain.[40] Therefore, objective measurement of brain stem-mediated autonomic tone that is not affected by any

factor other than anaesthetic depth may be a good indicator of depth of anaesthesia.

Kiode[41] investigated beat to beat variability of heart rate and observed that it may provide information, which would be useful for monitoring depth of anaesthesia. The special analysis of HRV revealed 3 components:

1) Low frequency fluctuations; believed to be circadian. 2) Medium frequency fluctuations; attributed to baroreceptor reflex. 3) High frequency fluctuations

HRV coincides with the frequency of ventilation, in which heart rate increases during inspiration and decreases during expiration, through a predominantly parasympathetic reflex connecting stretch receptors in the lungs and aorta to vagal motor neurons innervating the heart. This is called as respiratory sinus arrhythmia (RSA). It is typically characterized by greater than 10% variation in the ECG P-wave interval over 5 minutes. RSA is easily visible on an ECG monitor that is time locked to an ECG R-wave peak, but is difficult to distinguish with a rolling display. Pomfrett and colleagues[42] reported, using on line analysis of RSA, reduction in RSA during anaesthesia, together with increase in RSA during recovery. Various studies[43,44] have shown that the level of RSA reflects the level of anaesthetic depth. In addition, surgical stimulation during light anaesthesia elicits a greater increase on RSA than seen during lightening anaesthesia alone (Fig.4).

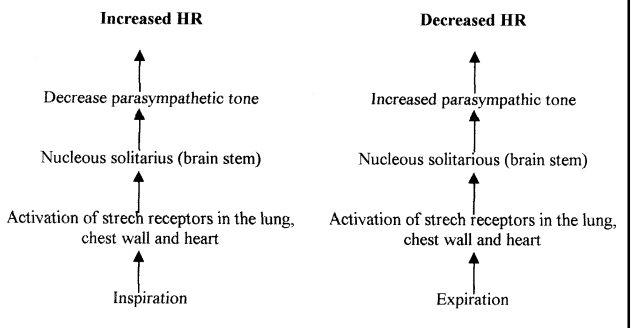

Fig. 4:The mechanism responsible for respiratory sinus arrhythmia (RSA)

Electroencephalogram and derived indices

The raw EEG is a complex small (1-50 □v) voltage deflection, which does not correlate with specific underlying events. The electronic filtering of EEG with the integrated amplitude of EEG waveform indicates the level of brain activity. The cerebral function monitor (CFM) gives a single trace of integrated EEG amplitude, increasing level of cerebral activity appears as a broadening of the trace, which ranges from 5-18 □v peak to peak amplitude. The cerebral frequency analysing monitor (CFAM) filters the EEG into five frequency bands and adds one extra trace demonstrating periods of burst-suppression. The main drawback of these monitors is that they are influenced by diathermy and the periods of poor electrode contact.

The modern EEG monitors, process and obtain EEG analog signals over a period of time and display the information in the form of histograms as compressed spectral array (CSA) or numerical parameters (e.g. spectral edge frequency, median frequency). The most common is the fast fourier transform (FFT). By squaring the results of FFT, the power spectrum of EEG may be obtained which, when plotted as power against frequency gives a frequency distribution of EEG. The individual distributions can be considered as time-slices and joined together into a 3-D plot, most frequently called as compressed spectral array (CSA). The CSA has been used to monitor the depth of anaesthesia.[45] During deeper anaesthesia the peaks of CSA shifts from higher frequencies to low frequency activity. While at recovery, there is a progressive increase in the amount of high frequency activity with a corresponding decrease in low frequency activity.

Although the CSA is considered more compact than the raw EEG, it is still a complex display that takes time to comprehend, and changes within it are difficult to quantify. Several single-figure numeric indices have been derived from power spectral analysis of EEG. These include:

1) Spectral edge frequency (SEF) 2) Median frequency (MF) 3) Bispectral index (BIS)

The spectral edge frequency is that below which 95% of EEG power is contained. The median frequency is described as, above and below which 50% of EEG power spectrum is distributed. Both SEF and MF have been correlated to clinical signs using numerous anaesthetic agents.[19,20,46,47] Median frequency of 5 Hz has been used as an empirical guide with closed loop propofol anaesthesia for providing adequate surgical anaesthesia.[47]

Bispectral index (BIS) is a statistically based, empirically derived complex parameter that is composed of a combination of time domain, frequency domain and high order spectral sub parameters. It is unique in the sense that it integrates several disparate descriptors of the EEG into a single variable, based on a large volume of clinical data to synthesize a combination that correlates behavioral assessments of sedation

and hypnosis, yet is insensitive to the specific anaesthetic or sedative agent chosen. It is a numerical index, ranging from 100 (awake) to 0 (isoelectric EEG). The BIS correlates well with the level of the responsiveness (responsiveness scores of modified observer's assessment of alertness/sedation level) and provide an excellent prediction of the level of consciousness with propofol, midazolam and isoflurane anaesthesia.[48] Various studies (50-52) have shown that BIS also correlates with the haemodynamic response to intubation,[49] patient's response to skin incision[50] and verbal command during inhalational as well as total intravenous anaesthesia.[50,51] Patients with BIS < 40 had a response rate of 12%, whereas those with BIS > 60 had 25%.[52] BIS is a useful monitor to adjust the anaesthetic dosages with decreased incidence of haemodynamic disturbances and improved recovery.[53] It reduces the cost by saving anaesthetic use and stay in PACU and provides a useful guide for titration of anaesthetic agents in cardiac surgery, elderly and paediatric patients.[54,55]

Inspite of its excellent usefulness BIS has some shortcomings. The presence of senile dementia may be a confounding factor in interpretation of BIS value. In some instances BIS has been observed to increase with the use of N_2O and ketamine.[56,57]

Evoked Potentials (EPs)

Evoked potentials show the response of more localized areas of the brainstem, mid brain and cerebral cortex to specific stimuli. Recording of EPs consists of recording EEG epochs and time-referencing them to sensory stimuli that have been applied in a repeated fashion. Therefore, EPs represents a time versus voltage relationship that can be quantitated by measuring the post stimulus latency and interpret amplitudes in the waveform. For intraoperative monitoring, 3 types of EPs are commonly used based on the sensory stimulus.

1. **Somatosensory evoked potential (SEP) :** SEP is recorded over the somatosensory cortex in response to tibial, peroneal or median nerve stimulation.
2. **Visual evoked potentials (VEP) :** VEP is recorded over occipital cortex in response to photic stimulation of the eyes.

   Flash stimulation **õ** retina **õ** lateral geniculate nucleus **õ** primary visual cortex.

4. **Auditory evoked potential (AEP) :** AEP is recorded at primary auditory cortex in response to auditory canal stimulation by audible clicks. It is most commonly used for the assessment of anaesthetic drug effect,

   Ear **õ** superior olivary nucleus **õ** inferior colliculus **õ** Medial geniculate nucleus **õ** primary auditory cortex.

AEP may be divided into (Fig 6)

1) Brain stem responses: potentials occurring during the first 10 ms after stimulation. 2) Early cortical response (from 15-80 ms). 3) Late cortical response (from 80-100 ms).

As the concentration of potent inhaled anaesthetic (halothane, enflurane, isoflurane) increases, the latencies of SEP, VEP and AEP increases and amplitude decreases.[58] In contrast N_2O produces a dose-related decrease in the amplitude of VEP & SEP, but no effect on latency.

Newton et al[59] have demonstrated the change in specific components of AEP during anaesthesia and recovery. Potent inhalational agents tend to increase the latencies of brain stem AEP waves III and V as anaesthetic deepens. They also increased the latency and decreased the amplitude of early cortical AEP. Intravenous barbiturates also increased the latency of brain stem components III & V, but other intravenous anaesthetics (etomidate, propofol, althesin) do not change the brain stem response, but change the cortical latency and amplitude in similar manner.

Using evoked potentials to monitor depth of anaesthesia entails some technical, clinical and practical complexities of recording evoked responses. Many confounding artifacts can alter evoked potentials: stimulus characteristics (intensity, duration, inter-stimulus interval), electrode placement, technique, age and gender of the subject and choice of anaesthetic drugs.[60]

Middle latency auditory evoked response (MLAER)

Thromton and Sharpe.[61] investigated in 1998, the use of MLAER in the detection of awareness by focussing on the latencies and amplitude of Pa & Nb waves. Thereafter several studies have suggested the use of MLAER as an effective indicator of depth of anaesthesia.[62,63,64] Schwender et al,[62] using different anaesthetic agents observed that implicit memory occurred only in patients in whom latency increase in Pa was less than 12 ms.

Newton et al[63] demonstrated that Nb frequency of 47 ms was 100% sensitive and specific for explicit memory of words presented during isoflurane inhalation. Recent studies have shown that MLAER derivatives confirm high level of sensitivity and specificity as in case of BIS.[64] The

only drawback is that MLAEP are usually obtained intermittently and the waveforms are difficult to use in the clinical situation.

Auditory evoked potential index

This has been derived from auditory evoked potentials and represent as a single numerical variable for monitoring depth of anaesthesia.[65] The auditory evoked potential index reflects the morphology of the AEP curves and is calculated from the amplitude difference between successive segments of the curve. A moving time average of AEP index is obtained at 3 sec intervals. AEP index of 37 was 100% specific and 52% sensitive for unconsciousness. It correlated best with BIS to distinguish awake from sleep state.[66]

Gajraj et al[67] compared the autitory evoked potential (AEP) index, 95% spectral edge frequency (SEF), median frequency (MF) and the bispectral index (BIS) during alternating periods of consciousness and unconsciousness produced by target controlled infusions of propofol. They found, of the four measurements, AEP index was the best and highly sensitive for distinguishing the transition from unconsciousness to consciousness (Table 4).

Table 4: Values of auditory evoked potential (AEP) index, bispectral index (BIS), 95% spectral edge frequency (SEF) and median frequency (MF) with 100% specificity and values with approximately 85% sensitivity for consciousness and unconsciousness

	Threshold	Sensitivity (%)	Specificity
Unconscious			
AEP index	37 44	52 85	100 87
BIS	55 76	15 86	100 83
SEF	16.0 21.0	9 85	100 92
MF	1.4 10.7	0 85	100 55
Conscious			
AEP index	56 45	60 87	100 85
BIS	95 75	14 88	100 80
SEF	26.6 21.9	15 84	100 92
MF	13.8 7.9	18 85	100 25

Future

At present, it is unlikely that any single method is found to measure the depth of anaesthesia reliably for all anaesthetic agents. The only reliable way of determining depth of anaesthesia will require a measure of cerebral activity and a localization of the activity to specific cortical regions and areas in brain stem, in real time.

Position emission tomography (PET)

It has been used in limited studies. PET scanning revealed that propofol anaesthesia has a widespread suppressive effect on cerebral metabolism.[68] This approach may lead to the adoption of a standard, absolute scale of anaesthetic depth; against which other measures can be calibrated. However, it is an invasive method and can not be used in routine cases.

Ultra sensitive super conducting quantum interference device (SQUIDS)

It is a non-invasive method, which measures functional activity of brain. Although expensive at present, this may provide the ultimate monitor to the anaesthesiologists. It is capable of determining not just anaesthetic depth but also awareness, anoxia, ischaemia and unusual pathology.

Summary and conclusion

Measuring depth of anaesthesia represents one of the most controversial and subjective aspect of modern anaesthesia, with the introduction of the concept of balanced anaesthesia using multiple drugs and muscle relaxants. It is unlikely that any single method will be found to measure the depth of anaesthesia reliably for all patients and all anaesthetic agents. All the methods for determining the depth of anaesthesia to date have some potential exclusion criteria.

Therefore, using more than one method at a time may provide more accuracy. The rapid advancement in the microcomputer technology and our understanding of the basic sciences will allow us a greater scope to interpret our observations of the anaesthetic state in near future.

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