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CENTENARY REVIEW ARTICLE

Intraoperative monitoring of the central and peripheral nervous systems: a narrative review

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Summary

The central and peripheral nervous systems are the primary target organs during anaesthesia. At the time of the inception of the *British Journal of Anaesthesia*, monitoring of the central nervous system comprised clinical observation, which provided only limited information. During the 100 yr since then, and particularly in the past few decades, significant progress has been made, providing anaesthetists with tools to obtain real-time assessments of cerebral neurophysiology during surgical procedures. In this narrative review article, we discuss the rationale and uses of electroencephalography, evoked potentials, near-infrared spectroscopy, and transcranial Doppler ultrasonography for intraoperative monitoring of the central and peripheral nervous systems.

Keywords: CNS monitoring; depth of anaesthesia; electroencephalography; evoked potentials; intraoperative neurophysiology; near-infrared spectroscopy; transcranial Doppler

Editor's key points

- Over the last 100 yr, significant progress has been made in intraoperative neuromonitoring.
- This review covers the use of the raw electroencephalogram, evoked potentials, near infrared spectroscopy, and transcranial Doppler techniques.
- Although significant advances have been made, future studies should concentrate on enhancing the sensitivity of monitoring techniques.

A century ago, the only tool available to anaesthetists to monitor the central nervous system was clinical observation. Recent technological developments have led to the introduction of more reliable and objective monitoring methods.

To assess hypnotic drug effects, anaesthetists traditionally relied on observation of heart rate, blood pressure, and signs of movement, sweating, or tears, to judge whether anaesthesia was adequate. After advances in signal acquisition and processing techniques, electroencephalography (EEG) monitoring has been used since the 1990s to assess the depth of anaesthesia. Work is also underway on methods of monitoring the adequacy of analgesic administration.

During operations which put the functional integrity of the nervous system at risk, the wake-up test was previously the only method available to assess the integrity of the spinal motor and sensory pathways. Anaesthetic drug administration was stopped intraoperatively, and once the patient regained consciousness, they were asked to move their hands or feet. The usefulness of this test was limited because it assessed neurological function at a single point in time when any injury might already have been irreversible. It was also associated with risks such as unintentional extubation.

Intraoperative neurophysiological monitoring (IONM) of the spinal cord using evoked potentials can now be used to

identify intraoperative neural insults to facilitate early intervention to prevent postoperative neurologic deficits and eliminate or significantly reduce irreversible damage to the spinal cord and nerves. Optimal anaesthetic choices and management are, however, essential to the successful application of IONM.

Neuromonitoring has also been used to detect cerebral ischaemia during carotid surgery since the 1970s, initially with EEG[1] and somatosensory evoked potentials (SSEPs),[2] and more recently motor evoked potentials (MEPs).[3]

In recent decades, noninvasive techniques for monitoring the physiology of the brain have been developed. Cerebral ischaemia and hyperaemia (see Fig. 1[4]) are both deleterious for the brain, and near-infrared spectroscopy (NIRS) has been used to assess regional cerebral tissue oxygenation, indicating the balance between cerebral oxygen delivery and demand.[5] Transcranial Doppler (TCD) monitoring can measure cerebral blood flow (CBF) velocity in the major cerebral arteries.

This narrative review briefly describes recent developments and scientific principles underlying the use, clinical applications, benefits, and limitations of different techniques. We focus on using raw EEG to monitor the depth of anaesthesia and detect cerebral ischaemia, IONM of the functional integrity of the spinal cord, and NIRS and TCD to monitor cerebral oxygenation and flow.

Electroencephalographic monitoring

Signal origin

EEG is a technique for recording the electrical activity of the brain.[6] As brain activity reflects cognitive activity and conscious status, which are influenced by anaesthetic drugs, dose-related EEG changes occur. Pathological conditions,

Fig 1. Qualitative representation of the relationships between oxygen demand, shown on the y axis (quantified as cerebral metabolic rate of oxygen [$CMRO_2$]) and oxygen delivery, shown on the x axis (quantified as the product of cerebral blood flow [CBF]) and arterial content of oxygen [Ca or CaO_2]). Causes of changes to supply and demand are shown. In the green zone demand and supply are matched. The red zones represent ischaemia and hyperaemia, occurring when demand exceeds supply or supply exceeds demand, respectively. Reprinted with permission.

including epileptiform activity, cerebral ischaemia, hypoxia, and hypoglycaemia, can also alter brain activity and EEG activity. A recent consensus statement recommended that every anaesthesiologist and intensivist should possess knowledge of EEG and be able to interpret common conditions in the electroencephalogram (EEG recording).[7]

The human brain contains ~100 billion highly interconnected neurons forming several functional networks.[8] Neuronal cells are electrically charged because they contain transmembrane proteins that maintain ion gradients across the cell wall. The most important is the sodium−potassium channel, which pumps three Na^+ out of the cell for every two K^+ pumped into the cell,[9] maintaining a resting potential of −70 mV inside the cell.[10] An action potential depolarises a neuron by activating voltage-gated Na/K channels, allowing a gradient-induced influx of Na^+ to enter the cell and raising the intracellular potential to +20 mV. As the action potential is propagated along the axon, it causes tiny local ion currents.
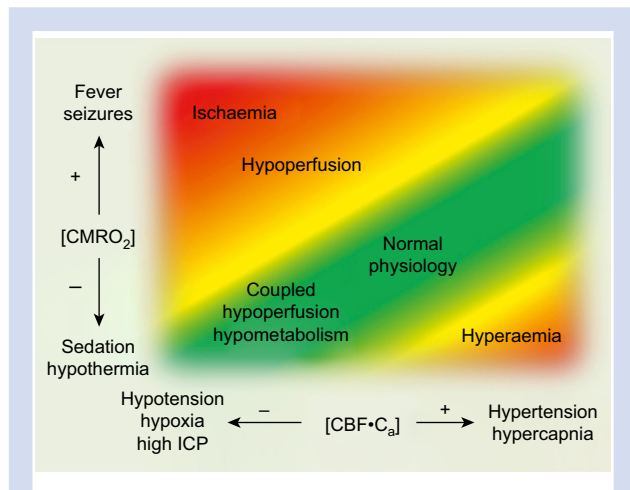
When an action potential reaches the presynaptic terminal, it causes release of neurotransmitters, which bind to postsynaptic neuronal membrane receptors and cause or modulate inhibitory or excitatory postsynaptic membrane potentials, depending on the nature of the neurotransmitter and its receptor. Inhibitory postsynaptic potentials (IPSP) arise when the neurotransmitter binds to a receptor that lowers the resting intracellular voltage (usually from −70 mV to −100 mV) by causing an efflux of K^+ from the cell or an influx of Cl^- (as in the case of $GABA_A$ receptors). An excitatory postsynaptic potential (EPSP) arises when an excitatory neurotransmitter such as glutamate binds to a postsynaptic receptor that causes temporary local depolarisation (e.g. by an influx of Ca^{2+} in the case of an *N*-methyl-D-aspartate receptor). Temporal and spatial summation of EPSPs and IPSPs occurs. If the combined change is sufficient to raise the transmembrane potential above a threshold, then an action potential will be generated.[11]

The dendrites of pyramidal neurons orientated perpendicularly to the scalp, receive inhibitory and excitatory inputs, which influence extracellular ion content and generate extracellular ionic currents. The thousands or millions of pyramidal cells near each electrode receive synchronous input from sub-cortical structures, and the signal detected by an EEG electrode is the integral of these combined cortical electrical signals.[1]

EEG essentially records the differences in electrical potentials between an electrode and one or more reference electrodes. Multiple electrodes are necessitated by the topographical variation inherent in cortical electrical activity. The international 10−20 system serves as a standard template for electrode positioning.[12]

Electroencephalography signal processing and analysis

EEG waveforms are usually described by their registration location, morphology, amplitude, frequency content, and the clinical context. In average adults, the amplitude recorded from the scalp ranges from ~10 to 100 μV. Morphology refers to the overall shape of the signal in the time domain. Individual waves can be said to be monophasic, biphasic, or polyphasic. Morphological features are essential in diagnosing and monitoring seizures and sleep staging. K-complexes and spindles are seen during stage 2 non-rapid eye movement (NREM) sleep, while spindles are also seen during dexmedetomidine sedation and propofol anaesthesia.[13]

The frequency content of the EEG has traditionally been classified into bands named delta (0.5–4 Hz), theta (4–8 Hz), alpha (8–13 Hz), and beta (13–30 Hz). In the healthy brain, the EEG almost always comprises a combination of frequencies. The relationship between amplitude and frequency is typically inverse.[14]

Fast Fourier transformation (FFT) of the signal enables more complex mathematical analyses of the EEG. It provides information about the component frequencies in the signal, their power (relative and absolute), and the phase relationships among the component frequencies. A frequency spectrogram represents EEG activity in the frequency domain, showing the power in each of the frequencies present in the signal. More sophisticated versions represent the changes in the power in each frequency recorded by a given electrode pair over time. During sedation and anaesthesia, there are distinct regional differences in frequency content, power, and coherence changes, and newer techniques for graphically representing these changes have been developed.[15]

Clinical EEG recordings are almost always contaminated by noise from electromagnetic (power lines, electric lights, and equipment) and biological sources (signals from face or neck muscles).[6] EEG systems usually contain notch filters to remove (50 or 60 Hz) electrical power supply interference. Further visual inspection of the EEG is essential to evaluate other sources of interference.

Burst suppression is a morphological feature that all anaesthetists should be able to recognise (Fig. 2[16]). It is characterised by systematic and quasiperiodic phases of isoelectric (or near isoelectric) signal, alternating with bursts of higher voltage activity.[4] Generally, it is associated with profound brain inactivation caused by high doses of GABAergic drugs, but it can also manifest in comas induced by hypothermia or structural lesions resulting from trauma or stroke.[17] In certain genetic or metabolic conditions, it can persist because of encephalopathy.[18] The exact neurophysiological mechanism remains unknown.[19]

The burst suppression patterns induced by different anaesthetic drugs exhibit notable differences.[20] The burst suppression ratio (BSR), the fraction of time that the EEG is (near) isoelectric, quantifies the extent of burst suppression and is displayed by some depth of anaesthesia devices. However, visual inspection of the raw electroencephalogram is superior to current machine-generated detection and quantification of burst suppression.[21]

Clinical use

Raw electroencephalography

Continuous unprocessed 'raw' EEG monitoring can be used for intraoperative seizure detection. During awake craniotomies, scalp and cortically recorded EEG signals are monitored for, among others, signs of impending seizure activity after electrical cortical stimulation.[22,23] When 'after-discharges' are detected, steps to reduce cortical excitability, such as administration of an additional dose of antiepileptic agent, should be considered. Scalp EEG monitoring is also used to assess cortical state during surgical procedures associated with a risk of spinal cord injury.[2]

Continuous raw EEG monitoring can be used to detect acute cerebral ischaemia.[24] When CBF is compromised, the metabolic and electrical activity of cortical neurons is impaired,[25] leading to EEG slowing. When CBF decreases to 25–35 ml 100 g^{-1} min^{-1}, faster frequencies disappear. Slower frequencies then predominate, however, with further reduction of CBF, they also disappear. Below the infarction threshold (plus or minus 10 ml 100 g^{-1} min^{-1}), cellular functions fail, and

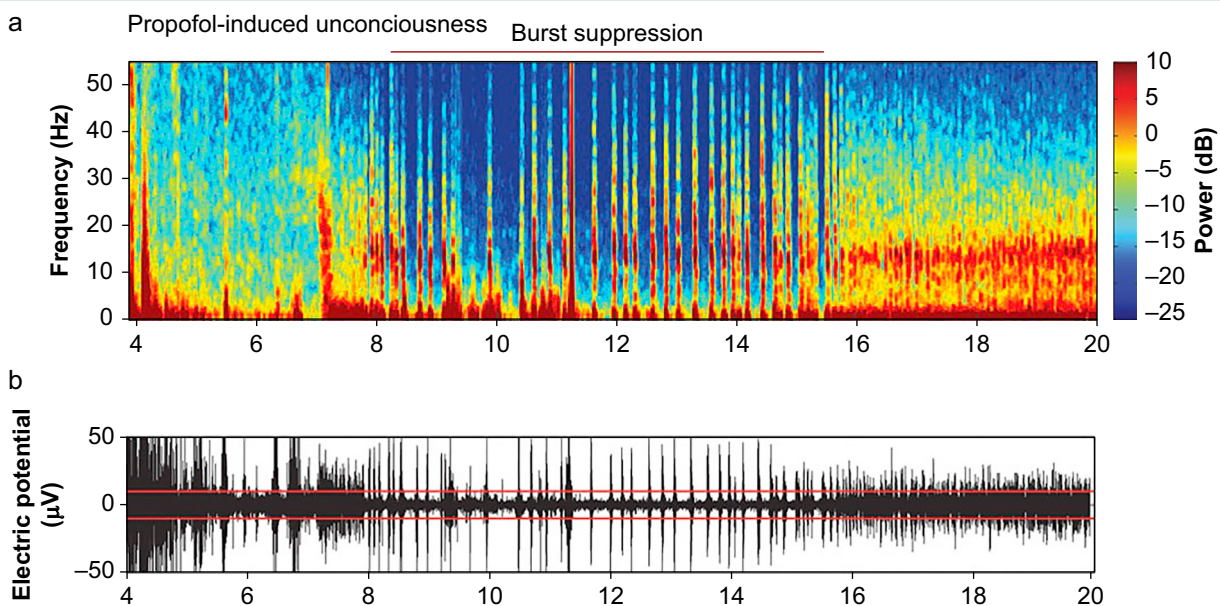Fig 2. (a) Spectrogram depicting relationships between frequency and power over time, illustrating a period of burst suppression, depicted by the crimson line, involve alternating isoelectric activity and slow-delta and alpha oscillations. (b) Corresponding raw electroencephalogram showing the alternating bursts (≥5 μV amplitude) and suppression (<5 μV, displayed between the two crimson lines). Reprinted with permission.

neurons lose their transmembrane gradients in neurons, which consequently undergo necrosis.

During a carotid endarterectomy (CEA), carotid clamping can cause cerebral ischaemia if the collateral flow is inadequate, resulting in EEG changes within 20 s. In some centres, shunts are placed routinely to prevent ischaemia,[26] but this carries significant risks (e.g. thrombosis, carotid dissection).[27] In other centres, they are placed selectively based on neurophysiological parameters.[26] EEG monitoring is a well-accepted method of detecting cerebral ischemia during CEA.[28] Small decreases in CBF can cause EEG changes within seconds, so EEG monitoring can facilitate rapid detection of cerebral ischemia and increase the window of opportunity for effective intervention.[29] EEG criteria considered indicative of cerebral ischaemia necessitating shunt placement include a >50% decrease in amplitude or a significant decline in fast activity on the ipsilateral side.[28,30]

Hypnotic anaesthetic drugs induce complex, dose-related, non-linear EEG changes.[16] Starting from the awake state, characterised by low-amplitude, high-frequency activity, sedative doses initially cause some activation in the beta frequencies. Subsequently, increasing doses lead to a gradual transition to high-amplitude, low-frequency activity before reaching burst suppression activity. At very high doses, iso-electricity occurs.[31] Frequency analyses reveal that the SEF 95 (spectral edge frequency: the frequency below which 95% of the total EEG power is located) and the median frequency exhibit a biphasic relationship with depth of anaesthesia. These measurements become numerically unstable when burst suppression occurs, and poses challenges for FFT algorithms in processing the alternating periods of electrical silence and bursts.

Processed EEG (pEEG) monitors incorporate mathematical algorithms developed to deal with this complexity. Most of them also display the raw EEG, and current guidelines recommend that anaesthetists also observe the raw EEG signal when interpreting the index displayed by the device.[32] Interpreting the raw EEG requires some training, for which there are published resources[1,16] and helpful social media resources. Several monitors also display changes in quantitative EEG parameters, such as SEF or frequency spectrogram, which can also aid interpretation of the raw EEG waveform.

EEG burst suppression is sometimes a therapeutic goal in the intensive care unit, such as when managing status epilepticus or refractory intracranial hypertension. In operating theatres, it may be a goal before deep hypothermic cardiac arrest or before neurovascular procedures, but it is generally considered a sign of profound anaesthesia. Intraoperative burst suppression is associated with emergence delirium, especially when the emergence phase lacks spindle-dominant slow wave activity.[33] The duration of burst suppression correlates with the risk of postoperative delirium, especially when occurring at low anaesthetic doses.[34,35]

The aforementioned studies of associations between burst suppression and delirium were observational.[33–35] The Electroencephalography Guidance of Anaesthesia to Alleviate Geriatric Syndromes (ENGAGES) trial was a randomised controlled trial that sought to investigate the clinical benefit of avoidance of burst suppression and low bispectral index (BIS) values in 1232 older patients.[36] It found that burst suppression avoidance did not reduce the incidences of postoperative delirium, 30-day mortality[36] and 1-yr mortality.[37] The authors attributed this discrepancy between their findings and those of the observational studies, to the methodological differences.[36]

Processed electroencephalography: depth of anaesthesia

The most common use of the EEG during anaesthesia is for depth of anaesthesia monitoring, using commercially available pEEG monitors. These monitors perform complex mathematical analyses of the EEG signal, usually acquired from a frontal montage, and display an index indicating the depth of anaesthesia. There is extensive literature on this topic, explaining how the indices are calculated and reporting the purported benefits associated with their use to various degrees. Given the breadth of this literature and the diversity of opinions concerning the interpretation of the findings, also within the pages of this journal,[38] a detailed analysis of this topic is not feasible here. Interested readers wishing to explore this topic further may wish to consult recent guidelines on intraoperative monitoring, particularly during total intravenous anaesthesia, and a recent Cochrane Review.[32,39–42]

Processed electroencephalography: nociception—anti-nociception balance

In routine clinical practice, anaesthetists determine opioid medication dose requirements empirically based on a combination of tradition, intuition, observation of clinical signs, and pharmacological knowledge. There is, however, marked interindividual variability in opioid pharmacokinetics and dynamics, and the intensity of the noxious stimuli changes during surgery. Attempts have therefore been made to quantify the nociception—antinociception balance objectively.

Some EEG-based monitoring systems have been developed. The Conox monitor (Fresenius-Kabi, Bad Homburg, Germany) also calculates the qNOX, an index of the nociception/antinociception balance (Fresenius-Kabi),[43] using adaptive neuro-fuzzy inference involving the ratios of power in different EEG frequency bands and burst suppression.[44] The composite variability index (CVI, Medtronic, Dublin, Ireland) is calculated from the variability in the BIS values and the electromyographic power.[45]

Opioids, such as remifentanil, generally only cause significant changes in summary measures of the EEG spectral content (e.g. SEF) at supraclinical doses.[46] Recently, a group of experts has proposed three changes in the EEG frequency content associated with inadequate analgesia in a patient under general anaesthesia.[47] These features—beta arousal (i.e. an increase in beta frequency power), paradoxical delta arousal, and alpha dropout (a reduction in alpha power)—have yet to be used to titrate analgesic administration in prospective studies.

Several other monitors have been developed that use other signals of autonomic function status, such as the surgical pleth index (SPI, GE Healthcare, Helsinki, Finland)[48] and the nociception level monitor (NOL, Medasense Biometrics Ltd, Ramat Gan, Israel).[49] The SPI calculates an index based on the normalised heartbeat interval and plethysmographic pulse wave amplitude,[50] and the NOL is a combination of finger photoplethysmogram amplitude, skin conductance, heart rate and heart rate variability and their time derivatives.

There is some evidence that using nociception monitoring to guide opioid administration may have benefits. For example, NOL guidance resulted in lower intraoperative stress hormone levels and less postoperative pain.[51] A review of available nociception monitoring devices concluded that none appeared to offer 'sufficiently broad applicability' and that there was no firm evidence that using the devices provided

clinically relevant improvements in outcome.[52] A more recent study showed that nociception monitoring guidance with different devices was associated with markedly different opioid doses,[53] suggesting that these devices are not assessing the same physiological construct.

Limitations

EEG monitoring in operating theatres has some technical and practical limitations. The complexity of interpreting EEG patterns has already been mentioned. Not only do different hypnotic drugs cause different patterns of changes, but EEG signals are also influenced by other factors such as age, use of other medications, medical conditions, and surgical stimuli.[47,54–56] Accurate interpretation of intraoperative changes in the raw EEG data requires training and experience.

Future directions

The complexity of EEG changes during sedation and anaesthesia lend themselves to machine learning techniques, which may result in better systems detecting accidental awareness and assisting with more accurate titration of drug doses.[57–59] Although the current literature is inconclusive, evidence suggests that pEEG-guided anaesthetic drug titration might reduce the incidence of postoperative delirium.[36,60,61] Future applications may extend the period of EEG monitoring into the postoperative period as there is some evidence that analyses of EEG signals before, during, and after anaesthesia could help early identification of cognitive deficits or neurological complications,[62] allowing for interventions and rehabilitation plans to be optimised.

Evoked response monitoring

Basic concepts

IONM involves using evoked responses to facilitate repeated mapping and surveillance of the central and peripheral nervous system. This enables early detection and correction of surgical, physiological, and mechanical factors that may threaten the integrity of these systems, thereby improving postoperative outcomes.[63]

With advancing monitoring capabilities and the increasing complexity of surgical interventions, the number of indications for IONM has grown in past decades. IONM is used during a wide range of procedures during which the central and peripheral nervous system are at risk, for example, during intracranial, spinal, and cardiovascular operations. Anaesthetists require basic understanding of IONM and should maintain close communication and cooperation with surgeons and neurophysiologists to ensure optimal monitoring and outcomes.

Monitoring modalities and applied anatomy of intraoperative neurophysiological monitoring

Commonly used monitoring modalities during IONM include SSEPs, MEPs, and brainstem auditory evoked potentials (BAEPs), often used in combination. Each modality involves the application of stimuli and subsequent recording of responses at distinct anatomicals.[64] Real-time free-running electromyography (EMG) and EEG monitoring are usually used as well. Monitoring the unprocessed EEG is essential, as excessive anaesthetic depth causes cortical suppression, which particularly influences MEPs.[65]

Somatosensory-evoked potentials

Somatosensory-evoked potentials (SSEPs) are used to monitor ascending large fibre sensory pathways. An electrical stimulus is applied to a peripheral nerve, typically the median or ulnar nerve at the wrist for upper extremity monitoring or to the tibial nerve at the ankle for lower extremity monitoring. This stimulus activates type Ia and type II sensory nerve fibres producing an ascending signal that enters the spinal cord via the dorsal root of the spinal nerve and ascends the spinal cord in the dorsal (posterior) column (Fig. 3). At the medulla, the signal decussates. Subsequently, it is conducted through the ventroposterolateral nucleus of the thalamus to the contralateral (of the stimulation side) primary somatosensory cortex, where the SSEP can be detected with scalp electrodes.[66]

Motor-evoked potentials

Motor-evoked potentials (MEPs) are used to monitor the descending motor pathways. They are elicited by transcranial (Tc-MEP) or direct stimulation of the motor cortex or pyramidal tract. With Tc-MEP, the electrical stimulus is transmitted by the fast-conducting cortico-spinal tract fibres, which decussate in the medulla oblongata and travel further through the anterior part of the spinal cord, where the descending signal can be detected in the epidural space as 'D-waves' (Fig. 4). The fibres synapse at the anterior horn cells, which then propagate the signal along the nerve root and peripheral nerve, ultimately reaching the neuromuscular junction. Afterward, if the muscle is activated, it results in an MEP that can be detected using intramuscular needles or surface electrodes.[64]

Although a single electrical stimulus applied to the motor cortex can readily evoke an MEP in awake subjects, during anaesthesia an MEP can only be evoked by a pulse train (i.e. a brief series of stimuli).[67] The amplitude and shape of the MEP recordings are inherently variable because of the polysynaptic nature of their generation. The amplitude reduction method is generally used for warning criteria, but this variability makes the definition of thresholds for warning criteria challenging. One approach used to reduce this variability is the supramaximal stimulation method (i.e. use of stimuli with higher voltage, slightly higher than necessary to evoke the maximum MEP amplitude).[68]

Brainstem auditory-evoked potentials

Brainstem auditory-evoked potentials (BAEPs) are used to monitor the vestibulocochlear nerve (VCN) and brainstem function during some posterior fossa procedures. BAEPs can be elicited by applying high-intensity acoustic stimuli (typically a series of clicks at 70 dB above the hearing threshold) to the external auditory canal. In response, the cochlear nerve generates an electrical signal that is propagated along the auditory pathway to the auditory cortex of the temporal lobe via synapses in the ipsilateral cochlear nucleus and the contralateral superior olivary complex (both in the medulla), the pontine inferior colliculus (pons), and the thalamus.[69] The resulting potential is usually recorded on the scalp with electrodes placed at Cz and the left and right mastoid processes or anterior to each ear. Anaesthetic drugs and various pathological conditions can cause characteristic alterations in the BAEP.[70]

Free running electromyography

Electrical activity of the muscles can be continuously recorded with needle or surface electrodes.[71] An increase in muscle
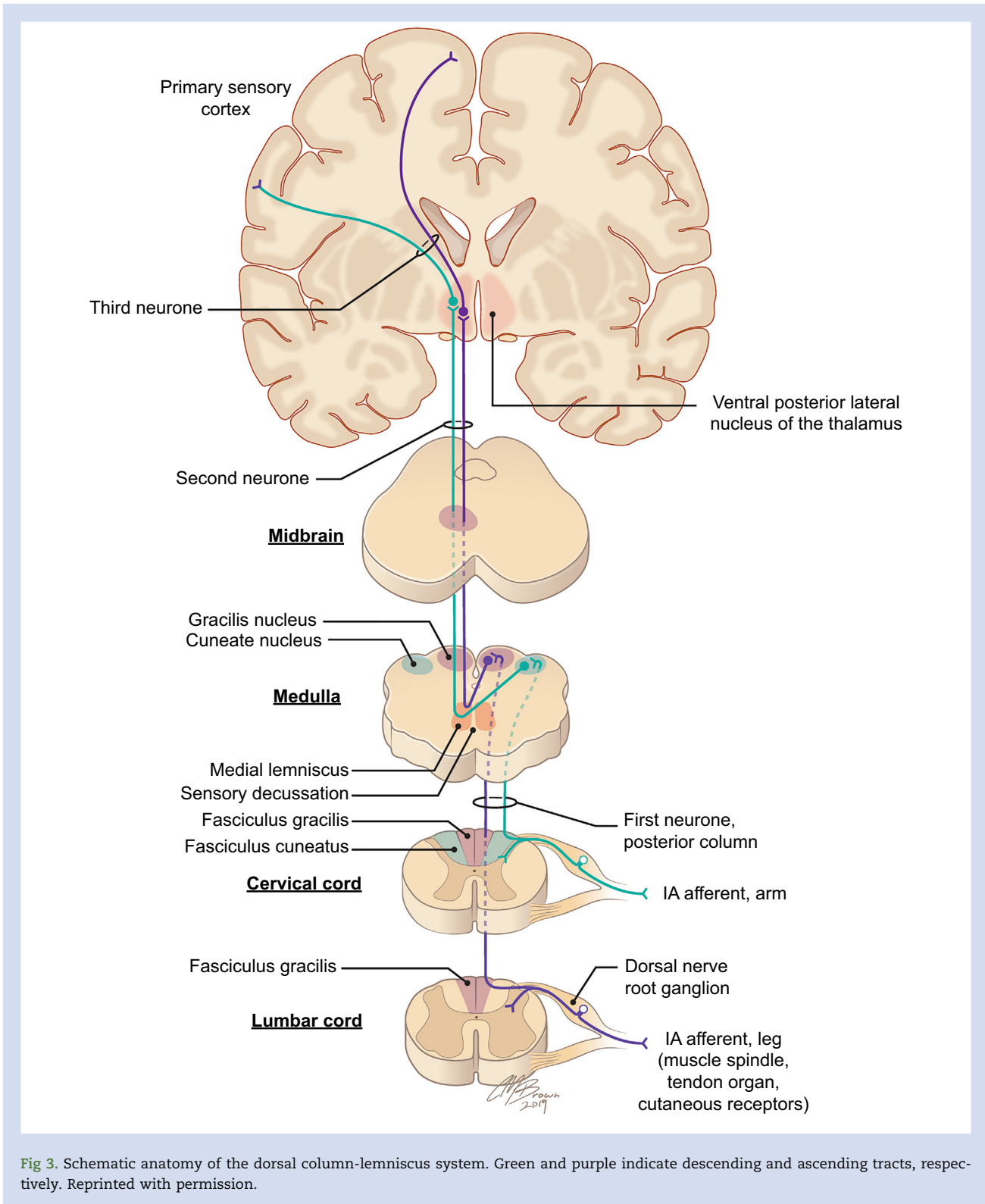
Fig 3. Schematic anatomy of the dorsal column-lemniscus system. Green and purple indicate descending and ascending tracts, respectively. Reprinted with permission.

activity against a low activity background can be seen with mechanical (stretching, compression, ischaemia) or thermal irritation, potentially signalling nerve injury, allowing quick identification and alleviation of the causative factor.[72] This can be useful during maxillofacial or ENT procedures that put the facial nerve at risk.
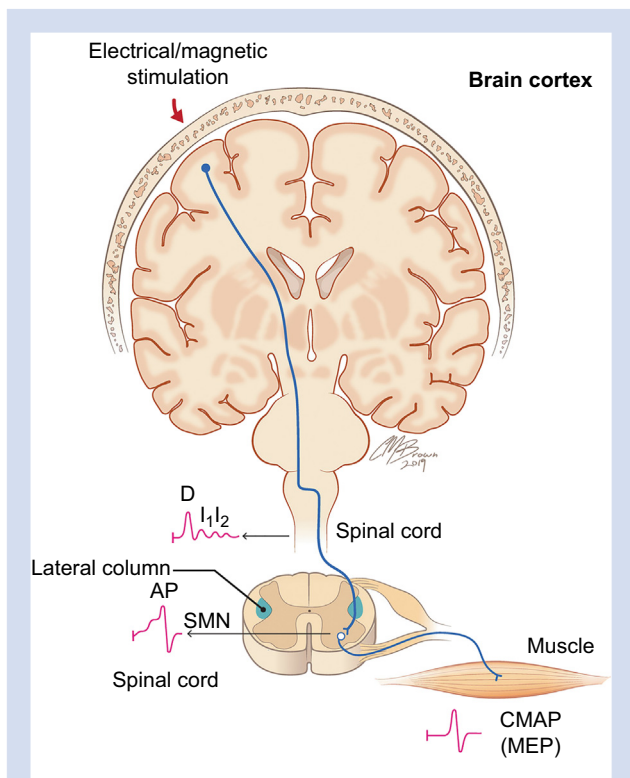
Fig 4. Schematic illustration of transcranial electric/magnetic stimulation of the motor cortex. The D and I waves were obtained from the spinal cord by epidural electrodes and the motor response (MEP) from the target muscle. The lower motor neuron (LMN) requires temporal summation of excitatory postsynaptic potentials in order to activate the nerve action potential, which then produces the muscle response. AP, action potential; CMAP, compound muscle action potential; MEP, motor evoked potential; LMN, lower motor neuron. Reprinted with permission.

Anaesthetic management

Multimodality IONM is best facilitated by an anaesthetic regimen that interferes least with reliable generation and recording of neurophysiological signals. This is usually achieved with total intravenous anaesthesia (TIVA) and avoidance of neuromuscular blocking agents after intubation.[28] The European Society of Anaesthesiology and Intensive Care has published recommendations for preoperative screening.[73] During IONM, a clinical neurophysiologist frequently monitors the amplitude and latency of the evoked potentials. A reduction in amplitude below a threshold is taken as a warning of potential neuronal injury. The optimal threshold for a warning indicative of impeding neuronal injury is controversial, differs per type of surgery and is the topic of ongoing research.[74] Careful anaesthetic management is required to reduce the incidence of false positive warnings, as anaesthetic drugs can directly influence CNS and muscular function and significantly impact the quality of IONM signals. Furthermore, CNS function, and therefore IONM signals, can also be affected by other factors that are influenced by anaesthetic

management, such as brain and spinal cord perfusion (which are in turn influenced by arterial blood pressure, Pa_{CO_2}, and Pa_{O_2}) and body temperature.

Propofol-based TIVA is considered more suitable than volatile anaesthesia for induction and maintenance of anaesthesia during surgery with IONM, as the effects of propofol on especially MEPs but also SSEPs are less profound.[75] Although not preferred, when volatiles are used, IONM is only possible when <0.5 MAC is used.[76]

Propofol effects on evoked potentials are dose-related, and so even with TIVA, it is essential to (a) optimise/minimise the dose, (b) maintain a steady drug effect where possible, and (c) avoid administering bolus doses. These goals can be achieved by administering propofol using a target-controlled infusion (TCI) pump and a pEEG monitor to guide drug titration.[77]

Opioid drugs have negligible effects on IONM signals. Optimal doses can facilitate IONM by (a) minimising physiological disturbances caused by the adrenergic response attributable to surgery and (b) enabling synergistic potentiation and reduction of hypnotic drugs, thereby attenuating their adverse effect. Bolus administration of opioid drugs should also be avoided, which is why TCI administration of opioids is also recommended.[78]

To prevent prolonged muscle relaxation, judicious doses of neuromuscular blocking agents should be used for tracheal intubation. Before the start of MEP monitoring, the possibility of the residual blockade should be excluded. Bite blocks are essential to prevent damage to the tongue, teeth, and tracheal tube when using MEPs.

As changes in physiological status can cause changes in evoked potential latency and amplitude, stable drug concentrations and optimal patient physiology should be maintained. Pa_{CO_2} levels should be kept in the normal range as hypocapnia causes cerebral vasoconstriction thereby reducing cerebral perfusion. Adequate oxygen delivery to the affected tissues is essential. Attention should be paid to maintaining normal blood oxygen content, normal blood haemoglobin concentration, and adequate cardiac output and tissue perfusion by administering fluids and vasopressor agents. Because blood flow and tissue perfusion are seldom measured in clinical practice, haemodynamic management usually focuses on maintaining the mean arterial blood pressure within the cerebral autoregulation range (60−140 mm Hg). Lastly, body core temperature predominantly affects MEP latency and should be kept between 35°C and 37°C.[2]

Interpretation of any changes in IONM signals is complex and should best be performed by a clinical neurophysiologist in close communication with the anaesthetist and surgeon.

Limitations

The variability of documented responses in IONM because of factors such as anaesthesia depth, subcutaneous tissue thickness variation, and electrode placement is a significant obstacle.[71,74] Changes in anaesthesia depth can affect response amplitudes and latencies, potentially confounding the evaluation of the actual neural function. Additionally, surgical manipulation introduces an additional limitation, as mechanical factors such as retraction, pressure, and blood flow modifications can cause transient changes in responses that may or may not indicate persistent neural damage.[79]

IONM also incurs additional expenses in terms of costs related to surgery and anaesthesia.[80] Nevertheless, this allows

the surgical team to prevent an iatrogenic neurological injury or rectify a temporary neurological insult. Interpretation requires expertise, and the possibility of artifact interference necessitates skilled personnel and specialised instruments for accurate monitoring. Furthermore, in the past decade there has been an almost three-fold increase in the utilisation of MEPs in spine surgery, hence its cost may be too high for use in smaller-income areas.[81]

Another limitation is the lack of universally agreed-upon thresholds used for warning criteria indicating that neural function is at risk or compromised. Differences in surgical procedures, patient populations, monitoring modalities, and monitoring systems are associated with differences in signal amplitudes, latencies, and waveforms. This has led to a wide range of warning criteria (for MEPs criteria range from 50% reduction in amplitude to complete loss).[2,82]

Future directions

Although regional practice guidelines[83,84] are available, efforts are still being made by researchers and professional organisations to agree more standardised protocols and criteria for IONM interpretation. Furthermore, efforts to train clinicians in interpreting IONM data should continue and will contribute to improved patient outcomes and widespread adoption of IONM in various surgical settings.

Further work is needed to address current technological and methodological limitations and optimise the technique further. Better electrode designs and signal processing algorithms may, for example, improve the sensitivity and specificity of IONM.

Despite a growing literature, IONM has not yet been proved to improve outcomes.[85] Design of large-scaled randomised controlled trials is made challenging by lack of equipoise and concerns that inclusion of a control group without IONM may be unethical.[86]

Near-infrared spectroscopy

NIRS is a noninvasive technique used to estimate the concentrations of molecules that absorb infrared light.[87] Visible light (wavelength 380–700 nm) penetrates tissues poorly, as it is rapidly reflected, scattered, or absorbed. NIR radiation with a wavelength between 700 and 1100 nm can penetrate myocardial and cerebral tissues and even bone for several centimetres.[88] This enables absorption spectra analysis of the underlying tissues and calculating concentrations of absorbing chromatophores in these tissues. Haemoglobin is a chromatophore the absorption properties of which are altered when it binds oxygen. Oxygenated haemoglobin (O_2Hb) and deoxygenated haemoglobin (HHb) therefore have different absorption spectra. Using different NIR wavelengths, applying the Beer–Lambert Law, and making various assumptions (such as a venous-to-arterial blood volume ratio of 70:30), cerebral NIRS devices can estimate regional cerebral tissue oxyhaemoglobin (ScO_2), deoxyhaemoglobin, and total haemoglobin concentrations.[89]

Clinical use

Jöbsis, who originally described NIRS principles in 1977, proposed its use for cerebral and cardiac oxygenation monitoring.[90] Currently, although no guidelines explicitly state clinical indications for NIRS monitoring, it is generally accepted that cerebral tissue oxygenation should be monitored during aortic arch and paediatric cardiac surgery.[91] It is also advisable to monitor ScO_2 in patients at risk of cerebral ischaemia, such as those undergoing surgery in the beach chair or sitting position, and those with poorly controlled hypertension or carotid artery stenosis.[87]

Clinical interpretation of cerebral NIRS measurements is complicated because different monitors use different techniques (i.e. different emitter and detector technologies, NIR wavelengths, and analytical algorithms), and there are no universally accepted standards.[92] As a result, the absolute ScO_2 levels estimated by different monitors are not directly comparable.[93] Consequently, although ScO_2 values in healthy, conscious subjects are typically plus or minus 70%, the range of values reported is wide (58–82%).[93]

It is common for the interpretation of intraoperative NIRS values to be based on relative changes rather than absolute values, although some studies suggest that absolute ScO_2 values also provide valuable clinical information.[94,95] Commonly used criteria are an absolute ScO_2 <55%, a decline from baseline of >20%, or both. When these criteria are reached, consideration should be given to improving cardiac output (fluids, inotropes, vasopressors), cerebral perfusion (increasing Pa_{CO_2} in case of hypocarbia, increasing arterial blood pressure to above the likely lower limit of autoregulation), and arterial blood oxygen content (increasing FiO_2, blood transfusion in the case of anaemia).

Carotid surgery

During carotid surgery, adequate blood and oxygen delivery to the brain is important to prevent cerebral ischaemia. Compared with other devices used to monitor cerebral ischaemia (e.g. EEG, MEP, SSEP, and TCD), NIRS is presumed to measure cerebral tissue oxygenation directly. However, it has not been proved superior to other modalities in detecting and preventing cerebral ischaemia.[96] Furthermore, the thresholds for identifying ischaemia remain contentious, partially because of lack of standardisation.

Noncardiac surgery

NIRS monitors provide an attractive goal for 'goal-directed therapy' as optimising cerebral oxygenation might decrease the incidence of intraoperative stroke, cognitive decline, and delirium, all associated with increased mortality and morbidity.[97] The evidence for such a benefit is, however, equivocal. A previous review suggested an association between perioperative cerebral tissue desaturation and complication rate suggesting a potential benefit of supports goal-directed therapy.[93] However, other reports[21,98–100] have outlined the uncertainty concerning the clinical benefits of NIRS as a monitoring tool in reducing the incidence of adverse events.

Cardiac surgery

The relatively high incidence of perioperative neurological injury and postoperative neurocognitive dysfunction has led numerous groups to study the effectiveness of NIRS-guided treatment algorithms in reducing the incidence of neurological complications.[101] Even though prolonged perioperative cerebral tissue desaturation has been associated with poor clinical outcomes after cardiac surgery,[102] the effectiveness of

NIRS-guided strategies to minimise these events in improving outcomes remains unproved.[103] Despite the lack of definite evidence, NIRS-guided strategies are increasingly being used because of their low cost and convenience of use.[87]

Limitations

Use of NIRS monitoring in the operating room is limited, possibly because current systems can only assess oxygenation in relatively superficial tissues.[104] When used to assess cerebral oxygenation, light must first pass through extracerebral tissues (scalp, periosteum, skull) and the dura mater. These tissues also contain chromophores that absorb NIR light, thereby interfering with accurate cerebral oxygen saturation measurement.

Another fundamental limitation is that NIRS devices measure volume-weighted mean arterial, capillary, and venous blood saturation in the sampled tissue volume. Most NIRS devices assume a fixed venous-to-arterial (V−A) blood volume ratio of 70:30 or 75:25, thereby ignoring the capillary blood volume (2% of the total). Although this is technically convenient, it is also a limitation. A study has demonstrated considerable variability in the contribution of venous and arterial vessels to tissue saturation between individuals.[105] Furthermore, cerebral V−A blood volume ratio is influenced by pathophysiological conditions (e.g. sepsis and hypovolemia)[106] and patient position (e.g. Beach-chair vs Trendelenburg), further confounding measurements.[107] It is also possible that vasopressor use, which influences sympathetic tone and cardiac output, can influence the V−A ratio. This may partly explain why phenylephrine administration in healthy volunteers causes a decrease in ScO_2.[108,109]

Several other conditions confound NIRS measurements, such as haemoglobinopathies,[110,111] elevated carboxyhaemoglobin,[112] hyperbilirubinemia,[113] intravascular dye,[114] skin pigmentation,[91] subcutaneous haematoma,[115] surgical device noises,[116] excessive ambient light,[115] and hair colour.[117] Furthermore, the absence of standardisation poses a challenge, as there is a lack of consensus regarding the protocols for data acquisition, interpretation, and analysis across different clinical settings. The absence of standardisation may give rise to discrepancies in study outcomes and impede the capacity to compare research findings across various studies or institutions.[118]

Finally, the ability of NIRS-based measurements to accurately assess brain oxygenation is unproved and robust evidence of clinical benefits of cerebral NIRS oximetry is lacking.[119−122] A recent study in an acute ischaemic stroke population undergoing endovascular treatment showed that, regardless of sensor position, NIRS could not detect spatial (interhemispheric) differences in ScO_2 or temporal changes after revascularisation of the ischaemic hemisphere.[123]

Future directions

Industrial, clinical, and academic partners need to agree on standardised protocols, guidelines, and thresholds for data acquisition, interpretation, and analysis of NIRS data in different surgical settings to compare findings across diverse studies and institutions. Further work is also needed to verify and improve the accuracy of NIRS methods for cerebral oxygenation assessment and to better quantify the influence of extracerebral tissues on the measurements with different

monitors. Among others, methods to attenuate errors caused by the abovementioned confounding factors need to be found.[104]

Telemedicine and remote monitoring innovations may allow NIRS data to be transmitted and analysed remotely, enabling experts to provide real-time guidance and support for surgeries in remote locations. Further incorporation of machine learning and artificial intelligence (AI) into the analysis of NIRS data could result in more complex algorithms for real-time data interpretation. AI models may aid in predicting adverse events, detecting subtle changes, and providing surgical teams with actionable insights to optimise patient outcomes.

Transcranial Doppler ultrasonography monitoring

Doppler ultrasonography can measure the velocity of moving bodies by using the Doppler effect or Doppler shift, first described by Christian Doppler in 1842 as an apparent change in the frequency of a wave when the observer moves relative to the source. TCD ultrasonography has been used to determine CBF velocity (CBFV) since the early 1980s. Portable TCD systems contain a probe capable of transmitting and detecting high-frequency sound waves. The detecting sensor on the probe receives reflected signals and analyses their frequencies. Signals reflected from moving red blood cells will have a different frequency than that of the emitted waves, with the difference proportional to the velocity of the red blood cells. The system can also calculate the depth of the signal source from the time gap between pulse emission and reception. When the operator insonates a cerebral artery, the system can calculate the CBFV in that cerebral artery. The mean CBFV is calculated as the integral of the velocity-time curve.

The correlation between CBF and middle cerebral artery (MCA) flow velocity has long been established.[124−126] A fundamental premise of TCD ultrasonography is that the diameter of cerebral arteries is constant, in which case CBFV (mm s^{-1}) is proportional to CBF (ml s^{-1}).[127] Conversely, when diagnosing delayed cerebral ischaemia after subarachnoid haemorrhage, an increase in CBFV is typically interpreted as indicating a decrease in arterial diameter. This interpretation underlies the diagnostic use of the Lindegaard index (the ratio of middle cerebral and internal carotid artery CBFV).

The skull is thinner in four regions, providing acoustic windows (at temporal, suboccipital, orbital, and submandibular) through which the main branches of the circle of Willis can be investigated. Each window offers benefits for examining individual arteries.[128] Although a comprehensive TCD study should include measurements from each window, the temporal window is the most commonly used for intraoperative purposes.

Clinical use

In operating theatres, TCD is most commonly used to monitor CBFV when there is a risk of cerebral ischaemia, such as during CEA.[129] A >90% decline of CBFV is associated with a high risk of stroke,[130,131] and has been used in conjunction with relevant EEG changes as a warning criteria for cerebral ischaemia.

TCD has also become the gold standard for predicting cerebral hyperperfusion syndrome (CHS) after CEA under general anaesthesia.[132] Cerebral hyperperfusion detected 3 min

after carotid de-clamping (defined as a 100% increase in CBFV compared with pre-clamping) is a predictor of CHS, and should prompt consideration of attempts to lower arterial blood pressure; and CBFV measurements at 24 h accurately identify patients unlikely to subsequently develop CHS.[132,133]

TCD is also a sensitive tool for detecting cerebral micro-emboli.[131,134–136] This has prognostic value as microemboli are associated with perioperative stroke or stroke-related mortality.[131] Detection may also help prompt surgical caution particularly during carotid artery[136] or aortic manipulation during cardiac surgery, and may attenuate embolic load and improve outcome.[137]

TCD is used during cardiac surgery to monitor cerebral perfusion and guide titration of cardiopulmonary bypass pump flow, especially during low-flow cardiopulmonary bypass,[138] and during congenital heart defect correction procedures under moderate and severe hypothermia.[139]

Limitations

Like other ultrasound-based modalities, the utility of TCD is operator-dependent, and interpretation complex. Operators should, therefore, be trained, certified, and experienced. Advanced knowledge is required of not only three-dimensional brain anatomy, but also factors that alter TCD measurements.[140] Normal physiological CBFV values vary widely from 35 to 90 cm s^{-1} and are influenced by age, gender, and race, and by intraoperative variables such as arterial blood pressure, haematocrit, and Pa_{CO_2}.[130,141–143]

Adequate fixation can be challenging, but is important as changes in insonation angle influence calculated CBFV. Additionally, certain populations, especially older individuals, sometimes have inadequate bone windows which impedes ultrasound penetration.[140]

Finally, TCD measurements can only provide an overview of the main cerebral arteries and cannot be used to identify small diameter vessel pathology.

Future directions

TCD is increasingly used as a research tool for assessing cerebral autoregulation,[144] and with further validation may enter clinical practice. Combining TCD with other neuromonitoring modalities (e.g. EEG and NIRS) has been proposed[140] to enable a more comprehensive view of cerebral physiology.

Future directions for TCD usage include its potential application in patients with acute ischaemic stroke eligible for endovascular treatment. This includes patient selection for direct transfer to specialised endovascular centres,[145] post-intervention use to guide blood pressure management,[146] and outcome prediction.[147]

As mentioned above, the value of TCD monitoring is operator-dependent. It has been proposed that this can be addressed by the use of fully robotic TCD systems to improve signal acquisition and standardisation.[148]

Conclusions

For the last half-century monitoring the central nervous system during anaesthesia primarily involved clinical observation. During the past few decades, considerable advances have been made. This progress includes the development of raw and processed EEG systems to assess hypnotic and analgesic effects, intraoperative neuromonitoring techniques for assessing the integrity of the central nervous system during operations with a high risk of neuronal injury, NIRS-based systems for evaluation of cerebral oxygenation, and TCD-based assessments of CBFV.

This review describes the underlying principles of these monitoring modalities, clinical use, and limitations. Advances in neuromonitoring have helped provide anaesthetists with a deeper understanding of how the surgical procedure and their anaesthetic management influence CNS function. None of the described modalities are perfect. Better pEEG systems are needed to reliably detect whether patients are conscious, and further research is required to quantify the impact of extra-cranial tissue signal attenuation on NIRS measurements of cerebral oxygenation. More sensitive and specific warning criteria for spinal injury, and cerebral ischaemia are needed, and finally, further research is required to investigate the influence of these monitoring modalities on patient outcomes.

Authors' contributions

Conception and design of study: CR, MMS, ARA
Literature search, review and synthesis: CR, MMS, GD, ARA
Drafting and revision of manuscript: CR, MMS, GD, ARA
Approval of final manuscript: CR, MMS, GD, ARA

Declaration of interest

The authors declare that they have no conflicts of interest.

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