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Editorial

Transcranial cerebral oximetry, transcranial Doppler sonography, and heart rate variability: useful neuromonitoring tools in anaesthesia and intensive care?

Sophisticated software algorithms and miniaturized hardware components have opened new non-invasive vistas to monitor the central nervous system. Electrophysiological modalities (electroencephalography (EEG), evoked potentials) can be used to assess the integrity (or compromise) of neuronal structures at different levels. Spectroscopic methods are used to evaluate oxygen metabolism in the brain and ultrasound techniques can depict cerebral perfusion. Quantifying oscillations of the heart-rate sequence sheds light on the regulatory systems governing complex autonomic feedback loops.

Transcranial cerebral oximetry

Transcranial near infra-red spectroscopy (NIRS) is a fascinating technique that promises to provide information on the balance between oxygen supply and demand in the brain through the intact skull. It can detect situations in which the oxygen status of the brain can change dangerously and where the peripheral systemic haemodynamics and oxygen saturation would not predict the changes.

Transcranial NIRS is a technique based on the Beer-Lambert Law [1,2]. The values obtained with cerebral oximetry depict primarily the oxygen status of the chromophores (haemoglobin-deoxyhaemoglobin) in the venous compartment (75%) [3] and on the intracellular redox state (cytochrome aa3) [4]. NIRS monitoring is used in a number of surgical procedures (e.g., carotid, neuroendovascular, open heart and aortic arch surgery) [5–10]. It is also applied in the critical care setting for detecting cerebral hypoxia in patients with severe brain injury [11–17], aneurysmal subarachnoid haemorrhage [18,19], low cardiac output states, pulmonary and vascular diseases, sepsis and anaemia [20]. Unfortunately the appealing prospect of simply placing a sensor on the forehead and obtaining a numeric readout of the oxygen status of the brain has led to over simplifications and premature expectations that could not be fulfilled. NIRS data have to be interpreted in the context of the underlying pathophysiology. Information is required on systemic arterial pressure, peripheral oxygen saturation, oxygen carrying capacity, body temperature, carbon dioxide, cerebral arterial or venous obstruction, and cerebral seizures. Mistakes by the user (e.g., insufficient light shielding, ineffective probe fixation and incorrect positioning of optodes) affect the results [21]. The problem of NIRS is the hydra-like quality of the technique: NIRS can have remarkably high sensitivity for minimal physiological [22] or pathophysiological [23] shifts and therapeutic effects [21]. By the same token the technique is limited by its reach: the saturation values are representative only of the region directly beneath the sensor and may not be sensitive to changes in other locations. Furthermore, the computational algorithms used in several NIRS devices assume that the infra-red signal exclusively reflects intravascular haemoglobin. Admixture of this signal with that obtained from a stagnant pool of deoxygenated blood can result in values of no clinical significance. The spatial orientation of the optode to the underlying healthy or abnormal anatomical structures is critical [24]. Measurements over regions of infarct or absent brain tissue can produce spurious readings. Metal plates implanted after craniotomy make monitoring impossible and the absence of frontal bone can result in overscale reflected signals.

A further methodological problem with NIRS is the extracerebral contribution to cerebral oximetry. Results from carotid surgery show that the contribution of the extracranial circulation to the measured oxygen values is insignificant [25]. In contrast, changes in scalp oxygenation or in extracerebral perfusion of the head have a significant effect on NIRS readings [26–29]. Numerous studies show a close correlation between changes in cerebral oxygenation assessed with NIRS and other monitoring modalities

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under varying clinical conditions. But correlation does not prove causation, and many studies have not controlled for potential changes in extracerebral attenuation [30].

NIRS has been used in patients with severe head trauma. Successful early identification of intracranial haematomas has been reported [11–16]. However, false-negative results are possible in patients with scalp haematoma, bilateral haematoma, or deep intracranial haematoma [11]. Changes in NIRS readings seem to be sensitive indicators of desaturation events in patients with severe head injury so that this monitoring could be useful to detect intracranial haemodynamic changes. In contrast, some authors question the usefulness of NIRS to detect ischaemic events in patients with head injuries [29,31–35]. Dramatic intracranial volume shifts such as those occurring during transtentorial herniation are not adequately reflected by NIRS in all patients [36]. In a comparison of NIRS and invasive oxygen tension monitoring of cerebral tissue, which is also locally limited, the latter technique provided significantly more valid data [32].

It is difficult to classify and interpret individual data readings provided by NIRS. Values in the range of the normal population have been recorded in brain dead subjects, cadavers after cardiocirculatory arrest and even after removal of the brain at autopsy [33,37]. This means that valid conclusions cannot be drawn from single readings of absolute NIRS values alone. In contrast, continuous monitoring with NIRS can document minimal dynamic changes. Although drops up to 25–30% in cerebral oxygen saturation seem to be associated with reversible neurological dysfunction, at the moment we do not have clinically useful intervention thresholds.

The use of NIRS to provide continuous, real time imaging of tissue oxygenation at the bedside is conceptually very appealing. Cerebral oximeters should be equipped with an indicator of signal quality and strength to distinguish physiological declines from artefacts. In the future, the ability to detect and observe the progress of cerebral events as they occur will require NIRS devices that can accurately measure photon path length [20] and integrate data from multiple detectors [38] into tomographic images. When the technical problems are solved, NIRS devices promise to become valuable tools in monitoring intracranial oxygen saturation in patients at cerebral risk.

Transcranial Doppler sonography

Transcranial Doppler sonography (TCD), introduced in 1982 by Aaslid and colleagues [39], has become one of the most useful non-invasive methods to examine cerebral haemodynamics. If the limitations of the technology are recognized (e.g., lack of a means for fixing the ultrasound probe in position), the information on the cerebral circulation can be used perioperatively and during critical care of patients at risk of cerebral ischaemia [40].

Transcranial Doppler sonography has numerous clinical applications in anaesthesia and critical care. It is used to monitor patients during cardiopulmonary bypass, controlled hypotension and carotid endarterectomy [41–43]. Additional software algorithms and electronic elements (e.g., Hanning window, multirange technique) [44] have improved the validity of TCD for detecting emboli.

The quantification of the degree of vasospasm after subarachnoid haemorrhage is an important application of TCD. Recording cerebral blood flow velocity in critical care patients could provide information for the treatment of patients with meningitis, head injury, or ischaemic–anoxic conditions [41,43].

Transcranial Doppler sonography is also used to document cerebral circulatory arrest [45–47] and has been incorporated into a number of national guidelines for determining brain death. The essential requirements are systolic spikes, oscillating flow or loss of signals in any cerebral artery in patients without ventricular drains or large craniotomy. In patients with severe head injuries it is important to obtain an initial recording as soon as possible so as to then be able to document later changes and especially the loss of signals. For example, loss of signals cannot be documented in patients without a sonographic window for anatomical reasons. Therefore 'neurosonologic silence' has to be interpreted with caution. Furthermore, vessel diameters cannot be assumed to be constant – neither during surgery nor in the critical care setting. Therefore by TCD alone you cannot distinguish between central changes due to increased intracranial pressure and vasoconstriction of whatever aetiology. So the usefulness of TCD depends on the skill and clinical experience of the examiner.

Multidirectional ultrasound probe holders have recently been designed [48,49]. This equipment is suitable for continuous and simultaneous monitoring of extracerebral and intracerebral arteries under conditions such as intensive care or acupuncture research (Fig. 1) [50].

We have also constructed a multifunctional helmet apparatus to hold TCD robotic probes, near infra-red spectroscopy sensors and active electrodes for measuring bioelectric neural activity. This apparatus can simultaneously record a variety of signals over longer periods of time [48,51]. However, the sonic energy emitted from the probes may hypothetically produce local warming of tissue during prolonged monitoring, the relevance of which still has not been clarified in detail.

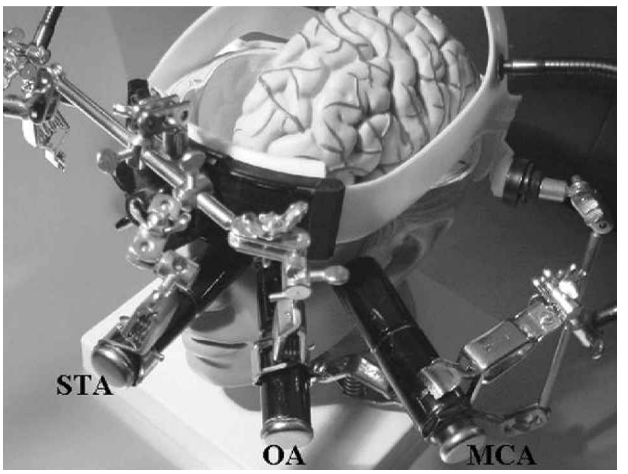

Figure 1.
Multidirectional ultrasound probe holder construction for simultaneous non-invasive monitoring of transcranial Doppler signals in different arteries of the brain (STA: supratrochlear artery; OA: ophthalmic artery; MCA: middle cerebral artery). Supported by the Jubiläumsfonds der Oesterreichischen Nationalbank (Project 8134).

The brain is the most complex organ and we need more knowledge about the interactions of different signals and parameters, especially when normal function is disturbed. It is also necessary to keep in mind that monitoring half a brain (Fig. 1) is not enough [48]. Biomedical engineers, clinicians and manufacturers working in close collaboration should develop and improve technological solutions and prototypes.

Heart rate variability

Heart rate variability (HRV) describes fluctuations in the intervals between heart beats in an ECG. It is distinct from the mean heart rate: two subjects can have the same mean heart rate but very different HRVs. While the raw data are easily obtained from the ECG, complex computerized algorithms are necessary to analyse the ECG recordings. However, a number of different algorithms are in use and these are not standardized. Accordingly, results obtained with different techniques are thus difficult to compare with one another [52].

Heart rate variability is a result of rhythmic and stochastic components. It reflects the complex modulation of the heart rate by the autonomic nervous system and other physiological regulatory mechanisms. HRV reflects the dynamic response to a number of feedback mechanisms which exert an effect on the sinus node via neural, humoral, metabolic and thermoregulatory influences. HRV is mediated primarily via parasympathetic pathways and only to a slight degree by the sympathetic nervous system [53,54]. The structures responsible for regulating HRV are the medullary circulatory centres (nucleus tractus solitarii, nucleus ambiguus) [55]. Peripheral afferents from stretch receptors in the lungs and from the great vessels interact with the central control systems [56]. Modulation occurs by the limbic system up to the neocortex [57,58].

Heart rate variability abnormalities can result from abnormal reflex afferents or efferents, abnormal central modulation between afferent and efferent impulses, central supramedullary influences, central neural transmission, or abnormalities of the receptors, or the heart itself as effector [59].

Heart rate variability can be analysed in a number of different ways: in the time domain, by non-linear and frequency domain methods [60–62]. In the time domain the standard deviation of the duration of the RR intervals of the electrocardiogram (parameter of total variability) or the differences between consecutive RR intervals have been used. This results in a number of differing HRV parameters [61,62].

Three frequency ranges can be distinguished by spectral analysis within the power spectrum. Oscillations at very low frequencies (to approximately 0.05 Hz) are probably regulated via the effects of the renin–angiotensin system, temperature regulation and metabolic processes [53,63]. At low frequencies (about 0.05–0.15 Hz) the regulatory oscillations seem to be mediated by both vagal and sympathetic influences but its relevance to the quantification of sympathetic tone is controversial [64–66]. The regulatory mechanism appears to be the intrinsic rhythm of the neurons of the lower brainstem that govern the cardiovascular system and modifications thereof by the intrinsic vasomotor rhythms and feedback from baroreceptors [57]. The high frequency range of the power spectrum (0.15–0.5 Hz) is generated primarily by central respiratory control systems and by interactions with pulmonary afferents [56,67] and reflects the modulation of parasympathetic influences on the heart.

Assuming that HRV shows complex fractal components [68] and is thus a chaotic system, non-linear methods were developed to characterize them. However, these are not yet established in clinical practice.

In the critical care setting HRV analysis provides valuable information for the detection of myocardial ischaemia and helps predict cardiac problems after acute myocardial infarction. Reduced HRV has been reported to predict an unfavourable course [69]. After heart transplantation the HRV factor, a time domain parameter for quantifying the overall variability, is suppressed because the autonomic pathways are interrupted [70]. HRV is markedly suppressed in all frequency ranges, especially in the low-frequency range.

Very similar HRV patterns with minimal residual variability are seen in brain dead subjects [71], both children [72] and adults [73]. After an initial autonomic storm, HRV is diminished both in the time domain and in spectral analysis [74]. Although a statistically defined limit of the variability coefficient is not exceeded in brain dead subjects, unfortunately variability is also diminished in comatose patients without clinical or electrophysiological features of brain death [71]. Concomitant conditions such as diabetes [75], renal failure [76], myocardial disease [69], alcoholic polyneuropathy [77], age [78] and medications used in the management of patients with severe head injuries (e.g., thiopental, propofol, benzodiazepines) [79] can markedly suppress HRV. Thus HRV has low specificity in the determination of brain death because markedly diminished HRV is not only found in brain death. Conversely, physiological HRV in a patient being suspected for brain death should prompt a careful reassessment.

Narcotic agents reduce the overall variability of HRV [79–82]. This has led to speculation that HRV could be used to monitor the depth of anaesthesia, and particularly to avoid superficial levels of anaesthesia [83]. This idea is supported by the increase in HRV that is seen with surgical stimuli or intubation and at the end of anaesthesia [84–86]. But these results have been interpreted in different ways. HRV is influenced by a number of factors in addition to the depth of anaesthesia. These include preoperative medications [73], concomitant medical conditions, and the positioning of the patient [87]. Also, HRV can be reduced in patients even without premedication immediately before surgery and the induction of anaesthesia (e.g., with propofol) causes a further reduction on total variability and in all components of the spectral analysis [88].

The respiratory rate is another factor that has a considerable effect on the power spectrum of HRV. A respiratory rate which is too low can shift the high frequency components of the power spectrum into the low frequency range so that the two ranges can be nearly impossible to distinguish. Thus, for intraoperative monitoring of ventilated patients, the respiratory rate setting should be noted [60].

A problem is that there is little consensus on which analytic process is the most appropriate. Because there is no standardization, the results reported by different groups cannot really be compared. There are no normal values for the whole perioperative period. The accuracy of measurements of the RR interval is inconsistent. The acquisition frequency measurement of the RR intervals which should be as high as possible is not uniform. The methods by which R waves are detected and artefacts eliminated and how data are interpolated are also inconsistent [64]. In the future better data acquisition and analysis should provide a methodological basis for validated data. Expansion of the analysis spectrum such as approximative entropy, which as in the EEG is a measure of the regularity of the oscillations, may be a further step toward making HRV more meaningful [89]. Standardized methods and large randomized studies will be needed to evaluate the role of HRV in the perioperative phase of anaesthesia care.

In conclusion, transcranial cerebral oximetry can be expected to provide important insights into the non-invasive evaluation of cerebral oxygen metabolism. Transcranial Doppler sonography is already an established technique for specific issues and assessing HRV may complement established techniques.

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