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Review

Clinical applications of cerebral function monitoring in neonates

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SUMMARY

The cerebral function monitor is a device for trend monitoring of changes in the amplitude of the electroencephalogram, typically recorded from one or two pairs of electrodes. Initially developed and introduced to monitor cerebral activity in encephalopathic adult patients or during anaesthesia, it is now most widely used in newborns to assess the severity of encephalopathy and for determining prognosis. The duration and severity of abnormalities of the amplitude-integrated electroencephalogram tracing is highly predictive of subsequent neurologic outcome following neonatal hypoxic–ischemic encephalopathy, including in newborns receiving neuroprotective treatment with prolonged moderate hypothermia. The cerebral function monitor is also used for seizure detection and to monitor response to anticonvulsant therapies. Amplitude-integrated electroencephalography compares well with standard electroencephalography when used to assess the severity of neonatal encephalopathy, but a standard electroencephalogram is still required to provide important information about changes in frequency, and in the synchrony and distribution and other characteristics of cerebral cortical activity. The role of the amplitude-integrated electroencephalogram to identify brain injury in preterm infants remains to be determined.

1. Introduction

The cerebral function monitor (CFM) was invented more than 40 years ago at the London Hospital, UK, by Douglas Maynard and was first applied clinically by Pamela Prior [1–3]. It was designed as a method for the continuous recording of cerebral electrical activity in adult patients with severe encephalopathy, in most cases following cardiac arrest. The intention was to design a simple device that allowed bedside continuous electroencephalographic (EEG) monitoring in an intensive care unit environment to detect changes between intermittent standard EEG recordings. The device proved invaluable for detecting seizures and deterioration in cerebral activity in unconscious patients, and to monitor response to therapy and the depth of anaesthesia [3–6]. The original CFM recorded (on heat-sensitive paper) the change in amplitude of the EEG – usually called the amplitude-integrated EEG (aEEG), measured in microvolts (μV) – and the impedance between the recording electrodes.

A few years after its invention, following a visit to the London unit, Ingmar Rosen and Nils Svenningsen introduced the CFM to the neonatal nursery in Lund, Sweden, to monitor brain function in sick neonates [7]. Subsequently, other clinical studies defined the characteristic abnormalities of the aEEG in term infants with hypoxic–ischaemic encephalopathy (HIE) and described its prognostic accuracy for neurodevelopmental outcome following HIE [7–12]. Later it was suggested that the CFM could be used as a tool for the selection of infants for trials of neuroprotective therapies [13]. Following the pilot study, an abnormal aEEG was used as a selection criterion in three randomized clinical trials of moderate hypothermia in infants with HIE [14–16]. The success of these trials stimulated the development and production of new digital CFM devices, and now the CFM is increasingly routinely used in neonatal intensive care units as part of standard monitoring of infants with HIE [17].

The CFM has also been used in preterm infants to detect complications such as intraventricular hemorrhage and for prognostication [18,19]. The characteristic changes in the amplitude of the aEEG tracing that occur with increasing maturity, analogous to developmental changes in continuity observed on standard EEG, have been defined [20,21]. Delay in the normal developmental changes in aEEG pattern and continuity during the first few weeks after birth may correlate with subsequent neurodevelopmental outcome.

Modern CFM devices, in addition to the aEEG, also display the unprocessed (raw) EEG signal, and some devices can display other

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EEG parameters such as the power, intensity, and spectral edge frequency of the signal. Algorithms for automated seizure detection have also been developed. In this article, CFM refers to the device and aEEG to the tracing displayed by the CFM.

2. Technology

The design of the original device has been described by Maynard [2] and is summarized in Fig. 1. The unique features of the device are a special wideband filter, which weights the EEG spectrum to counteract the normal tendency of slow components to be of larger amplitude; logarithmic compression and envelope detection; and a display that continually moves between minimum and maximum peak-to-peak amplitudes of the filtered EEG.

The frequency response of the CFM is shown in Fig. 2. The filter is designed to reject most activity <2 cycles per second so as to eliminate low-frequency fluctuations caused by movement. There is a sharp cut-off >15 cycles per second with a particularly strong rejection at 50 cycles per second to reduce muscle potential and mains interference.

After filtering, the signal is passed through a semi-logarithmic amplitude compression process to accommodate the large fluctuations of the level of EEG and to circumvent the need for gain adjustment. After peak-to-peak rectification (so that the signal is in a positive direction), the output is effectively a smooth line drawn through the peaks of the compressed signal. As cerebral activity fluctuates, the signal moves up and down, and as this is displayed at a slow speed (typically 6 cm/h), the tracing appears as a wide band. In the original device, the display was written on a recorder with heat-sensitive paper, but current systems use an LCD display.

CFM devices also incorporate an impedance monitoring system. This is used to record the state of conductivity of electrodes and to indicate the occurrence of artifacts. In the original device, the method employed to monitor impedance was based on the change in phase of a high-frequency signal injected across the electrodes after that signal was extracted from the EEG.

Several CFM devices are now available. The cerebral function analyzing monitor (CFAM) was also designed by Maynard (RDM consultants, Uckfield, UK). The latest version, the CFAM4, has four channels and can display in a CFM or CFAM format, which shows the $\log_{10}$-weighted mean amplitude distribution in μV plus 10th and 90th centiles and maximum and minimum excursions in 2 s epochs. The Brainz (BRM3) is a two-channel CFM monitor with additional trend and seizure detection capabilities (Natus Medical Inc., Pleasanton, CA, USA). The Olympic Brainz monitor (Natus Medical Inc.), is a single channel CFM that aims to replicate the characteristics of the original CFM device but with the capability to display the standard EEG. Some EEG devices such as the NicoletOne (Natus Medical, Inc.) can record a full standard multichannel EEG with the option to display the CFM. By combining this with video recording, a comprehensive video EEG and trend CFM monitoring is possible at the bedside. It is not clear whether all these devices use the same filtering and EEG processing parameters as the original CFM device; the CFAM4 and Olympic CFM claim to use identical parameters as the original CFM, but this information about the other devices is lacking.

Conventional silver–silver EEG electrodes, with screened coaxial cable leads to minimize artifact from movement or from adjacent leads and equipment, were provided with the original CFM device. The electrodes were applied to the scalp with Collodion adhesive gel (SLE, Croydon, UK) and were injected with electrode contact gel. The newer devices tend to use disposable self-adhesive and pre-gelled or needle electrodes. Skin preparation with a skin abrasive paste such as Nuprep (Bio-Medical Instruments, Warren, MI, USA) is required with the adhesive electrodes and these electrodes need to be replaced or re-injected with conducting gel after 24–48 h. The needle electrodes are quick and easy to use, can be securely attached with a smear of Collodion adhesive gel over the plastic hub of the electrode and the scalp, and function well for several days. The aEEG tracing obtained with either type of electrode seems to be identical.

3. Classification of the aEEG

The standard CFM display consists of the minimum and maximum peak-to-peak variability of the amplitude of the filtered EEG (aEEG) and appears as a band of activity moving slowly across the display screen. The lower edge of the band indicates the lowest peak-to-peak amplitude reached by the filtered EEG over a period of time, whereas the upper edge is related to the highest levels. The width of the band indicates the variability of the EEG amplitude. In normal neonates the band fluctuates approximately between 10

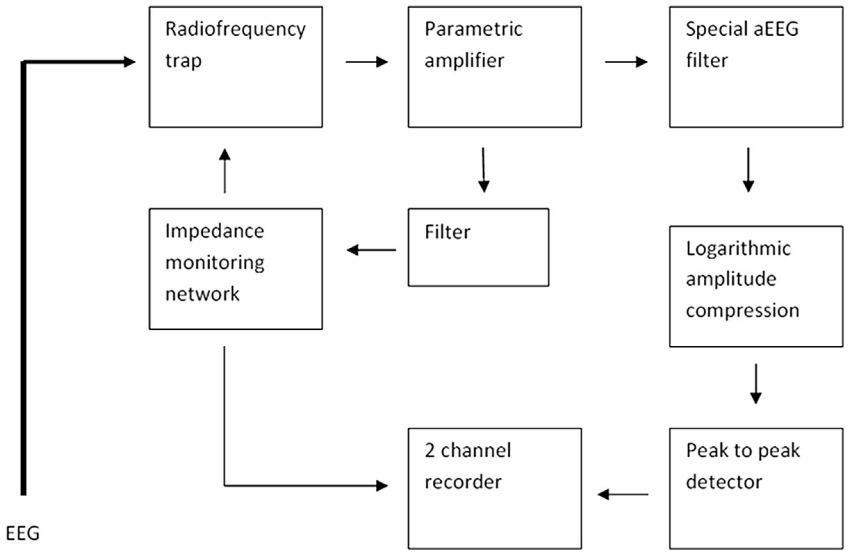

Fig. 1. Summary of the design of the cerebral function monitor. aEEG, amplitude-integrated electroencephalography.