Due to the remarkable developments in neonatal and perinatal care, a rapidly increasing number of neurologically challenged babies are now surviving. Recent studies have revealed that even more than 30% of these babies (birth asphyxia, intracerebral bleeding, brain infections) experience very frequent seizures, and importantly, a vast majority of these seizures have no clear clinical signs (Hellström-Westas et al., 1985; Boylan et al., 2004; Rennie and Boylan, 2007). The “subclinical” presentation of seizures will often lead to their ignorance, despite their potential adverse effects on the neurological development (Rennie and Boylan, 2007; Lombroso, 2007). It has become clear that neonatal seizures can only be diagnosed by using ictal EEG recordings (preferably with a video), and that an optimal diagnosis and antiepileptic treatment do require a possibility to perform (video)EEG-recordings over extended periods of time in the neonatal intensive care unit (see Clancy, 2006; Hellström-Westas et al., 1985; Boylan et al., 2002, 2004; Murray et al., 2006).

Neurophysiologists in most places have refrained themselves from performing longer EEG studies in neonatal units. The neonatologists have hence adopted an independent practice of performing simplified, one-channel EEG recordings, which is most often visualized by using a trend paradigm called aEEG or CFM (amplitude integrated EEG or cerebral function monitor, respectively; Hellstrom-Westas and Rosen, 2006). aEEG/CFM signal is typically recorded from a centro-parietal derivation (e.g. P3–P4), and the interpretation is based on a trend display that shows heavily time-compressed (3–6 h/display) signal after it has been strongly filtered (mostly 8–13 Hz) and plotted on a semi-logarithmic scale to emphasize the low amplitudes. Since many seizures in babies show a change at this frequency range, such technique has been very fruitful for the accumulation of data that pertains to various clinical aspects of neonatal seizures. In addition to seizure detection, aEEG/CFM paradigm has been especially successful in the early detection of severe disturbances in the background activity, such as inactive or burst suppression traces (Hellstrom-Westas and Rosen, 2006).

However, the shortage of technical and/or neurophysiological expertise available in neonatal units has led to a situation where aEEG/CFM might easily change from a mere monitoring aid to a gold standard in neonatal seizure identification. This change in practice is understandable from the standpoint that, in most places, a single-channel aEEG/CFM is the only available option for brain monitoring. When aEEG/CFM methodology was implemented into neonatal use, the pioneering authors (Profs Rosen, Hellström-Westas, and their collaborators) performed elegant studies to compare aEEG/CFM and conventional EEG. Those studies were mostly pragmatic, with the primary aim to demonstrate the clinical utility of aEEG/CFM recordings. While it is now well established that aEEG/CFM can show many seizures, it is often less appreciated that seizures may also go unnoticed with aEEG/CFM. In other words, clinicians may forget that absence of proof (of seizures in the aEEG/CFM) is not a proof of absence!

There are only few studies that have put the question the other way around, and assessed the loss of information with a reduced channel number (see e.g. Rennie et al., 2004). The paper by Shellhaas and Clancy (2007) re-opens this important question. Any visual, let alone automated, identification of seizures is possible only if the relevant aspects of seizure activity are recorded in the first place. It is a common experience among consulting EEGers, that it may be very tricky or impossible to judge seizures from a single channel recording (raw signal display in the aEEG/CFM machine). Difficulties in the interpretation may be either because seizure focus is not exactly under the recording electrode, or because neonatal seizures may present with so varying waveforms. The spatial information obtained from a conventional EEG (the gold standard) is currently considered to permit proper seizure identification. This has prompted the leading aEEG/CFM authors to always request conventional EEGs for diagnostic confirmation of neonatal seizures (Hellstrom-Westas and Rosen, 2006).

In this paper, Shellhaas and Clancy studied a large (n = 125) dataset of neonatal EEG recordings with a very
high number (n = 851) of seizures. They quantified the proportions of seizure onsets in each brain area. Their main target was to assess how often the seizure activity was seen in a single derivation (C3–C4) when the investigator could use the visual aid from the other EEG curves. In addition, they evaluated how much of the total “seizure burden” was noticed in the C3–C4 derivation. Shellhaas and Clancy show here that, at the population level, seizure onsets have a preferential distribution over the central and temporal areas, and that C3–C4 derivation exhibits electrographic discharges in majority of these seizures.

What are the contributions of this paper to the literature? Prior studies have shown that neonatal seizures are often spatially limited, that they often arise in the central and temporal areas (e.g. Bye and Flanagan, 1995), and that neonatal EEG has a much higher spatial resolution than adult EEG (i.e. signals do not spread so much by volume conduction; see Grieve et al., 2003; Fifer et al., 2006). Thus, both the common feelings and prior papers would support the basic notion that one channel sees less than many channels. As the neonatal brain monitoring is more and more often becoming a single-channel practice by neonatologists (see above), it is especially important that the attention of EEGers is focused on the potential caveats by presenting formal and systematical studies of this kind. The paper by Shellhaas and Clancy presents some aspects that merit special attention:

First, brain monitoring takes place at individual level. While many seizures in most patients might be seen in a single channel, the other side of the coin is that there may be many individuals whose seizures are completely ignored by the single channel. Hence the loss of seizure information at individual level may be complete or near-complete (i.e. not only a relative underestimation of seizure burden). The study of Shellhaas and Clancy shows that almost one-fifth (19%) of seizures initiated in frontal and occipital areas, and less than half (42–46%) of these were anyhow reflected in the C3–C4 derivation. This suggests indirectly that it may not be rare to have babies whose seizures are not seen at all in a single derivation. More alarmingly, over half (10 out of 17) of the status epilepticus cases were missed in this study when looking at one single channel only. More future studies are urgently needed to show how often the seizures are fully ignored and/or how much the seizure burden is underestimated when using a single channel recording. It is notable here that such studies are possible only by performing first a full array EEG recording (like Shellhaas and Clancy) from which the information (i.e. channels) can be reduced to mimic a single channel recording.

Second, Shellhaas and Clancy assessed the performance of C3–C4 derivation after seizure was first recognized in the full EEG montage. As C3–C4 reading was not blinded, it is possible that their C3–C4 detection rate (they call it “theoretical ceiling on sensitivity”) was significantly higher than what it would be in real single channel recordings. Further studies are needed to perform a blinded analysis from a dataset of this kind. A recent study with a little different setting (Rennie et al., 2004) suggested that the practical sensitivity of seizure identification from aEEG/CFM paradigm may be alarmingly much smaller.

Third, mere visual identification of seizure activity (with or without aid from other channels) does not yet prove that seizures could be picked up by aEEG/CFM paradigm or by any other automated EEG analysis tool. Seizure detection does always rely on specific features in the EEG waveform. For instance, aEEG/CFM paradigm does request that seizures contain an abruptly increased amount of power at a relatively narrow frequency bandwidth, which by default ignores seizures characterized by slow frequency oscillations only.

In conclusion, the present study and several other papers have shown that neonatal seizures are variable, both between and within individuals. Some babies will have all that is needed from the established aEEG/CFM paradigm, but there are babies whose seizures are either neglected or significantly underestimated with the fixed, single-channel monitoring paradigms. It is possible that some of those babies can be successfully monitored by modifying the single-channel electrode placements after knowing the seizure distribution in the given baby. The intra-individual variability of electrographic seizures, however, may present a challenge to such tailoring of recordings. In general, if the monitoring tools (e.g. aEEG/CFM) are allowed to shape our studies, there is a possibility that our view into neonatal seizures becomes biased by the detection tool. Shellhaas and Clancy have shown here an example of a rational approach to seizure detection: Only a good understanding about the phenomenon (neonatal seizure) itself can allow one to decide what tools it may take to properly see it.

References


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