Chapter 12
Monitoring Brain Development in Preterm Infants:
The Value of Automated Analysis of the Electroencephalogram (EEG)

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ABSTRACT

As neurocognitive deficits a still common in preterm infants and the exact etiology of these problems is not elucidated, investigation of preterm brain development is warranted. Electroencephalography (EEG) can provide important information about brain development, although it is hard and time consuming to interpret for neonatologists. Automated EEG analysis can overcome these problems, making brain monitoring more feasible in the neonatal intensive care unit. This chapter discusses different aspects of EEG maturation which are suitable for automated analysis: 1. changes in continuity and 2. changes in frequency. The most important pitfalls for automated EEG analysis are the complex validation process, the lack of a good gold standard, and EEG artifacts. However, when these limitations are addressed, automated EEG analysis can be the cornerstone for a brain monitor, which helps in evaluating premature brain development, in identifying factors which endanger or interfere with normal brain development and in evaluating neuroprotective strategies.

INTRODUCTION

Advances in the care for preterm infants have led to an increased survival. However, a large number of these infants still experience neurological deficits later in life, even in the absence of neurosonographic abnormalities (Bayless & Stevenson, 2007; Cooke, 2006; Larroque et al., 2008). The exact etiology of these neurodevelopmental deficits remains to be clarified, but it is suggested that different medical, environmental and iatrogenic conditions may interfere with the development of the vulnerable preterm brain

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(Gressens, Rogido, Paindaveine, & Sola, 2002; Perlman, 2002; Volpe, 2009).

Therefore, the monitoring of brain development in preterm infants during their stay at the Neonatal Intensive Care Unit may be valuable in detecting conditions which interfere with brain development and in the development of therapeutic strategies directed to protect preterm brain development. The conventional electroencephalogram (EEG) may be regarded as the gold standard in the assessment of cerebral function. EEG patterns of preterm infants change with postmenstrual age (PMA) and have been extensively studied.

EEG patterns which run behind actual PMA are called dysmature (Lombroso, 1985) Dysmature EEG patterns have been related to adverse outcome later in life (Tharp, Scher, & Clancy, 1989). Hayakawa et al. have made a distinction between "disorganized" patterns, following an acute brain insult, related to white matter injury and motor outcome and "dysmature" patterns, reflecting deviations in neuro-development, related to grey matter injury and cognitive outcome (Hayakawa, Okumura, Kato, Kuno, & Watanabe, 1997a, 1997b; Okumura, Hayakawa, Kato, Kuno, & Watanabe, 2002; Watanabe, Hayakawa, & Okumura, 1999).

Although this distinction of EEG abnormalities is rather resolute and arbitrary, it emphasizes the importance of studying EEG maturation.

However, most studies on EEG maturation were performed in the "pre-digital" era and made use of qualitative visual inspection by EEG experts. This process is very time consuming and may lead to inter-observer variability. The modern digital EEG recorders provide the opportunity to analyze the EEG by automated quantification. In fact, automated EEG quantification techniques are used by anesthesiologists to monitor brain activity in sedated patients. Besides, automated EEG analysis is already often performed in healthy and asphyxiated full term infants (Korotchikova, Stevenson, Walsh, Murray, & Boylan, 2011; Larroque et al., 2008; Lofhede et al., 2008, 2010). In order to monitor neurophysiologic maturation by more objective and uniform means and make the EEG more accessible to neonatologists, automated quantitative EEG analysis of preterm infants may be of value. In this chapter we review the aspects of the preterm EEG maturation which are or may be used for automated analysis. Furthermore, we discuss the most important pitfalls and limitations of automated EEG analysis of preterm infants and give future research directions. This chapter focuses on quantitative analysis of EEG maturation in preterm infants. However, the EEG is generally used for the detection of seizures. This will be discussed in another chapter of this book.

QUANTITATIVE ANALYSIS OF EEG MATURATION

1. Changes in Continuity

An important aspect of EEG maturation is the development in EEG background activity. In infants with PMA < 34 weeks the EEG consists of mainly two background patterns. First, the trace discontinue in which bursts of EEG activity are alternated with tracing of low or no EEG activity (named inter burst interval, or IBI) Second, trace continue comprising continuous EEG activity without marked frequency or voltage changes in time and space (Anderson, Torres, & Faoro, 1985; Andre et al., 2010; Selton, Andre, & Hascoet, 2000) (Figure 1)

With advancing PMA, the preterm EEG shows more continuous pattern. EEG discontinuity has been investigated in various ways.

Originally, the percentage of discontinuous tracings has been assessed by visual recognition of EEG experts. With increasing PMA, lower percentages of discontinuous tracings were found (Connell, Oozeer, & Dubowitz, 1987; Goto, Wakayama, Sonoda, & Ogawa, 1992; Van Sweden et al., 1991).