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Characteristics of sleep EEG power spectra in healthy infants in the first two years of life

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ABSTRACT

Objective: This study characterises and describes the maturational evolution of the healthy infant sleep electroencephalogram (EEG) longitudinally from 2 weeks to 24 months of age, by means of power spectral analysis.
Methods: A prospective cohort of 34 healthy infants underwent overnight polysomnography (PSG) at 2 weeks, and at 3, 6, 12 and 24 months of age. Sleep epochs were scored as Active Sleep (AS) and Quiet Sleep (QS) at 2 weeks of age and as Rapid Eye Movement (REM) and Non-REM (NREM) stages from 3 months onwards. Representative epochs were used to generate the EEG power spectra, from the central C3 derivation. These were analysed visually and quantitatively in AS/REM and QS/NREM sleep in the following bandwidths: delta (0.5–4 Hz); theta (4–8 Hz); alpha (8–11 Hz); sigma (11–15 Hz) and 0.5–25 Hz.
Results: Sleep EEG (central derivation) power spectra changed significantly in the different bandwidths as the infants matured. The emergence of a peak in the sigma bandwidth in NREM N2 sleep corresponded with the development of sleep spindles. Maturational changes were also seen in NREM N3 and in theta and alpha bandwidths in both AS/REM and QS/NREM.
Conclusions: Sleep EEG power spectra characteristics in healthy infants evolve in keeping with maturation and neurodevelopmental milestones.
Significance: This study provides an atlas of healthy infant sleep EEG in the early years of life, providing a basis for association with other neurodevelopmental measures and a normative dataset on which disease may be discriminated.

1. Introduction

It is generally believed that sleep plays an important role in brain development in early life. Roffwarg et al. (1966) found abundant Rapid Eye Movement (REM) sleep in infancy and proposed that information processing occurs during sleep, thus facilitating brain maturation in infants. In animal models, it has been found that REM sleep deprivation affects the development of the feline visual system (Marks et al., 1995). Subsequently, further evidence has shown that learned activities are rehearsed during sleep. The timing and structure of activity elicited by the playback of song during sleep was found to match activity during daytime singing in zebra finches, suggesting that sleep is important for consolidation of neuronal temporal codes for spatial memory (Dave and Margoliash, 2000).

Electroencephalogram (EEG) is a non-invasive indicator of regional brain activity and maturation in infants (Hrachovy et al., 1990; Lombroso, 1989; Stockard-Pope et al., 1992). Structural changes such as dendritic arborisation (Speckmann and Elger, 2005), myelination (Niedermeyer, 2005) and synaptogenesis (Marosi et al., 1992) are associated with changes on EEG. There are known correlates between disease states and EEG, such as the link between periventricular leukomalacia in infants and delayed maturation of EEG cerebral processes (Blumenthal, 2004).

The analysis of infant sleep EEG obtained during polysomnography (PSG) may therefore have the potential to provide information relevant to brain maturation (Scher, 1997). The analysis of sleep EEG in infants has generally been limited to a qualitative time-domain focus on sleep stage description, looking at quality of sleep, relative percentages and organization of sleep states and sleep

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cycles (Anders and Keener, 1985; Bes et al., 1991; Coons and Guilleminault, 1982; Hoppenbrouwers et al., 1982; Louis et al., 1997; Navelet et al., 1982; Roffwarg et al., 1966). However, quantitative analysis of sleep EEG can be achieved by transforming the EEG signal into the frequency domain. The power spectrum consequently produced permits robust comparison of EEG characteristic across long data samples (>8 h), across multiple bandwidths, across age and between individual subjects (Sterman et al., 1977). Consequently, power spectra analysis of sleep EEG is a powerful tool to chart the sleep maturation of normal infants and establish a basis for normative EEG power spectra in sleeping infants.

To date, the description of sleep EEG power spectra of infants has been fragmented and visually qualitative. In addition, studies have been limited to small sample sizes (Jenni et al., 2003; Parmelee, 1969; Schulte and Bell, 1973), cross-sectional design (Samson-Dollfus et al., 1983; Schulte and Bell, 1973), duration less than the full first year of life (Jenni et al., 2003; Parmelee, 1969; Samson-Dollfus et al., 1983; Schechtman et al., 1994; Scher et al., 1994), analysis of specific sleep stages or specific bandwidths (Schechtman et al., 1994; Sterman et al., 1977), and provision of either graphical (Jenni et al., 2003; Schulte and Bell, 1973) or quantitative (Samson-Dollfus et al., 1983) description of sleep EEG power spectra. For example, the appearance of sleep spindles in infants corresponds with a noticeable peak in the QS/NREM N2 power spectra in the sigma (11–15 Hz) bandwidth (Jenni et al., 2003). However, maturational changes in the sigma bandwidth have not been previously quantified.

The aims of this study were to characterise the maturation of sleep EEG power spectra in healthy infants, both graphically and quantitatively, and to expand on previous work by studying a larger prospective cohort from 2 weeks to 2 years. In addition, this study aimed to provide novel normative information on differentiated NREM sleep stages in infancy, using the new America Academy of Sleep Medicine (AASM) recommendations for paediatric sleep scoring (Iber et al., 2007).

2. Methods

2.1. Subjects

Thirty-four infants (16 females and 18 males) were enrolled following an uncomplicated delivery at term (gestation 38–42 weeks); with normal birth weight 10th to 90th percentile (Kuczmarski et al., 2000); and Apgar score; if they had caucasian parents and were from a non-smoking household. Infants were excluded if there was a history of Sudden Infant Death Syndrome (SIDS) in a sibling. Written consent was obtained from the parents. The project was conducted under the approval of the Mater Health Services Human Research Ethics Committee (Number 952C). This study was conducted from March 2006 to January 2009.

2.2. Study procedures

Full overnight PSG was performed within the Queensland Paediatric Sleep and Chronic Respiratory Failure Service in the Mater Children's Hospital. Other measures studied, but not reported here, were actigraphy and electrical impedance tomography. PSG was performed at 5–20 days old, 3, 6, 12 and 24 months of age. Studies were rescheduled to at least 2 weeks after clinical resolution of viral respiratory tract illness.

Sleep studies were carried out between 4 pm and 8 am. As part of the full computerised PSG (Embla N7000 system, EMBLA, 2009), the following were recorded: electroencephalogram (EEG), submental electromyogram (EMG), electro-oculogram (EOG), electrocardiogram (ECG), un-calibrated respiratory inductance plethsmography (RIP), arterial oxygen saturation by pulse oximetry (SpO_2), transcutaneous CO_2 and nasal airflow, with digital video recording. EEG electrodes were placed in the C3, C4, A1, A2, O1 and O2 positions.

2.3. Sleep stage scoring

The first study (at 2 weeks old) was scored according to Anders et al. (1971). For subjects aged 3 months and over, sleep staging was performed according to the AASM manual for Scoring Sleep (Iber et al., 2007) as recommended by Grigg-Damberger et al. (2007). The AASM manual was published midway through the data collection period, and studies conducted prior to this on infants aged 3 months and over were re-scored from the then contemporary standards of Rechtschaffen and Kales (1968). Following an initial training period within the QPSS for the new AASM paediatric guidelines, a single trained experienced scorer undertook the AASM scoring. Somnologica Version 3.3.2 Build 1559 (Somnologica, 2009) software was used to store and score the PSG signals.

2.4. Spectral analysis of EEG

The C3A2 channel was selected for the spectral analysis, with C4A1 as backup in the event of signal failure (although this did not eventuate), to optimise detection of spindles and central phenomena. Three 5 min (10 epochs) segments of both AS and QS were selected from the sleep study at 2 weeks of age for spectral analysis. For subsequent sleep studies, three 5 min (10 epochs) segments were selected from each of REM, NREM N2 and NREM N3 for spectral analysis. The EEG signals were exported in raw format. Stage NREM N1 and N were not analysed as there were less than 20 epochs present in each sleep study.

Segments were selected to optimise representation of sleep stage and minimise signal noise and artefact. The segments were selected manually at the beginning and end of the study, and also mid study by reviewing the hyponogram of each infant. This ensured representation of sleep over the night. The segments selected were always more than two complete sleep cycles apart (a sleep cycle being defined as a sustained period of QS/NREM sleep followed by a period of AS/REM sleep). Segments selected were free of artefacts, motion or other noise. Segments were sampled at least 2 min into a stable sleep stage, to avoid sleep stage transition epochs.

The duration of segments selected was determined to optimise resolution and minimise noise for Fast Fourier Transformation (FFT) analysis. Thus, even 5 min of EEG data at 200 Hz provides 60,000 data points for FFT analysis, with adequate frequency resolution. The desire to accurately encapsulate a given sleep state is a compromise between a shorter sample better representing the sleep state and a longer period consisting of more samples, which in turn, increases the ultimate resolution of the calculated power spectrum. Therefore, 15 min of each sleep state is a relatively long period for this analysis technique, with further increases in duration acting to increase noise, with minimal increase in resolution.

The EEG data was digitised at 200 Hz and digitally filtered using a highpass butterworth filter at 0.3 Hz and a lowpass Bessel filter at 70 Hz. Fast Fourier Transformation (FFT) with a averaged overlapping ten second (2000 data points) Hamming window was computed resulting in a frequency resolution of 0.1 Hz. Frequencies below 0.5 Hz were not used for analysis because of their sensitivity to artefacts. Matlab Signal Processing Toolbox V6.11 (MATLAB, 2009a) was used to compute the FFT. Spectral data were analysed between 0.5 and 25 Hz.

The absolute mean power spectra of selected frequency range were calculated by binning each AS/QS and REM/NREM episode into four frequency intervals. The intervals are defined as delta

(0.5–3.9 Hz), theta (4–7.9 Hz), alpha (8–10.9 Hz), sigma (11–14.9 Hz) and 15–25 Hz bandwidth (Grigg-Damberger et al., 2007).

Integral Mean Power Spectra (IMPS) was calculated for each interval for each infant and averaged across subjects. IMPS is defined as the area between the EEG power spectra (*y*-axis) and the frequency axis (*x*-axis). IMPS = $\int_a^b f(x)\ \ dx$ where *a* is the lower frequency limit, *b* is the higher frequency limit, *f(x)* is the EEG power spectra function and *x* the frequency. The log of IMPS calculated was used to statistically analyse the changes across the age. The log IMPS of the infants was not normally distributed, with severe skewness ($-0.2 <$ skewness > 0.2). Thus, Wilcoxon signed rank test, rather than *t*-test, was used to test the IMPS changes between the different ages for the delta, theta, alpha, sigma and 15–25 Hz bandwidth. Matlab Statistical Toolbox V7.1 (MATLAB, 2009a) was used for all statistical analysis.

3. Results

3.1. Recording quality and duration

The PSG parameters for the infants are summarised in Table 1, including the number of infants completing each study. There were a number of withdrawals, which were accounted for in recruitment numbers and were expected, due to the logistic difficulty for families of undertaking an overnight study in infancy.

3.2. Sleep stage and cycle variables derived from visual scoring

The mean values for the visually scored sleep variable are shown in Table 1. As expected, the duration of AS/REM (both mean and percentage of TST) decreased with maturation, while QS/NREM percentage of TST increased from 2 week until 24 months. Sleep spindles were identified in all the infants at 3 months of age during sleep stage NREM N2.

3.3. EEG power spectra of AS/REM and QS/NREM

3.3.1. AS/REM sleep stage

At 12 and 24 months of age, a small peak with decreasing power is observed in the EEG power spectra of REM sleep in the delta bandwidth (Fig. 1a). There are also significant changes ($p < 0.05$) in the log IMPS of the AS/REM theta and alpha bandwidths from 2 weeks to 12 months of age (Fig. 1b). The IMPS of the REM sigma bandwidth changes significantly ($p < 0.05$) from 3 to 24 months, while delta and alpha bandwidth changed significantly ($p < 0.01$) from 12 to 24 months.

3.3.2. QS/NREM N2 sleep stage

At 3 months of age, a peak emerged in the NREM N2 sigma bandwidth (as seen in Fig. 2a). This was at 12.9 Hz ($\mu V^2 = 1.65$) with a Width at Half Height (WHH) of 1.7 Hz. At 6 months, the peak was at 13.3 Hz with a lower power ($\mu V^2 = 1.16$) and WHH of 2 Hz. At 12 months the peak was at 13 Hz ($\mu V^2 = 0.64$) with WHH of 2 Hz and a second peak with decreasing power was noted the theta bandwidth. From 3 to 12 months of age, the peak in the sigma bandwidth became flatter (denoted with decreasing WHH). By 24 months, the peak in sigma had moved from the mid region of the sigma bandwidth to 11.4 Hz ($\mu V^2 = 1.01$). A peak in the theta bandwidth emerged at 24 months at 5 Hz ($\mu V^2 = 13.01$). However, as noted in Fig. 2b, the IMPS of the infants only changed significantly ($p < 0.01$) from 2 weeks (QS) to 3 months (NREM N2). There were no further changes in the IMPS of NREM N2 sleep in the sigma bandwidth after 3 months. The IMPS of all bandwidths in QS/NREM N2 significantly changed ($p < 0.01$) from 2 weeks to 3 months (Fig. 2b). From 3 to 24 months, only the IMPS of the theta and alpha bandwidths changed significantly in NREM N2 ($p < 0.01$).

3.3.3. QS/NREM N3 sleep stage

At 3 months of age, in QS/NREM N3 (Fig. 3a), a peak emerged in the sigma bandwidth at 12.6 Hz ($\mu V^2 = 1.16$) with a WHH of 1.6 Hz. At 6 months, the peak in the sigma bandwidth was at 12.8 Hz ($\mu V^2 = 1.26$) with a WHH of 1.7 Hz and at 12 months at 13.3 Hz ($\mu V^2 = 0.94$) with a WHH of 1.8 Hz. The peak in the sigma bandwidth in N3 underwent similar changes as to those found in N2, with the peak becoming flatter (denoted by increasing WHH) from 3 months to 12 months of age. The IMPS in the sigma region changed significantly ($p < 0.05$) from 2 weeks to 6 months, with no further changes until 24 months (Fig. 3b). At 24 months, the peak in the sigma bandwidth was no longer visible, and a peak with decreasing power was seen in the theta bandwidth. The IMPS of bandwidths in QS/NREM N3 changed significantly ($p < 0.05$) from

Table 1
Polysomnography parameters in infants in the first two year of life.

	Age (mean ± standard deviation (days))				
	2 weeks (14 ± 3.0) *n* = 31	3 months (97 ± 9) *n* = 25	6 months (187 ± 6) *n* = 27	12 months (371 ± 14) *n* = 26	24 months (725 ± 8) *n* = 20
Duration, (min)					
Total recording time (TRT)	568 ± 70	530 ± 73	510 ± 81	479 ± 87	501 ± 53
Total sleep time (TST)	389 ± 60	441 ± 96	415 ± 81	390 ± 84	443 ± 68
Awake time (AT)	163 ± 64	78 ± 52	90 ± 45	87 ± 60	47 ± 45
QS/NREM	192 ± 32	249 ± 53	269 ± 57	265 ± 58	325 ± 52
NREM N1	–	3 ± 3	5 ± 6	4 ± 4	9 ± 5
NREM N2	–	154 ± 59	186 ± 43	195 ± 53	234 ± 46
NREM N3	–	71 ± 39	73 ± 26	66 ± 21	75 ± 16
NREM-N	–	21 ± 19	5 ± 6	3 ± 6	7 ± 16
AS/REM	197 ± 48	192 ± 51	146 ± 34	125 ± 35	117 ± 31
Movement time (MT)	10 ± 7	8 ± 8	4 ± 4	3 ± 2	6 ± 5
Percentage of TST (%)					
Sleep efficiency	69 ± 10	83 ± 12	81 ± 8	81 ± 11	88 ± 9
Percentage of QS/NREM	50 ± 8	57 ± 5	65 ± 5	68 ± 5	73 ± 5
NREM N1	–	1 ± 1	2 ± 2	1 ± 1	2 ± 1
NREM N2	–	35 ± 10	45 ± 6	50 ± 7	53 ± 5
NREM N3	–	18 ± 11	18 ± 6	17 ± 5	17 ± 3
NREM-N	–	5 ± 4	2 ± 2	4 ± 2	6 ± 4
Percentage of AS/REM	50 ± 8	43 ± 5	35 ± 5	32 ± 5	27 ± 5

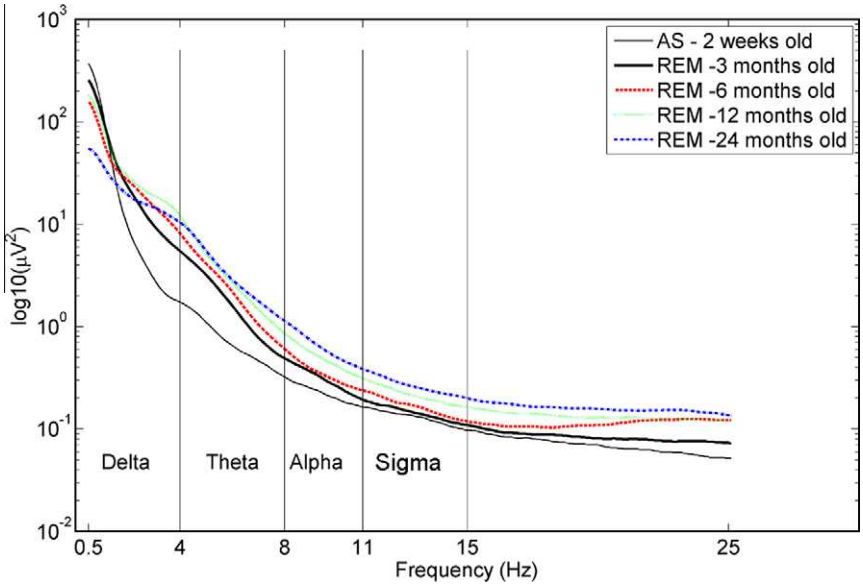

Fig. 1a. EEG power spectra of AS/REM from 0.5 to 25 Hz from 2 weeks to 24 months. Note the slight deflection in the delta/theta bandwidth at 12 and 24 months of age.

2 weeks to 6 months (Fig. 3b). The IMPS of the delta and theta bandwidth changed significantly ($p < 0.05$) from 6 to 24 months in NREM N3, while the IMPS of the alpha bandwidth changed from 6 to 12 months.

Fig. 4 compares the NREM N3 EEG power spectra of all the individual infants in the study at 6 and 24 months of age. The EEG power spectra of individual infants at 6 months of age were relatively uniform, with evident peaks in the sigma bandwidth seen in all the infants. However, at 24 months of age, the uniformity was less apparent. Infants appeared to develop individualistic peaks at various frequencies.

4. Discussion

In this longitudinal study, the power spectra of sleep EEG (central derivation) of normal infants was examined in the first 2 years of life at 2 weeks, 3, 6, 12 and 24 months. The EEG power spectra and the IMPS were presented graphically and statistically analysed for maturational changes with age. Previous studies of sleep EEG power spectra analysis have been limited by small sample size, cross-sectional design, analysis of specific sleep stages only and provision of either graphical descriptors or statistical analysis of sleep EEG power spectra (but not both). Jenni et al. (2003) graphically described the sleep EEG power spectra of seven infants longitudinally from 2 weeks to 9 months of age. Schulte and Bell (1973) also graphically presented the sleep EEG power spectra of 19 normal children chosen cross-sectionally, as control for other projects. Alternatively, Samson-Dollfus et al. (1983) statistically analysed the sleep EEG power spectra of 20 infants younger than 5 months and 23 infants older than 5 months in a cross-sectional study. This study has addressed previous limitations by examining a larger prospective healthy cohort, by spanning the first 2 years of life, and by including both graphical and quantitative analysis of sleep EEG power spectra, with novel normative information on discriminated NREM sleep stages in infancy. This study also included the difficult early study at 2 weeks of age.

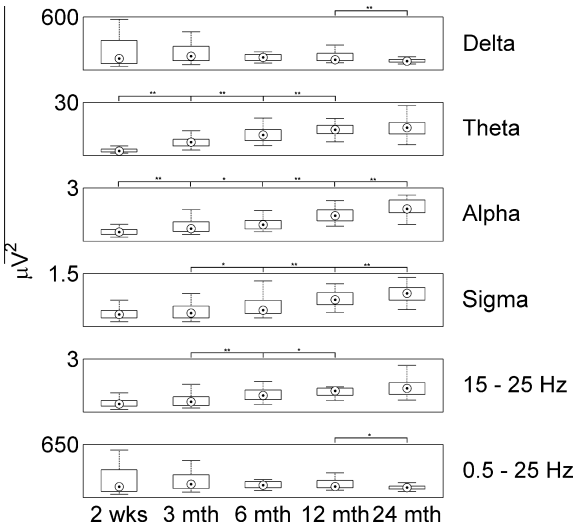

Fig. 1b. The median Integrated Mean Power Spectra (IMPS) of all infants in the frequency bandwidths for AS/REM sleep stage (boxplot outliers not plotted). *Difference in IMPS between the ages, at $p = 0.05$, **Difference in IMPS between the ages, at $p = 0.01$.

Historically, sleep studies for infants younger than 9 months of age were scored as AS and QS according to Anders et al. (1971). However, studies by Coons and Guilleminault (1982); Lenard (1972); Tanguay et al. (1975) and Hoppenbrouwers et al. (1982) all found that NREM stages 2 and slow wave sleep were distinguishable in infants between 3 and 6 months of age. Consequently in 2007, The Paediatric Task force (Iber et al., 2007; Grigg-Damberger et al., 2007) recommended that NREM sleep stages be characterised into stage N1, N2 and N3 (slow wave sleep) from the age of 4–4.5 months. This is the first study investigating EEG power spectra in healthy infants which differentiates NREM sleep stages by adopting the new staging criteria recommended by AASM (Iber et al., 2007). In the sleep studies of all infants aged 3 months and older, NREM stages 2 and 3 were identifiable from scoring criteria.

There were a number of potential limitations to this study. For practical reasons, infants were not studied at 9 months of age, to minimise the burden on families, and optimise key points in maturation of breathing control. However, this may have resulted in discontinuity of EEG maturational processes, as suggested by Louis et al. (1997), who found that this age may be significant in the sleep maturation process and is also an important time for frontal area myelination. An additional potential limitation is the discontinuity of sleep stage scoring rules from 2 weeks to 3 months,

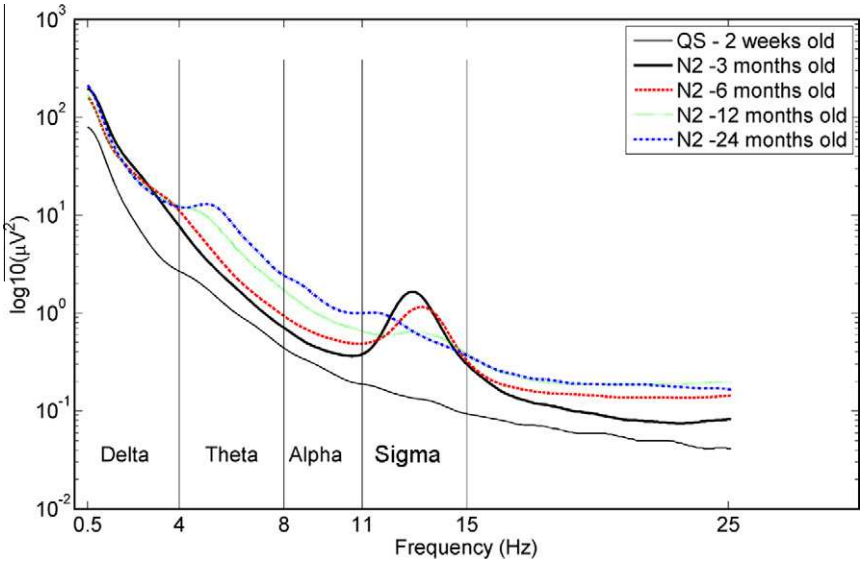

Fig. 2a. EEG power spectra of QS/NREM N2 from 0.5 to 25 Hz from 2 weeks to 24 months of age. Note the emergence of peak in the sigma bandwidth at 3 months. The peak changes in shape until 24 months of age. A second deflection emerges at 24 months in the theta bandwidth.

occurring of necessity due to the age range covered by the scoring rules. Artefact free sample segments of each sleep stage were selected through the night for spectral analysis. The samples were selected at least 2 min into a stable sleep stage, to avoid sleep stage transition epochs. Thus, 5 min segment length was considered optimal length to fulfil the sampling criteria. This technique used for segments selection for analysis through the night might not be able to fully describe the changing spectral content over the night, but was designed to analyse representative samples of sleep.

The data collection period for this study spanned the first change in scoring rules for nearly 40 years, from Rechtschaffen and Kales (1968) to the new AASM guidelines (Iber et al., 2007; Grigg-Damberger et al., 2007). This necessitated re-scoring of studies already undertaken, using the new guidelines. As was standard practice for paediatric studies, frontal EEG derivations were not part of the PSG montage (American Thoracic Society, 1996). These

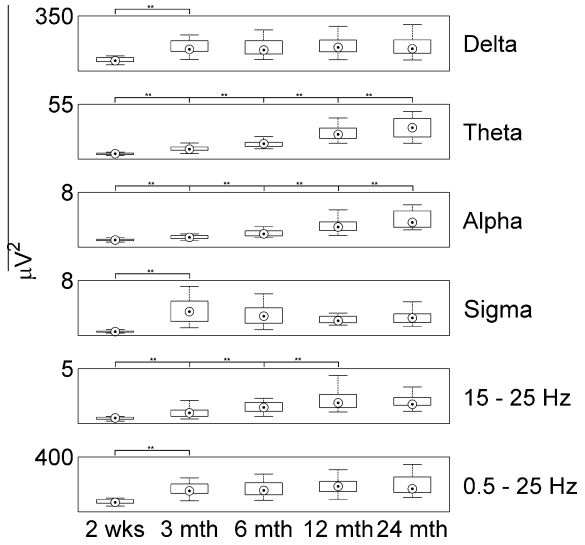

Fig. 2b. The median Integrated Mean Power Spectra (IMPS) of all infants in the frequency bandwidths for QS/NREM N2 sleep stage (boxplot outliers not plotted). *Difference in IMPS between the ages, at $p = 0.05$, **Difference in IMPS between the ages, at $p = 0.01$.

are mandated in the new AASM guidelines for studies on adults, but not children (Iber et al., 2007). This is a reasonable distinction, as the inclusion of frontal derivations in adults may increase scored slow wave sleep in those with borderline slow wave amplitudes at central derivations. However, this has not been found to be the case in children, and the omission of frontal leads in the age group of this study is unlikely to have altered sleep stage scoring. As stated by Novelli et al. (2009), in agreement with Grigg-Damberger et al. (2007), the relatively high voltage slow wave activity in children, compared with adults, results in minimal visual amplitude differences between frontal and central derivations, and voltages well above the amplitude threshold. The addition of the frontal derivation was not found to affect N3 scoring, as had been found in adults (Novelli et al., 2009).

Several studies have examined the differences in sleep scoring between Rechtschaffen and Kales (1968) and the new AASM criteria: Moser et al. (2009) for adults and Novelli et al. (2009) for children aged 3–16 years. As stated by both Moser et al. (2009) and Novelli et al. (2009), the majority of the differences in sleep scoring parameters between Rechtschaffen and Kales (1968) and AASM standard are attributable to the changes in terminology and definition, rather than EEG location.

The change in scoring to the AASM guidelines will unfortunately result in potential difficulties comparing findings with studies scored according to the previous standard. The analysis of central EEG derivations in this study is potentially retrospectively and prospectively applicable; however this may be viewed as a limitation for the comparison of these data with future studies applying more strictly the new AASM montage to include frontal EEG derivation.

4.1. Maturational changes in EEG Power spectra (central derivation)

Graphical plots of the sleep EEG power spectra demonstrated the emergence and disappearance of peaks in various bandwidths with maturation at the different ages studied.

4.2. EEG power spectra at 2 weeks of age

At 2 weeks of age, Schulte and Bell (1973) ($n = 4$) and Jenni et al. (2003) ($n = 7$) described a peak in the delta–theta bandwidth in the

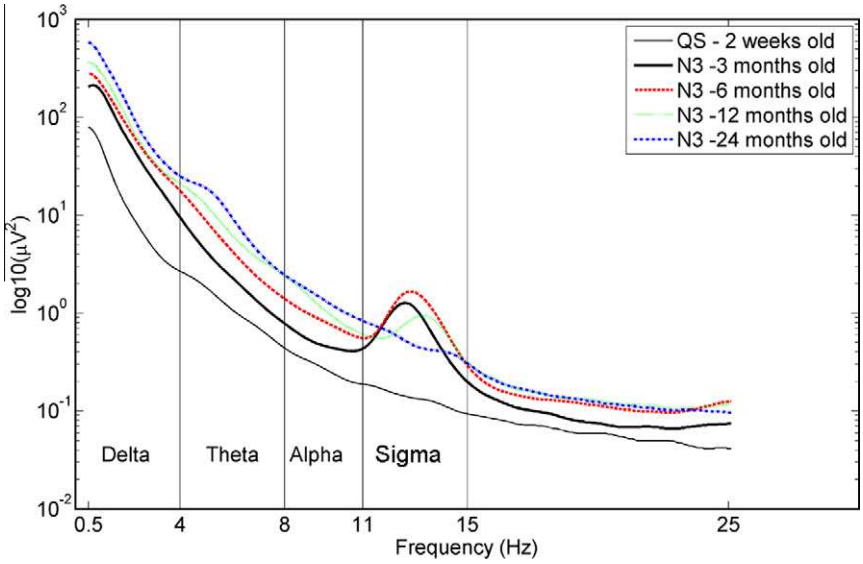

Fig. 3a. EEG power spectra of QS/REM N3 from 0.5 to 25 Hz from 2 weeks to 24 months of age. Note the emergence of peak in the sigma bandwidth at 3 months. The peak changes in shape until 12 months of age and is not well defined at 24 months of age. A peak emerges at 24 months in the theta bandwidth.

AS and QS, which was not present in the current study. Overall, at 2 weeks, Jenni et al. (2003) described a power difference between AS and QS in the sleep EEG power spectra, with the power of QS being higher than AS between 1 and 16 Hz. This too was not observed in the current study. This was potentially a type 1 error, which was not apparent with a larger cohort size.

4.3. NREM N2 sigma bandwidth and sleep spindles

At 3 months of age, the peak in the NREM N2 EEG power spectra sigma frequency was observed in all infants. Jenni et al. (2003) too observed the same feature in infants at 2 months of age and noted that this corresponds chronologically with the emergence of sleep spindles. A decrease in spindle density is noticed in developmentally delayed children compared to normal full term infants (De Gennaro and Ferrara, 2003). Dreyfus and Curzi-Dascalova (1975) have also suggested that the complete absence of spindles at 3 to 8 months of age may indicate a severe abnormality. Interestingly, Jenni et al. (2003) postulated that sleep spindles in infants promote the formation of thalamocortical network by providing endogenous neural signal with repetitive and synchronized activity.

The IMPS of QS/NREM N2 sigma bandwidth changed significantly from 2 weeks to 3 months, with no further statistically significant changes after that, even though the appearance of the peaks changed graphically. The lack of statistical change in the sigma IMPS from 3 months of age corresponds with the previously described finding that sleep spindles are well developed by 3 months of age (Metcalf and Jordon, 1972). According to Hughes (1996) the peak in sleep spindle duration at 13 weeks of age, is related to increase in size of the reticular nucleus of the thalamus, where sleep spindles are generated.

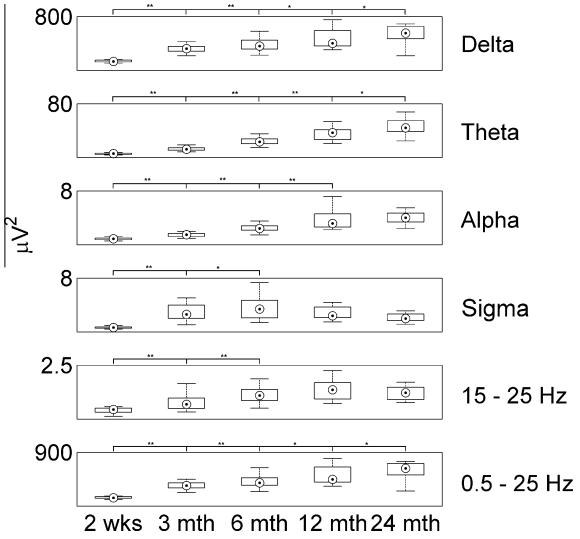

Fig. 3b. The median Integrated Mean Power Spectra (IMPS) of all infants in the frequency bandwidths for QS/NREM N3 sleep stage (boxplot outliers not plotted). *Difference in IMPS between the ages, at $p = 0.05$, **Difference in IMPS between the ages, at $p = 0.01$.

4.4. NREM N3 delta bandwidth

Interestingly, the IMPS of QS/NREM N3 delta and 0.5–25 Hz bandwidth changed throughout the entire study. The IMPS of QS/NREM N3 delta bandwidth consisted of high absolute power (up to 800 μV^2) when compared to other bandwidths (theta bandwidth up to 50 μV^2, alpha and sigma bandwidth up to 4 μV^2, 15–25 Hz bandwidth up to 2 μV^2). Hence, changes in the delta bandwidth in QS/NREM N3 may dominate the changes in the entire 0.5–25 Hz bandwidth. Slow Wave sleep (NREM N3 and N4) and sleep spindles both are dependent on hyperpolarization of the thalamocortical neurons where membrane potential may exhibit oscillations first in the spindle frequency range and then in the range of slow wave sleep (Aeschbach and Borbely, 2009; Dijk, 1995). Thus, the changes in the IMPS of QS/NREM N3 delta bandwidth may reflect maturation of the central brain structure during infancy.

4.5. REM sleep stage power spectra

At 12 and 24 months of age, the delta REM bandwidths had a peak with decreasing power at about 3 Hz (report by Schulte and Bell (1973) at 24 months). The appearance of the peak at 24 months of age is noted by a significant change in the IMPS of the delta REM bandwidth, even though there was no significant change in the first year (reported by Samson-Dollfus et al.

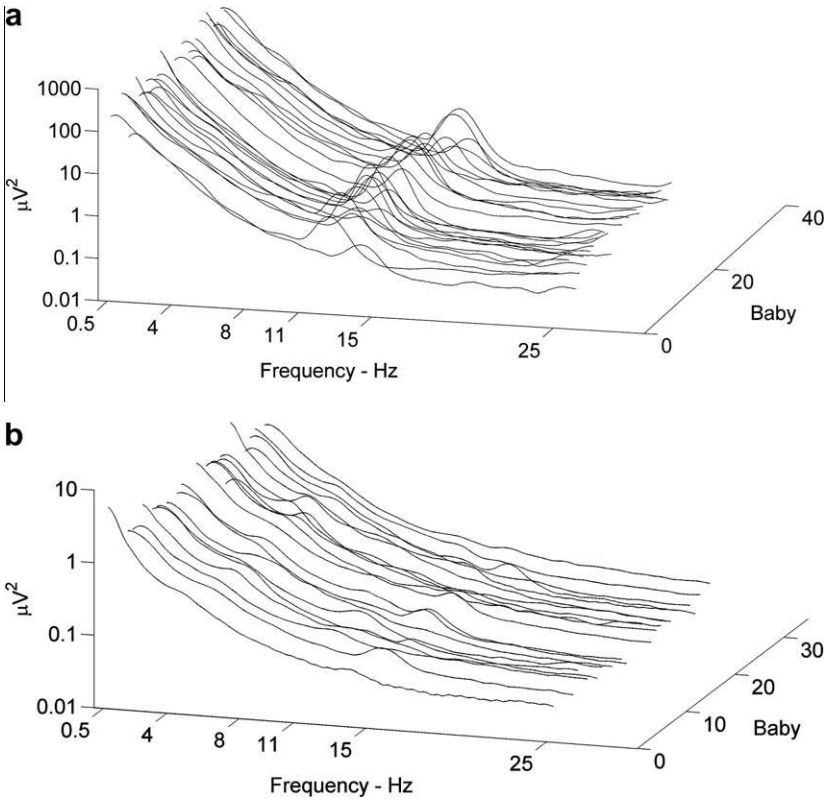

Fig. 4. NREM N3 EEG IMPS of each infant at (a) 6 months and (b) 24 months of age. Note the uniformity of peak frequency at 6 months of age but not 24 months of age.

(1983)). The IMPS of sigma bandwidth in REM sleep also changed significantly from 3 to 24 months (also reported by Samson-Dollfus et al. (1983) in the first year of infancy). These changes in REM sleep may reflect the role of AS/REM in brain maturation. Roffwarg et al. (1966) and Marks et al. (1995) postulated that AS/REM facilitates brain maturation by internal stimulation when sensory input is still minimal during infancy.

4.6. Increase in EEG Power

Overall within the first two years of life, there was a rise in spectral power in both AS/REM and QS/NREM. This agrees with the finding by Jenni et al. (2003) in infants up to 9 months of age. The changes are similar in AS/REM and QS/NREM thus may represent a sleep state-independent aspect of EEG development. The marked increase in central sleep EEG power spectra during the first 2 years of life may be related to structural brain development, potentially reflecting the increasing myelination of brain white matter observed on MR images (Paus et al., 2001).

4.7. Theta and alpha bandwidths

Graphically, the theta and alpha bandwidths in both AS/REM and QS/REM increased in power in the first 2 years of life. The IMPS of the alpha bandwidth in AS/REM and QS/NREM N2 changed significantly for the entire 2 years of infancy, and in QS/NREM N3 for the first year only. Statistically the IMPS of theta bandwidth changed in AS/REM only in the first year and in QS/NREM (both N2 and N3) for the entire 2 years of infancy. These changes in alpha and theta bandwidth were reported by Samson-Dollfus et al. (1983) for the first year only. This study has extended previous observations on the maturational changes in the theta and alpha bandwidth to the second year of life. A potentially interesting association is that theta activity has been related to the propensity for sleep and implicated in development of attention in infancy by Orekhova et al. (2006).

The emergence of individual variability in the frequency of NREM power spectra peaks, found at various bandwidths at 24 months of age, was an interesting phenomenon. This suggests that the EEG power distribution pattern in NREM sleep is characteristic for an individual and may reflect individual traits or development. To date, this has only been observed in adults NREM EEG by Finelli et al. (2001).

5. Conclusion

The current study provides longitudinal information on a prospective cohort of normal infants from 2 weeks to 24 months of age, using the new sleep scoring guidelines, which differentiate NREM stages N2 and N3 from the age of 3 months. The characteristics of central sleep EEG power spectra in healthy infants correspond with maturational and neurodevelopmental milestones. In particular, the emergence of the peak in the NREM N2 sigma bandwidth corresponds with the development of sleep spindles, while lack of quantitative changes in the sigma bandwidth power after 3 months is consistent with the finding that sleep spindles are well developed by 3 months of age. The changes in the NREM N3 delta bandwidth may correspond with central brain maturation. In addition, the relationship between developmental maturation and the changes in the theta and alpha bandwidths in both AS/REM and QS/NREM sleep warrant further exploration. This study provides a normative sleep EEG power spectra dataset on which disease may be discriminated.

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