

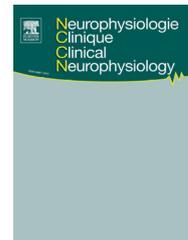


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COMPREHENSIVE REVIEW

Normal EEG during the neonatal period: maturational aspects from premature to full-term newborns



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Abstract Electroencephalography (EEG) is the reference tool for the analysis of brain function, reflecting normal and pathological neuronal network activity. During the neonatal period, EEG patterns evolve weekly, according to gestational age. The first analytical criteria for the various maturational stages and standardized neonatal EEG terminology were published by a group of French neurophysiologists training in Paris (France) in 1999. These criteria, defined from analog EEG, were completed in 2010 with digital EEG analysis. Since then, this work has continued, aided by the technical progress in EEG acquisition, the improvement of knowledge on the maturing processes of neuronal networks, and the evolution of critical care. In this review, we present an exhaustive and didactic overview of EEG characteristics from extremely premature to full-term infants. This update is based on the scientific literature, enhanced by the study of normal EEGs of extremely premature infants by our group of neurophysiologists. For educational purposes, particular attention has been paid to illustrations using new digital tools.

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Introduction

Electroencephalography (EEG) is the reference tool for the analysis of brain function, reflecting normal and pathological neuronal network activity. During the neonatal period, EEG activity presents specific characteristics that evolve weekly, according to gestational age (GA). Such maturation is due to the progressive establishment of neuronal networks and the sequential activation of spontaneous endogenous generators.

Starting more than 50 years ago, numerous studies have been conducted to determine the normal and pathological EEG characteristics of premature newborns. These studies included major fundamental issues of EEG of premature and full-term newborns from the “*Groupe de Neurophysiologie Clinique de l’Enfant*” under the auspices of the French Clinical Neurophysiology Society [2,4,38,69]. In the wake of these publications, pediatric clinical neurophysiologists, specialized in neonatology, have continued this work. Given the technical progress in EEG acquisition and evolution of critical care, including ethical considerations, they published an exhaustive and didactic overview of EEG characteristics from extremely premature to full-term infants. This description of EEG patterns has been enriched by recently acquired knowledge on the maturation processes of neuronal networks. This updated review, based on the scientific literature, is enhanced by the study of normal EEGs in extremely premature infants conducted by our experienced group of neurophysiologists. Moreover, for educational purposes, particular attention has been paid to illustrations using new digital tools.

Terminology

Given the evolution of EEG with cerebral maturation, consistent definitions are required to compare their neurodevelopmental aspects (Fig. 1).

Clinical terminology

Gestational age (GA) (or menstrual age)

Time elapsed between the first day of the last normal menstrual period and the day of birth [46].

Conceptional age

Time elapsed between the day of conception and the day of birth [46]. The terms gestational age and conceptional age are not synonymous. The convention for calculating gestational age is to add two weeks to the conceptional age. Nevertheless, except in cases of assisted reproductive technologies, the precise date of conception is uncertain. Thus, according to the American Academy of Pediatrics, conceptional age should not be used in clinical practice [46].

Chronological age (or postnatal age)

Time elapsed after birth.

Postmenstrual age or corrected gestational age

Time elapsed between the first day of the last menstrual period and birth (gestational age) plus the time elapsed after birth (chronological age) [46].

Corrected age (or adjusted age)

Time elapsed between the expected date of birth and the date of assessment. Corrected age is a term most appropriately used to describe prematurely born infants up to three years of age.

Full-term neonate

Neonate born after 37 weeks of amenorrhea calculated from the first day of the last normal menstrual period.

Premature infant

Infant born before 37 weeks of amenorrhea (Table 1).

EEG definitions

Quiescent and active periods

The normal EEG pattern of premature infants is discontinuous, alternating between high-amplitude and low-amplitude activity periods.

Low-amplitude activity periods are commonly called inter-burst intervals (IBIs) or periods of discontinuity. They are also called quiescent periods (QPs) from the Latin *quiescens* from *quiescere*, which means “to rest” or “to be quiet” [72]. These periods reflect synchronous neuronal silence. Indeed, extracellular recordings of multiple unit activity in somatosensory and visual cortices of rats demonstrated that QPs result from a decrease in neuronal activity [17,35,53]. As it refers to a physiological process, the term ‘quiescent period’ appears to be more relevant and is used in this review.

QPs are interspersed with periods of high-voltage and mixed-frequency activity (also called active periods or bursts of activity). Active periods (APs) are comprised of complex age-specific EEG activities (also called EEG-specific features) and intermediate activity and are generated by the interaction between subcortical and cortical plates (for more details, see Wallois et al., 2021 in the same issue [72].

With cerebral maturation, the duration of QPs decreases and that of APs increases, with the distinction between active and quiescent periods becoming progressively less detectable. The determination of normal and pathological EEG aspects requires knowledge of the normal ranges of duration for each gestational age. The definition of these normal ranges in the literature are based on various amplitude thresholds (from 10 to 100 μ V) and minimum durations (from 1 to 5 s) (Tables S1–S3) [3,4,9–11,18,19,27,28,59,68,71]. After reviewing the literature data and analyzing serial EEGs, the following definitions appear to be the most relevant with respect to personal observations:

- Active period (AP): period with an amplitude $> 50 \mu$ V lasting at least 1 s and observed across at least 2 derivations. APs associate EEG-specific features and mixed-frequency low-amplitude activity (50–100 μ V) (also called intermediate activity or background activity).

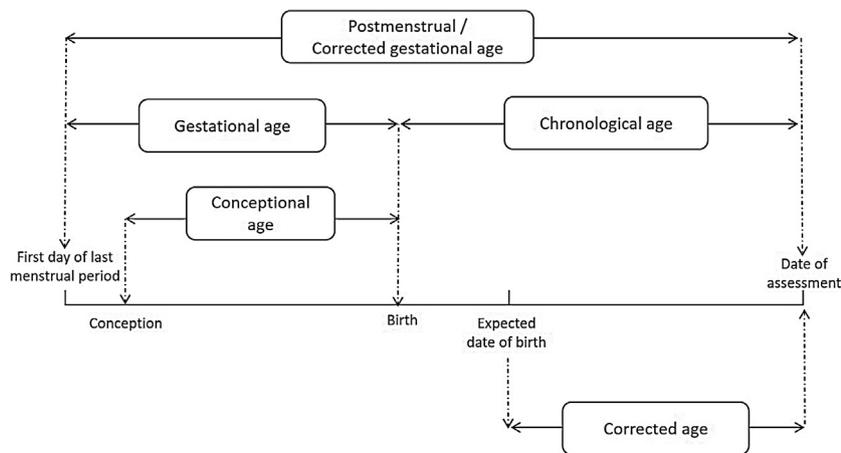


Figure 1 Age terminology for the perinatal period, adapted from the American Academy of Pediatrics, 2004 [46].

Table 1 Summary of EEG definitions.

Terminology	Definition
Quiescent period	Period of low-amplitude activity (<50 μV) lasting at least 1 s recorded under all but one derivation.
Active period	Period of high-amplitude activity (>50 μV) lasting at least 1 s recorded across at least 2 derivations and composed of specific EEG features and intermediate activity (50-100 μV).
EEG amplitude	Voltage of the EEG measured from peak to peak between the maximum positive and negative deflections of each feature, expressed in microvolts (μV).
Interhemispheric asymmetry	Differences in amplitude (>50%) and/or frequency and/or morphology of the EEG activity in homologous areas of opposite hemispheres.
Interhemispheric synchrony	Simultaneous occurrence of active periods across both hemispheres.
Interhemispheric asynchrony	Any delay (>1.5 s) between periods of activity between the two hemispheres.
Lability	The existence of fluctuations in the duration of quiescent and active periods or fluctuations of amplitude or frequency of the EEG features.
Reactivity	Amplitude and frequency EEG fluctuations in response to a sensory stimulus
Spatial organization	The predominant regional localization of specific EEG features.

- Quiescent period (QP): period of low amplitude activity (<50 μV) lasting at least 1 s observed for all but one derivation.

Based on these definitions, we present normal minimal, maximal, and median durations for each gestational age (see supplemental information, SI-2). The minimal and maximal values are of interest but cannot be considered in isolation. The variability of the duration and the most frequently observed durations need to be interpreted according to the GA and state of vigilance. Because of the non-Gaussian distribution, median values appear to be the most appropriate measure of the general tendency of QP and AP duration rather than the mean values generally expressed in the literature data. Contrary to the mean value, which is shifted

away from the typical value in a non-Gaussian distribution, the median value is less affected by extreme values. Thus, we present normal durations expressed in terms of the minimal, maximal, and median duration and inter-quartile ranges (IQR, Q_1 ; Q_3) for various states of vigilance for each GA. Nevertheless, these values of discontinuity duration are indicative and should be considered within the context of all EEG analysis criteria. Furthermore, the conditions of EEG acquisition, in particular the administration of drugs, must always be considered for evaluating discontinuity.

EEG amplitude

The voltage of the EEG signal determines its amplitude and is expressed in microvolts (μV). Amplitude is measured from peak to peak; between the maximum positive and negative deflections of each feature of background activity.

The signal amplitude depends on the aspects of technical acquisition (impedance, electrodes, etc.) and interpretation conditions (montages, reference, etc.). The EEG amplitude analysis should be comparative between homologous cerebral regions and should simultaneously consider the signal frequency. The amplitude measured in conventional EEGs should not be confused with that of an amplitude-integrated EEG, which refers to a specific type of EEG signal processing.

Interhemispheric symmetry and asymmetry

Interhemispheric asymmetry is defined by differences in amplitude (>50%) and/or frequency and/or morphology of the EEG activity in homologous areas of opposite hemispheres.

Interhemispheric asymmetry of the amplitude is considered physiological if the difference does not exceed 50% and if it is transiently observed [4,7,15,39,52,67]. Interhemispheric asymmetry of the morphology and/or frequency of EEG patterns is pathological. If asymmetry of the amplitude is observed without other pathological patterns, technical aspects must be checked (e.g. asymmetry in positioning of the electrodes, etc.). Asymmetry of the amplitude may also be related to a subcutaneous hematoma or an intra-cerebral hemorrhage without brain dysfunction (for more details see Malfilâtre et al., 2021 in the same issue [42]).

Interhemispheric synchrony and asynchrony

Interhemispheric synchrony is considered to reflect the level of interaction between the two hemispheres and constitutes one of the key features in the classification of the neonatal EEG background. There is no unanimous definition of interhemispheric synchrony. In the broad sense, synchrony is the presence of similar EEG features of comparable duration measured almost simultaneously in different regions of the cortex [79]. In preterm infants, interhemispheric synchrony is traditionally defined by the simultaneous occurrence of active periods across both hemispheres, with a visually estimated difference below 2 s [3,4]. Interhemispheric asynchrony is also defined by a difference between the onset of APs between the two hemispheres of more than 1.5 s [40]. After reviewing the literature data and analyzing serial EEGs, the following definitions of synchrony and asynchrony appear to be the most relevant:

- Interhemispheric synchrony in the EEG is characterized by the simultaneous occurrence of APs between the two hemispheres.
- Interhemispheric asynchrony is defined by a difference (>1.5 s) between the onset of APs between the two hemispheres [4,38].
- The level of interhemispheric asynchrony refers to the proportion of APs that exceed the 1.5-s difference of onset between the two hemispheres. Interhemispheric synchrony is almost >80% for all GAs [19,36,39,61].
- The term synchrony can also refer to the simultaneous occurrence of isolated specific EEG features between homologous areas of the two hemispheres.

Labiality and reactivity

Labiality corresponds to fluctuations in EEG activity, such as fluctuations in the duration of APs and QPs and fluctuations

of amplitude and frequency of the EEG features. In a normal EEG, labiality should always be observed, even without complete recognition of sleep cycles in extreme premature infants [4,68].

Reactivity refers to fluctuations in the amplitude and frequency in the EEG in response to a sensory stimulus.

Spatial organization

Spatial organization refers to the localization of specific EEG features with a regional predominance. Spatial organization evolves with cerebral maturation [4,38] (Fig. 2).

General maturational aspects and specific EEG features

Maturational aspects of EEG activity in the preterm infant evolve according to two main dynamics: network-based dynamics and generator-based dynamics [72].

General EEG organization: network-based dynamics

The length of QPs tends to decrease with the establishment of functional interactions within cortical neuronal networks. EEG activity becomes more continuous, leading to a 'tracé alternant' at term [3,19,24,26,28,38,48,66]. In parallel, the length of periods of spontaneous activity (APs) increases [48]. The neonatal EEG thus matures to a less dichotomous form between the QPs and APs.

Simultaneously, the amplitude of the EEG activity gradually decreases. The amplitude of specific EEG features observed in the early stages of maturation (24–26 weeks gestational age, wGA) can range from 400 to 500 μV and even up to 600–800 μV . The amplitude of the EEG activity decreases to 50–100 μV by the period around term.

The frequency content of the EEG shows a significant shift from lower to higher frequencies, with the predominant frequency increasing from 0.3 to 4 Hz [10,28,31,39,55,60].

Interhemispheric synchrony is present at early stages of maturation, with up to 80% of APs being synchronous independently of GA [19,36]. Physiological transient interhemispheric asynchrony is observed during changes in vigilance state, notably between 32 and 36 wGA [36,39,61,62].

Behavioral states and the differentiation of sleep states

Sleep states in premature newborns consist of active and quiet sleep. Active sleep (AS) is characterized by the presence of rapid eye movements (REMs), an irregular respiratory rate, the absence of a tonic chin by electromyography (EMG), body and facial movements (notably smiles), and more continuous EEG activity, depending on the GA. It consists of the state of falling asleep in premature newborns. Quiet sleep (QS) is characterized by the absence of REMs, a regular respiratory rate, the presence of a tonic chin by EMG, few body movements, and more discontinuous EEG activity. QS is observed after a period of AS. Behavioral, clinical features, and EEG activity do not always correspond to a definitive sleep state. The presence of an indeterminate sleep state (IS) indicates immature sleep organization.

Quiet and active wakefulness are observed in most mature infants. They are characterized by bright open eyes,

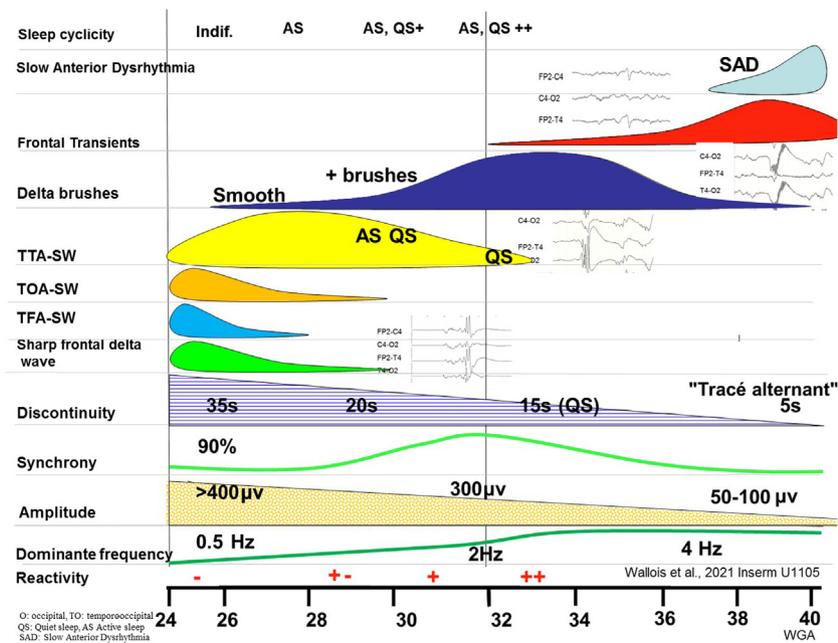


Figure 2 Synopsis, from Wallois et al. 2021 with permission [72].

with or without exploratory eye movements, a stable heart rate, and irregular respiration. Active wakefulness is distinguished from quiet wakefulness by the presence of gross body movements.

Sleep stages appear progressively with the development of interactions between the neuronal networks of sub-cortical and cortical structures. As early as 24–26 wGA, preterm neonates show rudimentary sleep state cyclicity [56]. At this GA, sleep states with REMs and more continuous activity can be distinguished from non-REM periods [68]. From 27 to 28 wGA, a stable concordance between EEG activity and polysomnographic criteria (autonomic functions (EKG and respiration), motor activity, and behavior) progressively appears. AS (considered to be a precursor of REM-sleep) is the first sleep state observed. From 28 to 29 wGA, QS (or non-REM sleep (NREM)) can be identified. On EEGs, the activity is discontinuous and the duration of QPs depends on the GA. From 30 wGA, active wakefulness is observed, followed (34–36 wGA) by quiet wakefulness (for more details, see Bourel-Ponchel et al., 2021, in the same issue [13]).

Reactivity

Before 28 wGA, provoked EEG reactivity during sensory stimulation, particularly during tactile and auditory stimulation, is not visible by EEG and is variable before 30 wGA [3,4,38].

EEG reactivity appears after 28–30 wGA. During AS, sensory stimulation is associated with a diffuse and transient decrease of EEG amplitude. During QS, provoked EEG reactivity is characterized by the transient appearance of continuous slow-wave activity. These reactivity patterns are observed until 37–38 wGA [3,4,38].

After 38 wGA, reactivity appears more often as an attenuation rather than reinforcement of the background activity, depending on the behavioral state [4,38].

Specific EEG features: generator-based dynamics

In parallel with the gradual establishment of neuronal networks, interactions developed within the subcortical and cortical plates generate spontaneous endogenous activities. Before 28 wGA, the activation of these generators is non-sensory driven [8,16,45,78]. At approximately 28 wGA, the relocation of thalamic afferents from the cortical subplate to cortical plate provides sensory inputs to the immature network. In addition to their spontaneous endogenous origin, generators become progressively sensory-driven [17,43,44,76]. These generators are sequentially activated with different spatio-temporal and frequency characteristics (for more details and discussion, see Wallois et al., 2021 in the same issue [72]).

Specific age-related EEG features rely on the sequential activation of these endogenous generators. The sequential appearance/disappearance of EEG age-related specific features is one of the most important hallmarks of early developing EEG activity. These specific age-related EEG features result frequently from the coalescence of theta activity with slow waves [45,54] (for more details about definition and discussion about the coalescence, see Wallois et al., 2021 in the same issue [72]).

These age-specific EEG features consist of:

- 1 Theta occipital activity in coalescence with slow waves (TOA-SW)
- 2 Theta frontal activity in coalescence with slow waves (TFA-SW)
- 3 Theta temporal activity in coalescence with slow waves (TTA-SW)
- 4 Sharp frontal delta activity
- 5 Slow delta waves that are smooth or superimposed with fast rhythms (delta brushes)
- 6 Frontal transient sharp waves

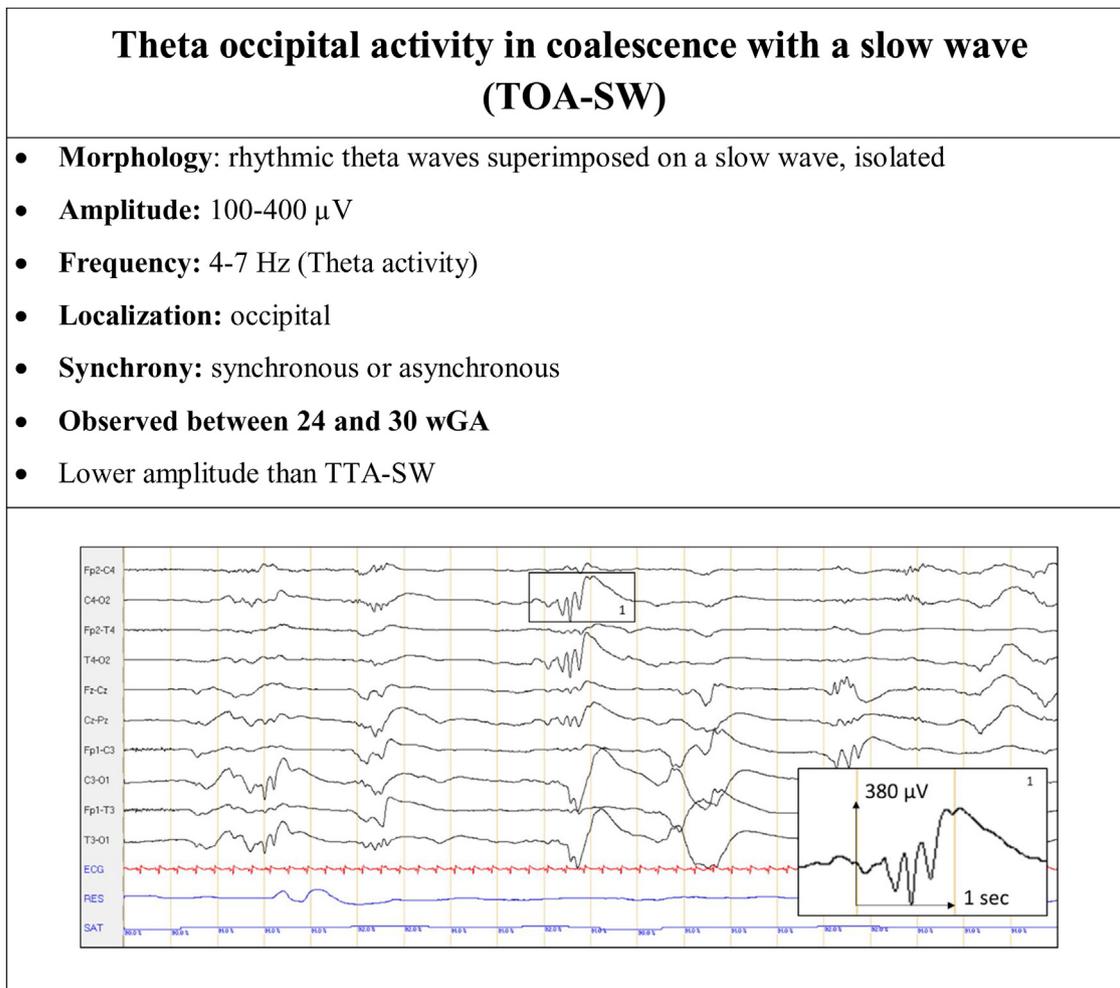


Figure 3 Theta occipital activity in coalescence with slow waves (TOA-SW). TOA-SW characteristics (on the left) illustrated with an example (20 s) of an EEG recorded at 24 wGA + 5 days. *low pass filter: 70 Hz, high pass filter: 0.5 Hz, notch filter: 50 Hz (Amiens).*

7 Anterior slow dysrhythmia

Theta occipital activity in coalescence with slow waves (TOA-SW)

The first description of this specific feature was reported by Werner et al. in 1977 [75]. It was described as a "brief occipital theta burst" [75] and has been called an "occipital sawtooth" [11,12,32]. This specific feature is one of the EEG characteristics of the earliest stage of maturation. It appears as soon as 24 wGA and generally disappears at 27–28 weeks GA and always before 30 wGA. The morphology consists of a burst of sharp 4- to 7-Hz waves in coalescence with a delta slow wave observed in occipital areas [72]. Its amplitude ranges from 100 to 400 μV [11,12,33,59] (personal study). It is mostly isolated and occurs asynchronously between the two hemispheres (Fig. 3, Table S4).

Theta frontal activity in coalescence with slow waves (TFA-SW)

Several descriptions of this EEG-specific feature, also called delta crests, are available in the literature [3,59]. This feature characterizes the earliest stage of maturation but is

inconstantly observed. It appears as soon as 24 wGA and disappears by 28 wGA. This feature consists of a burst of sharp 4- to 7-Hz waves in coalescence with a slow wave, observed in frontal areas [72]. Its amplitude ranges from 100 to 500 μV [11,59,68] (personal study). TFA-SW is observed both synchronously and asynchronously between the two hemispheres and appears to be more frequently observed in the right hemisphere. TFA-SW is mostly observed synchronously with TTA-SW (Fig. 4, Table S6).

Theta temporal activity in coalescence with slow waves (TTA-SW) [45,54]

This specific EEG feature has also been called a "temporal sawtooth" [75], a "theta burst" [23,63], "temporal sharp transients", and "bursts of sharp theta" by Lombroso et al. [39–41] and Anderson et al. [3]. TTA-SW appears at 24–26 wGA but is maximally expressed between 27–30 wGA. It disappears at 32 wGA during AS and at 34–36 wGA during QS [32]. This feature consists of a burst of sharp 4- to 7-Hz waves coalescent with a biphasic slow wave [1,45,54], localized in temporal areas. TTA-SW is both synchronous and asynchronous and equally distributed between the two

Theta frontal activity in coalescence with a slow wave (TFA-SW)

- **Morphology:** rhythmic theta waves superimposed on a slow wave, isolated
- **Amplitude:** 100-500 μV
- **Frequency:** 4-7 Hz (Theta activity)
- **Localization:** frontal
- **Synchrony:** synchronous / asynchronous
- **Observed between 24 and 28 wGA**
- Mostly observed synchronously with TTA-SW
- Inconsistently observed

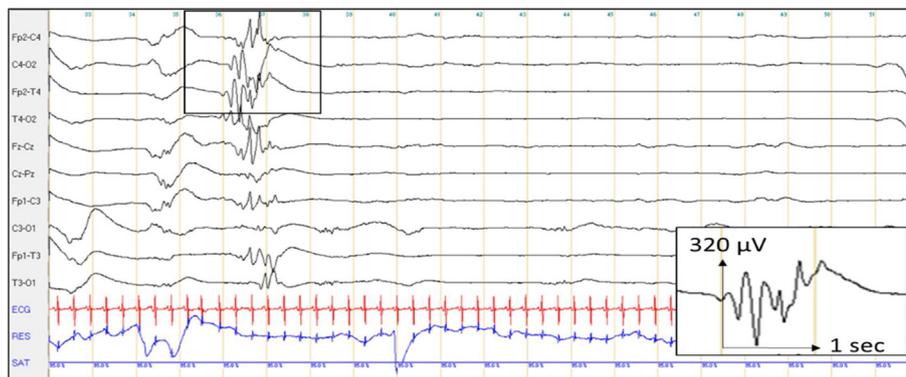


Figure 4 Theta frontal activity in coalescence with slow waves (TFA-SW).

TFA-SW characteristics (on the left) illustrated with an example (20s) of an EEG recorded at 25 wGA + 2 days. *low pass filter: 70Hz, high pass filter: 0.5Hz, notch filter: 50Hz (Amiens).*

hemispheres. Its amplitude ranges from 100 to 600 μV and exceptionally up to 800 μV at 27–28 wGA [32,59,68] (personal study) (Fig. 5, Table S5).

Sharp frontal delta waves

There are only a few descriptions of this EEG-specific feature [3,59,68]. Sharp frontal delta waves are inconstantly observed. They appear at 24–26 wGA and disappear at 27–28 wGA and always before 30 wGA. Sharp delta waves consist of high amplitude bi- or triphasic slow waves localized in the frontal areas. The amplitude of sharp frontal delta waves ranges from 100 to 600 μV and exceptionally up to 800 μV , with a duration of 0.5–1 s. This feature is mostly isolated and occurs asynchronously between the two hemispheres [59,68] (personal study) (Fig. 6, Table S7).

Slow delta waves

Slow delta waves consist of monophasic or diphasic delta waves (0.3–2 Hz) [2,4,22,49,51,55,63] that are smooth or with superimposed fast rhythms (8–30 Hz) [4,10,25,29,37,38,40,43,51,55,63], generally on the ascending slope of the slow wave [18,64,73] (Fig. 7, Tables S8–S11).

The morphology of slow delta waves evolves with maturation. The frequency of both the slow component and the superimposed fast rhythms increases with age [77]. Slow delta waves with superimposed rapid alpha-beta rhythms are called delta brushes. Their amplitudes range from 100 to 600 μV and decrease with age [4,38,65].

Initially diffuse or multifocal, they become progressively temporo-occipital and occur exclusively across the occipital areas from 36 wGA.

Slow delta waves appear at 24 wGA (smooth delta waves) [69]. They become progressively superimposed with fast rhythms from 28 to 30 wGA, at which time they are called "delta brushes" [14,38,47,70]. The peak of incidence is observed between 32 and 35 wGA [4,14,22,38]. Delta brushes disappear between 38 and 42 wGA [4,14,37,38].

Transient frontal sharp waves, "Encoche frontale"

This specific EEG feature has been called a "transient frontal sharp wave", "frontal transient" [4,38], and "encoche frontale". It consists of a diphasic wave (50–200 μV) with a small initial negative deflection followed by a wider positive deflection of higher amplitude. The duration of transient frontal sharp waves is approximately 0.5 to 0.75 s [4,38].

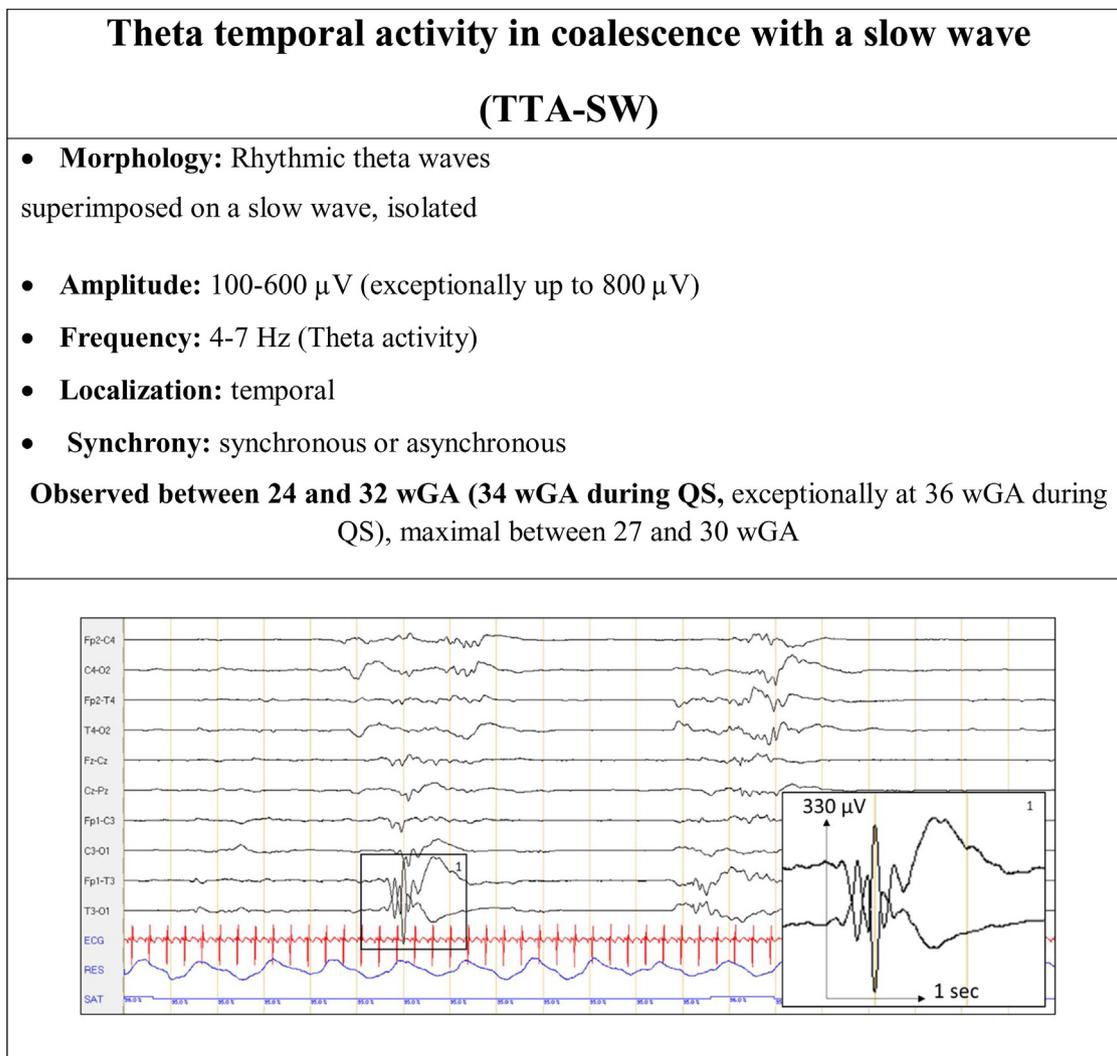


Figure 5 Theta temporal activity in coalescence with slow waves (TTA-SW). TTA-SW characteristics (on the left) illustrated with an example (20s) of an EEG recorded 26 at wGA +3 days. *low pass filter: 70 Hz, high pass filter: 0.5 Hz, notch filter: 50 Hz (Amiens).*

They are localized to the frontal areas and are generally synchronous between the two hemispheres but can also be observed unilaterally [20]. Frequently isolated, with variable occurrence, they are preferentially observed during active sleep 1 (AS 1) before the transition to QS [5]. They appear at 35–36 wGA and disappear during the first month of life. “Encoches frontales” may be observed from 33 wGA onwards, with an immature aspect and are often repetitive, incomplete, and asymmetric [4,38] (Fig. 8).

Anterior slow dysrhythmia, « Dysrythmie lente antérieure »

Anterior slow dysrhythmia consists of monomorphic and/or polymorphic delta waves (1–3 Hz, 50–100 μV) observed in short bursts (1–3 s) during active sleep 1 (AS 1). They occur in the frontal areas and are generally synchronous between the two hemispheres. They appear at 36–37 wGA and disappear during the first month of life [4,38] (Fig. 9).

Specific maturational EEG aspects according to GA: 24–26 weeks GA

General organization of the EEG (network-based dynamics)

Quiescent periods

The duration of QPs is variable and never exceeds 60 s [3,9–11,18,19,27,28,68,71]. However, such a long duration is uncommon. In our experience, the duration of QPs generally ranges from 1 to 22 s and exceptionally up to 35 s.

The mean duration of QPs reported in the literature is between 6 and 40 s [3,9–11,18,19,27,28,68,71]. In personal observations, we calculated the median duration of QPs to be 3 s. During the most discontinuous and continuous EEG activity, the first and third quartiles were 2–6 s and 2–4 s, respectively. More than 90% of QPs had a duration of < 8 s (fig S2) (Fig. 10, Video 1).

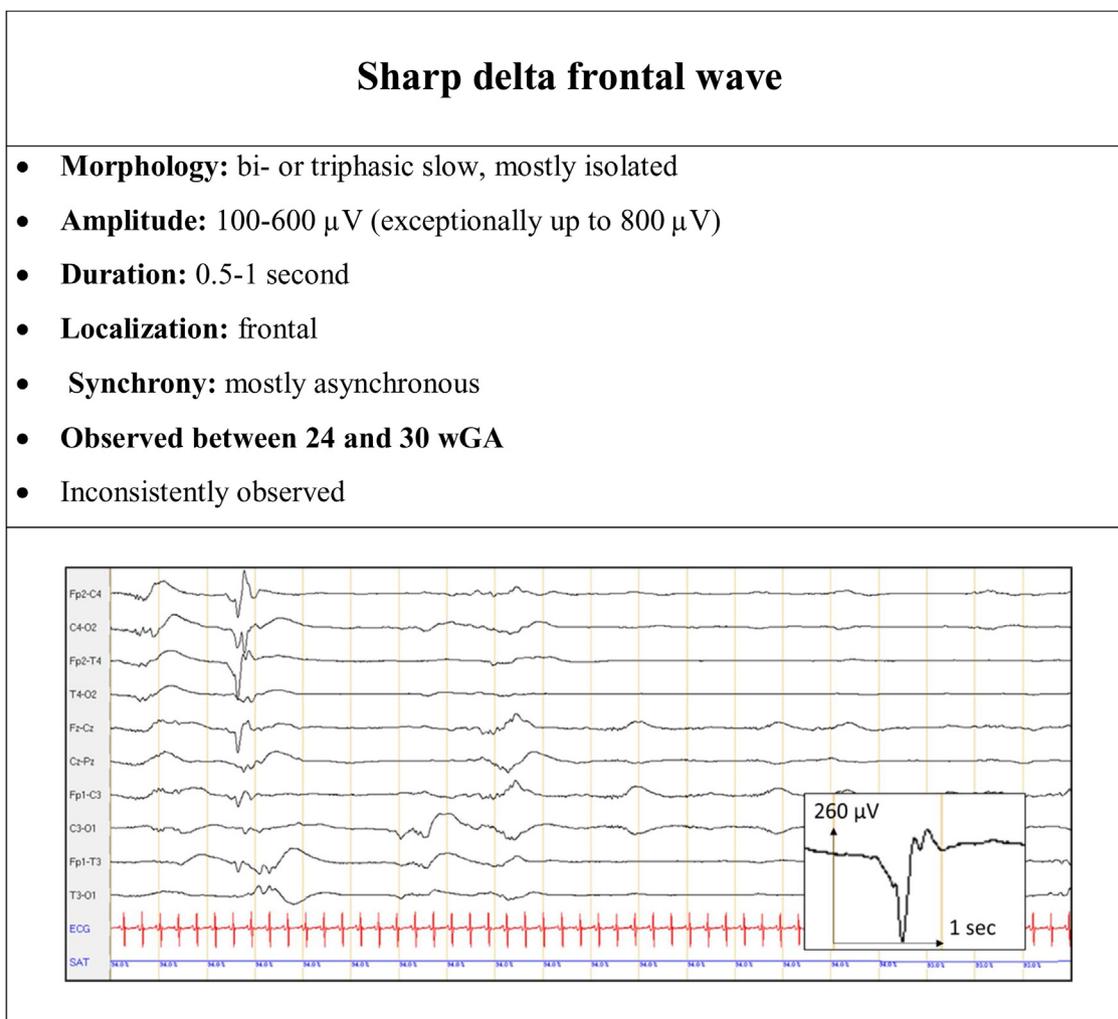


Figure 6 Sharp delta frontal wave.

Sharp delta frontal wave characteristics (on the left) illustrated with an example (20 s) of an EEG recorded at 26 wGA + 3 days. *low pass filter:* 70 Hz, *high pass filter:* 0.5 Hz, *notch filter:* 50 Hz (Amiens).

QPs represent between 20 and 50% (from 20 to 40% in personal observations) [68] of the recording time.

Active periods

APs are composed of EEG-specific features and mixed-frequency activities of relatively low amplitude (50–100 μV).

The duration of APs is variable. In our experience, more than 90% of APs last from 1 to 40 s. Nevertheless, APs can last up to 3 min [28,59,68] (personal observations). APs are abundant and represent between 40 and 50% of the recording time [68], up to 78% in our experience. In personal observations, the median duration of APs during the most discontinuous EEG activity was calculated to be 3 s (IQR 2–7) and 7 s (IQR 3–15) during the most continuous EEG activity.

Mixed activity (intermediate or background activity) consists predominantly of delta frequencies, but frequencies ranging from delta to beta bands have been observed [19,68]. Intermediate activity represents approximately 10–20% of the tracing (personal observations).

More than 90% of APs are synchronous and symmetrical [3,68] (personal observations).

Lability/Sleep state cyclicity

Rudimentary sleep state cyclicity is already observed as early as 24 wGA [30,58] (personal observations). Periods with eye movements are associated with less discontinuous EEG activity and higher voltage [68].

Reactivity

Reactivity is not observed within this age group [4].

EEG-specific features (generator-based dynamics)

The predominant features observed at this GA are TOA-SW and TTA-SW. They consist both of bursts of sharp 4- to 7-Hz waves in coalescence with a biphasic slow wave.

TOA-SW is localized to occipital areas and can be either synchronous or asynchronous. At this GA, its amplitude

Slow delta waves

- **Morphology:** monophasic or diphasic delta waves that are smooth or with fast rhythms superimposed on the ascending slope of the slow wave, evolves with GA
- **Amplitude:** 100-600 μV
- **Frequency:** 0.3-2 Hz (slow wave), 8 -30 Hz (fast rhythms)
- **Localization:** diffuse or multifocal, becoming progressively temporo-occipital and exclusively across occipital areas from 36 weeks GA
- **Synchrony:** synchronous / asynchronous
- **Observed from 24 wGA but maximal between 32 and 35 wGA**
- **Disappears between 38 and 42 wGA**

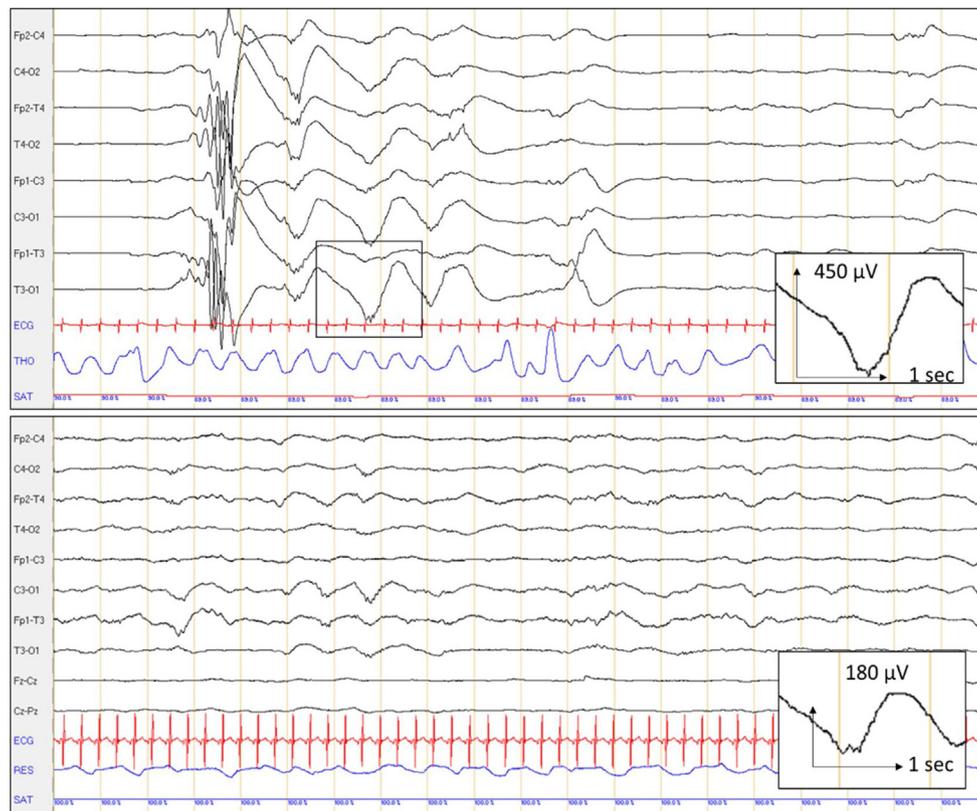


Figure 7 Slow delta waves.

Slow delta wave characteristics (on the left) illustrated with two examples (20s) of EEGs recorded at 27 wGA (on the top) and 36 wGA above.

low pass filter: 70 Hz, *high pass filter:* 0.5 Hz, *notch filter:* 50 Hz (Amiens).

Transient frontal sharp wave: "Encoche frontale"

- **Morphology:** biphasic wave with a small initial negative deflection followed by a wider positive deflection of higher amplitude, isolated
- **Amplitude:** 50-200 μV
- **Duration:** 0.5-0.75 second
- **Localization:** frontal
- **Synchrony:** mostly synchronous
- **Observed from 35 to 36 wGA, disappears during the first month of life**
- Often observed during AS1 and at the beginning of QS
- Immature aspects can be observed from 33 to 34 wGA

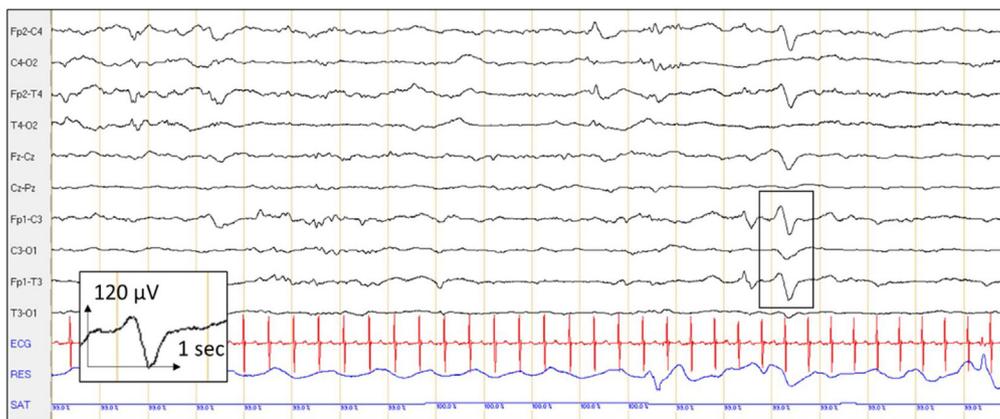


Figure 8 Transient frontal sharp wave, 'encoche frontale'.

Transient frontal sharp wave characteristics (on the left) illustrated with an example (20s) of an EEG recorded at 39 wGA. *low pass filter: 70 Hz, high pass filter: 0.5 Hz, notch filter: 50 Hz (Amiens).*

ranges from 100 to 300 μV (100–350 μV , including the slow wave) (personal observations) [11,12,33,59].

TTA-SW is localized to temporal areas and can be either synchronous or asynchronous between the two hemispheres or unilaterally equally distributed within the right and the left hemispheres [68] (personal observations). It appears progressively at this GA but remains less frequent than in the 27–28 wGA group [59]. Its amplitude ranges from 100 to 600 μV , including the slow wave [11,12,32,59,68] (personal observations).

TFA-SW and Sharp frontal delta waves are also observed at this GA but are infrequent. TFA-SW is characterized by bursts of sharp 4- to 7-Hz waves in coalescence with a biphasic slow wave. It is localized to frontal areas. It can be either synchronous or asynchronous between the two hemispheres but is mostly observed synchronously with TTA-SW. Its amplitude ranges from 100 to 500 μV (personal observations). Sharp frontal delta waves consist of bi- or triphasic slow waves, with an amplitude from 100

to 600 μV (personal observations). They are mostly asynchronous between the two hemispheres, observed in the frontal areas, and last between 0.5 and 1 s [59,68] (personal observations).

Slow delta waves are observed at this GA. They are characterized by a very low frequency of 0.5–1 Hz and mono- or biphasic morphology and are often smooth or already superimposed with fast rhythms (5–25 Hz), irrespective of their localization. Occipital slow delta waves, also called "posterior slow waves" [24], are the most abundant [68] and have the highest amplitude (100–600 μV). They occur in sequences lasting from 1 to 20 s and are often bilaterally synchronous [68]. Temporal delta waves, also called "temporal positive slow waves" [24], occur nearly as frequently as occipital delta waves. They also occur mostly in sequences lasting from 2 to 20 s and have a lower amplitude than occipital slow waves (100–500 μV). Frontal and central delta waves are the least frequent delta slow waves. They are frequently isolated and asynchronous and have

Anterior slow dysrhythmia : « Dysrythmie lente antérieure »

- **Morphology:** monomorphic and/or polymorphic delta waves, observed in short bursts (1-3 s)
- **Amplitude:** 50-100 μV
- **Frequency:** 1- 3 Hz
- **Localization:** frontal
- **Synchrony:** mostly synchronous
- **Observed from 36 wGA, disappears during the first month of life**
- Often observed during AS1

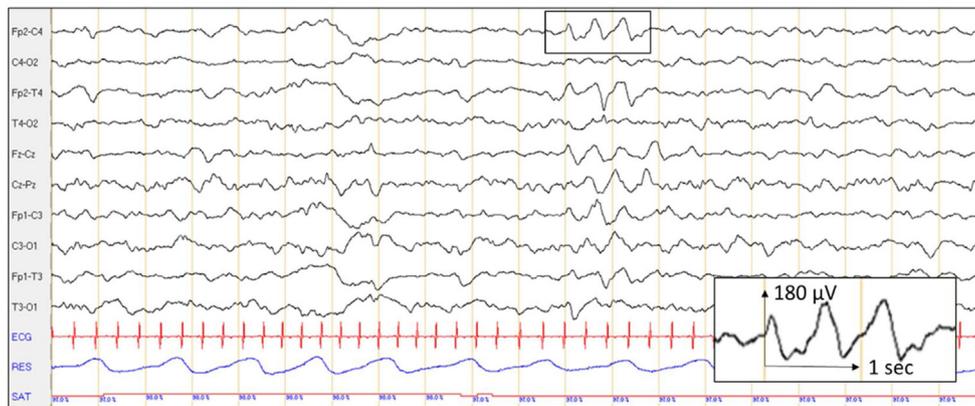


Figure 9 Anterior slow dysrhythmia, dysrythmie lente antérieure: Anterior slow dysrhythmia characteristics (on the left) illustrated with an example (20s) of an EEG recorded at 41wGA. *high pass filter: 70 Hz, low pass filter: 0.5 Hz, notch filter: 50 Hz (Amiens).*

the lowest amplitude of the slow delta waves (<400 μV , exceptionally up to 600 μV). When slow delta waves appear simultaneously in different areas, they have an aspect of diffuse synchronous high-amplitude activity, lasting a few seconds to several minutes (up to 3 min in personal observations) [3,11,24,34,59,68] (personal observations).

27–28 weeks GA

General organization of the EEG (network-based dynamics)

Quiescent periods

The duration of QPs is close to the 24- to 26-wGA values. According to the literature, QPs last between 1 and 60 s for this age group [3,9–11,18,19,27,59,71]. In personal observations, the duration of QPs was similar to that of infants of 24–26 wGA, mostly from 1 to 30 s. The median values were 3 s (IQR 2–5) during QS and 2 s (IQR 2–4) during AS. More than 90% of QPs were < 8 s in length. The longest QPs were

between 10 and 30 s (personal observations) (Fig. 11, Video 2).

QPs represent 10–30% of the EEG trace in published studies [68] and 22% (from 12 to 30%) in personal observations (Fig S2).

Active periods

APs are composed of EEG-specific features (see below) and mixed-frequency activity of lower amplitude (50–100 μV).

The duration of APs is variable. According to the literature, APs can last up to 3 min [3,59]. In our experience, more than 90% of APs last between 2 and 40 s, the longest AP observed lasting up to 5 min. We calculated the median duration of APs to be approximately 4.5 s (IQR 2–8) during QS and 10 s (IQR 6–22) during AS.

This mixed activity (intermediate or background activity) consists of frequencies ranging from delta to beta bands, predominantly delta [19,68], and represents approximately 10–20% of the tracing (personal observations).

More than 90% of APs are synchronous and symmetrical [3,68] (personal observations).

General organization of EEG at 24-26 GA				
Sleep state cyclicity	Rudimentary sleep state differentiation			
Background activity	Quiescent periods: 1-35 sec, never exceeds 60 sec, median: 3 sec [2-6]*, 3 sec : [2-4]* (according to the sleep state differentiation), 20-50 % of the EEG trace Active periods: 1-40 sec, up to 3 min, median: 3 sec: [2-7]*, 7 sec [3-15]*, (according to the sleep state differentiation), 50-80 % of the EEG trace Intermediate activity: delta to beta (predominantly delta), 10-20% of the EEG trace			
Provoked reactivity	Absent			
EEG specific features				
	Morphology	Amplitude μV	Localization	Remarks
TOA-SW +++ (1)	Burst of 4-7 Hz sharp waves in coalescence with a biphasic slow wave	100-350	Occipital	Synchronous / asynchronous Occurs isolated
TTA-SW + (2)	Burst of 4-7 Hz sharp waves in coalescence with a biphasic slow wave	100-600	Temporal	Synchronous / asynchronous
TFA-SW +/- (3)	Burst of 4-7 Hz sharp waves often in coalescence with a slow wave	100-500	Frontal	synchronous/asynchronous Occurs isolated Mostly synchronous with TTA-SW Inconstant
Sharp Frontal Delta wave +/- (4)	Bi- or triphasic slow- wave (0.5-1 sec)	100-600	Frontal	Mostly asynchronous Inconsistently observed
Slow Delta waves + (5)	Mono or biphasic slow waves (0.5-1 Hz) Smooth or superimposed with fast rhythms (5-25 Hz)	<i>Occipital:</i> 100-600 <i>Temporal:</i> 100-500 <i>Frontal/central:</i> <400	<i>Occipital</i> +++ <i>Temporal</i> ++ <i>Frontal/central</i> +	<i>Occipital:</i> often synchronous <i>Temporal / Frontal / central:</i> often asynchronous



Figure 10 Specific maturational aspects of EEGs at 24 to 26 wGA. The EEG alternates between continuous (A) and more discontinuous activity, with long quiescent periods (B-C-D-E). The duration of each period is variable, indicating the presence of rudimentary sleep state cyclicity. EEG age-related specific features are observed: TOA-SW (1), TTA-SW (2), TFA-SW (3), sharp frontal delta waves (4), and slow delta waves (5).
 low pass filter: 70Hz, high pass filter: 0.5Hz, notch filter: 50Hz (Amiens)* [Q1-Q3]

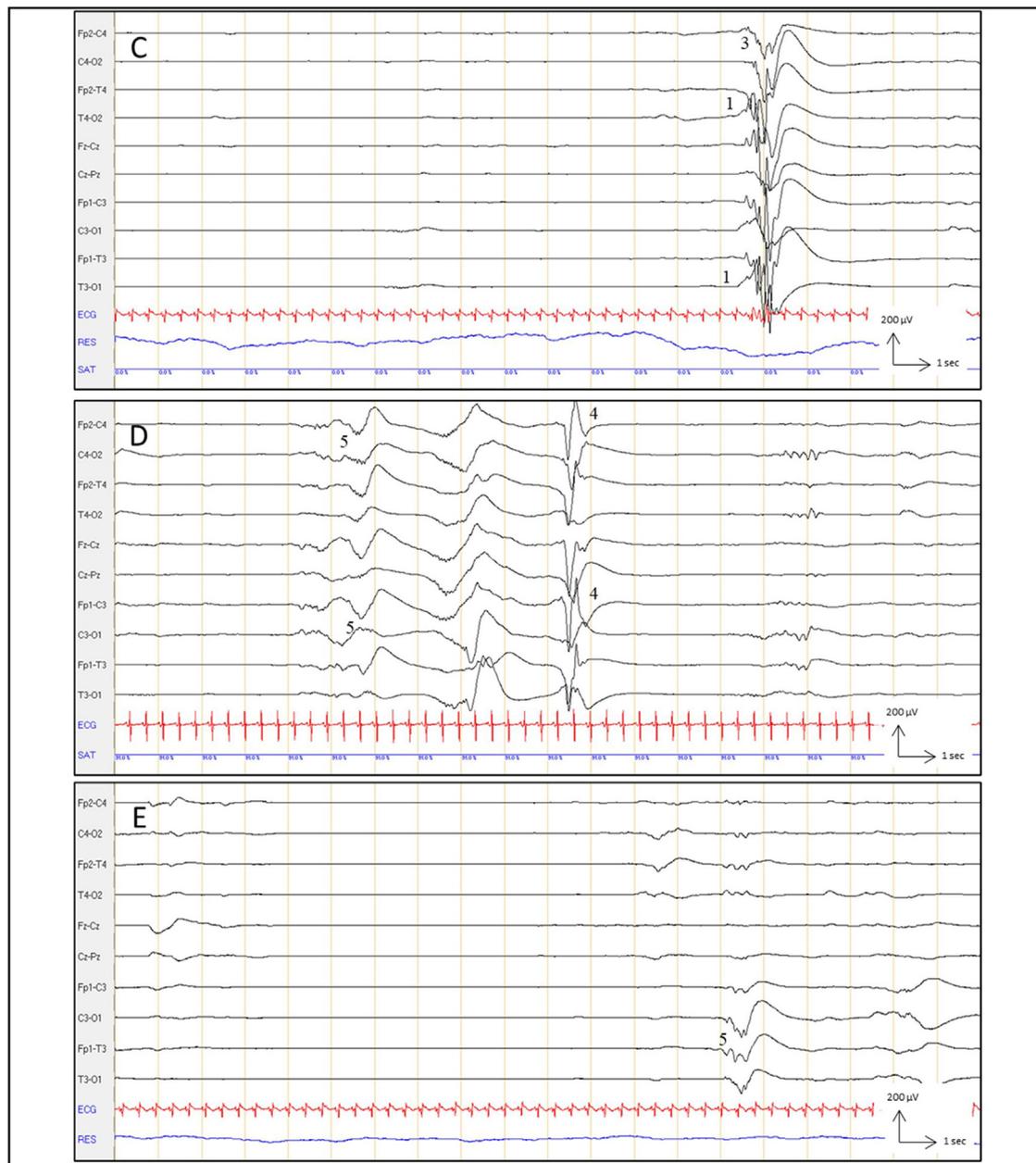


Figure 10 (Continued)

Sleep state cyclicity

Sleep state cyclicity is already observed. Concordance between EEG patterns and the presence or absence of REM allows differentiation between the AS and QS states. The time spent in AS is significantly higher than that in QS. In AS, the EEG trace is continuous or nearly continuous, with APs lasting up to several minutes [21].

Reactivity

Reactivity appears progressively within this age group and is marked by a generalized transient decrease in amplitude [3,4,38].

EEG-specific features (generator-based dynamics)

The most frequent feature is represented by TTA-SW (personal observations) [11,59]. Its incidence increases over

that from 24 to 26 wGA. Its amplitude ranges from 100 to 600 μV (exceptionally up to 800 μV , including the slow wave) (personal observations). It is localized to temporal areas, synchronous or asynchronous, and equally distributed between the right and left hemispheres [11,32,59,68] (personal observations).

The incidence of TOA-SW decreases during this period and it is inconsistently observed (50% of EEG tracing) (personal observations) [3]. Its amplitude ranges from 100 to 310 μV , including the slow wave (personal observations) and remains localized to the occipital areas [11,12,33,59] (personal observations).

TFA-SW remain variable and disappear at this GA. They have the same characteristics as at 24–26 wGA [59,68] (personal observations).

Sharp Frontal Delta waves are inconsistently observed. When present, they are localized to frontal areas, mostly asynchronous, and predominantly observed in the right hemisphere (needs to be confirmed) [59,68] (personal observations).

Slow delta waves tend to increase in number between 27 and 32 wGA [3,74]. Occipital and temporal slow delta waves are the most frequently occurring and have the highest amplitudes. Their amplitude ranges from 100 to 500

µV and are mostly superimposed with fast rhythms on the ascending slope of the slow wave (10–60 µV, 5–25 Hz). They occur in sequences lasting from 1 to 95 s. Frontal and central delta waves occur less frequently than temporal and occipital delta slow waves, as at 24–26 wGA, are isolated, and are mostly unilateral and asynchronous or occur in sequences lasting from 1 to 20 s. They are of lower voltage than temporal and occipital delta slow waves (100–400 µV [3,11,24,34,59,68] (personal observations).

General organization of EEG at 27-28 GA				
Sleep state cyclicly	+/- Active sleep / quiet sleep			
Background activity	Quiescent periods: 1-30 sec, median: 3[2-5]* (QS), 2 [2-4]* (AS), 10-30 % of the EEG trace Periods of activity: 1-40 sec, up to 5 min in active sleep, median 5 [2-8]* (QS), 10 [5-22]* (AS) Intermediate activity: delta to beta (predominantly delta), 10-20% of the EEG trace			
Provoked reactivity	+/- (appear progressively) Transient generalized decrease in amplitude			
EEG specific features				
	Morphology	Amplitude µV	Localization	Remarks
TTA-SW ++ (2)	Burst of theta (4-7 Hz) sharp waves in coalescence with a biphasic slow wave	100-600 (exceptionally up to 800)	Temporal	Synchronous / Asynchronous
TOA-SW + (1)	Burst of 4-7 Hz sharp waves, often in coalescence with a biphasic slow wave	100-310	Occipital	Mostly asynchronous Inconsistently observed (50%)
TFA-SW +/- (3)	Burst of 4-7 Hz sharp waves often in coalescence with a biphasic slow wave	100-500	Frontal	Mostly asynchronous Mostly synchronous with TTA-SW Inconsistently observed Disappears at this GA
Sharp Frontal Delta wave +/- (4)	bi- or triphasic slow waves (0.5-1 sec)	100-600 (exceptionally up to 800)	Frontal	Mostly asynchronous Inconsistently observed
Slow Delta waves + (5)	Mono or biphasic slow waves (0.5-1 Hz) Smooth or superimposed with fast rhythms (5-25 Hz)	<i>Occipital:</i> 100-600 <i>Temporal:</i> 100-500 <i>Central/frontal:</i> 100-400	<i>Occipital</i> +++ <i>Temporal</i> ++ <i>Central/frontal</i> +	<i>Occipital/temporal:</i> Occur in sequences, often bilateral synchronous <i>Central/ frontal:</i> frequently isolated asynchronous

Figure 11 Specific maturational aspects of EEGs at 27 to 28 wGA.

EEG activity remains labile. Sleep state cyclicly appears progressively. Continuous activity (A) or sub-continuous activity (B), associated with an irregular respiratory rate (AS), alternates with more discontinuous activity and regular respiratory and cardiac rates (C–D) (QS). EEG age-related specific features are observed: TOA-SW (1), TTA-SW (2), TFA-SW (3), sharp frontal delta waves (4), and slow delta waves (5).

low pass filter: 70 Hz, high pass filter: 0.5 Hz, notch filter: 50 Hz (Amiens)* [Q1-Q3]

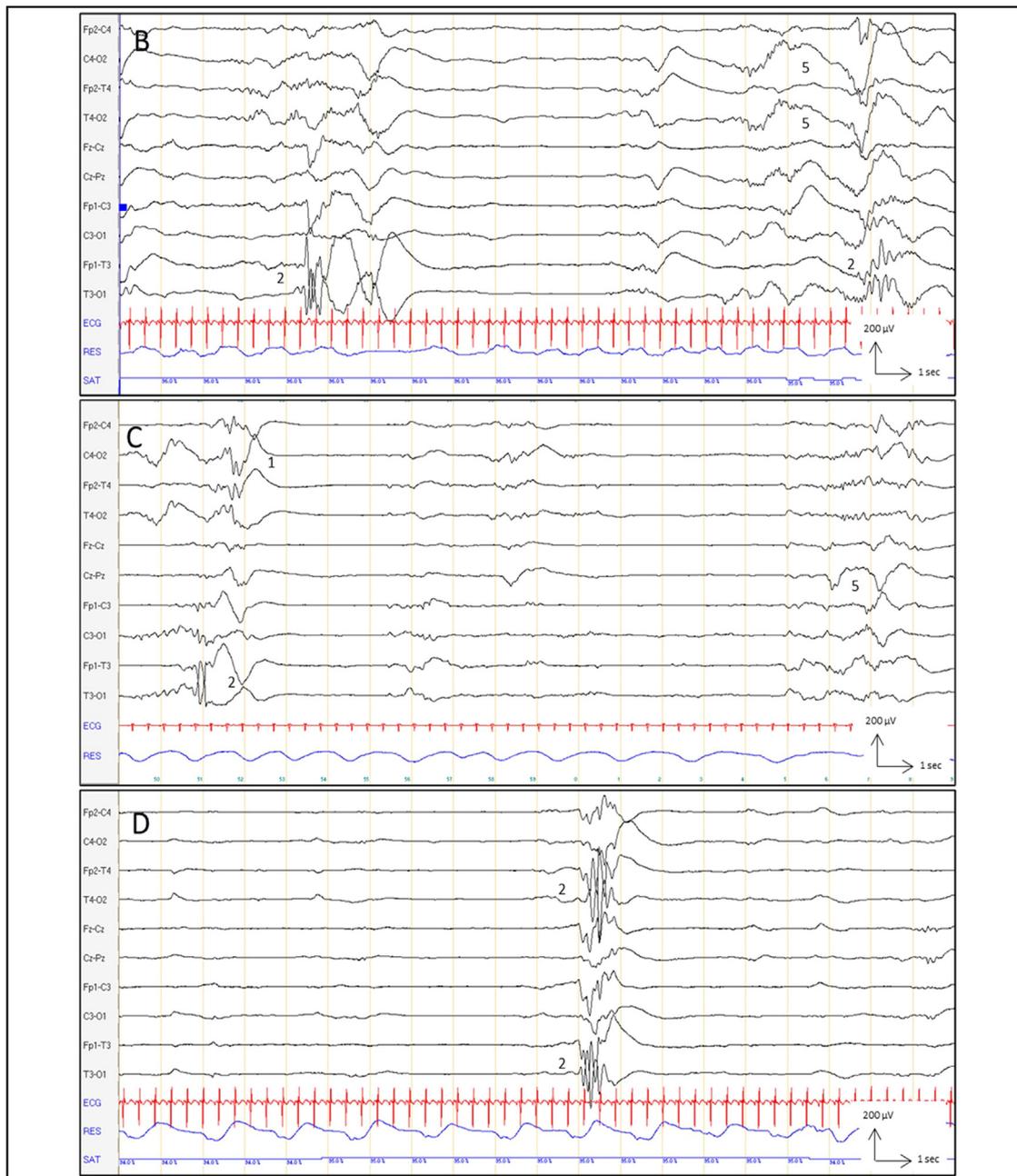


Figure 11 (Continued)

General organization of the EEG (network-based dynamics)

Quiescent periods

The duration of QPs decreases and depends on the vigilance state. In personal observations, the duration of QPs ranged from 1 to 27 s [9,11,18,27,59,71]. QPs lasting between 30 and 40 s are also acceptable, although rare [50,57] (Fig. 12, Video 3).

The median values were 3 s (IQR 2–5) during QS and 3 s (IQR 2–4) during AS. More than 90% of the QPs were <8 s in length. QPs represent from 20 to 30% of the EEG recording time.

Active periods

APs are composed of EEG-specific features (see below) and mixed-frequency activity of lower amplitude (50–100 μV).

The duration of APs increases during this period and depends on the vigilance state. In personal observations, the duration of APs ranged from 1 to 4 min but APs lasting up to 10 min have been reported [27,59]. In personal observations, the median value was 6 s (IQR 3–10) during QS and 11 s (IQR 4–25) during AS.

This mixed activity (intermediate or background activity), consists of frequencies ranging from delta to beta bands, predominantly delta [19,68], and represents <10% of the tracing (personal observations).

General organization of EEG at 29-30 GA				
Sleep state cyclicity	+ active wakefulness, active sleep, quiet sleep			
Background activity	Quiescent periods: 1-27 sec, exceptionally 40 sec, median 3 [2-5]* (QS), 3 [2-4]* (AS), 20-30 % of the EEG trace Active periods: 1 sec – 4 min, up to 10 min, median 6 [3-10]* (QS), 11 [4-25]* (AS) Intermediate activity: delta to beta (predominantly delta), 10-20 % of the EEG trace AW: continuous activity, AS/QS: discontinuous activity			
Provoked reactivity	+ AS: transient generalized decrease in amplitude, QS: transient appearance of continuous EEG			
EEG specific features				
	Morphology	Amplitude μ V	Localization	Remarks
TTA-SW +++ (2)	Burst of theta (4-7 Hz) sharp waves in coalescence with a biphasic slow wave	100-300	Temporal	Synchronous or asynchronous
Slow Delta waves ++ (5)	Mono or biphasic slow waves (0.5-2 Hz) superimposed with fast rhythms (5-25 Hz)	<i>Occipital:</i> 100 -400 <i>Temporal:</i> 100-400 <i>Frontal/central:</i> 100-300	<i>Occipital</i> +++ <i>Temporal</i> +++ <i>Frontal/central</i> +	<i>occipital:</i> often synchronous in sequences <i>temporal:</i> often asynchronous <i>Frontal and central:</i> frequently isolated, asynchronous
TOA-SW +/- (1)	Burst of 4-7 Hz sharp waves in coalescence with a biphasic slow wave	100-400	Occipital	Mostly asynchronous Inconsistently observed at (20 % of EEG tracing) Disappears at this GA
Sharp Frontal Delta wave +/- (4)	Bi- or triphasic slow waves (0.5-1 sec)	100-400	Frontal	Mostly asynchronous Rarely observed Disappears at this GA

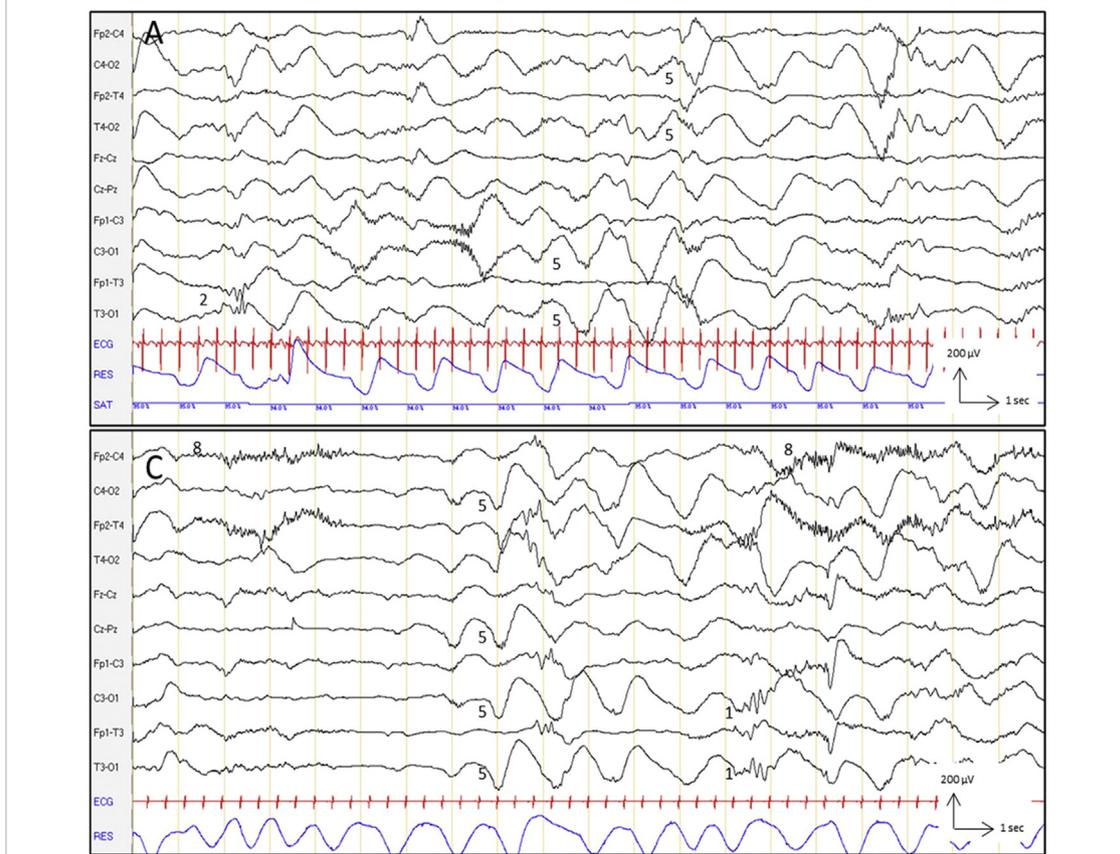


Figure 12 Specific maturational aspects of EEGs at 29 to 30 wGA.

The three states of vigilance are distinguishable: active wakefulness (A), active sleep (B), and quiet sleep (D–E). Activity is continuous during wakefulness and remains discontinuous during sleep, with the longest duration of quiescent periods during quiet sleep. EEG age-related specific features are observed: TOA-SW (1), TTA-SW (2), sharp frontal delta waves (4), and slow delta waves (5) observed in sequences in occipital areas (A–B).

low pass filter: 70Hz, high pass filter: 0.5 Hz, notch filter: 50Hz (Amiens)* [Q1-Q3]

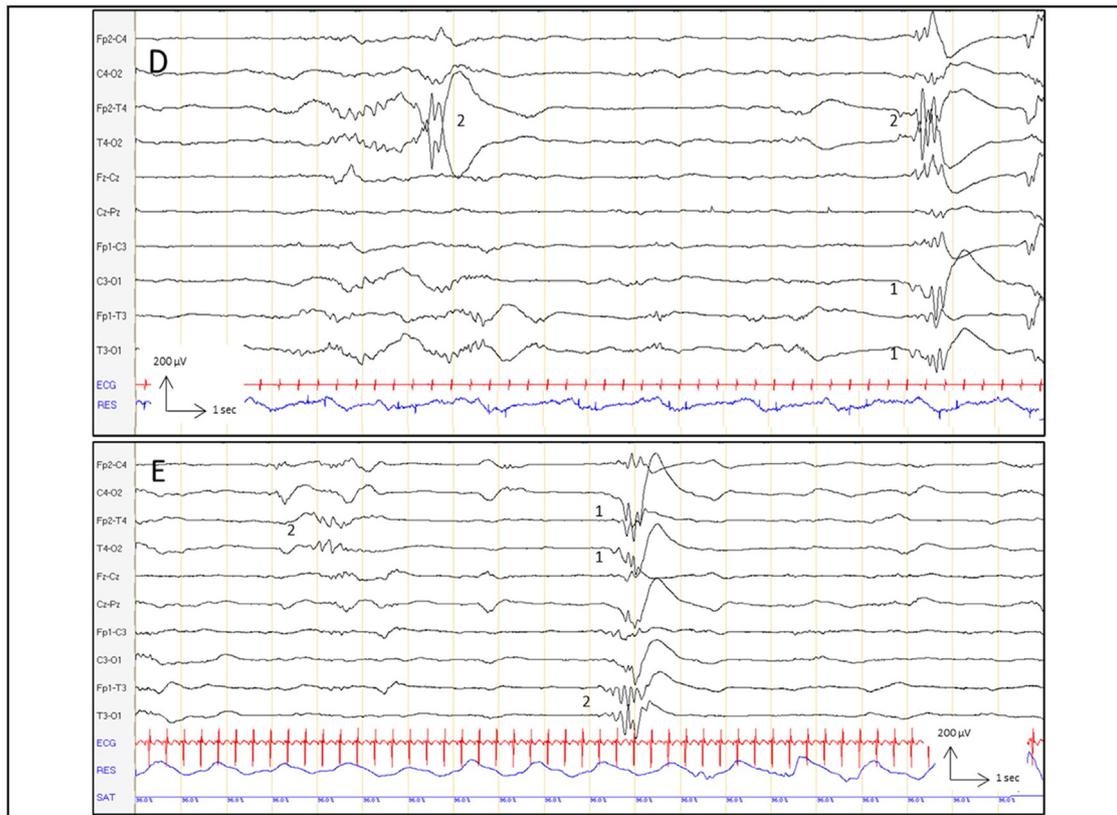


Figure 12 (Continued)

From 28 wGA, interhemispheric burst synchrony and symmetry is almost total [3,68] (personal observations).

Sleep state cyclicity

From 30 wGA, a clear agreement between EEG activity and the behavioral state is recognizable. The three vigilance states are distinguishable (active wakefulness, AS, QS). During arousal, the EEG trace is almost continuous. Discontinuity persists during AS and QS. During sleep, the longest periods of discontinuity are observed during QS.

Reactivity

Reactivity is present during this period. It is marked by a transient generalized decrease in amplitude during AS and the transient appearance of continuous EEG during QS [3,4,38].

EEG-specific features (generator-based dynamics)

The most frequent features observed are TTA-SW and slow delta waves.

TTA-SW is the most frequent theta activity at this age (personal observations) [11]. Its amplitude decreases and ranges from 100 to 130 μV (100–300 μV , including the slow wave, and exceptionally up to 600 μV) (personal observations) [11,32,59,68].

Slow Delta waves are characterized by frequencies ranging from 0.5 to 2 Hz, superimposed with fast rhythms (5–25 Hz), irrespective of their localization. The amplitude of the delta waves peaks from 100 to 400 μV (exception-

ally up to 600 μV). Occipital and temporal slow delta waves remain the most abundant. Frontal and central slow delta waves are less frequent and their amplitude varies from 100 to 300 μV (exceptionally up to 500 μV) [3,11,24,34,59,68] (personal observations).

TOA-SW is observed in only 20% of EEG tracings (personal observations) and always disappears at this GA [3] (personal observations). Its amplitude ranges from 100 to 400 μV .

Sharp frontal delta waves are rarely observed and disappear at this GA (personal observations). Their amplitude ranges from 100 and 400 μV .

31–33 weeks GA

General organization of the EEG (network-based dynamics)

With cerebral maturation and the organization of sleep cycling, QPs first disappear during wakefulness and AS. EEG activity becomes more continuous during active/quiet wakefulness. During AS, EEG activity is continuous, and QPs < 10 s can persist [4,38]. During QS, QPs persist but their duration decreases with increasing GA (< 15 s at 32 wGA) [9,18,27] (Fig. 13, Video 4).

In parallel, the duration of QPs increases. More than 80% of APs are synchronous and symmetrical [3]. Asynchronous activity is mainly seen at the beginning of QS [4,55].

General organization of EEG at 31-33 GA				
Sleep state cyclicity	+ Active wakefulness, quiet wakefulness (+/-), active sleep, quiet sleep AS: continuous activity, QS: discontinuous activity			
Background activity	Quiescent periods: <15 sec (QS), <10 sec (AS) Active periods: AW/ QW: continuous activity, period of activity lengths in active and quiet sleep Synchrony / symmetry: transitory asynchronous activity at the beginning of the QS			
Provoked reactivity	+ AS: transient generalized decrease in amplitude, QS: transient appearance of continuous EEG			
EEG specific features				
	Morphology	Amplitude μV	Localization	Remarks
TTA-SW + (2)	Burst of theta (4-7 Hz) sharp waves in coalescence with a biphasic slow wave	100-300	Temporal	Synchronous or not Disappear in AS (32 wGA) Persist in QS
Slow Delta waves +++ (5)	Mono or biphasic slow waves (0.5-2 Hz) superimposed with fast rhythms (5-25 Hz)	100-300	Temporal Temporo-occipital	Occur in sequences

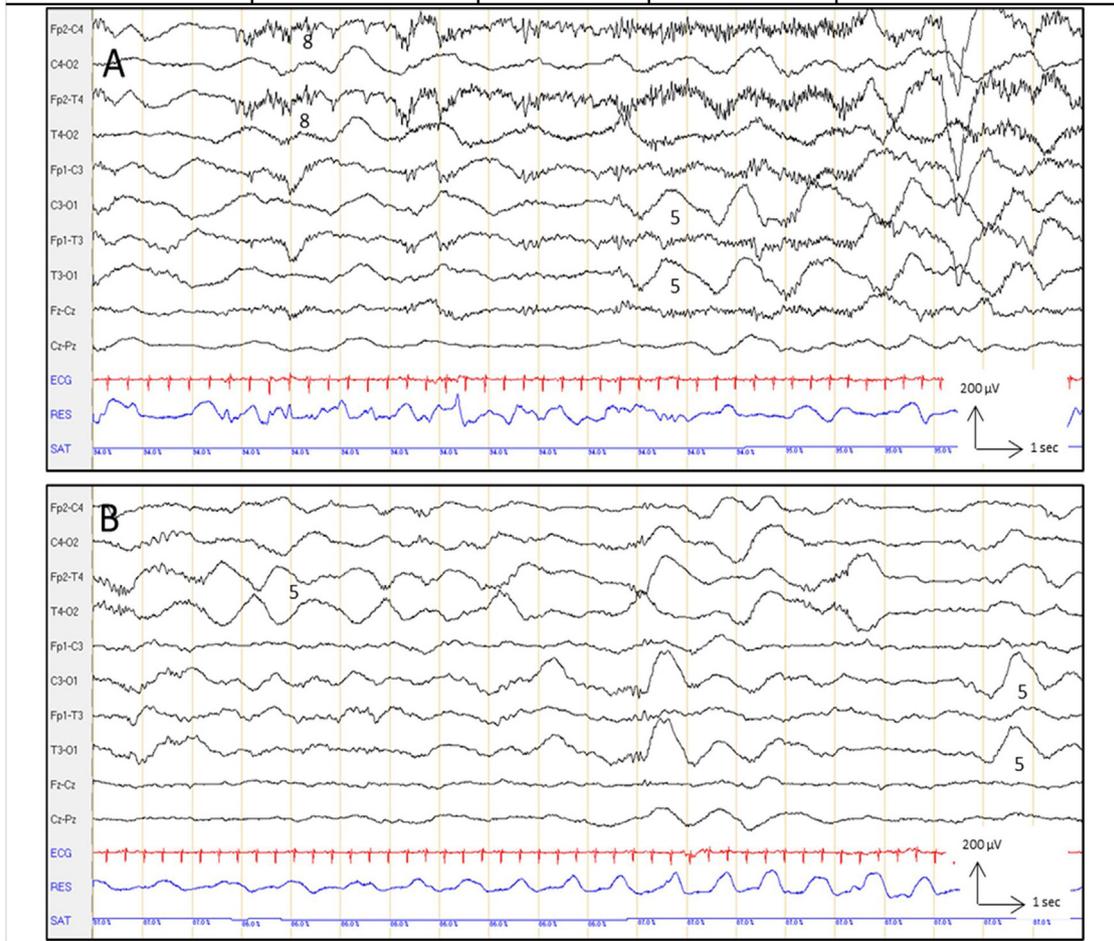


Figure 13 Specific maturational aspects of EEGs at 31 to 33 wGA.

The three states of vigilance are distinguishable: active wakefulness (A), active sleep (B), transition to quiet sleep (C), and quiet sleep (D–E). Activity is continuous during wakefulness, with muscle artefacts (8) and remains discontinuous during sleep, with the longest duration of quiescent periods during quiet sleep. The transient decrease of amplitude indicates reactivity during active sleep (9). Transitory asynchrony can be observed during the transition between vigilance states (C). EEG age-related specific features are observed: TTA-SW (2) and slow delta waves (5) observed in sequences in occipital areas (A–B)

low pass filter: 70 Hz, high pass filter: 0.5 Hz, notch filter: 50 Hz (Amiens) [Q1-Q3]*

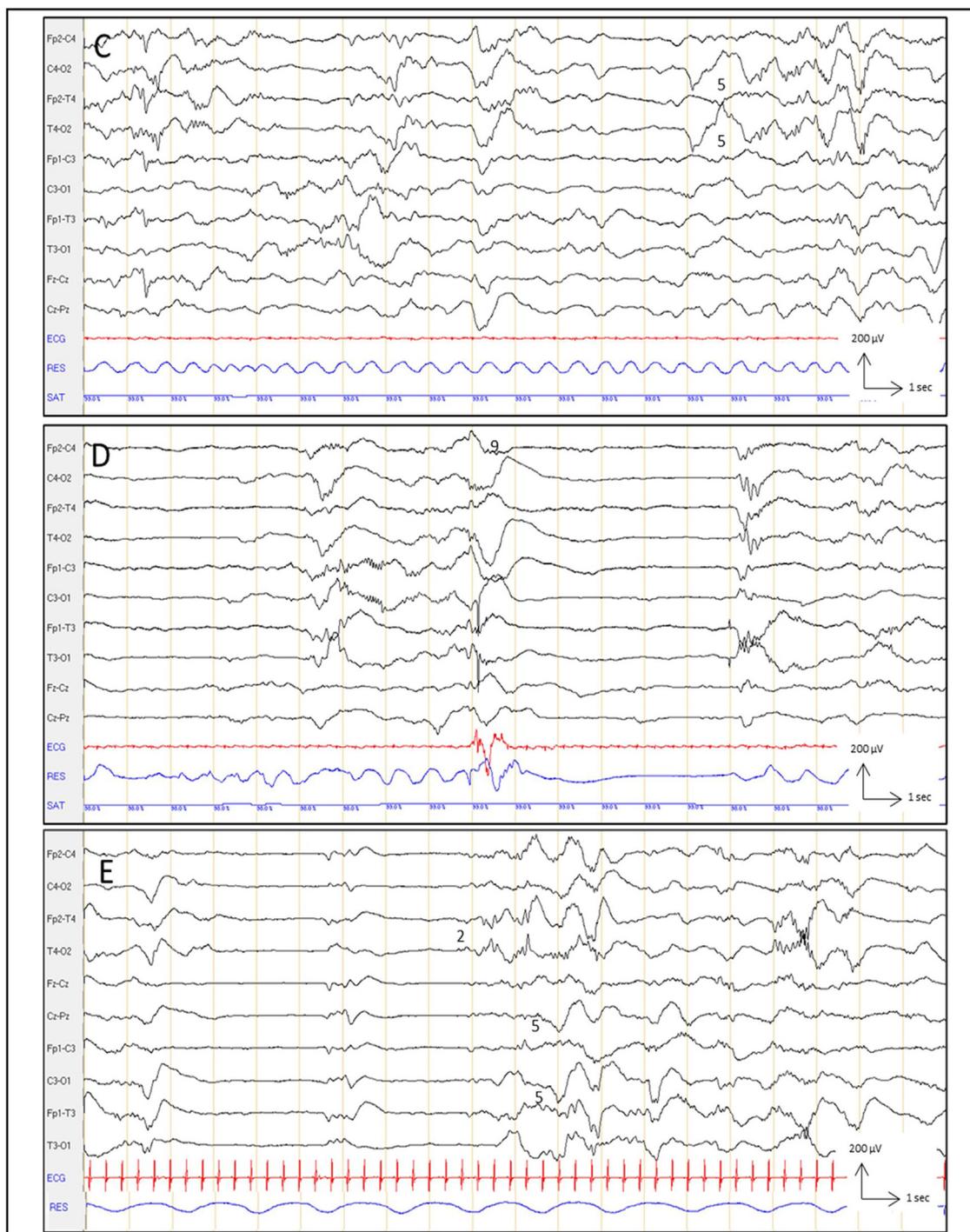


Figure 13 (Continued)

Sleep state cyclicity

After 30 wGA, there is a clear association between the EEG state and behavioral state. AW, AS, and QS are easily distinguishable, but periods of quiet wakefulness are still rare.

Reactivity

Reactivity is clearly identifiable at this stage [3,4,38]. During AS, reactivity is marked by a general transient decrease

in amplitude. During QS, reactivity is characterized by the transient appearance of continuous slow-wave EEG activity [4,38].

EEG specific features (generator based dynamic)

TTA-SW is the only theta activity at this stage [3]. Its incidence decreases after 30 wGA and disappears during AS at 32 wGA but persists during QS up to 34–36 wGA [4,32].

General organization of EEG at 34-36 wGA				
Sleep state cyclicity	++ Active wakefulness, quiet wakefulness, active sleep, quiet sleep			
Background activity	Quiescent periods: < 10 sec, only in QS Periods of activity: Continuous EEG except in QS Synchrony / symmetry: frequent transitory asynchrony at the QS onset			
Provoked reactivity	+ AS: transient generalized decrease in amplitude QS: transient appearance of continuous high amplitude slow wave activity			
EEG specific features				
	Morphology	Amplitude μ V	Localization	Remarks
Local Slow Delta waves +++ (5)	Mono or biphasic slow waves (1-2 Hz), superimposed with fast rhythms (5-25 Hz)	100-300	Occipital	More diffuse in QS Occur in sequences More numerous than at 32 wGA
TTA-SW +/- (2)	Burst of theta (4-7 Hz) sharp waves in coalescence with a biphasic slow wave	100-300	Temporal	Mostly asynchronous +/- unilateral Only in QS, Disappear at this GA
Transient frontal sharp wave, "encoches frontales" +/- (6)	Smooth, incomplete and asymmetrical	50-200	Frontal	Synchronous +/- repetitive

Figure 14 Specific maturational aspects of EEGs at 34 to 36 wGA.

The three states of vigilance are distinguishable: wakefulness (A), active sleep (B–C), and quiet sleep (D–E). Activity is continuous during wakefulness and active sleep, but some quiescent periods persist during active sleep. Transitory asynchrony is physiological during the transition between active and quiet sleep (D). EEG age-related specific features are observed: TTA-SW (2) exclusively observed during quiet sleep and slow delta waves (5) observed in sequences in occipital areas and transiently in frontal areas (6). low pass filter: 70 Hz, high pass filter: 0.5 Hz, notch filter: 50 Hz (Amiens)* [Q1-Q3]

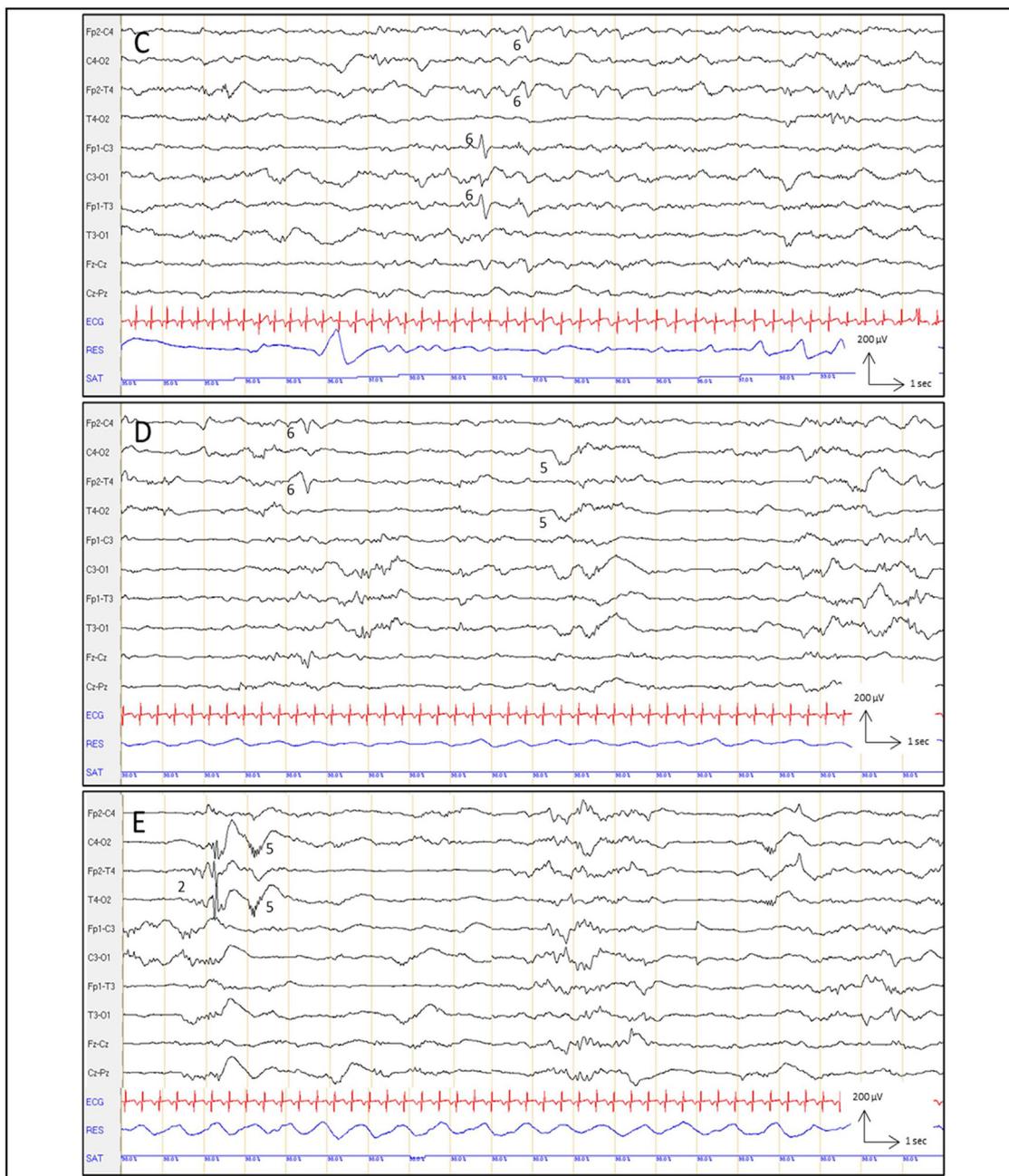


Figure 14 (Continued)

Local slow delta waves (delta brushes) are the most common specific feature at this stage [4,38]. They are characterized by delta frequencies (0.5–2 Hz). Their amplitude decreases with GA and is between 100 and 300 μV , with a higher amplitude during QS than AS [4,25,37,40,55,58,63,74]. They are superimposed with fast-rhythm theta waves and peaks of high frequency (14–20 Hz) [77]. They become more localized to the temporal and temporo-occipital areas with increasing GA [4,6,22,64].

34–36 weeks GA

General organization of the EEG (network-based dynamics)

At 34–36 wGA, the EEG is continuous, except during QS. These persisting QPs last < 10 s [4,38,50]. The EEG AP amplitude decreases to between 50 and 300 μV .

Interhemispheric asynchrony increases at this stage. Transient asynchrony may be observed at the onset of QS [4,55] (Fig. 14, Videos 5–6).

General organization of EEG at 37-41 GA				
Sleep state cyclicality	++ Active and quiet wakefulness, active sleep 1 (before QS), quiet sleep, active sleep 2 (after QS)			
Background activity	Quiescent periods: absent (only some QP in quiet sleep at 37-38 wGA < 5 sec) Active periods: Continuous in all vigilance states AW, QW, AS2: 'activité moyenne' (continuous poly-frequencies activity) AS1: high amplitude mixed frequencies continuous tracing QS: 'tracé alternant' and 'tracé lent continu' (slow continuous tracing, appears after 38 wGA) Synchrony / symmetry: Inconstant and transitory asynchrony at the QS onset			
Provoked reactivity	+ AS: transient generalized decrease in amplitude QS: transient reinforcement or more often attenuation of the background activity			
EEG specific features				
	Morphology	Amplitude μV	Localization	Remarks
Local Slow Delta waves + (5)	Mono or biphasic slow waves (1-3 Hz) Superimposed with fast rhythms (5-25 Hz)	100-200	Occipital	Occur in sequences Predominate in AS1 and QS (only QS after 38 wGA)
"Encoches frontales" ++ (6)	Diphasic with a small initial negative deflexion followed by a wider positive deflexion with higher amplitude (0.5-0.75 seconds)	50-200	Frontal	Mostly synchronous Frequently isolated Predominantly in AS1 and the onset of QS
Slow anterior dysrhythmia ++ (7)	short burst of monomorphic or polymorphic delta waves of 1-3 Hz	50-100	Frontal	Predominantly in AS1
Burst of rolandic theta rhythms +/- (11)	Burst of theta activity, sometimes sharp in QS Sequences 1-3 sec	25-50	Rolandic Central	More frequent in QS

Figure 15 Specific maturational aspects of EEG at 37 to 40 wGA.

The four states of vigilance are distinguishable: active wakefulness (A), quiet wakefulness, active sleep 1 (AS1) (B-C-D), quiet sleep (E-F), and active sleep 2 (AS2) (G). Activity is continuous during all states of vigilance. 'Activité moyenne' is observed during wakefulness and AS2 (A-B-C-D-G). The 'tracé alternant' is observed during quiet sleep (E-F). EEG age-related specific features are observed: transient frontal sharp wave (6), anterior slow dysrhythmia (7), bursts of theta Rolandic waves (11), and artefacts (muscular artefacts (8), ocular movements (10)).

low pass filter: 70 Hz, high pass filter: 0.5 Hz, notch filter: 50 Hz (Amiens)* [Q1-Q3]

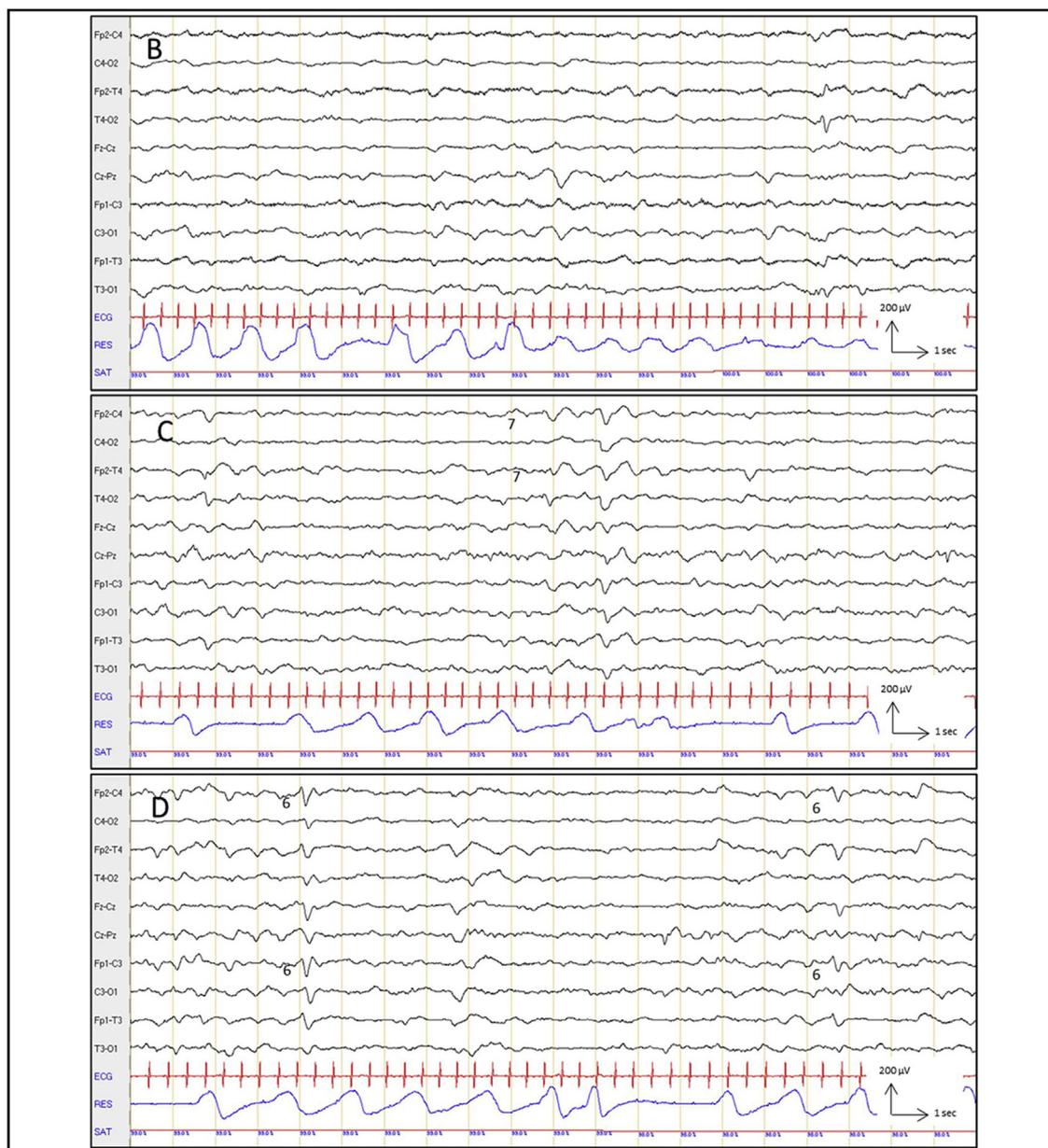


Figure 15 (Continued)

Sleep state cyclicity

The four vigilance states are distinguishable at this stage (active and quiet wakefulness, AS, and QS). During arousal and AS, the EEG trace is almost continuous, but discontinuity persists during QS.

Reactivity

Reactivity is clear and reproducible. In QS, EEG reactivity is characterized by a general transient decrease in background activity. In AS, the reactivity takes the appearance of continuous high-amplitude slow-wave activity [4,38].

EEG specific features (generator-based dynamics)

At 34–36 wGA, the principal age-related specific features are represented by slow delta waves superimposed

with fast rhythms (delta brushes). They are observed during all vigilance states but are more numerous during AS and QS [4,38]. They are predominant in the occipital areas and more diffuse during QS than AS [4,6,22,64]. The frequency of delta waves increases to 1–2 Hz and superimposed fast rhythms range from 5 to 25 Hz. The amplitude of the delta waves decreases (100–300 μV) [22] and is higher during QS than AS [4,25,37,40,58,63,74].

TTA-SW is rare and only observed during QS. It is mostly asynchronous and can be unilateral. It disappears during this stage.

Immature frontal transients may appear. They can be isolated or repetitive and can be clearly differentiated during the transition between AS and QS and at the beginning of QS.

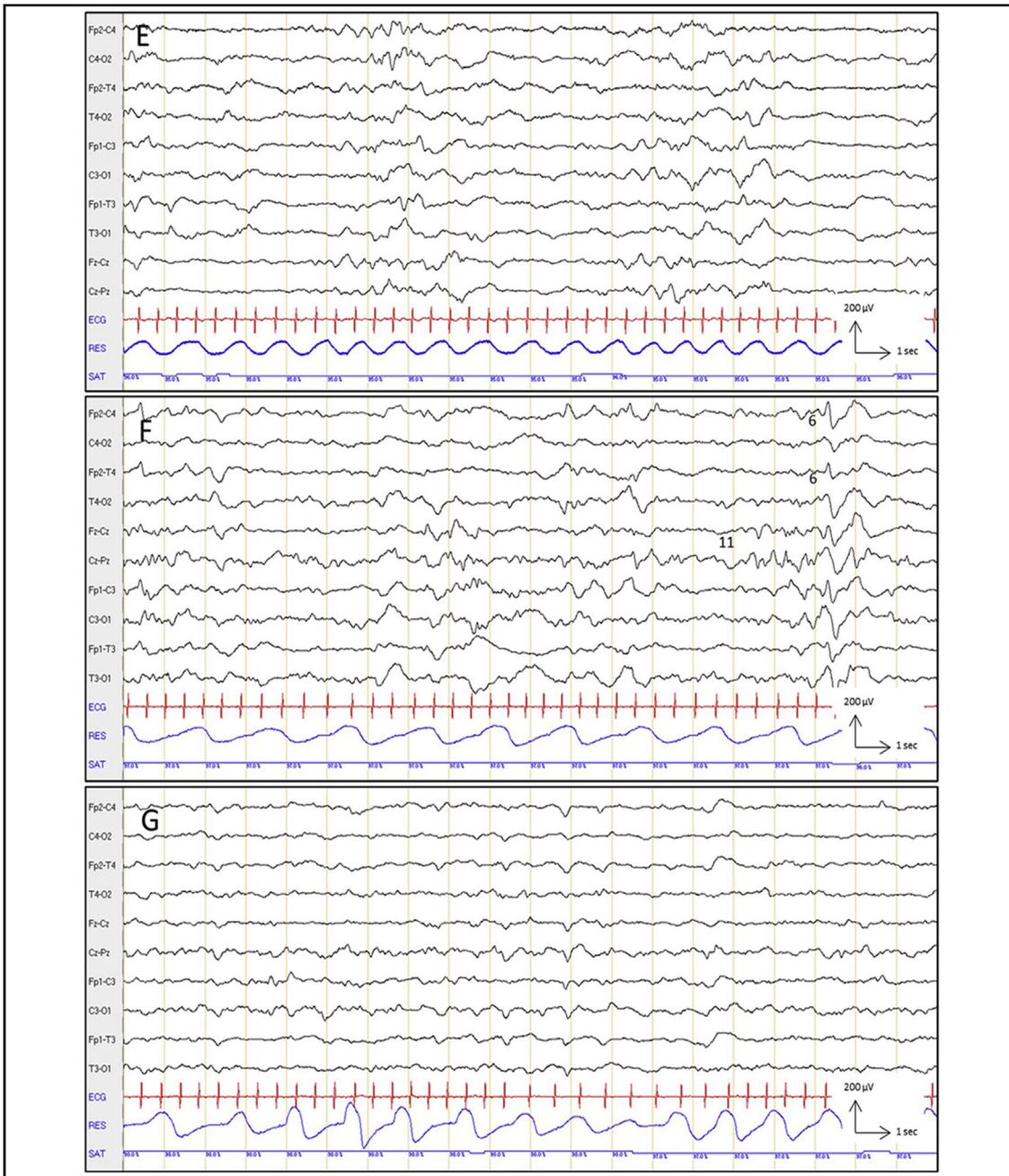


Figure 15 (Continued)

37–40 weeks GA

General organization of the EEG (network-based dynamics)

The EEG trace is continuous, irrespective of the vigilance state (some QPs < 5 s can persist during QS at 37–38 wGA). Active and quite wakefulness (AW-QW) and AS and QS (AS-QS) can be clearly identified and distinguished. AS1 (AS1) precedes QS followed by AS2 (AS2). They show different characteristics. Interhemispheric synchrony is permanent during AS and very frequent during QS (Fig. 15, Video 7).

During AW, QW, and AS2, the continuous activity, composed of mixed frequencies, is called 'activité moyenne'. It is characterized by irregular diffuse activity with a Rolandic predominance, mainly in the theta band (4–7 Hz), with an amplitude of 25–50 µV lasting 1–3 s; occipital delta waves (1–3 Hz) of 25–50 µV may also be observed, as well as irregular alpha and beta activity, with amplitudes up to 30 µV over all areas [4,38].

A mixed-frequency tracing is observed during AS1 and is characterized by continuous low-amplitude activity with superimposed slow waves (2–4 Hz) of high amplitude (> 10 µV).

During QS, quiescent periods < 5 s can still be observed at 37–38 wGA. After 37–38 wGA, the so called ‘tracé alternant’ is observed. It is characterized by a bilateral synchronous and symmetrical burst of delta-theta activity (1–7 Hz) of 25–200 μ V. Delta waves have a smoother morphology in occipital areas and a sharper morphology in frontal areas. Bursts generally last 5–6 s (varying from 3–8 s) and alternate with periods of lower amplitude that have nearly the same duration as the slow wave burst. The ‘tracé alternant’ disappears after 44 wGA. In more mature infants (39–41 wGA), slow continuous tracing (‘tracé lent continu’) is present during QS. It is characterized by continuous delta-wave activity (1–3 Hz), with occipital predominance and a variable amplitude of 50–200 μ V. When the ‘tracé alternant’ and ‘tracé lent continu’ occur in the same infant, the ‘tracé lent continu’ precedes the ‘tracé alternant’ [4,38].

Reactivity

Reactivity is clear and reproducible. During AS, sensory stimulation induces a general transient decrease in EEG activity. During QS, a slow transient wave burst, or transient lengthening of hypoactive activity can be observed.

EEG-specific features (generator-based dynamics)

Delta waves with superimposed fast rhythms (delta brushes) persist during all behavioral states, at 37–38 wGA. They have a higher amplitude during QS and predominate in the occipital areas [4,38]. At 39 to 41wGA, delta brushes are only observed during QS, with an amplitude <200 μ V.

Mature frontal transients are clearly differentiated in frontal areas during AS1 and the onset of QS. These frontal transients are a good maturational index. They are rare during AS2.

Slow anterior dysrhythmia (short bursts of monomorphic or polymorphic delta waves of 1–3 Hz with an amplitude of 50–100 μ V) are observed in the frontal areas during AS1.

The appearance of clearly differentiated short-burst theta waves in the Rolandic areas, which are sometimes sharp and of high amplitude, are observed during QS.

Conclusion

This review presents the normal characteristics of background EEG activity (continuity, discontinuity, lability, cyclicity), as well as the spatio-temporal organization and morphological aspects of EEG-specific features, during brain maturation. This is a well-illustrated didactic tool that includes summary tables for each GA. This should help in the interpretation of EEGs of premature infants to differentiate between normal and pathological patterns. Abnormal features or background activity disturbances should warn clinicians of possible neurological complications. Further studies are nevertheless required to precisely define the neurodevelopmental prognostic value of such abnormalities.

Conflicts of interest

The authors disclose no conflict of interest related to this work.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.neucli.2020.10.004>.

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