

Physiological Activity Recorded With Intracranial EEG: From Wakefulness to Sleep

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KEY CONCEPTS

- Physiological electroencephalography (EEG) rhythms exhibit local specificities when recorded with intracranial EEG (ICEEG).
- It is important to recognize these rhythms, as they should be clearly differentiated from pathological activities.
- Study of wakefulness requires a routine protocol with activation tasks and study of sleep should include additional scalp EEG combined with electrooculography and electromyography of the mentalis muscle.
- ICEEG explorations have allowed the description of physiological activity of deep structures, such as the hippocampus, which contribute only very little to scalp EEG.
- ICEEG study of physiological activity has changed our understanding of wakefulness and sleep, with the demonstration of spatial and temporal inhomogeneities suggesting that vigilance states evolve along a continuum and are regulated locally.

INTRODUCTION

EEG activity recorded with intracranial electrodes shares many characteristics with scalp EEG. Thus, physiological rhythms of wakefulness and sleep recorded with scalp electroencephalography (EEG) are detected, such as alpha activity, mu rhythm, sleep spindles, or saw-tooth waves. These activities exhibit some local specificities in the intracranial EEG (ICEEG). Moreover, other less well-known EEG patterns are observed which are particularly evident in deep structures such as the hippocampus. These latter structures contribute only very little to what we know from the scalp EEG. Such graphoelements are important to recognize, as they should not be misinterpreted as pathological activities. In the present chapter, we provide a description of physiological activity throughout the sleep–wake cycle, regarding both spectral particularities and specific rhythms, inside and beyond the Berger frequency band.

METHODOLOGICAL CONSIDERATIONS FOR THE RECORDING OF PHYSIOLOGICAL ACTIVITY IN INTRACRANIAL EEG

Among ICEEG methods, the major advantage of stereoelectroencephalography (SEEG) is that it is excellently suited to explore deep structures and it provides the unique opportunity

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to investigate local specificities of brain electrophysiological activity. These advantages are opposed by its limited cortical sampling. What type of physiological EEG activity will be recorded is dependent on the cortical sampling of the individual SEEG exploration. For example, mu rhythm will be captured only in case of sensorimotor explorations, whereas lambda waves are captured only in case of posterior cortex explorations. One way to normalize the variable location of SEEG electrodes is to investigate a large number of patients and to standardize the electrode positions in a common stereotactic space allowing intersubject comparisons, as recently done in the Montreal Neurological Institute multicenter ICEEG atlas project (mni-open-iieegatlas.research.mcgill.ca).^{1,2} One has to be aware that selecting “true” normal healthy cortex represents an inaccurate task, since we essentially analyze EEGs from the brains of epileptic patients. Moreover, electrodes are implanted with the objective to identify the epileptogenic zone. Nevertheless a portion of approximately 20% of channels³ contains electrode contacts localized in nonlesional tissue (electrodes placed for studying seizure propagation or neocortical contacts in case of deep-seated targets), showing no slow wave anomaly and no, or only very rare, epileptic spikes. Studies aiming to investigate brain physiology selected these channels and performed their studies in intervals clearly outside of ictal event (for a review see Frauscher and Gotman⁴). The fact that this activity is actually physiological is further supported by comparisons with noninvasive neurophysiological results obtained with EEG, magnetoencephalography, or functional MRI. Nevertheless, the effect of antiepileptic treatment has to be kept in mind, and knowledge about specific treatment effects such as benzodiazepines on EEG rhythms with an increase in fast activities is important. Moreover, it is recommended to await a certain time after electrode insertion, given the effect of anesthesia and cicatrization of tissue, before studying physiological brain activity. Based on our experience we suggest waiting 48 to 72 hours after SEEG insertion and 7 days in case of grids/strips.¹ For studying sleep, it is further important to have simultaneous scalp EEG fulfilling the minimum criteria of the American Academy of Sleep Medicine combined with electrooculography and electromyography of the mentalis muscle. At our Institution, we introduced a routine protocol, which is performed in all patients at the beginning of the recording (see Table 24.1). It facilitates the identification of physiological rhythms and the assessment of reactivity of EEG patterns in different conditions.

TABLE 24.1 MONTREAL NEUROLOGICAL INSTITUTE ROUTINE INTRACEREBRAL SEEG PROTOCOL (TOTAL DURATION OF 30 MIN)

NO.	SEEG PROTOCOL
1.	Eyes opened 1 min, closed 1 min, opened 1 min, and closed 1 min
2.	Saccades. Look to the right, to the left, upward, downward. 1 min
3.	Clench left fist 5-10 sec, right fist 5-10 sec, few times
4.	Jaw clenching 5-10 sec, few times
5.	Hyperventilation. 3 min. 3 additional min for relaxation
6.	Intermittent photic stimulation at 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 30, 40, and 50 Hz
7.	Attention. 1. Serial 7s (100-7, 93-7, 86-7, etc.). 1 min 2. Months of the year forward and backward. 1 min
8.	Reading. 1 min
9.	Writing. 1 min
10.	Various stages of sleep, if possible, in epochs of at least 1 min

SEEG, stereoelectroencephalography.

PHYSIOLOGICAL ACTIVITY DURING WAKEFULNESS

Signal Spectral Composition

The spectral composition of the ICEEG signal during wakefulness has been investigated in a large number of brain regions thanks to multicenter collaboration.¹ This work allowed the description of local specificities regarding spectral density distribution, with a spectral peak localized in the beta range (20–24 Hz) in the frontal lobe, in the alpha band (9.25–10.25 Hz) in the occipital lobe, in the intermediate alpha (8.25–9.25 Hz) and beta ranges (17–20 Hz) in the parietal lobe, in the lower alpha (7.75–8.25) and delta (0.75–2.25 Hz) bands in the temporal lobe (the delta peak was mostly due to the spectral composition of the mesiotemporal lobe), and in the beta (20 Hz) frequencies in the anterior insula. Some brain regions exhibit a specific signature, such as the precentral gyrus (beta peak), the cuneus (alpha peak), and the hippocampus (delta peak; Figure 24.1). The particular slow activity of the hippocampus during wakefulness, described

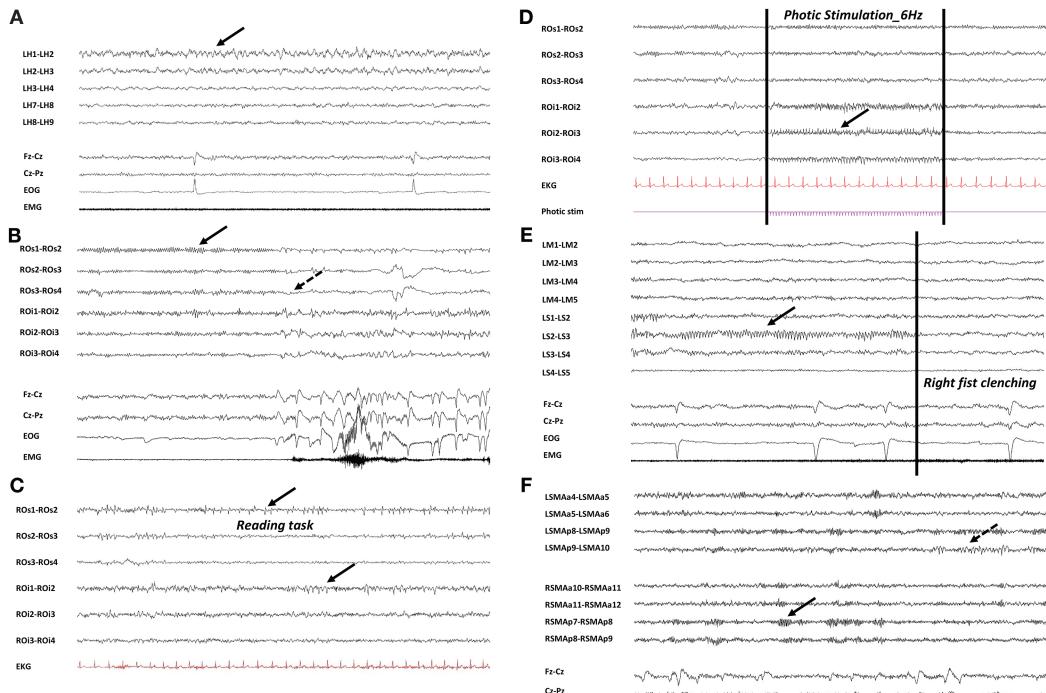


FIGURE 24.1 Examples of physiological wakefulness ICEEG features. In each figure (A–F), the ICEEG is presented above the scalp EEG. (A) Hippocampus rhythmic delta oscillations (line arrow) associated with high frequency oscillations (LH1–LH2). This activity differs from the fast activity observed in the temporal neocortex (LH7–LH8 and LH8–LH9). (B) Alpha rhythm is observed in the cuneus and lingual gyrus (line arrow). It is suppressed by eyes opening (dotted arrow), which is followed by lambda waves in the same derivations. (C) Lambda triangular waves (line arrow) are observed in the cuneus and lingual gyrus while the patient is reading. (D) Photic response to intermittent photic stimulation in the lingual gyrus (line arrow). (E) This example shows a mu rhythm in the postcentral gyrus (line arrow); the typical arch-shaped oscillations are blocked by contralateral fist clenching. (F) Beta oscillations (20 Hz) in the supplementary motor area. In this example, bursts of beta oscillations are observed in both hemispheres, but they are particularly well seen in the posterior right supplementary motor area (line arrow). Note that a mu rhythm appears in the second part of the EEG in channel LSMAp9–LSMP10 (dotted arrow).

a, anterior; EMG, electromyogram (chin); EOG, electrooculogram; H, hippocampus (the superficial channels are located in the temporal neocortex T2); ICEEG, intracranial EEG; L, left; M, motor cortex; Oi, lingual gyrus; Os, cuneus; p, posterior; R, right; S, somatosensory cortex; SMA, supplementary motor area.

since the first ICEEG studies, has been defined as a “rhythmic slow oscillation” (rhythmic slow activity [RSA]; 1.5–3 Hz) and is also observed during rapid eye movement (REM) sleep; it may be the counterpart of the theta activity observed in rodents during this vigilance stage as well as during active wakefulness (Figure 24.1A).^{5–9} It is associated with specific cognitive functions such as navigation and memory formation.^{5,9,10} The hippocampus activity during wakefulness and sleep also includes high-frequency oscillations (HFO).¹¹ In subcortical structures, wakefulness is associated with fast activities in the alpha to gamma range for the thalamus (medial pulvinar) and in the theta-alpha to beta range in the basal ganglia.^{12,13}

Specific Graphoelements

Alpha activity

Alpha rhythm is the most salient EEG rhythm observed during quiet wakefulness with eyes closed.¹⁴ It is defined as a 8 to 12 Hz oscillation recorded over the posterior regions, suppressed by eyes opening, and is thought to play a key role in top-down cognitive processes.¹⁵ Cortical alpha activity is found not only in the occipital lobe but extends to posterior parietal and temporal cortices (Figure 24.1B).¹ Interestingly, the alpha peak is not observed in all occipital structures; it is particularly prominent in the mesio-occipital cortex (cuneus) but not in the inferior occipital gyrus.¹ Alpha rhythm generation is thought to involve cortico-cortical and cortico-thalamic components.¹⁶ Recent studies combining SEEG and electrocorticography (ECOG), including microelectrodes, have shown that alpha oscillations are generated in supragranular layers of the cortex, that they propagate as travelling waves from higher order associative to primary visual but also somatosensory areas, and that cortical alpha may drive rather than be driven by thalamic alpha.^{17,18}

Lambda waves

Lambda waves are transient sharp surface-positive waves recorded over the posterior region and considered as a normal variant of the wakefulness EEG as they are not observed in all individuals.¹⁹ They seem more frequent in children, are evoked by saccadic visual exploration, and their generator is thought to be occipital.²⁰ Intracranial explorations have reported that lambda waves could be recorded in or near the calcarine region, but also in the infero- and superolateral portions of the occipital lobe.²¹ In our experience, lambda waves can be observed during the reading task of our routine protocol (see Table 24.1), particularly in areas associated with responses to photic stimulation (Figures 24.1C and D).²¹ This stimulus-specific reactivity helps to not confound them with epileptic activity.

Mu activity

The mu rhythm is a physiological activity in the theta to beta range (7–13 Hz) present over the central derivations.²² It may be uni- or bilateral, and if bilateral, symmetrical and synchronous or not. It is present when the body is at rest, and suppressed by the realization of a movement with the contralateral upper member, as well as by passive movements or somatosensory stimulations.²³ This suppression, also called “event-related desynchronization,” can also be elicited by the observation of another person executing an action, which may be considered as a marker of mirror neuron system activation.²⁴ Intracranial recordings have allowed localizing mu rhythm in the sensorimotor cortex as well as in premotor areas (Figure 24.1E).^{25,26}

Beta oscillations

Beta oscillations (from 13 to 30 Hz) predominate in the central region and the dorsolateral part of the frontal lobe and are observed both in scalp and ICEEG explorations.^{1,25,27} They are involved in cortico-muscular coupling for movement initiation but also in the proprioceptive feedback, thus playing a key role in sensorimotor integration (Figure 24.1F).²⁵

Gamma oscillations

Gamma activity in the 30 to 80 Hz range is diffusely distributed in the whole brain and generated within the cortex.²⁸ Gamma oscillations are thought to support various cognitive functions and to synchronize spatially separated cell assemblies, allowing large-scale integration.²⁹ For several reasons, including their low amplitude and the attenuation by the skull, gamma oscillations are hardly detected with scalp EEG whereas they can be easily observed in ICEEG. Thus, focal gamma reactivity to movement execution over the primary sensorimotor cortex has been described in patients explored with electrocorticography (ECoG) and SEEG.^{26,30}

PHYSIOLOGICAL ACTIVITY DURING NONREM SLEEP

Most of the nonREM (NREM) oscillations (slow oscillations, delta waves, spindles, and ripples [see the following]) exhibit a high level of synchronization within and between structures including the neocortex, thalamus, and hippocampus.³¹ This fine-tuned temporal coupling is thought to control neuronal excitability, stimulus processing, and to participate in memory consolidation processes including the transfer and the integration of new information into the preexisting cortical networks during sleep.^{32,33}

Signal Spectral Composition

The spectral composition of the ICEEG signal of various brain regions during NREM sleep has been recently described.² Overall, there is a global increase in spectral density power of 2.3 times in N2 and 6.0 times in N3, as compared to wakefulness. This increase reflects higher power mostly in delta to alpha (which includes spindles) frequencies, whereas beta and gamma power are lower. However, local specificities regarding particular frequencies are observed, with more high frequencies in the frontal lobe and less high frequencies in the temporo-occipital areas (Figure 24.2). Spectral peaks also differ from one region to another. They are generally well defined in mesial and deep-seated regions, where they are distinct from what is observed in the scalp EEG which represents mainly surface neocortical activity.

Specific Graphoelements

The main graphoelements of NREM sleep are presented from the lowest to the highest frequency.

Slow oscillations

NREM deep sleep (mainly N3 or slow wave sleep) is characterized by the presence of very slow oscillations less than 1 Hz which are spontaneously generated in the cortex. They are distinct from the delta (1–4 Hz) activity also associated with NREM sleep. First described in animals explored with local field potentials (scalp + depth EEG) as well as intracellular recordings, these slow oscillations have also been observed in the human scalp EEG.^{34,35} They reflect the bistability of cortical neurons, which alternate from a hyperpolarized state with low firing rate, called “OFF period” or “down-state,” associated with a negative half-wave on scalp EEG (often positive on depth EEG, depending on montage and anatomical location of the electrodes), to a depolarized state with high firing rate, called “ON period” or “up-state,” associated with a positive half-wave on scalp EEG (and often negative on depth EEG).³⁴ SEEG recordings, including macro- and microwire electrodes, have also demonstrated the modulation of gamma activity by the phase of the slow wave and provided more information about these oscillations by showing that a majority of them occurs locally, mostly in the medial frontal cortex, and propagates to other regions such as the thalamus but also the hippocampus, where their power is however lower than in the cortex.^{7,36–39}

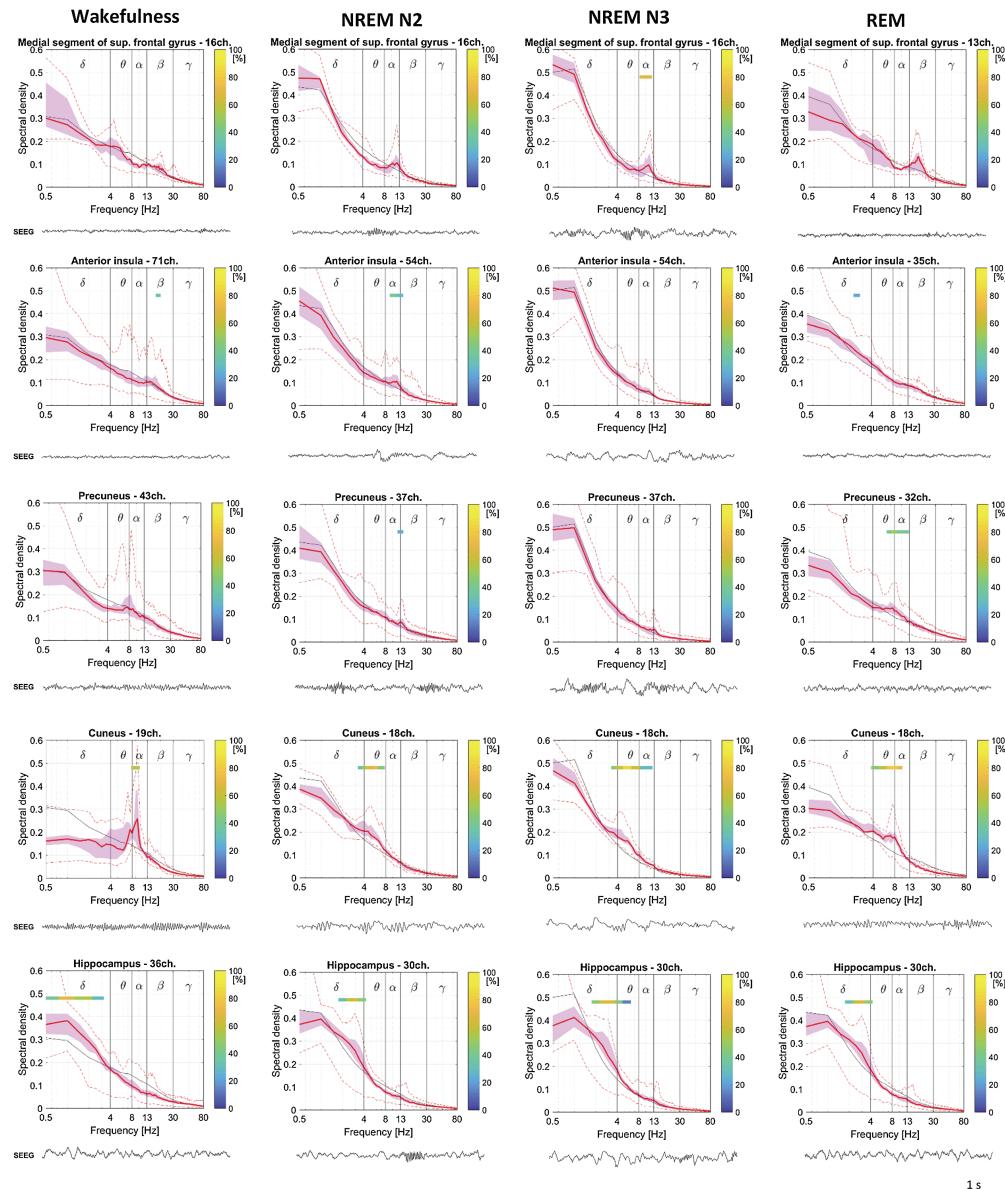


FIGURE 24.2 Intracranial EEG signal spectrum according to vigilance states in deep-seated brain areas. For each vigilance state (wakefulness, nonREM [NREM] N2, NREM N3, and REM), spectra of different deep-seated brain regions are provided. Semilogarithmic graphs are shown. The red line corresponds to the median spectral density of all channels in the region. The 25 and 75 percentiles are indicated by the shaded region. The broken lines show upper and lower bounds of the spectral distribution at every frequency. The thin black line shows the median spectrum of the baseline used to determine the presence of peaks. For definition of the baseline, see Frauscher et al.¹ Vertical black lines separate the common clinical frequency bands indicated by Greek letters. The horizontal segment in the upper part of some graphs indicates the presence of a significant peak as compared to baseline. If the segment is present, it indicates that the distribution of the channel spectral densities is significantly higher than the distribution of the baseline. The color level of the line indicates the percentage of channels that have a significant deviation compared to the baseline at each frequency. Below the spectra, an example of 10 sec of raw SEEG signal in one bipolar derivation is shown. Note that the spectrum corresponds to a pool of many channels (number of channels is indicated above each spectrum) and not to the specific example of EEG.

SEEG, stereoelectroencephalography.

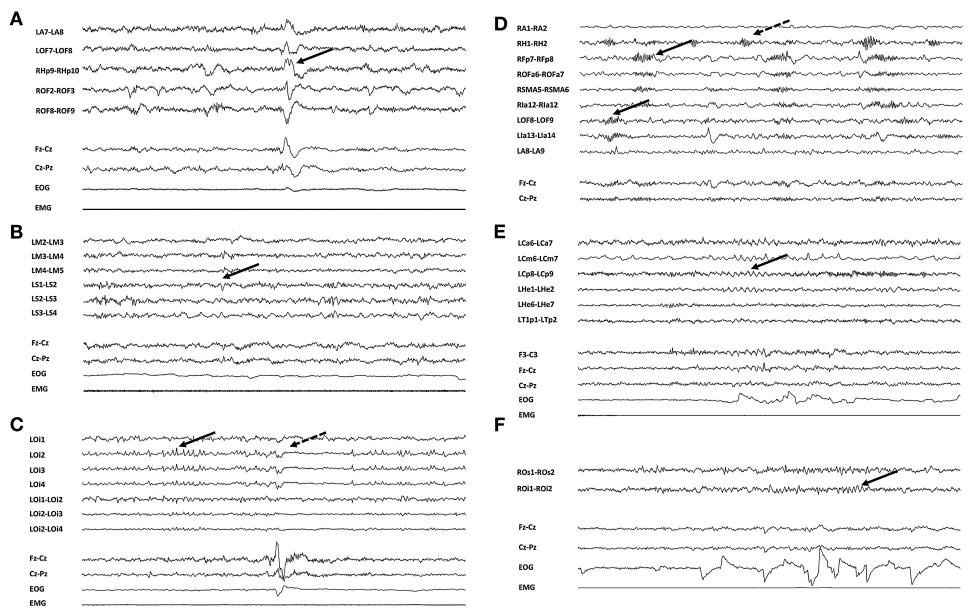


FIGURE 24.3 Examples of physiological sleep intracranial EEG features. In each figure (**A-F**), the intracranial EEG is presented above the scalp EEG. (**A**) K-complex, nonREM (NREM) N2. The K-complex is widespread; in this example, it is recorded both in the right and left hemispheres in the frontal and temporal lobes. (**B**) Vertex wave, NREM N1. Vertex waves are well seen in primary sensorimotor cortices. (**C**) Positive occipital sharp transients of sleep (POSTS), NREM N2 (the monopolar and bipolar intracerebral montages explore the lingual gyrus). Note that the POSTS are suppressed during the microarousal (dotted arrow). (**D**) Sleep spindles, NREM N2. Spindles are recorded in the hippocampus (dotted arrow) and in widespread cortical areas in the left and right hemispheres (line arrows). Note the asynchrony between spindles. Note also that hippocampal spindles are not evident in the scalp EEG. (**E**) Saw-tooth waves (STW), REM sleep. STW frequently occur after the onset of muscle tone reduction (see electromyogram). In this example, they are observed in the frontal, parietal, and temporal neocortex. (**F**) Ponto-geniculo-occipital (PGO)-like activity, REM sleep. PGO-like activity occurs during a burst of REM.

A, amygdala (the superficial contacts are in the temporal neocortex T2); Ca, anterior cingulate cortex (the superficial contacts are in the dorsolateral frontal cortex); Cm, middle cingulate cortex (the superficial contacts are in dorsolateral frontal cortex); Cp, posterior cingulate cortex (the superficial leads are in the dorsolateral parietal cortex); EMG, electromyogram (chin); EOG, electrooculogram; Fp, frontopolar cortex; H, hippocampus (the superficial contacts are in the temporal neocortex T2); He, Heschl gyrus; Hp, posterior hippocampus (the superficial contacts are in the temporal neocortex T2); Ia, anterior insular cortex (the superficial contacts are in the frontal operculum); L, left; M, motor cortex; OF, orbito-frontal cortex; Oi, lingual gyrus; Os, cuneus; R, right; S, somatosensory cortex; SMA, supplementary motor area; T1p, superior temporal gyrus, posterior part.

K-complex

The K-complex (KC) is a particular form of a high-voltage biphasic slow wave (Figure 24.3A).⁴⁰ It is considered as a reactive graphoelement as it can be evoked by internal or external stimulations in NREM sleep.^{41,42} SEEG recordings have shown that the KC represents an isolated cortical down state, associated with strong and consistent decreases in gamma frequencies and multiunit activity.⁴³ It may involve small or large cortical regions, but its amplitude is maximal over the anterior and superior part of the frontal cortex.^{44,45} Recently, KC associated with an arousal were shown to be preceded by awake-like activity (increase in beta frequencies) in the motor cortex. Moreover, region-specific sleep- or arousal-promoting responses were observed following KC, suggesting a dual role for the human KC supported by local specificities.⁴⁶

Delta waves

Delta (1–4 Hz) waves represent the main feature of NREM sleep and are generated in the thalamus.⁴⁷ They involve all cortical areas but scalp and SEEG studies have shown local differences, with delta power being higher in frontal areas especially during the first sleep cycle.^{2,48} The hippocampus and the amygdala also exhibit NREM sleep delta oscillations with homeostatic properties resembling those observed both in scalp EEG and depth cortical recordings.^{7,49}

Vertex waves

Vertex waves are a particular form of slow waves with a maximal amplitude over the central midline region, considered as evoked potentials elicited by an internal or external stimulation in N1 (Figure 24.3B).⁴¹ Vertex waves generators explored with EEG-functional MRI were found to include the primary sensorimotor cortical regions including medial central, lateral precentral, posterior superior temporal, and medial occipital cortices.⁵⁰ To our knowledge, no specific investigation of vertex sharp waves through SEEG has been published yet.

Positive occipital sharp transients of sleep

Positive occipital sharp transients of sleep (POSTS) are considered as a physiological variant observed in NREM sleep, mainly in young subjects; they consist in posterior triangular waves, bilateral but often asymmetric (Figure 24.3C).⁵¹ They predominate during the first part of the night, after sleep onset, and exhibit similarities with lambda waves with which they are strongly associated, potentially sharing a common occipital generator.⁵² In SEEG, POSTS are observed in mesial and lateral occipital cortex.^{21,53}

Spindles

Sleep spindles are a hallmark of NREM sleep, consisting in phasic waxing-and-waning 10 to 16 Hz oscillations lasting 0.5 to 2 seconds and resulting from oscillations within reticulo-thalamo-cortical loops (Figure 24.3D).^{47,54} They have been observed with ICEEG recordings by numerous teams in almost all brain areas, including the thalamus and temporal limbic structures such as the hippocampus and the entorhinal cortex, whereas they seem rare or absent in the amygdala.^{5,49,55–57} They present region-specific differences in frequency (caudo-rostral gradient with faster frequencies in posterior areas) and density (higher rates in parietal and frontal lobe and lower rate in the temporal neocortex), and they can occur locally or asynchronously between cortical areas (Figure 24.4).^{37,56–58}

PHYSIOLOGICAL ACTIVITY DURING REM SLEEP

As in NREM sleep, faster oscillations of REM sleep in the hippocampus and in the cortex preferentially express at a particular phase of the slower rhythm, exhibiting cross-frequency phase-amplitude (especially between gamma and delta frequencies) coupling, which strength is lower than in NREM sleep.^{2,8,59}

Signal Spectral Composition

In REM sleep, global spectral composition of SEEG signal shows mild differences with wakefulness, namely an increase in delta and a decrease in theta to beta bands' activity while gamma band remains unchanged (Figure 24.2).² It is important to note that REM sleep is not a homogeneous state; one usually distinguishes phasic REM sleep, characterized by bursts of rapid eye movements (REM), increased muscle tone (“twitches”) and ponto-geniculo-occipital (PGO) waves, and tonic REM sleep where muscle tone is abolished and REM are absent.⁶⁰ The EEG differs between these two states, as a higher level of EEG desynchronization is observed during phasic REM sleep, associated with an enhanced suppressive effect on interictal epileptic

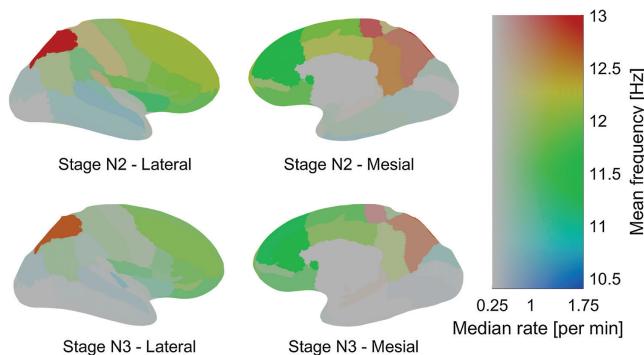


FIGURE 24.4 Spatial distribution of rate and frequency of sleep spindles. Median rates of sleep spindles are the highest in the parietofrontal regions compared to the rest of the brain. The frequency of sleep spindles follow a caudorostral transient, with faster frequencies in the centroparietal regions and slower frequencies in the frontal lobe. The median rate and mean frequency is shown for the 38 studied brain regions on the inflated cortex. The hue indicates the mean frequency and the saturation the median rate, that is, gray corresponds to low rates and vivid colors to high rates. The top images correspond to results during sleep stage N2 and the bottom images to sleep stage N3 shown in the lateral and mesial views of the brain.

Source: Reproduced with permission from von Ellenrieder N, Gotman J, Zelmann R, et al. How the human brain sleeps: direct cortical recordings of normal brain activity. *Ann Neurol*. 2020;87(2):289–301. doi:10.1002/ana.25651

SEEG, stereoelectroencephalography.

activity.⁶¹ Moreover, local specificities are found, such as a decrease in delta and an increase in beta-gamma frequencies in the frontal lobe and an increase in theta to alpha frequencies in posterior areas but also in the anterior cingulate cortex.^{2,62} During tonic REM sleep, the motor cortex presents an activity similar to that of relaxed wakefulness (mu-activity), whereas it is “activated” during phasic REM with disappearance of this mu activity, like during active motor execution.⁶³ The amygdala exhibits an activity resembling what is observed during wakefulness except for higher 9-Hz values during the latter state, and a higher level of activation (gamma 44–48 Hz) during REM than during waking eye movements.^{49,64} In the hippocampus, tonic delta oscillations persist, as a “rhythmic slow oscillation” (RSA; 1.5–3 Hz) also associated with specific cognitive tasks during wakefulness.^{6–9} Hippocampus activity is also marked by the presence of slower oscillations less than 2 Hz, gamma oscillations, and spindles resembling those observed in NREM sleep.⁷ Regarding subcortical structures, a paradoxical slow activity (2 to 3 Hz) with a low amount of high-frequency activities has been described in the medial pulvinar nucleus of the thalamus.¹³ Other thalamic nuclei (also the globus pallidus and the subthalamic nucleus) might however present high beta or gamma activity in REM sleep.^{65,66}

Specific Graphoelements

Saw-tooth waves

Saw-tooth waves are defined as a burst of delta (2–3 Hz)-notched triangular waves with highest amplitude over the vertex of the fronto-central regions.^{67,68} (Figure 24.3E). They occur after the onset of muscle tone reduction, before a burst of REM, and show an increase in density between the first and last sleep cycles.⁶⁸ A high-density EEG (HD-EEG) analysis has shown that saw-tooth waves are associated with an increase in gamma activity and REM.⁶⁹ Recently, we reported using SEEG recordings that a large set of regions in the parietal, frontal and insular cortices shows an increase in 2–4 Hz power during scalp saw-tooth waves, and that a strong and widespread increase in high frequency activity, including limbic structures, is observed at the same time.⁹⁸

Ponto-geniculo-occipital waves

PGO waves are biphasic sharp waves which have been studied mostly in animals (Figure 24.3F). They originate in the reticular pontine formation, propagate to the lateral geniculate nucleus of the thalamus and to the occipital cortex, and are associated with REM.⁷⁰ In humans, the majority of studies about PGO waves have been performed with scalp EEG or functional imaging.⁷¹ Intracranial recordings in subcortical structures performed in patients with Parkinson's disease have shown the presence of graphoelements sharing some characteristics with animal PGO waves. Among these graphoelements, P-waves lasting 150–200 ms have been recorded in the ponto-mesencephalic tegmentum; these waves partially correlate with bursts of REM and precede cortical potentials with a 20–140 ms latency.⁷² In the subthalamic nucleus, singlets or cluster of delta waves have been observed before and during bursts of REM.⁷³ In epileptic patients, sharply contoured theta waves occurring specifically in the primary visual cortex during phasic REM sleep have been proposed to be the correlate of the occipital part of the PGO waves in humans.^{74,75} PGO waves have been suggested to be local potentials time-locked with REM, associated with modulation of neuronal firing, not only in occipital cortex but also in the medial temporal lobe, similar to activity patterns observed upon image presentation during fixation without eye movements.⁷⁶ It has been proposed that saw-tooth waves may represent the cortical extra-occipital part of ponto-geniculocortical waves.⁹⁹

BEYOND THE BERGER FREQUENCY SPECTRUM: FROM DIRECT CURRENT (DC) SHIFTS TO RIPPLES (>80 Hz)

“Full-band EEG” aims at taking into account all EEG bandwidths, from infra slow to higher EEG frequencies as they may be physiologically and clinically relevant.⁷⁷

Infraslow Oscillations

Infraslow oscillations (0.01–0.2 Hz) in cortical excitability have been described in scalp EEG recording. Their observation needs specific recording set-ups and direct-current (DC) coupled amplifiers.⁷⁷ During transitional states from wakefulness to NREM and from NREM to REM, one can observe systematic shifts in the scalp-recorded DC potential. These shifts may depend on subcortical neuromodulatory influences and modulate spindles, delta and slow wave activities.⁷⁸ No ICEEG study of physiological infraslow oscillations has been reported, but in epilepsy, ictal DC shifts have been associated with the epileptogenic areas.⁷⁹

High-Frequency Oscillations

High-frequency oscillations (HFO) defined as ripples (80–250 Hz) and fast ripples (>250 Hz) depending on the spectral frequency have been described in ICEEG recordings during wakefulness and sleep, both in cortical and mesial temporal structures. HFO can be visually detected by filtering the EEG signal (ICEEG or scalp EEG) with a high-pass filter set at 80 Hz, by reducing the time window to around 1 second, and by increasing the gain. They have generated much interest over the past years given their physiological role in cognitive functions, including memory consolidation during sleep, but also given their recent description as a biomarker for epileptogenicity.^{80–83} Several characteristics have been proposed to differentiate physiological from pathological HFO, with a large overlap however between these two entities. Physiological ripples are predominant (rate >0.2/minute) in the occipital cortex, temporal lobe (medial and basal region, transverse temporal gyrus), and pre- and postcentral gyri.⁵ They predominate during NREM sleep and show a temporal coupling with slow wave oscillations, with an occurrence after the peak of the down state.^{5,84} For further information on HFO, the reader is referred to Chapter 26 in this book.

PHYSIOLOGICAL ACTIVITY DURING TRANSITIONAL STATES

A major contribution of ICEEG studies in sleep investigation has concerned transitional states (from wakefulness to sleep and from sleep to wakefulness), as well as transient, and mostly focal intrusions of a vigilance state into another one, such as arousals. Indeed, ICEEG recordings in humans have provided evidence that electrophysiological features of sleep and wakefulness could coexist at the same time in different brain areas.⁸⁵

Sleep Onset

The demonstration that the process of falling asleep did not involve the whole brain at the same time was made by Magnin et al.,⁸⁶ who quantified findings of Caderas et al.⁵⁵ In this work, the authors used the dimension of activation (DA) which is global measure of the signal complexity allowing signal quantification and thus discrimination between vigilance stages. They reported that thalamic deactivation (decrease in DA) at sleep onset most often preceded that of the cortex by several minutes and that an asynchrony was also observed within the cortex.⁸⁶ Such delay was also found in the hippocampus, where spindles not only precede neocortical spindles, but may occur several minutes before scalp-detected sleep onset.^{55,87}

Awakening

Imaging and EEG studies have suggested that awakening was also a progressive process associated with the sequential reactivation of brain structures underlying sleep inertia phenomena.⁸⁸ In rodents, awakening from sleep is characterized by the presence, during several minutes, of remaining local slow waves associated with “OFF-periods.”⁸⁹ Few SEEG studies have specifically studied the sleep-to-wake transition except in pathological situations such as parasomnia.⁹⁰ Regarding physiological awakening from NREM sleep, Magnin et al. did not report thalamo-cortical nor intra-cortical asynchrony; however, except for the thalamus (mostly the medial pulvinar), no other subcortical region was investigated and it is possible that DA may not explore short-lasting events such as “OFF periods”.⁸⁶

Micro-Arousals

Arousal are defined as brief (3–15 seconds) activations during sleep, associated with an abrupt shift of EEG spectrum toward higher frequencies and, for REM sleep arousals, with an increase in muscle tone.⁹¹ Such activations can be observed locally during NREM sleep in the motor cortex (blockage of slow waves and increase in alpha-beta frequencies) whereas other areas, especially the dorsolateral prefrontal cortex, exhibit an increase in slow wave activity.⁹² They occur also during REM sleep, allowing initiation of a motor response without global awakening.⁹³ Stereotypical arousals at the thalamic level are associated with heterogeneous patterns of cortical arousals mainly depending on the cortical area considered and the ongoing sleep stage.⁹⁴ Interestingly, the SEEG signal during arousals differs from that recorded during awakenings, suggesting that the shift between sleep and wake may actually be progressive.⁹⁴

Micro-Sleep

The presence of local cortical slow waves and “OFF periods” after extended wakefulness in rats, correlated with impaired performance, suggests that intrusion of sleep features during wakefulness may represent a sleep homeostatic phenomenon.⁹⁵ Such “micro-sleep” could constitute the electrophysiological correlate of sleepiness. Accordingly, HD-EEG recordings have provided evidence of local aspects of sleep during wakefulness in children.⁹⁶ Only one study with ECoG

has reported that the detection of such local inactive micro-states, associated with decrease in theta-alpha and increase in delta frequencies, increased with the time spent awake.⁹⁷

SUMMARY

ICEEG recordings have allowed not only confirmation of the presence of most previously scalp EEG-defined features of sleep, but also advancement of their description and presentation of hypotheses regarding their functional significance. The most important contributions of ICEEG recordings concern detailed analyses of topography and the investigation of deep structures. Thus, our understanding of sleep has evolved over the last 10 years with the demonstration of spatial and temporal inhomogeneities suggesting that vigilance states evolve along a continuum and are regulated locally. Moreover, intracranial recordings including investigation of mesio-temporal structures during sleep have provided evidence that within and across area coupling of sleep oscillations support cognitive functions of sleep. However, several fields remain incompletely explored, and could benefit from larger database analysis, which could allow overcoming the spatial sampling bias of SEEG, and translational approaches, especially regarding subcortical structures recordings in movement disorders, simultaneous multimodal explorations including functional imaging, and age-specific investigation of maturational aspects of sleep.

KEY REFERENCES

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