Local aspects of sleep: observations from intracerebral recordings in humans

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The boundaries between sleep and wakefulness local behaviors of brain activity
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The wake-sleep transition is characterized by clear-cut modifications of EEG activity: from low-amplitude high-frequency activity to high-amplitude low-frequency slow waves and sleep spindles.
During deep NREM sleep the membrane potential of cortical neurons engages in a Slow Oscillation

Steriade M., Nunez A., Amzica F., 1993

Vyazovsky et al, Neuron 2009

Hill and Tononi, J. Neurophysiol 93:1671-98, 2005
EEG (cortex)

Intracellular cortex

20 mV

2 s

ACh depolarizes Thalamic Relay Cells

Mc Carley 1988

Moruzzi and Magoun 1949
Steriade 1999
Sleep as a local phenomenon

• Experimental studies suggest that sleep is a fundamental property of local neuronal networks in different brain structures.

• These local networks are orchestrated, but not fundamentally driven, by central mechanisms.

• According to this view, global sleep (behaviorally and electroencephalographically defined) emerges when the altered input–output state, that characterizes the sleep-like state at the local network level, involves a large and widespread number of cortical regions

(Krueger et al., 2008 Nat Neurosci Rev)
Brain-sleep state may be spatially non-uniform
Unihemispheric slow-wave sleep

Fig. 1. EEG recorded from the parieto-occipital cortex (A) of a bottlenose dolphin during unihemispheric slow-wave sleep with either the left (B) or right (C) hemisphere asleep. Note the high-amplitude, low-frequency EEG activity in the sleeping hemisphere and the low-amplitude, high-frequency EEG activity in the awake hemisphere. Reprinted from Brain Research, Vol 134, Mukhametov, L.M., Supin, A.Y., Polyakova, I.G., Interhemispheric asymmetry of the electroencephalographic sleep patterns in dolphins, 581–584, 1977, with permission from Elsevier Science.
Topographic differences in the distribution of Slow Wave Activity (SWA), the marker of sleep homeostasis, are evident

Brain areas in which regional cerebral blood flow (rCBF) decreases as a function of delta power during non-REM sleep (stages 2–4)

Sleep EEG delta power can be locally increased or reduced as a function of previous waking activity.

Sleep as an use-dependent phenomenon.

From wake to sleep
A behavioral transition through local brain changes
the reduced reticular formation tone is interpreted as the main determinant of the electroencephalographic (EEG) synchronization characterizing the sleep state

Moruzzi and Magoun, 1949
Local sleep in wakefulness

Sleep and wakefulness can be restricted to small groups of neurons (Pigarev et al., 1997) or individual cortical columns (Rector et al., 2005).
Local sleep in awake rats

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At high sleep pressure levels populations of neurons in different cortical areas can suddenly go ‘offline’ in a way that resembles the off periods of NREM sleep.

Local awake off periods are associated with locally increased excitability after intensive training and with failures in performance; they could represent a form of neuronal tiredness due to use-dependent factors, such as synaptic overload.
Local Experience-Dependent Changes in the Wake EEG after Prolonged Wakefulness

Extended experience-dependent plasticity of specific circuits results in a local increase of the wake theta EEG power in those regions, followed by more intense sleep, as reflected by SWA, over the same areas.
If signs and symptoms:

- Are not in agreement with MR or interictal EEG
- Identify the lobe but not the side
- Suggest a precocious diffusion in wide areas
- Are not pointing to an univocal origin of seizures

And Video-EEG doesn’t resolve the doubtful points.
The thalamus and the cortical mantle are not strictly coupled during the wake–sleep transition
Extensive cortical territories maintained an activated pattern for several minutes after the thalamic deactivation.
Sleep onset in the hippocampus

**Aim:**
To explore the possibility of transient decoupling between limbic and neocortical structures during wake–sleep transition

**Methods and patients:**
simultaneous intracerebral hippocampal, neocortical and scalp EEG recordings in 9 patients with refractory epilepsy
Sleep in the Human Hippocampus: A Stereo-EEG Study

Fabio Moroni¹, Lino Nobili², Giuseppe Curcio¹, Fabrizio De Corbi³, Fabiana Fratello¹, Cristina Marzano¹, Luigi De Gennaro¹, Franco Ferrillo⁴, Massimo Cossu⁵, Stefano Francione⁶, Giorgio Lo Russo⁷, Mario Bertini¹, Michele Ferrara⁸

[Graphs showing EEG power for different frequency bands (VLF, Delta, Theta, Alpha, Sigma, Beta) across time (min)]

2007
Wake 1 sec
Subj. 2
Subj. 2
From light off to sleep onset

Andrillon et al J Neuroscience 2011

Sarasso et al, Neuroimage, under review
Spindles detection
2 pts with electrodes in the thalamus
Sleep Onset (scalp EEG)

Th

Hc

Time (minutes)
Different temporal dynamics of state synchronization in different cortical areas at sleep onset

- Spindles in the hippocampus appeared 12.7 +/- 2.3 minutes before sleep onset (detected on scalp EEG by the emergence of the first spindle or K-complex)

- Spindles in the hippocampus preceded by about 2 and 8 minutes the appearance of spindles in the frontal and posterior regions respectively (parietal, occipital cortex)
Implications

- Cognitive impairment and performance deficits induced by sleep deprivation could be due to the occurrence of cortical and subcortical local “islands of sleep” in behaviorally fully awake subjects.

- The observation that the hippocampus displays typical sleep features (i.e., spindles) many minutes before the occurrence of sleep on scalp EEG might explain specific memory alteration or amnesia for events preceding the unequivocal occurrence of behavioral sleep onset (Wyatt et al., 1994, 1997).

- An impairment in the process of state-synchronization among different cortical regions, with cortical territories that remain activated for long time after the thalamic and hippocampus deactivation, could explain both long sleep latency in insomniac patients and the mismatch between subjective and objective measures frequently observed in subjects with paradoxical insomnia (Manconi et al., 2010; Marzano et al., 2008; Parrino et al., 2009)
Dissociated wake-like and sleep-like electro-cortical activity during NREM sleep
Sleep slow waves and the underlying active and inactive neuronal states occur locally. Especially in late sleep, some regions can be active while others are silent.
NREM arousal parasomnias
State Dissociation
(partial arousal)

The brain is partially awake and partially in NREM sleep

Awake enough to perform complex motor or verbal functions

Asleep enough not to have conscious awareness of these actions

Mahowald 2011
Clinical observations indicate that sleep and wakefulness could occur simultaneously in different parts of the brain.
Activation of the thalamocingulate pathways occurs with persistent deactivation of other thalamocortical arousal systems.
Thalamo-cortical dissociation in NREM parasomnias
Slow oscillations orchestrate fast oscillations

NREM sleep

A

NREM parasomnia

C

Up and Down state

Vyazovsky et al, 2009
Timofeev and Steriade, 2004
Evidence of Dissociated Arousal States During NREM Parasomnia from an Intracerebral Neurophysiological Study

Michele Tarzaghi, MD; Ivana Sartori, MD; Laura Tasari, MD; Giuseppe Didato, MD; Valter Ruzeloni, MD; Giorgio LoRusso, MD; Raffaele Manni, MD; Lino Nobili, MD, PhD.

Sleep 2009
Dissociated local arousal states underlying essential clinical features of non-rapid eye movement arousal parasomnia: an intracerebral stereo-electroencephalographic study

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• Intracerebral recordings show that brain activity can exhibit different local behaviors during arousal parasomnias.

• Typical features of arousal parasomnias could be explained by the activation of the limbic and motor network disengaged from the prefrontal control cortex (emotional activation, such as fear) and paralleled by the deactivation of the hippocampal and frontal associative cortices (amnesia for the event).
Five subjects

at least two electrode contacts which could be localized unequivocally within the prefrontal cortex and at least two contacts within the primary motor cortex.
Slow Wave Activity (0.5-4.0 Hz)
NREM

Motor cortex

PF Cortex

Fz-Cz

Eog

Chin

1 sec
Coupling of EEG rhythms

Motor cortex

PF Cortex

Fz-Cz

Eog

Chin

5 sec
Uncoupling of EEG rhythms

Motor cortex

PF Cortex

Fz-Cz

Eog

Chin

5 sec
Acoustic area (Heschl gyrus)
Conclusions

✓ Some parts of the brain can be electro-physiologically fully awake while others can be asleep (sleep and wakefulness are not two mutually exclusive states)

✓ The occurrence of local dissociated states is actually an intrinsic feature of physiological NREM sleep

✓ A lower arousal threshold and a higher level of activation in the motor cortex may have been selected, because they increase the probability of survival, facilitating motor behaviors in case of sudden awakenings

✓ The significant enhancement of slow frequencies in the PFc immediately before and during the Mc activation could be interpreted as a behavior that allows the global sleep process to proceed smoothly even when a local activation appears