Summary

What happens to our brain during those long hours of unconsciousness that we spend sleeping every day? Recent research has started to answer this fascinating question, by observing the differences in brain activity between wakefulness and sleep. One of the most striking differences is the change in the level of interaction between distant brain regions. Based on this observation, this thesis starts from the assumption that to understand sleep we should not limit our analysis to one circumscribed neuronal population, but we need to understand how the interplay between multiple areas emerges and evolves over numerous spatial and temporal scales. This thesis investigates how the interaction between brain regions changes in relation to the state of the brain, to learning, and to sleep deprivation, and how the anatomical structures of the brain might influence the connectivity between neuronal populations.

Chapter 1 presents the intriguing idea that sleep arises from the interplay between brain regions. This interaction is thought to be necessary for the emergence of two of the most emblematic elements of sleep, such as slow waves, oscillations at around 1 Hz, and spindles, 0.5–2 s long bursts of oscillatory activity between 11 and 18 Hz. To study this interaction, it is necessary to take advantage of advanced tools, such as electroencephalography (EEG), magnetoencephalography (MEG), diffusion tensor imaging (DTI), and functional Magnetic Resonance Imaging (fMRI), and to employ refined analysis techniques that can calculate the degree of correlation between distant areas. Each of these techniques can shed light on a specific aspect of connectivity, such as structural connectivity, which informs us about the anatomical pathways connecting brain regions, functional connectivity, which defines the correlation in brain activity, and effective connectivity, which describes a directional influence of one region onto another. Often, one single technique is not sufficient, and multiple chapters in this thesis employed multiple techniques in order to provide a more complete picture of the level of brain connectivity.

The combination of EEG and DTI was exploited in Chapter 2, where the expression profile of spindles and slow waves was investigated in relation to the anatomical structures of the connecting white-matter tracts. Because the appearance on the EEG of these sleep elements depends on the synchronization of the underlying neuronal population, we investigated whether stronger structural connectivity might be associated with higher synchronization of spindles and slow waves. We observed that participants who had larger spindle power and steeper slow wave slopes, two markers of neuronal synchronization, had stronger integrity in their white-matter tracts.

In addition to the anatomical aspects, the degree of synchrony of the slow waves is thought to be determined by the activity of nuclei located in the brainstem,
such as locus coeruleus (LC). Because of the very deep location of the LC, we employed, in Chapter 3, fMRI acquired together with EEG to investigate the temporal relationship between the propagation of slow waves and the neuronal activity of the LC. We observed that slow waves that travel along an anterior-to-posterior gradient were more likely to be accompanied by phasic activity in the LC, suggesting that this pontine nucleus can bias the emergence of the slow waves.

One crucial characteristic of the slow waves is the ability to synchronize the local activity between distant neuronal populations. Local activity is often associated with oscillations in the high-frequency bands, such as the spindle- and gamma-band. In Chapter 4, we observed on scalp EEG in school-aged children that spindles and gamma activity are more likely to occur during the rising slope of the slow wave. This precise synchronization between slower and faster oscillations is thought to provide a powerful mechanism for memory consolidation.

The fundamental contribution of sleep to memory was studied in Chapter 5 using MEG. Learning a complex memory task before sleep induced a specific pattern of inter-regional connectivity during task execution. The same pattern was present during subsequent sleep, but not during subsequent wakefulness, suggesting that sleep may support memory consolidation by reactivating long-range functional connectivity elicited during learning.

The importance of sleep to our well-being and optimal cognitive functioning becomes apparent after periods of sleep deprivation. In Chapter 6, we observed that the degree of effective connectivity, measured with EEG, was particularly strong in the posterior-to-anterior direction between two main hubs of the brain network. This increase in effective connectivity, however, was impaired after one night of sleep deprivation, and this impairment was correlated with worse performance on a vigilance attention task. Therefore, sleep may be necessary to maintain an efficient degree of connectivity within the brain network.

These findings are complemented by the observations in Chapter 7. One of the most severe consequences of sleep deprivation is the decrease in the flexibility to either remain focused on a particular target, or switch to another target. This is particularly evident in the case of bistable perception, whereby participants were less likely to switch to an alternative perceptual interpretation of the ambiguous figure. This perceptual perseveration was strongly correlated with the strength of the alpha oscillations, a marker of neuronal synchronization measured with EEG. We concluded that, by increasing alpha power, sleep deprivation may impair the flexibility of the brain to switch to alternative configurations.

Overall, the findings in this thesis support the hypothesis that sleep is associated with fundamental changes in the level of structural, functional, and effective connectivity of the brain network. Chapter 8 discusses how thinking of sleep as a property of the brain network represents an essential step towards our understanding of its origins and its functions. This interpretation provides a powerful framework to investigate the alterations in connectivity that are often observed after sleep deprivation and in association with sleep disorders. Because brain connectivity is thought to underpin the state of consciousness, studies of the complex interactions between neuronal populations during sleep might shed light on the nature of consciousness.