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REVIEW

Revolutionizing Sleep Science: A Narrative Review of the Historical Origins and Current Applications of Sleep Neuroimaging

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Abstract: Sleep neuroimaging is a subfield of sleep science that goes beyond polysomnography by combining neuroimaging techniques with validated sleep research methods to characterize sleep-wake states and investigate sleep-related processes across the 24-hour day. In this article, we review the historical advancements and applications that grew out of somnography leading to current sleep neuroimaging methods. We highlight the power of somnoimages to help visualize sleep research results and communicate complex information about sleep processes. We also suggest several ways in which applying neuroimaging during sleep has opened new avenues to more fully capture the nature of sleep, uncovered mechanisms of sleep-wake regulation, and increased understanding of sleep-related processes. Current applications and future directions of sleep neuroimaging are also discussed.

Plain Language Summary: Sleep neuroimaging is an advanced area of research that combines brain imaging techniques with other validated sleep measures to better understand sleep. This article reviews how sleep research has evolved from basic monitoring techniques like polysomnography to modern multimodal sleep neuroimaging methods. It highlights how these new approaches provide clearer insights into sleep processes and have led to discoveries about sleep that were previously inaccessible. The article also discusses future directions for using neuroimaging to further explore sleep and its related neuronal, behavioral, and experiential processes.

Keywords: sleep neuroimaging, sleep fMRI, EEG-fMRI, somnoimages, somnoimaging

Introduction

It is said that a picture tells a thousand words; in sleep science graphs, polysomnography (PSG) and the hypnograms in particular, have dominated as the scientific depiction of sleep and for nearly a century have likewise governed its conceptualization and classification. With advances in neuroimaging technology, a clearer picture of sleep is coming to light. Studies that combine neuroimaging techniques with polysomnography and other validated sleep methods have been called by various names, including "sleep fMRI" (functional magnetic resonance imaging) and somnoimaging. In this paper we use the term sleep neuroimaging, which we define *as a subfield of sleep science and sleep medicine that layers structural and functional neuroimaging with sleep methods including PSG to characterize sleep-wake states and study constructs across those states*. Sleep and sleep-related constructs, such as sleep quality, daytime sleepiness, and circadian preference, are theoretical concepts not directly observable but are inferred from empirical indicators. The images generated from sleep neuroimaging studies are referred to as somnoimages, as they vividly capture the regional dynamics of sleep-wake states in the brain in ways graphs alone cannot depict. Somnoimages are powerful depictions of regional dynamics of sleep-wake states. The aims of this narrative review are to provide the history of sleep neuroimaging from

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its deep roots in somnography (defined below), current methods, advantages/disadvantages of common neuroimaging modalities, highlighting their contributions to understanding sleep regulation and future research directions. Our objectives are to revisit the historical progression of sleep research from the earliest probes of brain processes to modern neuroimaging techniques, provide examples of how neuroimaging has enhanced our understanding of sleep processes and regulatory mechanisms, and to discuss future directions and potential advancements in neuroimaging applications for sleep research.

Methods

This narrative review synthesizes key literature in sleep neuroimaging, emphasizing historical context and expert insights to trace the origins, developments, and applications of neuroimaging modalities in sleep science. PubMed searches, citation tracking, and the lead author's years of compiled relevant sources, including gray literature and translated non-English manuscripts informed this narrative review. The review grouped studies thematically, highlighting the earliest applications of each modality and samples of current applications. While not exhaustive, the review prioritizes foundational studies and key advancements. Unlike systematic reviews, which aim to comprehensively answer specific questions, this narrative review focuses on providing an integrative overview of historical, theoretical, and methodological developments, allowing flexibility in study selection. We acknowledge that where we give precedence for a major advancement in sleep neuroimaging, there may be contributions we are unaware of or that were presented in outlets beyond the scope of our search. We welcome updates to this timeline should such information come to light. Such corrections to the history are natural and would not alter the main point message this review aims to communicate. Though this approach acknowledges potential biases and limited scope, it offers a nuanced synthesis to educate readers and foster scholarly dialogue on sleep neuroimaging's past, present, and future. A timeline of the various advancements in sleep neuroimaging is provided in Table 1, which corresponds by year with sample images presented in Figure 1.

History of Somnography

Somnography refers to the recording and study of sleep patterns and processes during sleep, with graphs as the primary vehicle for representing and communicating this knowledge. Conceptually, sleep neuroimaging grew out of somnography that emerged in the 19th century, as the brain's role in sleep and consciousness became more evident and a topic of scientific study. Definitions of sleep prior to the introduction of somnographs were largely based on personal experience, clinical judgments, and behavioral observations. Some of the first systematic and empirical depictions of sleep were represented in somnocharts, including those anonymously collected throughout the year 1755 in daily diaries, among other daily variables.[1] At the dawn of modern sleep science in the early 1860s, Ernst Kohlschütter produced the first somnographs of auditory threshold across the night demonstrating that exteroception varies over the course of sleep.[2,3] The somnograph of the auditory threshold from sleep produced by Kohlschütter represented a major innovation, helping to convey the patterns of sleep data more clearly than accompanying somnocharts. Making headlines in 1875, Richard Caton used the galvanometer to document electrophysiological changes in the brains of animals, empirically observing for the first neurophysiological changes across states, including reports of increased currents during sleep.[28–31] Using a different modality to investigate the brain changes associated with sleep (ie, plethysmography), Angelo Mosso produced the first neurophysiological somnographs of human sleep in 1876.[4] Mosso pioneered a method to measure brain pulsations in patients with skull defects, providing indirect access to volume, which he applied across sleep-wake states. His findings generally showed decreased and more uniform hemodynamic activity during sleep. Mosso also invented a weighted table upon which was shown to tip down toward the feet during behavioral sleep compared to wakefulness and toward the head during stimulation, suggesting cerebral blood flow (CBF) decreased during sleep.[32,33] Laying the groundwork for noninvasive brain activity studies, some consider these inventions to be the first rudimentary neuroimaging approach, and by exertion is a forerunner to sleep neuroimaging. At the time, the finding of lower pulsations and lower brain weight during sleep seemed to support the vascular theory of sleep that argued anemia marked by decreased CBF caused sleep. His finding aligns with modern sleep neuroimaging studies showing overall lower metabolic activity during non-rapid eye movement (NREM) sleep[34] and his observation of periodic increases in brain pulsations— which he speculated might correspond to dreaming—predated the discovery of EEG defined rapid eye

Table 1 Historical Timeline of Sleep Neuroimaging

Year	Event
1755	An anonymous writer kept a daily diary for a year, charting sleep patterns and habits, among other daily variables. The daily charts that were produced are an early example of what might be called a "somnochart"[1]
1862	This work marked the dawn of modern sleep science. A copy of Kohlschütter's somnograph from his dissertation is presented in Figure 1, representing a major innovation for summarizing and presenting sleep data.[2] Kohlschütter published somnocharts of changes in auditory threshold during sleep that he then plotted into a somnograph in his highly influential dissertation study, which he published in a medical journal a year later.[3]
1875	Caton observed the first changes in galvanic signals in the animal brain, showing changes in electrophysiology across sleep-wake states. We were unable to find somnographs showing these data.
1881	Mosso published the first human somnographic representation of brain activity across sleep-wake state. The sample image in Figure 1 shows brain pulsations measured with plethysmography of patient Catherina X around the moment of awakening from sleep, indicted by arrows across three tracings (A-C).[4] This image, along with those of his other patient Bertino, provided early empirical evidence for a neurophysiological change between sleep and wakefulness in humans.
Circa 1900	Somnographs of physiological processes are developed for numerous biological processes, showing changes across sleep and wakefulness. Although not depicted in Figure 1, this time period around the turn of the century was a renaissance in sleep science, and included the first sleep deprivation studies done in animal and human subjects.[5,6]
1930s	Hans Berger published the first somnograph using electroencephalography (EEG) of the human sleep state. In the image in Figure 1, signals were taken from the forehead and occipital areas of the scalp in a 35-year-old doctor, 2 hours after sleep onset.[7] These and other graphs he published demonstrated the presence of electrophysiological differences across sleep-wake states.
1935	Published in the journal *Science*, Loomis et al published polysomnographs (PSG) of distinct EEG features including K-complexes and sleep spindles along with staging criteria for sleep, showing that sleep is an endogenous, temporally and spatially dynamic, and active process. In the graph presented in Figure 1, numerous EEG signals show that responses to stimuli differ across different locations of the scalp.[8]
1955	Mangold et al conducted a multimodal sleep study by measuring EEG concurrent with the nitrous oxide technique.[9] In Figure 1, a depiction on the chart they presented showing the significant differences in cerebral blood flow (CBF) during wake (C) and sleep (S) in 6 participants. Findings of higher CBF during sleep challenged theories that argued sleep is caused by reduced CBF or metabolism.
Circa 1950s	Aserinsky, Kleitman, and Dement[10,11] characterize REM sleep, showing a new stage of sleep that they argued corresponded to dreaming. Some argue this was the birth of modern sleep science. As can be seen in this timeline, however, modern sleep science sprouted at least a century earlier.
1968	Reivich et al published the first somnoimages by combining autoradiography techniques concurrent with implantable EEG, and thermistors, marking the birth of sleep neuroimaging and showing regional functional brain differences across sleep-wake states.[12] As depicted in Figure 1, the somnoimages show two coronal slices of the brain (1 and 2) taken from animals in the awake (A), slow wave sleep (B), and REM sleep (C) state. Indicated brain areas include C (caudate nucleus), P (putamen), W (white matter), and G (lateral geniculate body). Also shown Figure 1, Rechtschaffen and Kales published, standardized criteria for PSG sleep-wake staging.[13] Although researchers had used EEG in combination with other biological measures from its first application to sleep in humans, the types and locations of electrodes used varied across researchers. Rechtschaffen and Kales led the effort to validate and manualize PSG.
1969	Risberg et al published the first somnoimages of humans, showing in simple hand drawings, state and regions specific differences in regional cerebral blood volume (rCBV) across sleep-wake states determined with Curie RISA (^{131}I) administered intravenously and measured with sensors positioned around the skull.[14] This is depicted in Figure 1 with the brain drawing (left) including numbered sensor locations corresponding to the plots (right) of rCBV during slow-wave sleep (first column labeled ORTHO) and paradoxical sleep (labeled PARA in columns 2–4) in 5 subjects.
1985	Heiss et al published the first computer generated somnoimage in humans using 2-deoxy-D-[2-aSF]glucose positron emission tomography (PET). The somnoimages in Figure 1 show reduced regional glucose metabolism during a nap (S) compared to wakefulness (W).[15]

(*Continued*)

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Table 1 (Continued).

Year	Event
1991	The first single photon emission computed tomography somnoimage (SPECT) were published in the early 1990s.[16] This method uses radioactive tracers to measure regional cerebral blood flow. When combined with PSG and high-resolution magnetic resonance structural images, SPECT is capable of producing detailed somnoimages of regional cerebral blood flow across sleep stages. The somnoimages depicted in Figure 1 shows regional differences in cerebral blood flow during REM sleep. This is one of the first color somnoimages published—the first was published in the same year in an animal study.[17]
1992	Hughes et al were first to use magnetoencephalogram (MEG) concurrent with EEG to study sleep in 1976 to pinpoint the maximal location of sleep spindles.[18] By 1990, technological advancement allowed simultaneous multichannel measures of MEG to better localize magnetic signals in the brain, such as sleep spindles as seen in Figure 1.[19] MEG is now able to generate topographic images and localize magnetic changes associated with a host of sleep features, including sleep onset, stages, saccades, consciousness, and depth.
1999	The first somnoimages using simultaneous EEG-fMRI was published by Løvblad et al in 1999[20] Due to copyright restrictions, the somnoimage could not be reproduced here. A sample EEG-fMRI somnoimage published the following year in 2000 by Portas et al[21] is shown in Figure 1. This image shows regional differences in auditory processing during sleep compared to wake in consciousness centers of the brain, including the posterior cingulate. This modality has since become a powerful set of sleep neuroimaging techniques that can measure functional connectivity, regional homogeneity, low-frequency fluctuations and more across sleep-wake states and has been used widely to investigate many sleep-related processes.
2001	Functional near-infrared spectroscopy (fNRIS) has been used to study sleep since the early 1990s, particularly in human infants.[22] With technological advancement, multi-channel fNIRS has been used in sleep neuroimaging to investigate regional cortical hemodynamic activity associated with sleep processing and produce more detailed somnoimages. The fNIRS somnoimages provided in Figure 1 shows differences in oxygenated hemoglobin during wakefulness (left side) and REM sleep (right side) in the right visual cortex.[23] Emerging in the 1990s, high-density EEG (hd-EEG) was first applied in sleep science to study regional neural processes in the sleeping infant in 2001,[24] and was later applied to the sleeping adult in 2004.[25] Sleep hd-EEG has since become the most widely used sleep neuroimaging approach in humans. The sample somnoimage in Figure 1 shows regional differences in auditory processing during sleep in neonates.[24]
2002	Published in the journal *Science*, Dehaene-Lambertz et al[26] produced the first sleep fRMI image in human infants, which highlights the power of sleep neuroimaging methods in researching sleep physiology across the development lifespan.[26] The somnoimages of this modality are depicted in Figure 1.
2025	Current sleep neuroimaging includes multimodal PET-fMRI-EEG that are capable of revealing the complex biological processes that occur across sleep-wake states.[27] In Figure 1, sample somnoimages from this paper are provided showing side-by-side regional differences in hemodynamic and metabolism collected simultaneously.

Notes: The dates in this timeline correspond to the image depicted in Figure 1. Bolded dates above are not shown in Figure 1.

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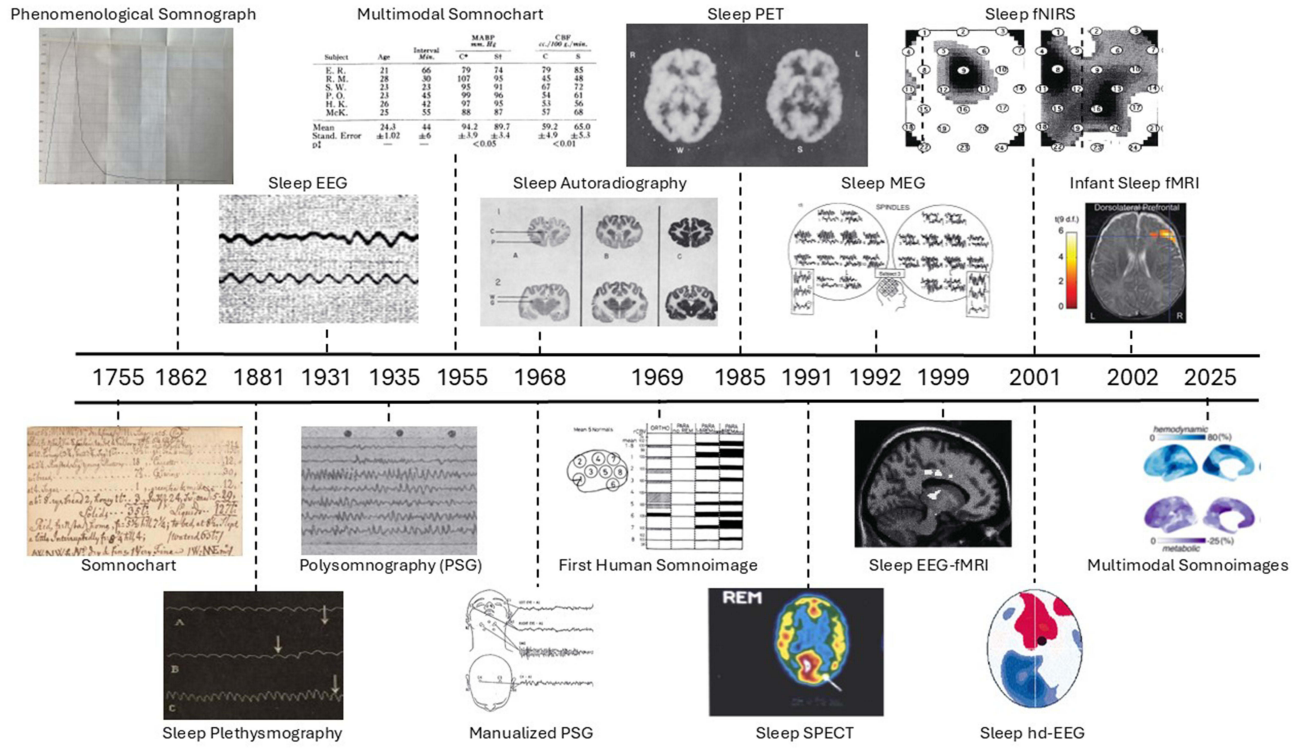

Figure 1 This figure is a timeline showing the major advancements made over the past 150 years in visualizing and communicating knowledge about sleep. This birds-eye view of the timeline shows the evolution of somnography into sleep neuroimaging moving from black and white somnochart and graphs, to colorful 3D somnoimages produced today. A description of each chart, graph, or image depicted in this timeline can be found in Table 1 corresponding by date. A description of each symbol in the figure is beyond the scope and purpose of this review.

Notes: **1930s image**: Reprinted from Berger H. Uber das Elektrenkephalogramm des Menschen. III. Mitteilung. *Archiv fur Psychiatrie und Nervenkrankheiten*. 1931;94:16–60.[7] **1935 image**: Loomis AL, Harvey EN, Hobart G. Potential rhythms of the cerebral cortex during sleep. Science. 1935;81(2111):5978.[8] **1955 image**: Reprinted from Mangold R, Sokoloff L, Conner E, Kleinerman J, Therman PO, Kety SS. The effects of sleep and lack of sleep on the cerebral circulation and metabolism of normal young men. J Clin Invest. 1955;34(7, Part 1):1092–1100. Creative Commons.[9] **1968 images**: Reprinted from Reivich M, Isaacs G, Evarts E, Kety S. The effect of slow wave sleep and REM sleep on regional cerebral blood flow in cats. J Neurochem. 1968;15(4):301–306[12] and Rechtschaffen A, Kales A. A Manual of Standardized Terminology, Techniques and Scoring System for Sleep Stages of Human Subjects. Bethesda, Md: U.S. Dept. of Health, Education, and Welfare; 1968. Creative Commons.[13] **1969 image**: Risberg LG J, Ingvar DH. Regional Cerebral Blood Volume During Paradoxical Sleep. *Cerebral Blood Flow*. Berlin: Springer; 1969:101–103, Springer Nature.[14] **1985 image:** Reprinted from *Brain Res*, volume 327(1-2), Heiss WD, Pawlik G, Herholz K, Wagner R, Wienhard K. Regional cerebral glucose metabolism in man during wakefulness, sleep, and dreaming. 1362–366, copyright 1985, with permission from Elsevier.[15] **1991 image**: Reprinted from Madsen PL, Holm S, Vorstrup S, Friberg L, Lassen NA, Wildschiodtz G. Human regional cerebral blood flow during rapid-eye-movement sleep. *J Cerebral Blood Flow Metab*. 1991;11(3):502–507. With permission from Sage Publication.[16] **1992 image**: Reprinted from *Electroencephalogr Clin Neurophysiol*, volume: 82(3), Lu ST, Kajola M, Joutsiniemi SL, Knuutila J, Hari R. Generator sites of spontaneous MEG activity during sleep. 182–196. Copyright 1992, with permission from Elsevier.[19] **1999 image**: Reprinted from *Neuron*, volume28(3), Portas CM, Krakow K, Allen P, Josephs O, Armony JL, Frith CD. Auditory processing across the sleep-wake cycle: simultaneous EEG and fMRI monitoring in humans. 991–999, Copyright 2000, with permission from Elsevier.[21] **2001 images**: Reprinted from Hoshi Y, Mizukami S, Tamura M. Dynamic features of hemodynamic and metabolic changes in the human brain during all-night sleep as revealed by near-infrared spectroscopy. *Brain Res*. 1994;652(2):257-62[22] and Igawa M, Atsumi Y, Takahashi K, Shiotsuka S, Hirasawa H, Yamamoto R, et al. Activation of visual cortex in REM sleep measured by 24-channel NIRS imaging. Psychiatry Clin Neurosci. 2001;55(3):187-8. Creative Commons.[23] **2002 image**: Reprinted from Dehaene-Lambertz G, Pena M Electrophysiological evidence for automatic phonetic processing in neonates. *Neuroreport*. 12(14):3155–3158. Available from: https://www.science.org/doi/10.1126/science.1077066.[26] **2025 image**: Reprinted from Chen JE, Lewis L, Coursey S, et al. Simultaneous EEG-PET-MRI identifies temporally coupled, spatially structured hemodynamic and metabolic dynamics across wakefulness and NREM sleep. *bioRxiv*. 2025. Creative Commons.[27]

Abbreviations: PET, Positron Emission Tomography; hd-EEG, high-density electroencephalography; fMRI, Functional Magnetic Resonance Imaging; SPECT, Single Photon Emission Computed Tomography; MEG, Magnetoencephalography; fNRIS, Functional Near-Infrared Spectroscopy.

movement (REM) sleep by over 50 years.[10,11] In hindsight these results could have suggested that reduced blood flow was not a prerequisite for sleep and the presence of multiple sleep states exist. However, the overall historical interpretation of his results were, regrettably, deemed unconvincing and inconclusive by some.[35] Somnographs of sleep phenominology and physiology produced by Kohlschütter and Mosso represented a major innovation, helping to convey the patterns of sleep data more clearly than text or somnocharts and by the early 20th century, graphical depictions of physiology came to dominate the conceptualization and study of sleep. Somnographs were rapidly created for every conceivable physiological process known at the time, including brain weight, cranial pressure, CBF, heart activity, muscle tone, respiration, pupillometry, skin conductance, salivation, digestion, body temperature, and eye movements.[32,36] This time period was a Renaissance in sleep science and the widespread adoption and use of somnographic methods in sleep research and clinical practice highlights the power of graphical depictions in portraying and

communicating sleep patterns to other researchers and the public. None of these graphs, however, generated as much interest or electrified the field of sleep science like electroencephalography (EEG).

Hans Berger is widely credited with first measuring human brain activity using EEG.[37] Less well known was his application of EEG, electrocardiography (ECG), and respiration patterns to study sleep in the early 1930s, thereby creating the first human PSG using EEG. The published images corresponding to his observations of a flattening in alpha EEG waves during sleep seemed to further confirm prior beliefs that sleep is a quiescent state of brain activity.[7,31,38] This overly simplistic conclusion, based on somnographs from limited electrophysiological measures (ie, few electrodes), using limited modes of measurement (ie, behavioral observation and electrophysiology), over a limited timeframe (ie, minutes to hours) reveals the persisting problem of PSG—its poor content validity in capturing the complexity of sleep-wake dynamics, incuding regional brain processes.

Mitigating this limitation, Loomis et al soon published more detailed images of EEG signals across sleep wake states in humans by using multiple EEG electrodes and recording sleep in varying conditions.[8] Their graphical depictions of characteristic sleep-related brain-wave patterns, "undoubtedly of cortical origin" including the K-complex that occurred in response to knocking on the door and sleep spindles, are important representations of their revolutionary work toward characterizing sleep stages. An important step forward in measuring and representing sleep-wake states was achieved by Gibbs et al who combined thermo-electric blood flow recorders with other physiological measures of sleep.[39] Their multimodal somnographs showing maintained CBF during sleep demonstrated that reduced blood flow was not a viable mechanism of sleep onset, effectively putting to rest the vascular theory of sleep.[39] Although they doubted that regional changes in blood flow to a "sleep center" was involved in sleep, they acknowledged the limited regional specificity of their method prevented comment on this theory. The somnographs produced by these early EEG investigations helped challenge conceptualizations of sleep as a quiescent physiological state for the body and demonstrated convincingly that the brain is endogenously active and dynamically reactive during sleep.

Despite early advances in CBF measurement across sleep-wake states, electrophysiology ultimately came to dominate the measurement and conceptualizations of sleep. Indeed, advancements in other brain measures of sleep were largely overshadowed by PSG within the emerging field of sleep and dream research following the discovery of REM sleep in the 1950s.[10,11] Compared to electrophysiological measures, alternative measures of sleep proved to be less accessible, technical, and expensive. Human brain measures also tended to yield less reliable or clear results. Nevertheless, the application of neuroimaging to study sleep remained an important subscript in the history of sleep science. For example, in 1955, Mangold et al conducted an early multimodal sleep study in young men by combining EEG with the Kety-Schmidt method to study CBF and global cerebral metabolic rate of oxygen during sleep states, defined by the presence of sleep spindles and slow-wave activity.[9] The Kety-Schmidt method involved having participants breathe low concentrations of nitrous oxide while researchers took blood measurements from the internal jugular bulb and the femoral artery to calculate N^2O uptake and estimate CBF and oxygen metabolism.[40] Their approach, though indirect, showed increased CBF during sleep compared to wakefulness and failed to find significant sleep-wake differences in oxygen metabolism. Although higher blood flow during sleep has subsequently been isolated to REM sleep, the results of this early CBF study demonstrated that reduced cerebral metabolism is neither necessary nor sufficient for sleep states to occur, which challenged contemporary sleep theories that sleep is caused by reduced gross nutrition or metabolism. Ultimately, this study demonstrated that multimodal brain measurement is needed to advance the field beyond what could be achieved with electroencephalography alone.

After the discovery of REM, the field of sleep research further emphasized electrophysiological measures of brain, body, eye, and heart movements. Standardizing PSG criteria for scoring sleep-wake stages became a priority for early sleep and dream researchers, particularly Allan Rechtschaffen, who outlined it as a key objective of the newly formed Association for the Psychophysiological Study of Sleep.[41] Before settling on specific electrophysiological measures to define sleep based on global rather than regional brain activity, the field of sleep medicine struggled to account for discrepancies across units of measurement. Some argued for a decoupling of CBF, metabolic rate, and electrophysiology across sleep-wake states, while others sought agreement across units of analysis. Well known discrepancies between self-reported sleep and electrophysiological measures were largely ignored and disregarded as subjective "misperceptions" on the part of the sleepers. By 1968, manualized PSG became a rallying point around which sleep researcher and clinicians

could call "objective", which provided the footing the field needed to advance, particularly in sleep medicine. The polysomnogram became the "gold standard" graphical representation of sleep.[13] Initially, produced with ink scratching on football fields worth of paper per night, digital PSG signals have become the image of scientific sleep to the present day. Although lacking the spatial resolution to characterize the subtle regional dynamics of global sleep-wake states suggested by contemporary animal research and sleep neuroimaging studies (described below), the establishment of a reference point in which neuroimaging results could be interpreted represented a major advancement in sleep science. The manualized Rechtschaffen and Kales (R&K) PSG staging criteria provided reliability and clarity to early brain studies, helping to reconcile contradictory findings of increased, decreased, or unchanged CBF and metabolism during sleep.[42] Although PSG has yielded important advances, like somnocharts, somnographs have failed to fully capture the complexity of the sleep's phenominology, behavior, and physiology needed to test sleep theories that have been debated for nearly two centuries.

Birth of Sleep Neuroimaging

The history of sleep neuroimaging is tied to theoretical debates over whether sleep is a local or global phenomena and whether there exist hypnogenic centers of the brain. In the modern age, local sleep theory was proposed by Robert Macnish.[43] His regrettable use of phrenology, a discredited and widely derided theory, to outline his version of local sleep may have contributed to its subsequent difficulties in gaining wide acceptance. Conducting the first experimental study on sleep deprivation, Marie de Manacéïne argued that sleep was localized to the higher brain centers and observed that the cortex was most affected by sleep loss.[44] Debate around sleep centers of the brain was revitalized by Ivan Pavlov in the early 1900s whose theory rejected the existence of a sleep center in favor of the view that every cell in the brain sleeps, some as a result of use, others as a result of chemical signaling that spread inhibition originating in the exhausted cells (Reviewed in 25). Nathaniel Kleitman, a sleep scientist whose views have had a much greater influence in the field of sleep research, panned Pavlov's sleep theory in favor of a whole brain theory of sleep.[45] Although concepts of local versus global sleep, sleep centers, and sleep systems continue to be debated, sleep neuroimaging has proved a powerful tool in settling these theoretical disputes.

Our knowledge of human sleep neurophysiology is largely derived from invasive animal research protocols. It is perhaps, therefore, not surprising that sleep neuroimaging was first developed and applied in animal models before its application in human sleep research. Using implantable EEG, thermistors, and autoradiography techniques, Reivich et al convincingly demonstrated regional differences in brain activity across sleep-wake states in the cat model.[12,46] To our knowledge, these studies produced the first published somnoimages. Subsequently, sleep neuroimaging methods using fMRI have been developed for use in basic animal studies,[47–49] making it a valuable tool for studying sleep physiology.

Sleep neuroimaging in humans began in the late-1960s, with the earliest human somnoimages being mere crude hand drawings produced by Risberg et al, who combined neuroimaging methods (ie, intravenous [^{131}I] scintigraphy) with PSG in human, showing state-specific regional dynamics in cerebral blood volume.[14] In 1973, Townsend et al used the xenon-133 inhalation method with PSG to investigate CBF across the recently developed R&K criteria for wake, NREM sleep, and REM sleep.[13] Applying the xenon approach, participants inhaled xenon-133 during sleep while extracranial scintillation detectors around the head measured CBF, revealing decreased flow during slow-wave sleep and increased flow during REM sleep compared to wakefulness.[50] Diagrams of the brain with accompanying plots of regional brain activity patterns were published, but a clear somnoimage was lacking. Nevertheless, the combination of neuroimaging with validated PSG criteria provided a clear picture of CBF during sleep and provided a possible solution to explain contradictory CBF findings in prior studies—inclusion of REM sleep.

Subsequent advances in xenon methods (eg, stable xenon methods that allowed for local CBF measures) demonstrated in humans that which was also being found in autoradiography studies in animals[46,51–53]—that there are regional changes in CBF and glucose metabolism during NREM and REM sleep.[16,54–58] Blood flow was shown to be lower in stage 1 sleep in the bilateral frontal cortex, left parietal lobe, bilateral inferior temporal, right Sylvian opercular, right posterior temporal cortex, cerebellum, and brainstem relative to wakefulness but reductions became more diffuse throughout the brain as sleep deepened into stage 3 and 4.[57] These subsequent human studies also provided hand-

drawn somnoimages with statistics and plots positioned over regions showing differences in blood flow across sleep-wake states.

The first computer-generated somnoimage in humans was published in 1985 by Heiss et al, who used 2-deoxy-D-[2-aSF]glucose positron emission tomography (FDG-PET) with EEG to investigate regional cerebral metabolism during a nap compared to wakefulness.[15] Although lacking R&K staging criteria, their investigation in 4 male participants demonstrated that sleep typically involves widespread reductions in glucose metabolism. However, in one volunteer who reported having a nightmare during the sleep period, regional increases in glucose metabolism were observed. In addition, these early studies showed the potential power of using sleep neuroimaging to elucidate regional dynamics of dreaming, state-specific regional differences in sleep disorders,[59] and other neuropsychiatric disorders. For example, using the xenon 133 method, Gozakirmizi et al demonstrated that while good sleepers experience a reduction in CBF during NREM sleep, patients with complex partial seizures show increased CBF in the temporal lobe during paroxysmal activity than occurs during NREM sleep and that increased blood flow occurs beyond the lateralized temporal lobe showing paroxysmal EEG activity.[54]

In a pioneering application of this technique, Greisen et al utilized 133-Xenon clearance after intravenous injection to explore sleep-wake shifts in 15 healthy preterm infants.[60] The team utilized concurrent biparietal EEG, heart rate, respiration, and clinical observation to investigate quiet and active sleep. They showed that in these infants active sleep was associated with lower CBF, comparable to the reductions seen in quiet sleep. They concluded that physiological and metabolic mechanisms governing REM sleep, typically characterized by greater neural activity, might not be fully developed in preterm infants. The first somnoimage in infants was published in 2002 by Dehaene-Lambertz et al who used sleep fMRI.[26] Sleep fMRI has proved to be a powerful tool for studying early life development.[61–63] These studies emphasized the crucial role sleep neuroimaging can play in elucidating the nuances of sleep physiology and development, particularly in vulnerable populations like preterm infants.

Although the basic approach was employed 2 years earlier,[64] the first to publish a somnoimage of R&K-defined NREM and REM sleep states was Buchsbaum et al in 1989.[65] Using the FDG-PET method, the authors demonstrated that NREM sleep involves widespread reductions in glucose metabolism compared to wakefulness, with the greatest reductions in the medial frontal cortex. They also showed that REM sleep involves lower glucose metabolism in some brain regions. In a subsequent re-analysis of these data, the authors published somnoimages that contrasted brain activity across states (activity during REM sleep compared to that occurring during NREM sleep).[66] The FDG-PET method proved to be a powerful sleep neuroimaging approach bringing a higher degree of reliability and detail than were possible in prior human research methods. As described below, PET methods continue to have place in the rapidly evolving field of sleep neuroimaging.

Current Sleep Neuroimaging Methods

Modern sleep neuroimaging methods include high-density EEG (hd-EEG), magnetoencephalography (MEG), single-photon emission computed tomography (SPECT), PET, functional near-infrared spectroscopy (fNIRS), and various MRI sequences, and multimodal imaging techniques, including EEG-fMRI.[19,42,65,67–81] Just as neuroimaging does not require the production of an actual image, the ability to measure brain functioning at a level capable of visualization is where the power lies in sleep neuroimaging. By combining dynamic neuroimaging (eg, fMRI, perfusion) with high-resolution structural scans, detailed somnoimages are now being produced that form a powerful communication tool for sleep science. Below we describe the major sleep neuroimaging modalities, outline their strengths and weakness (Table 2), and their applications in sleep science.

Hd-EEG

Almost immediately after EEG was applied to record human sleep, the natural evolution was to record multiple EEG signals simultaneously. With multiple simultaneous recordings, clues to local sleep patterns have challenged the prevailing view that sleep is a whole brain event. To overcome limitations in spatial resolution of standard PSG, hd-EEG utilizes 64+ electrode channels with computational modeling to provide real-time measurement of regional electrical brain activity and potential sources localization.[80] Since its introduction in the 1990s,[82] hd-EEG has become the most widely used sleep

Table 2 Strengths Limitations and Recommendations for Current Sleep Neuroimaging Modalities

Sleep Neuroimaging Modality	Strengths	Limitations	Recommendations for Use
High-density Electroencephalography (hd-EEG)	Excellent temporal resolution; a more naturalistic sleep obtained in a quiet space and bed.	Poor spatial resolution compared to fMRI; limited deep brain activity measurement.	Relatively inexpensive. Ideal for studying sleep disorders, local sleep phenomena, and sleep deprivation effects.
Magnetoencephalography (MEG)	High temporal and spatial resolution for tangential sources; sleep recordings occur in a quite space.	Requires sleeping in MEG helmet in an expensive shielded room	Best for investigating sleep spindles, brain oscillations, and cortical activity patterns.
Single Photon Emission Computed Tomography (SPECT)	Measures regional cerebral blood flow; available in clinical settings.	Lower spatial and temporal resolution than PET; radiation exposure.	Useful for examining blood flow abnormalities in sleep disorders. May be most feasible in medical settings and in combination with EEG
Positron Emission Tomography (PET)	Provides metabolic and neurotransmitter activity insights; good spatial resolution. For glucose metabolism, participants can sleep in a bed	Higher radiation exposure than other modalities; requires sleeping with catheter, expensive.	Best for studying metabolic and neurotransmitter activity changes across sleep-wake states.
Functional Near-Infrared Spectroscopy (fNIRS)	Portable, good for measuring cortical hemodynamics.	Lower spatial resolution; poor depth specificity. Bulky cap may disrupt sleep; limited to surface cortical sources	Good for portable sleep research and studying oxygenation changes in the cortex.
Functional Magnetic Resonance Imaging (fMRI)	High spatial resolution; enables measurement of a wide array of biological processes ; widely available.	Motion artifacts higher during sleep; scanner noise; scanner artifacts, requires sleeping in an MRI environment, selection effects to claustrophobia, metal in the body, etc.	Excellent for examining sleep-related constructs during wakefulness and global brain dynamics across sleep-states where simultaneous EEG is not possible including in the human fetus
EEG-fMRI	Combines the temporal precision of EEG with the spatial resolution of fMRI. Multiple modalities within fMRI make it versatile for studying many aspects of sleep	In addition to limitations of both EEG and fMRI listed above, subject discomfort due to EEG cap in MRI can further disrupt sleep; signal artifacts to EEG from MRI gradients.	Recommended multimodality for most sleep neuroimaging questions. Can also be combined with PET for complex processes.

neuroimaging modality. This modality was first applied to study neural processes during sleep in infants and was soon applied to study sleep more broadly.[24] Although it takes more time and expense to set up than PSG, hd-EEG has emerged as a versatile and powerful sleep neuroimaging technique used to investigate regional dynamics of sleep,[83–85] source of neural changes in sleep,[86,87] sleep deprivation,[87–89] sleep disorders,[83,90–93] dreams,[94,95] sleep and learning/memory,[25] sleep development,[96] consciousness[74,97] and numerous other sleep-related constructs (eg, concepts, phenomena, outcomes) across sleep-wake states, including mental illness.[95,98,99]

Like other sleep neuroimaging modalities, its introduction to the sleep community was met with some skepticism about its ability to measure naturally occurring sleep. The initial studies in adults were conducted in a testing room environment in which participants were reclined in a chair. Due to discomfort of the cap recording of sleep were limited to just a few hours.[25] Advancements in laboratory sleep methods and technology now allow for all night records that address most of the early criticisms. Hd-EEG nets often include the standard 10–20 electrodes or can be easily supplemented with additional lead, which allows for systematic placement, measurement, and scoring of sleep states. Ensuring consistent placement of the cap, particularly when making recordings across multiple nights is essential for correct localization. Low profile electrodes, soft pillows, and plush-pile pads allow participants to sleep more comfortably in a bed during recordings, providing a more naturalistic gauge of regional brain activity in the laboratory setting

than can be obtained using other neuroimaging modalities (as described below). Hd-EEG has traditionally had relatively poor spatial resolution compared to other modalities such as fMRI, particularly for deep brain activity. Advances in source localization, however, are beginning to overcome spatial limitation.[100,101] Its advantages make it an ideal modality for combination with the other sleep neuroimaging methods described below.

MEG

MEG measures changes in the magnetic fields generated by electrical activity generated along dendritic clusters of neurons aligned perpendicular to the MEG sensors, primarily in superficial cortical layers. Early applications of MEG to sleep research in the 1970s measured concurrent EEG to pinpoint the maximal location of sleep spindles.[18,102] Using simultaneous multichannel measures, MEG is now able to generate topographic images and localize magnetic changes associated with sleep onset, stages, saccades, consciousness, and depth.[79,103] MEG has been combined with evoked response potential to map the flow of information through the sleeping brain and to investigate other sleep-related processes, including the regional impact of sleep deprivation on the brain.[104] Compared to hd-EEG, MEG offers higher spatial resolution, especially for tangential oriented sources,[105] increased signal sensitivity, and the ability to measure some deep brain activity while retaining exceptional temporal resolution. Limitations of MEG include the necessity of sleeping in the MEG helmet that prevents naturalistic measures of sleep, reliance on source localization for deeper brain structures that prevents access to many deep structure, and high expense for both the machine and requirements for a dedicated shielded room to eliminate external magnetic interference. MEG can be combined with hd-EEG to allow for standard sleep scoring. Their combined signals can help improve accuracy of source localization. Optically pumped MEG (OPM-MEG) is an emerging technology that may overcome several limitations of traditional MEG and holds promise for sleep research. It is a cost-effective, wearable system capable of simultaneously recording neuronal activity with both high temporal and spatial resolution over extended periods.[106,107] OPM-MEG has already been combined with EEG and fNIRS,[108] making it a potentially valuable tool for multimodal sleep neuroimaging. While optimal data quality requires a magnetically shielded room, ongoing advancements are improving its accessibility and usability.

SPECT

SPECT is a neuroimaging method that uses radioactive tracers to measure regional CBF. SPECT provides information about patterns of brain activity and has been applied to show differences in regional CBF across sleep stages, investigate regional dynamics of sleep deprivation, characterized abnormalities in sleep disorders,[71,72,109] and study sleep-bound seizures.[110] Compared to fMRI and PET, SPECT has higher radiation exposure and worse temporal and spatial resolution. While tracers can be injected during sleep and scanned later, SPECT provides only snapshots rather than continuous data. Although its use in sleep neuroimaging is more limited, SPECT remains clinically available, is more affordable than PET, and has unique tracers. Advances in image processing and camera technology continue to enhance its role in studying sleep disorders.

PET

To study metabolic activity and CBF across sleep-wake states, PET scans have been widely employed in sleep research. FDG-PET and water-PET (H_2O-PET) allow for the quantitative analysis of changes in brain activity across the brain and have been used to study sleep stages,[111] sleep disorders,[34] and sleep deprivation.[112] For the FDG-PET method, a stable electrophysiological state is confirmed prior to and following the injection of the radioactive tracer, whereupon active neurons take up the glucose homologue.[113] Scans taken after the uptake period produce snapshot images reflecting the brain activity that occurred during the uptake period. In contrast, the shorter half-life of $[^{15}O]H_2O$-PET, these scans typically happen while the participant is sleeping in the scanner. This comes with higher temporal resolution but at the cost of ecological validity as the participant is not able to sleep quietly in a bed during the uptake period. PET offers typically higher spatial resolutions compared to SPECT, in addition to lower radiation exposure. Other PET methods have been used to measure neurotransmitter receptor activity, which provide a valuable window into regional molecular activity associated with sleep, sleep disorders, and sleep-related constructs.[114,115] However, PET scans have limitations

including higher radiation exposure, high expense, and relatively low temporal and spatial resolution compared to most alternatives except SPECT.

Assessing sleep using these methods has shown preliminary evidence that local sleep processes are associated with daytime outcomes. For example, Nofzinger et al studied healthy and depressed individuals using FDG-PET to show that increased glucose metabolism in the ventromedial prefrontal cortex and right lateral occipital cortex during sleep is associated with greater arousal and worse self-reported sleep quality, particularly in individuals who were clinically depressed.[116] Inversely, PET scans can help us better understand existing differences in individuals with mental health disorders. For example, Germain et al found that veterans with posttraumatic stress disorder experienced more REM sleep and had more activity in arousal areas of the brainstem, limbic and cortical regions compared to veterans with major depressive disorder.[117] These and other FDG-PET studies demonstrate the utility of this method as a sleep neuroimaging technique for identifying the role of sleep in mental health disorders and symptom presentation. In addition, PET radio-isotopes are an active area of research with new and exciting tracers being developed for inflammation, dopamine, serotonin, membrane-bound proteins (VMAT2), norepinephrine, amyloid, tau, GABA, nicotinic acetylcholine receptors that hold promise in future sleep neuroimaging studies. New hybrid imaging systems combine PET with MRI within a single machine that allow for simultaneous acquisition of structural, functional, and molecular data. The knowledge gained from sleep neuroimaging studies that use this these technologies will undoubtedly inform future psychiatric intervention efforts.

FNIRS

Multi-channel fNIRS utilizes near-infrared light to measure hemodynamics and oxygenation in underlying brain tissue.[78] As a sleep neuroimaging technique, it has been used to study sleep disorders, the neurophysiology of cognitive performance following sleep deprivation, and resting brain connectivity across sleep-wake states in adults and infants.[81,118–121] fNIRS enables measurement of cortical hemodynamic activity during sleep without requiring participants to sleep in an fMRI scanner.[78] However, fNIRS has limitations including low spatial resolution, poor depth specificity, and bulky optical fibers, sources/detector optodes.[78] This makes the somnoimages it produces somewhat less detailed than other modalities. Nevertheless, its high temporal resolution, low cost, and rapid engineering advances make fNIRS a promising sleep neuroimaging approach.

Nuclear Magnetic Resonance Modalities: FMRI, Magnetic Resonance Spectroscopy Imaging (MRSI), and Perfusion

Nuclear magnetic resonance is a non-invasive technique used to study the molecular and structural properties of materials, including biological tissues. It offers several powerful tools for studying sleep, including a host of scan sequences capable of tapping into many domains of brain physiology including fMRI, MRSI, and perfusion.

FMRI

fMRI is a particularly versatile sleep neuroimaging technique that measures brain activity by detecting the differential magnetic properties of oxyhemoglobin, deoxyhemoglobin, and total hemoglobin within brain tissues, enabling detection of cerebral cortex activity.[122] fMRI can be co-registered with high-resolution structural MRI images collected in the same scanning session, which offer high spatial resolution. Task-based fMRI can be conducted across sleep-wake states by introducing a stimulus (eg, auditory, visual, olfactory) and measuring hemodynamic brain responses.[21,123,124] Furthermore, as with resting-state scans, fMRI can continuously measure brain signals during sleep over extended periods, making it ideal for characterizing and imaging state-specific hemodynamics across sleep-wake state.[122] Functional connectivity analysis to assess brain network interactions[125] has been of particular interest but other measures used in sleep research include regional homogeneity to examine local synchronization of neural activity,[126] amplitude of low-frequency fluctuations and fractional low-frequency fluctuations to measure spontaneous brain activity,[127] degree centrality to identify hub regions in brain networks,[128] graph theory-based network analysis to map topological changes,[129] entropy-based methods to capture signal complexity,[130] ultraslow fMRI to investigate long-range neural

communication, global brain state transitions, cerebrospinal fluid (CSF) dynamics,[131] and ultrafast functional MRI to investigate rapid sleep-state transitions, microstates, and brain fluid dynamics across sleep-wake states.[132]

fMRI has limitations including motion sensitivity, slower temporal resolution compared to EEG and MEG, scanner noise, constrained sleep positions, and lower rate of data sampling.[122] Still, carefully applied, fMRI has provided valuable insights into regional sleep dynamics, as ways for prospective motion processing improved over the last decade.[133] Although early sleep fMRI studies lacked concurrent EEG, EEG is recommended when investigating sleep-wake states, as discussed in the next section.[134] Nevertheless, as a standalone modality, fMRI continues to have utility in investigating sleep disorders and other sleep-related constructs during the wake state. In these conditions, we recommend using tasks that require behavioral responses and eye tracking to ensure wakefulness, or at least require that eyes remain open and fixed on a cross during resting state scan, due to high rates of sleep occurrence in eyes-closed conditions.[125] fMRI is also a valuable sleep neuroimaging method in cases where concurrent EEG is not feasible, for example studies in some patient populations or studying sleep in the human fetus.[63,135] In such cases, behavioral measures may prove useful in helping determine the presence or absence of sleep. Machine learning may also be a viable alternative for staging sleep using fMRI in the absence of PSG, with the tantalizing possibility of one day untethering sleep neuroimaging from reliance on PSG staging criteria.[125]

MRSI

An exciting MR method of neuroimaging is MRSI, which measures stable changes in several metabolites, precursors and neurotransmitters, eg assessing the excitation-inhibition balance and oxidative stress within the human body.[136] MRSI is a promising approach capable of uncovering the regional chemical patterns involved in sleep regulation, processes, and disorders but has several limitations including long acquisition sequences with limited coverage of the brain, requiring focus on specific regions of interest and insensitivity to subtle chemical changes associated with sleep. To date, this approach has been used to study neurochemical differences associated with acute sleep loss and sleep disorders.[137,138] Sequences are now available on 3T scanners but high field (>3T) is recommended for greater spatial resolution and higher signal-to-noise ratio.[139] Functional MSRI, combines fMRI with MRSI to assess metabolic changes in the brain during functional tasks or in response to external stimuli that has merit as a sleep neuroimaging approach.

Perfusion

Perfusion refers to the delivery of blood to brain tissue, facilitating the supply of oxygen and nutrients while aiding in the removal of metabolic waste, with CBF serving as a key measure of this process. CBF is tightly regulated by cerebral autoregulation, which maintains stable perfusion despite fluctuations in systemic blood pressure. CBF can be assessed with several other neuroimaging modalities including PET, SPECT, transcranial Doppler Ultrasound (TCD), and arterial spin labeling (ASL). TCD has many advantages for indirectly assessing CBF based on velocity-based flow measures, including relatively low cost, portability for bedside assessment of sleep, ability to combine with PSG, no need for radioactive tracers, and high temporal resolution. Highlighting its utility, one computer-assisted pulsed Doppler system together with simultaneous PSG showed that middle cerebral artery blood flow velocity changes across sleep stages, suggesting that factors other than metabolic mechanisms contribute to the regulation of cerebral perfusion during human NREM sleep.[140] fMRI sequences sensitive to perfusion, such as ASL, have key advantages for sleep research: it is the only tool that provides a direct measure of absolute quantification of perfusion (without using a contrast agent) and provides better spatial resolution than these other options. Few studies have examined CBF changes using combined ASL perfusion and EEG measurements. Tüshaus et al (2017) found a dynamic relationship of CBF with slow-wave activity corroborated vigilance state specific (ie, wake, NREM sleep stages N1-N3, wake after sleep) differences of CBF, eg in the posterior cingulate, basal ganglia, and thalamus, indicating their role in sleep-wake regulation and sleep processes.[134] The authors concluded that some of these brain areas – known to be affected in disorders of consciousness – might also contribute to the emergence of consciousness. ASL perfusion can be used in a time series to monitor CBF changes across sleep-wake states or averaged over a window of time to provide snapshots of specific states, providing unique information about cerebral activity on a timescale in between the temporal resolution offered by PET and fMRI.

EEG-fMRI

Simultaneous EEG-fMRI emerged as a multimodal neuroimaging approach in the 1990s and was initially used to localize seizures in epilepsy patients.[20,21,77] Studies of epilepsy-related sleep patterns revealed a posterior-to-anterior shift in slow-wave activity in children[141] and age-related thalamic hemodynamic changes in healthy volunteers.[142,143] Since that time, EEG-fMRI has been used to advance sleep research considerably.[144,145] This approach allows researchers to simultaneously capture the electrical activity of the brain and its hemodynamic responses, providing a comprehensive view of brain function across sleep-wake states. One of the key advantages of dual modality is its ability to correlate the temporal resolution of EEG with the spatial resolution of fMRI enabling investigation into the intricate dynamics of sleep stages, such as REM and NREM sleep, and their associated neural correlates. Moreover, EEG-fMRI can help identify biomarkers for various sleep-related conditions, facilitating early diagnosis and targeted interventions. As sleep is crucial for cognitive processes, emotional regulation, and physical health, understanding its neural underpinnings through EEG-fMRI could lead to improved therapeutic strategies. Studies have shown that stimulus-induced BOLD decreases during NREM sleep correlate with EEG synchronization, suggesting cortical deactivation protects against arousing stimuli.[146] Research on sleep spindles found increased fMRI signals in the middle temporal gyrus during N2 compared to N3, with spindle-related activation negatively associated with N2 sleep duration.[147] Memory consolidation studies have linked slow wave–spindle coupling to task-specific brain reactivations, confined to the learning hemisphere, while uncoupled spindles were associated with sensory processing and sleep maintenance.[148] Additionally, EEG-fMRI has helped examine fatigue in insomnia, showing altered thalamic-cerebellar connectivity correlated with fatigue severity.[149] EEG-fMRI has been used to examine changes in CSF and blood flow that are coupled in time to slow waves during sleep, providing important evidence for potential role of sleep in brain clearance in humans.[150] A systematic review of EEG-fMRI studies is beyond the scope of this article but would be of great value and benefit to the field.

Despite its advantages, EEG-fMRI has several limitations that have been well characterized elsewhere, including considerable noise imposed on EEG in the MRI environment and potential distortions in MRI introduced by EEG electrodes.[151,152] The considerations noted above for hd-EEG and fMRI above generally apply when combined and present additional challenges. For artifact reduction, Bullock recommended using additional hardware not often included on commercial products that synchronize clocks, and directly record artifact at the head, including motion, reparation, vibration, ballistocardiogram, and eye blinks. In their review of the EEG-fMRI sleep field, Czisch and Wehrle outline several logistical and technical challenges of this method when applied to sleep including reduced signal quality over the time course of sleep, increased movement artifact during sleep compared to wakefulness, inability of a minority of participants to sleep in the MR environment, disruption to sleep (particularly suppression of REM) in the MR acoustic environment, limited control over sleep-wake states, and limited ability to capture more than 1–2 sleep cycles.[151] They suggest that habituating participants to the scanner environment, using sleep deprivation prior to sleep scans and using real-time scoring to confirm sleep-wake states may help overcome some of these challenges.

Although sleep deprivation may be advisable for nap protocols, prior studies indicate that most participants can sleep in the scanner at night without prior sleep deprivation, with 62% obtaining more than 10 minutes of N2 and/or N3 within a one-hour scan.[153,154] Our data align with these findings, as 85% of participants self-reported sleeping during partial-night scans conducted at habitual bedtime. To help participants habituate to the scanner, we conduct a morning scan before the evening sleep scan and instructed participants to avoid napping during the day to help them feel sleepy that night. Many participants (~50%) in our simultaneous EEG-fMRI studies report experiencing pain due to the electrode cap and sleeping on the scanner bed after about 2 hours in the scanner. The added bulk of the EEG cap prevents the use of a comfortable pillow when using a high-channel MR head coil. Individual foam disks placed around the EEG electrodes on the back of the head or weaving gauze padding around electrodes provides some comfort . The EEG cap presents changes in securing the head in the coil without disrupting the EEG electrodes and introducing additional discomfort. In the fMRI scanner environment, artifacts associated with the magnetic field, movement, compromised electrode impedances, and time-varying gradient fields can comprise EEG-fMRI recordings during longer (sleep-related) sessions and make real time observation and subsequent scoring for sleep stages more difficult. Several postprocessing option are currently available to remove scanner artifacts which are impressive but the resulting EEG signals are different

from those typically seen in PSG studies making processing the EEG data to the quality needed to score for sleep staging challenging. Nevertheless, advances in sleep neuroimaging and technology are rapidly overcoming these limitations. Requiring participants to shower (without conditioner) before the scan, utilizing a hd-EEG cap (64+ channels), and sampling at higher rates (≥5000 hz) can provide better postprocessing outcomes. Full-night fMRI-EEG studies have demonstrated that NREM-REM cycles occur in the scanner, with deep sleep typically emerging in the first part of the night (40–240 min), and sleep stage scoring during MRI scans has been validated.[153,154] Multimodal fMRI-EEG has recently been combined with PET to reveal the complex regional interplay of neuronal, hemodynamic, and metabolic dynamics that occur across sleep-wake states.[27] Sleep neuroimaging using fMRI-EEG is rapidly evolving and a white paper on best practices is needed.

Unlocking the Power of Sleep Neuroimaging

Human sleep researchers face a fundamental dilemma: prioritize temporal resolution to capture sleep patterns over time or use an unnaturalistic sleep environment to obtain the high spatial resolution needed to identify localized brain processes associated with sleep. While laboratory PSG balances these considerations, it lacks spatial resolution to localize sleep-related brain activity, fails to capture key aspects of sleep (eg, consciousness), and does not provide a fully naturalistic sleep setting. By comparison, neuroimaging techniques such as fMRI and PET offer detailed insights into sleep-related neural mechanisms but are constrained to controlled, short-term studies in an even more unnatural sleep environment than PSG. By integrating neuroimaging with sleep research methods, sleep neuroimaging leverages their respective strengths. When possible, we recommend conducting simultaneous PSG during scanning, supplemented by a post-scan sleep diary documenting participants' sleep experience in the scanner. Although we have emphasized the power of multimodal approaches, sleep neuroimaging also recognizes the importance of integrating multiple units of analysis into sleep research. Collecting a detailed clinical sleep history, self-reported sleep including daily sleep diaries for at least one week, psychological and cognitive variables, overnight PSG sleep study outside the scanner, and wearable data (eg, actigraphy) can provide valuable context needed to interpret the neuroimaging results. The field of modern sleep science began with graphing the phenomenology of sleep and incorporating valid measures of self-reported sleep and sleep related experience is critical. Just as the emergence of polysomnography revolutionized sleep science's conceptualization of sleep as well as the ability to directly measure sleep-related outcomes, we believe that sleep neuroimaging is the next revolutionary methodology that will advance the field of sleep science. The potential of sleep neuroimaging as a research and clinical tool truly feels unbounded, though our minds are drawn immediately to several direct applications of this method, including advancing our understanding of sleep neurophysiology including its most challenging aspects (ie, consciousness and dreaming), gaining insights into sleep disorders and mental health, and enhancing treatment strategies.

Sleep neuroimaging has significantly advanced our understanding of sleep mechanisms and disorders, resolving long-standing debates such as whether sleep is a whole-brain or localized process. Furthermore, neuroimaging provides crucial insights into the pathophysiology, diagnosis, and treatment of sleep disorders.[155] A prime example is in insomnia research. Our sleep neuroimaging research has shown that insomnia is not merely a "misperception" of sleep but is linked to altered brain activity.[156,157] Similarly, studies using hd-EEG have shown that the feeling of being awake during sleep correlated with increased localized high-frequency (ie, sigma and beta power) EEG activity in good sleepers and with more widespread changes in insomnia patients.[92,158,159] Using FDG-PET, we have also shown that individuals with insomnia exhibit reduced sleep-wake differences in glucose metabolism in regions involved in conscious awareness, executive control, and affective processing, which may underlie both nighttime sleep difficulties and daytime impairments.[34] Follow-up research demonstrated that sleep restriction lowers glucose metabolism in these regions during recovery sleep, for both individuals with insomnia and good sleepers, suggesting that sleep restriction therapy may enhance local sleep drive in areas of the brain involved in consciousness, sensory, and affective processing.[112,160] Using real-time fMRI neurofeedback training (of the amygdala) to enhance positive autobiographical memory, Li et al were able to alter resting state brain activity to improve sleep in individuals with insomnia disorder.[161] Collectively, these findings challenge the global hyperarousal model of insomnia and reinforce that sleep difficulties in these patients are not merely subjective experiences but involve a dynamic brain process across sleep-wake states.

Sleep neuroimaging also opens the door to investigate the neural mechanisms underlying dreaming and consciousness.[151] Historically, these phenomena were difficult to measure, either due to methodological challenges or a focus on phenomenology. However, sleep neuroimaging now enables physiological assessments of these processes, overcoming past concerns in dreaming and consciousness research. For instance, Siclari et al (2017) identified neural correlates of dreaming across sleep stages, revealing local EEG activations associated with dream experiences despite globally distinct REM and NREM profiles.[95] Additionally, high-frequency activity in these regions correlated with specific dream content. Using EEG-fMRI, neural differences between lucid and non-lucid dreaming have been demonstrated,[162] offering insights into conscious experiences during sleep. These findings could establish a new domain of dream imaging research, challenging traditional views on consciousness and altered states.

Beyond dreaming, sleep neuroimaging plays a pivotal role in understanding individual variability in responses to sleep disruption.[163,164] We have proposed that sleep may become disturbed regionally resulting in brain specific impairments during the day.[165] We are excited about the potential of sleep neuroimaging to test this "local sleep deprivation hypotheses" and provide greater insights into how sleep restores cognitive and affective functions and the local mechanisms through which sleep disturbance impacts subsequent daytime functioning, physical health, and risk for mental illness. Emerging applications, including fMRI and fNIRS, now allow researchers to study glymphatic function, a critical sleep process.[166] These sleep neuroimaging modalities may help us finally establish the functions of sleep.

Overall, sleep neuroimaging has transformed our understanding of sleep physiology, cognitive and behavioral functions, and its evolutionary significance.[48] Its continued advancement holds immense potential for refining sleep medicine, developing targeted therapies, and unraveling the complexities of human sleep health.

Challenges and Future Directions

Sleep neuroimaging confronts several challenges that need to be addressed before this method can be fully utilized. These include the high cost and limited accessibility of certain neuroimaging techniques, the need for standardization in data acquisition and analysis, and the potential for artifacts due to head movement. Emerging technologies, such as mobile EEG systems and wearable fNIRS, offer promising solutions by allowing for more naturalistic, at-home sleep monitoring while maintaining neurophysiological precision. Additionally, advancements in motion-correction algorithms and machine learning-based artifact detection may help mitigate movement-related distortions in neuroimaging data. Perhaps the most important recommendation for future use of EEG-fMRI in sleep neuroimaging, is for researchers to fully report their methods according to best practices,[152,167] hardware/software parameters, and artifact reduction procedures enable reproducibility and cross-study validation, thereby strengthening the reliability and advancement of sleep neuroimaging findings.

Beyond technical challenges, ethical considerations must also be addressed, especially when studying children, individuals with neurodevelopmental disorders, or patients with severe sleep disturbances. Ensuring informed consent, minimizing discomfort, and balancing scientific benefits with patient well-being are critical concerns. When conducting studies in these populations, we recommend designing the study around their specific needs. Future research should focus on refining sleep neuroimaging methods to be less disruptive to sleep and more adaptable to real-world settings, enhancing both the validity and ethical application of these techniques. The continuous evolution of sleep neuroimaging underscores the need for further interdisciplinary collaborations amongst neuroscientists, sleep researchers, MR-physicists, bioengineers, computer scientists, and clinicians to devise innovative methods for data collection and analysis. Such synergy will undoubtedly refine our understanding of the structural and functional aspects of sleep, eventually guiding the development of effective diagnostic and therapeutic strategies for sleep disorders, offering enhanced quality of life for affected individuals.

Conclusion

From the pioneering work of Angelo Mosso in the 19th century to the contemporary use of high-resolution techniques, the field of sleep science has made notable strides in elucidating the intricacies of sleep, whether in pathological samples, animal studies, or in unraveling the complexities of sleep disorders such as insomnia, obstructive sleep apnea, narcolepsy, restless legs syndrome, and REM sleep behavior disorder. The emergence and evolution of sleep neuroimaging have

profoundly transformed our understanding of sleep and its related constructs. By leveraging advanced neuroimaging methods, sleep research has shed light on the neural mechanisms underpinning sleep patterns, disorders, and the consequences of sleep deprivation. For example, neuroimaging studies have identified disrupted thalamocortical connectivity in insomnia, providing potential biomarkers that may improve diagnostic accuracy. In the case of narcolepsy, fMRI and PET imaging have been used to assess hypocretin/orexin deficiencies, leading to a better understanding of its pathophysiology and informing pharmacological treatments. Additionally, sleep neuroimaging has provided insights into the cognitive impairments associated with sleep deprivation, which has influenced the development of interventions such as cognitive training and neurofeedback therapies to mitigate these deficits.

Modern sleep neuroimaging studies have enriched our knowledge of sleep-wake regulation[66,168] and the pathophysiology of sleep disorders,[72,109,169] providing a level of detail that surpasses traditional sleep staging. As machine learning and AI-driven neuroimaging analyses continue to evolve, sleep-related brain changes are being explored as potential early indicators of neurodegenerative diseases, such as Alzheimer's disease. These advancements hold promise for developing predictive tools for early intervention and personalized treatments for sleep disorders. This revolution in sleep science is poised to redefine our understanding of the sleep-wake cycle, improve diagnostic precision, advance therapeutic strategies, and deepen our knowledge of the relationship between sleep, health, and overall well-being.

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