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Review

Sleep EEG in chronic insomnia disorder☆

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ABSTRACT

Chronic insomnia disorder is among the most prevalent sleep disorders, and decades of research investigated about its diagnosis and treatment. Yet, the pathophysiological mechanisms underlying insomnia symptoms remain only partially understood. Contemporary conceptual frameworks characterize insomnia as a 24-hour disorder, marked by persistent physiological, cognitive, and emotional hyperarousal, resulting in distinct insomnia phenotypes. However, objective sleep assessment through traditional polysomnography provided limited insight into the mechanisms underlying insomnia disorder. In contrast, the application of advanced analytical techniques to both sleep and wake EEG recordings holds promise for this purpose, with quantitative EEG metrics and sleep microstructure features increasingly recognized as potential biomarkers of insomnia pathophysiology and symptom expression. On the centenary of the first EEG recordings, this narrative review aims to frame and summarize current evidence on EEG applications in insomnia research within the context of modern clinical models. After reviewing contributions from EEG studies conducted during both wakefulness and sleep in characterizing hyperarousal, sleep instability, and sleep misperception, recent findings on EEG-based markers of insomnia treatment response are presented. Finally, directions for future EEG research on insomnia are proposed, building on past achievements and advancing toward precision treatment and clinical translation.

1. Introduction

A century after Hans Berger's first electroencephalographic (EEG) recordings (Berger, 1929) and the early characterization of sleep-related EEG activity by Alfred Lee Loomis and colleagues (Loomis et al., 1935), the field of sleep neurophysiology underwent remarkable advancements, significantly enhancing our understanding of the brain's dynamic transitions between wakefulness and sleep (Krueger et al., 2016). Despite this progress, insomnia—one of the most prevalent and well-studied sleep disorders—remains a complex clinical entity, challenging researchers and clinicians in its characterization at the neurophysiological, mechanistic, and pathophysiological level (Marques et al., 2020). Current diagnostic criteria define chronic insomnia as a condition marked by persistent difficulties in sleep initiation, maintenance or early awakening in the morning occurring at least three times a week and lasting for more than three months, accompanied by daytime dysfunction and clinically significant impairment directly attributable to sleep problems (American Academy of Sleep Medicine, 2014; American Psychiatric Association, 2022). Recent epidemiological studies estimate that insomnia disorder (ID), as defined by these criteria, affects up to 10 % of the adult population (Morin and Jarrin, 2022).

In clinical practice, insomnia is traditionally diagnosed based on subjective sleep complaints, and objective monitoring is not recommended in the assessment and management of the disorder (Krystal et al., 2019; Perlis et al., 2024; Riemann et al., 2023b). Therefore, ID should be treated at the time of diagnosis, using sleep diaries and questionnaires to confirm the clinical suspicion. In fact, the indication for polysomnography (PSG) is limited to treatment-resistant ID or in cases of concomitant suspicion of sleep apnea or limb movements that may lead to awakenings and sleep fragmentation.

Abbreviations: CAP, cyclic alternating pattern; CBT-I, cognitive behavioral therapy for insomnia; DORAs, dual orexin receptor antagonists; EEG, electroencephalography; ERPs, event-related potentials; ID, insomnia disorder; NREM, non-rapid eye movement; PSG, polysomnography; qEEG, quantitative electroencephalography; REM, rapid eye movement; SWS, slow-wave sleep.

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Nevertheless, research using PSG helped clinicians in better understanding the pathophysiological causes and consequences of ID, with PSG studies revealing distinct alterations in sleep microstructure (Perlis et al., 2001b; Zhao et al., 2021). Indeed, the accumulating body of EEG-based evidence underscores the role of sleep neurophysiology in redefining insomnia beyond self-reported symptoms, positioning EEG as a critical tool for improving insomnia phenotyping and treatment monitoring in both research and clinical settings (Krystal et al., 2002; Krystal and Edinger, 2010).

Over the past two decades, an increasing number of studies converged on the hyperarousal hypothesis of insomnia, which proposes a 24-hour dysregulation of the arousal systems as the pathophysiological basis of the disorder (Dressle and Riemann, 2023; Riemann et al., 2010). Studies using EEG spectral analysis have consistently demonstrated cortical hyperarousal, characterized by increased high-frequency activity (beta and faster frequency power) during both wakefulness and sleep, indicating heightened cortical excitability in individuals with insomnia. This persistent physiological overactivation extends beyond conventional sleep stage metrics and manifests as disruptions in sleep microstructure, increased sleep instability, and impaired homeostatic regulation (Feige et al., 2013). Consequently, EEG-based approaches may serve as critical tools for identifying the neurophysiological correlates of insomnia, offering deeper insights into its underlying mechanisms that extend beyond subjective sleep complaints. Moreover, beyond its role in the neurophysiological characterization of insomnia pathophysiology, EEG may also play a strategic role in clinical assessment and management, aiding in the identification of meaningful insomnia phenotypes and the longitudinal tracking of treatment efficacy. Traditional PSG markers, such as total sleep time and sleep efficiency, showed limited sensitivity in distinguishing insomnia from normal sleep patterns. This limitation is particularly evident in individuals exhibiting subjective–objective sleep discrepancy (Kay et al., 2015). In contrast, sleep EEG microstructural markers—including spectral power alterations and phasic sleep features characteristics—may provide more fine-grained information on individual differences in sleep regulation and arousal levels (Feige et al., 2013; Parrino et al., 2012). Thus, EEG research serves as a critical bridge between mechanistic insights and clinical applications, offering a more precise framework for insomnia diagnosis and treatment personalization.

Building on these foundations, this narrative review will examine the major contributions of EEG and sleep neurophysiology to the understanding of insomnia's etiology, summarizing key findings from EEG studies of both wakefulness and sleep and discussing their implications for future research and clinical practice.

2. Insomnia as a 24-hour disorder and the hyperarousal model

As previously outlined, the recognition that ID extends beyond nocturnal symptoms marked a critical shift in research, emphasizing persistent physiological and cognitive-emotional hyperarousal as a defining characteristic of the disorder across the entire 24-h rhythm (Dressle and Riemann, 2023). This hyperarousal model is supported by extensive physiological evidence demonstrating heightened central and autonomic activation in individuals with ID, including increased sympathetic nervous system activity (Bonnet and Arand, 2010), altered heart rate variability (Farina et al., 2014; Spiegelhalder et al., 2011), elevated metabolic rate (Chapman et al., 2018), and dysregulated core temperature rhythms (Lack et al., 2008). These findings, alongside EEG and neuroimaging evidence, reinforce the view of ID as a state of persistent chronic overactivation during the 24-h circadian rhythm rather than a disorder based on the disruption of sleep processes. Specifically, EEG studies—examined in detail later in this review—identified cortical hyperarousal markers, such as increased high-frequency cortical activity, during both sleep and wakefulness (Dai et al., 2024; Jang et al., 2024; Perlis et al., 2001c; Spiegelhalder et al., 2012), consistent with functional neuroimaging evidence showing greater glucose brain metabolism throughout wakefulness and sleep in individuals with subjectively disturbed sleep due to insomnia (Kay et al., 2016; Nofzinger et al., 2004). Taken together, these results suggest a failure to appropriately downregulate cortical activity across vigilance states, with this chronic cerebral overactivation likely contributing to a self-perpetuating cycle that exacerbates both subjective sleep complaints and objective sleep disturbances, highlighting the need for accessible, objective, and modifiable physiological biomarkers of hyperarousal in ID.

In addition, the persistence of hyperarousal may play a key role in explaining the long-standing clinical paradox of subjective–objective sleep discrepancy present in ID, wherein individuals with insomnia may report significantly poorer sleep quality than what is objectively measured via PSG (Harvey and Tang, 2012). However, quantitative EEG (qEEG) and sleep microstructural analyses provided critical insights into this phenomenon, revealing that even when macrostructural sleep parameters appear in the normal range, individuals with insomnia exhibit altered brain activity patterns that may underlie the perception of wakefulness (Stephan and Siclari, 2023). Furthermore, research suggests that disruptions in rapid eye movement (REM) sleep regulation—marked by frequent arousals and REM fragmentation—may further contribute to this discrepancy, as REM sleep, already characterized by heightened cortical activation, appears particularly vulnerable to disruption in chronically hyperaroused individuals (Riemann et al., 2024). Notably, REM sleep disturbances have been linked to deficits in emotional processing, a function closely associated with this sleep stage. Impairments in REM regulation may therefore contribute to emotional dysregulation and the heightened psychological distress often observed in ID, reinforcing the vicious cycle that perpetuates hyperarousal across the 24-h cycle (Galbiati et al., 2020; Riemann et al., 2024). Such REM-related dysfunction may exacerbate mood disturbances and reinforce maladaptive cognitive-emotional responses to sleep loss, further entrenching insomnia's bidirectional relationship with affective disorders (Baglioni et al., 2010).

Beyond cortical hyperactivation, sleep-state instability also emerged as a key neurophysiological marker of ID, providing additional support for the hyperarousal framework. Cyclic alternating pattern (CAP) analysis demonstrated that individuals with insomnia exhibit increased CAP rate, indicating sleep fragmentation and heightened arousal fluctuations, thus providing an objective electrophysiological index of disrupted sleep continuity, not captured by macrostructural PSG measures (Parrino et al., 2012). Consistently, CAP rate has been shown to correlate strongly with subjective sleep quality (Terzano et al., 2003), reinforcing the hypothesis that frequent microarousals contribute to sleep fragmentation and reflect the impairment in sleep regulatory mechanisms (Parrino et al., 2004).

Based on the studies reviewed to this point, the neurophysiological evidence supporting the hyperarousal model of ID has significant implications for both diagnostic refinement and treatment development. EEG spectral power, microstructural sleep parameters, and CAP analysis, as well as event-related potentials (ERPs) (Feige et al., 2021, 2013), may provide a more detailed understanding of sleep state instability and altered cortical and cognitive excitability. Collectively, these findings support the integration of EEG-based biomarkers into future insomnia classification models, allowing for differentiation based on the degree of physiological hyperarousal, microstructural sleep fragmentation, and REM sleep instability. Moreover, the well-documented persistence of hyperarousal across wakefulness and sleep raises the possibility that interventions modulating arousal networks —such as pharmacological approaches directly targeting the wake-promoting orexin system or non-invasive brain stimulation focused on modulating cortical excitability (Mogavero et al., 2023; Riemann et al., 2015)— could serve as tailored approaches to counteract the hyperarousal state of patients with ID.

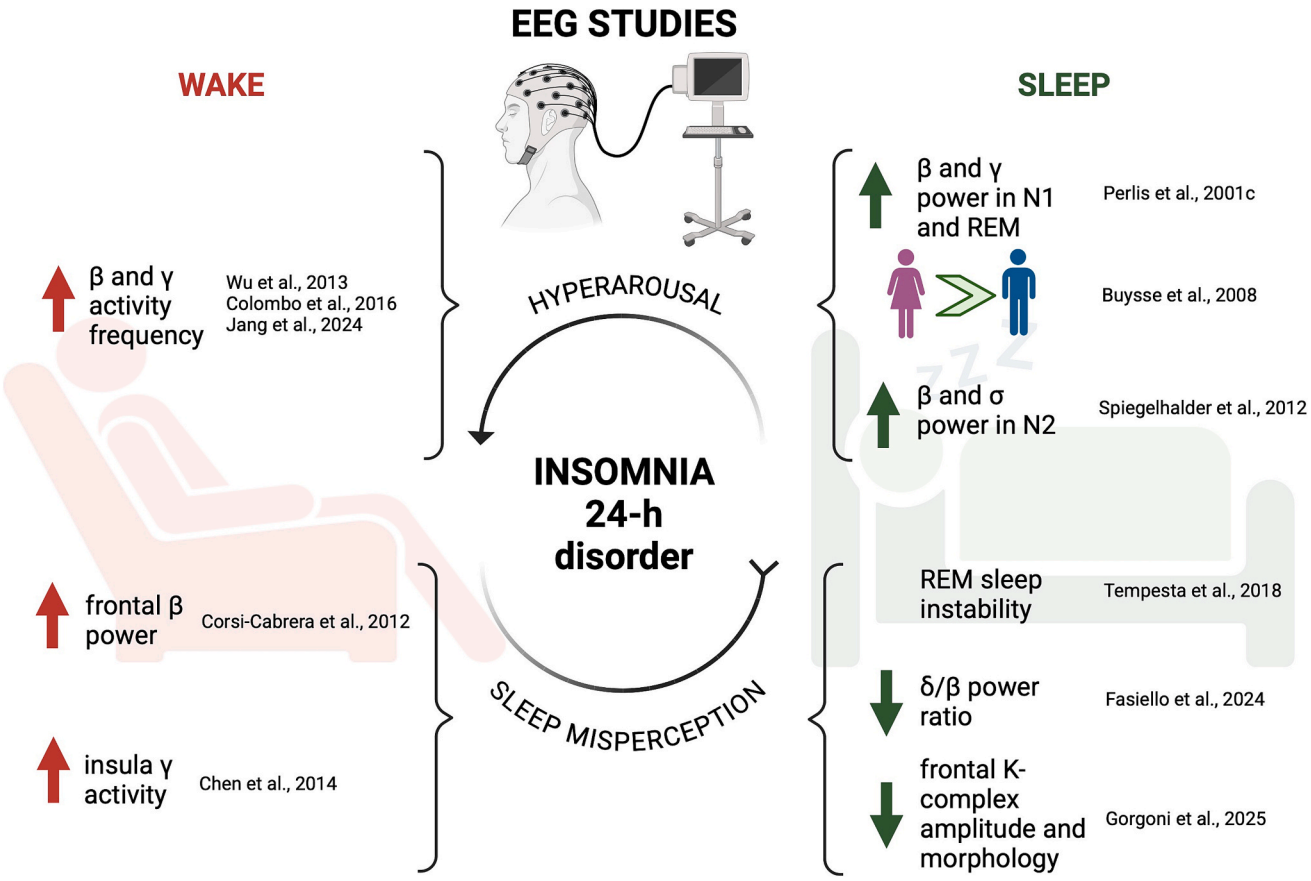

Fig. 1. Key findings from reviewed wake and sleep EEG studies in insomnia disorder. *Legend*: EEG: electroencephalography; REM: rapid eye movement.

3. EEG in wakefulness: Markers of cortical hyperarousal

In line with the 24-h conceptualization of ID within the hyperarousal model, wakefulness EEG activity may be just as relevant as nocturnal neurophysiological indices in characterizing the disorder and its underlying mechanisms. Several studies investigated resting-state neural activity during wakefulness, either independently or in conjunction with sleep EEG recordings, leveraging the idea that heightened physiological activation in the awake state and throughout sleep-wake transitions may be as impactful as sleep-related alterations in insomnia pathophysiology (Fig. 1).

Among these, Wu et al. (2013) examined EEG patterns during a five-minute eyes-closed recording at habitual sleep time (prior to PSG assessment) in insomnia patients (n = 50) and good sleepers (n = 32). While no significant group differences emerged in wakefulness or non-REM (NREM) sleep EEG power, a significant correlation between wake and NREM power was observed across several frequency bands. Despite the limited EEG setup (recording from C3 and C4 electrodes only), these results suggest that high-frequency wake EEG activity may persist into subsequent sleep periods, reinforcing the concept of cortical hyperarousal as a self-sustaining trait, independent of clinical status.

In another study, Corsi-Cabrera et al. (2012) employed a more extensive EEG montage with 19 scalp electrodes in a smaller sample of young participants (10 insomnia patients vs. 10 matched controls), examining EEG activity during the wake-sleep transition before overnight PSG. Insomnia patients exhibited increased frontal beta power and source-derived current density, alongside enhanced beta and gamma frontal-parietal-temporal activity coupling throughout wakefulness and stage 1 of NREM sleep. These findings align with the hypothesis of an impairment in the deactivation of frontally-led brain networks involved in executive control and self-awareness, which should naturally disengage during the transition from wake to sleep. The lack of frontal cortical activity during this wake-sleep transition may represent a candidate biomarker for sleep onset difficulties reported by patients with ID. Moreover, this persistent activation of frontal circuitry may also represent the electrophysiological basis of the subjective experience of wakefulness despite PSG-defined sleep, as expressed by the sleep misperception that commonly characterizes ID.

In agreement with this study, Chen et al. (2014) combined functional magnetic resonance imaging (fMRI) and resting state EEG, focusing specifically on the transition from wake to sleep, in female insomnia patients (n = 17) and healthy controls (n = 17). Their findings revealed increased engagement of the anterior insula within salience networks in insomnia patients, along with a positive correlation between insula activation and high-frequency EEG gamma activity during resting state. Given the insula's role in integrating bodily state information and interoceptive awareness, these alterations may underlie sleep-related misperception and heightened distress in individuals with insomnia symptoms.

Using high-density (256-electrode) EEG, Colombo et al. (2016) examined resting-state brain activity under eyes-open and eyes-closed conditions in insomnia patients (n = 51) and healthy controls (n = 43). Insomnia patients exhibited reduced upper-alpha power during eyes open and increased high-beta power during eyes closed, with source analysis indicating a global EEG pattern rather than a regionally localized effect. This evidence, obtained through high-resolution EEG, further confirms the persistence of generalized high-frequency hyperarousal in ID, and also points to a distinct pattern of reduced cortical inhibition in wakefulness, specifically in the eyes-open condition.

Another resting-state EEG study, employing a 19 EEG channels setup, explored the interaction between insomnia and depression, comparing insomnia patients with comorbid depression (n = 15), insomnia-only

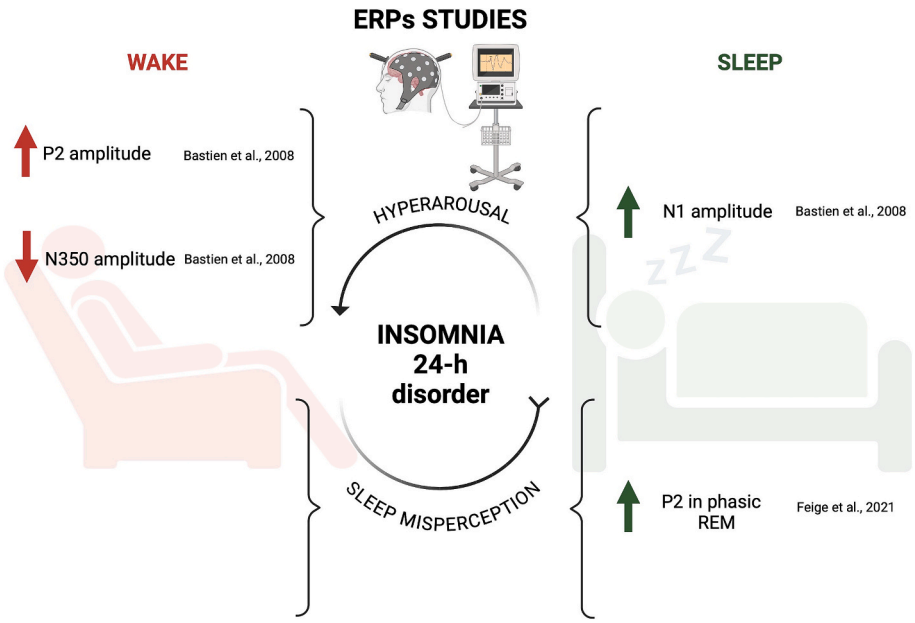

Fig. 2. Key findings from reviewed event related potentials EEG studies in insomnia disorder. *Legend:* EEG: electroencephalography; ERPs: event related potentials; REM; rapid eye movement.

patients (n = 15), and matched healthy controls (n = 15) (Kwan et al., 2018). While both insomnia groups exhibited the expected increase in high-frequency EEG activity compared to controls, no significant spectral power differences emerged between insomnia patients with and without depression. Although exploratory, this finding suggested that insomnia-related EEG patterns may take precedence over depression-associated neural signatures, providing a compelling perspective on the complex interplay between insomnia and depression and their comorbidity.

Finally, a recent study by Jang et al. (2024) examined wake qEEG parameters in a large sample of insomnia patients (n = 58) and healthy controls (n = 49), using a high-density 64-channel system during eyes-closed resting state. In addition to confirming the well-documented increase in beta and gamma EEG power in insomnia patients, their larger sample size enabled to demonstrate a positive association between beta and gamma spectral power density and self-reported insomnia symptom severity, even after controlling for anxiety.

In addition to reinforcing the core mechanisms postulated by the hyperarousal model, the findings reviewed here further support the conceptualization of insomnia as a disorder characterized by physiological dysregulation spanning the entire 24-h cycle. In addition, wake EEG studies highlight the potential utility of resting-state EEG as an accessible and practical biomarker for the assessment and characterization of insomnia. However, confirmatory studies with larger sample sizes, comprehensive clinical characterization —including both sleep and psychiatric comorbidities —and standardized EEG protocols are warranted to validate the most well-supported findings and to further investigate emerging evidence, such as altered eyes-open EEG patterns and network-level brain activity differences.

4. EEG during sleep: Macrostructure and microstructure

As previously mentioned, PSG studies investigating sleep macrostructural parameters have historically yielded inconsistent findings in insomnia research. To date, the *meta*-analysis by Baglioni et al. (2014) remains the most comprehensive synthesis of differences in PSG-derived macrostructural sleep variables between individuals with ID and healthy controls, reporting a significant reduction in total sleep time, longer sleep latency, and an increased number of nocturnal awakenings that may correlate with a prolonged wake time after sleep onset. Additionally, ID patients may exhibit reduced slow-wave sleep (SWS) and REM sleep compared to good sleepers. However, all of these differences were associated with small effect sizes, making them difficult to detect in routine clinical practice, and only weakly related to patient-reported subjective sleep complaints (Perlis et al., 2022). Consequently, PSG is not recommended as a standard diagnostic tool for insomnia assessment and monitoring (Frase et al., 2023; Riemann et al., 2023b).

Given the recent literature supporting the possibility of phenotyping ID according to total sleep time, the inclusion of PSG measures of sleep duration in the clinical definition of insomnia may be encouraged (Fernandez-Mendoza, 2017; Vgontzas et al., 2013; Vgontzas and Fernandez-Mendoza, 2013). Specifically, a clinical phenotype characterized by objectively short sleep duration (i.e., $\leq$ 5 h) has been identified, exhibiting stronger physiological hyperarousal, overactivation of the stress system, and heightened cardiometabolic and neurocognitive risks over time. In contrast, insomnia with objectively normal sleep duration appears to be strongly associated with cognitive-emotional hyperarousal and sleep misperception, but not with physiological overactivation or increased risk for medical complications.

Beyond this promising stratification hypothesis, the majority of sleep EEG-based studies in insomnia extend beyond macrostructural sleep staging, focusing instead on fine-grained sleep microstructural processes, including qEEG, ERPs, cyclic alternating pattern (CAP) analysis, and the morphology and occurrence of phasic sleep events (e.g., K-complexes, sleep spindles, and REM fragmentation) (Fig. 1 and Fig. 2).

4.1. qEEG, ERPs and spectral power alterations

The first neurophysiological evidence supporting the cortical hyperarousal model came from two seminal qEEG studies by Perlis and colleagues (Perlis et al., 2001a, 2001c). In a small cohort of individuals with primary insomnia (n = 9), patients with insomnia secondary to depression (n = 9), and good sleepers (n = 9), Perlis et al. (2001a) found a diffuse increase in high-frequency EEG activity (beta and gamma power) during sleep in insomnia patients, particularly in stage 1 of NREM sleep and REM sleep (Perlis et al., 2001c).

A larger study by Buysse et al. (2008) replicated these findings in a sample of 48 adults with insomnia and 25 healthy controls, observing an increase high-frequency EEG activity during NREM sleep in female

insomnia patients, but not in males. Interestingly, insomnia-related EEG alterations were not associated with subjective sleep complaints, raising questions about the direct perceptual relevance of spectral power differences.

Conversely, Spiegelhalder et al. (2012), using the same PSG setup (bilateral central EEG channels) in a different sample of 25 insomnia patients and 29 controls, found that beta and sigma power were increased only during stage 2 of NREM sleep, with no significant differences during other NREM sleep stages or REM sleep. This supports that EEG hyperarousal pattern may not be uniform across sleep stages and that specific microstructural features of stage 2 of NREM sleep may be particularly relevant in insomnia pathophysiology.

Studies employing expanded EEG montages provided further insights into the topography of hyperarousal in insomnia. Riedner et al. (2016) conducted all-night high-density (256-channel) EEG recordings in eight insomnia patients and matched controls, demonstrating that increased high-frequency activity during NREM sleep was distributed across the entire scalp rather than localized to specific brain regions. Additionally, source analysis revealed localized alpha activity differences during deep NREM sleep (stage 3 of NREM sleep), with insomnia patients exhibiting elevated alpha power in sensorimotor and sensory cortices. This persistence of cortical activation even during SWS suggests that impaired sensory deactivation may contribute to fragmented and nonrestorative sleep in insomnia.

Similarly, Perrier et al. (2015) used an eight-channel EEG system during PSG recordings to compare 14 insomnia patients and 11 good sleepers. Their findings showed elevated beta and reduced delta power during NREM sleep, with a spatially diffuse pattern across the scalp, except in the prefrontal cortex (Fp1 and Fp2 channels). Interestingly, during REM sleep, insomnia patients exhibited lower beta power in prefrontal regions, pointing to a specific pattern of altered EEG activity that varies across sleep stages. These findings support the need for spatially resolved EEG analyses to further delineate topographical biomarkers of insomnia.

Taken together, qEEG studies of spectral power in insomnia demonstrated the presence of persistent cortical hyperarousal, particularly during NREM sleep. However, further high-density EEG research on larger samples is needed to clarify the spatial characteristics of these alterations, their clinical significance, and the potential involvement of other frequency bands during both NREM and REM sleep. Notably, contrasting evidence emerged, such as the findings reported in the previously mentioned study by Wu et al. (2013), which failed to detect large-magnitude beta differences in a larger insomnia sample, emphasizing the need for standardized methodologies and replication efforts.

Further supporting the hyperarousal hypothesis, studies using auditory event-related potentials (ERPs) demonstrated increased cortical responsiveness to stimuli during sleep in individuals with insomnia. Bastien et al. (2008) examined arousal-related ERPs (N1, P2, and N350) using an oddball paradigm recorded across four consecutive nights of PSG (with seven EEG electrodes) in 15 individuals with chronic insomnia and 16 good sleepers. Their findings revealed that insomnia patients exhibited larger N1 amplitude on the fourth morning and evening, along with greater P2 amplitude at sleep onset, suggesting persistent cortical hyper-responsiveness across both nocturnal and diurnal states. Additionally, a smaller N350 amplitude at sleep onset in the insomnia group suggests difficulty in inhibiting cortical arousal, further reinforcing the notion of impaired disengagement from wakefulness to sleep-related neural inhibition.

Building on these findings, Feige et al. (2021) conducted a study specifically targeting sleep misperception, hypothesizing that individuals with insomnia may be oversensitive to external and internal stimuli while asleep. To test this aspect, they measured P1, N1, and P2 auditory ERPs in response to low-intensity synthesized tones presented continuously during two nights of PSG recordings with 21 EEG channels in 50 insomnia patients and 50 healthy controls. The main finding was an increased P2 amplitude during phasic REM sleep (i.e., REM sleep with bursts of eye movements linked to ponto-geniculo-occipital waves), which was inversely correlated with sleep misperception—meaning that higher P2 amplitude was associated with greater subjective wakefulness despite objective sleep. This result supports that REM P2 amplitude may serve as a biomarker of sleep misperception, reflecting heightened sensory processing during sleep, which could lead to an increased likelihood of detecting auditory stimuli, ultimately contributing to the subjective experience of being awake—particularly during phasic REM sleep.

A recent study by Fasiello et al. (2024) further explored the scalability of EEG biomarkers for subjective insomnia symptoms. Analyzing PSG data with 19 EEG channels from 21 insomnia patients and 20 matched healthy controls, they reported a topographically widespread reduction in the delta/beta power ratio in insomnia patients during both sleep onset and the entire night. Notably, this delta/beta ratio was significantly and negatively correlated with sleep misperception, with greater reductions linked to more pronounced subjective wakefulness across sleep onset, NREM, and REM sleep. These findings provide a synthetic EEG-based index of persistent cortical arousal, reinforcing the idea that insomnia is characterized by heightened wake-like neural activity that persists regardless of sleep stage.

4.2. K-complexes and sleep spindles characteristics in insomnia

In addition to cortical hyperarousal detected in insomnia patients, the role of sleep-protective mechanisms, such as K-complexes and sleep spindles, has been investigated, although findings remain mostly inconclusive. Bastien et al. examined K-complex (2009a) and spindle (2009b) characteristics in small samples of insomnia patients (n = 14–16) and healthy controls (n = 14–16), and they found no significant differences in either K-complex density and amplitude or spindle number and density during stage 2 of NREM sleep.

Conversely, Hairston et al. (2010) identified a lack of stimulus-induced increases in K-complexes among insomnia patients (n = 18) compared to good sleepers (n = 20). This suggests a potential impairment in the mechanisms responsible for filtering out sensory information during sleep, which may contribute to increased nocturnal reactivity and fragmented sleep architecture.

A more recent investigation by Gorgoni et al. (2025) took a high-resolution approach to K-complex analysis. In 19 insomnia patients and 18 healthy controls undergoing overnight PSG, the authors assessed K-complex density, amplitude, and area under the curve in midline frontal, central, and parietal derivations, alongside sleep misperception (defined as the discrepancy between objective and subjective total sleep time). Their findings revealed that insomnia patients exhibited reduced K-complex amplitude and morphology in frontal derivations, which was associated with greater total sleep time underestimation. Additionally, K-complex morphology correlated negatively with stage 3 of NREM sleep latency, sleep fragmentation, and arousal indices while being positively related to stage 3 of NREM sleep percentage and sleep efficiency—suggesting that deficits in K-complex production may reflect impaired sleep protection mechanisms, which may likely spill over into subjective sleep perception, heightening insomnia complaints and hyperarousal.

4.3. CAP rate analysis and sleep instability

As a further research avenue, CAP has been introduced as a key microstructural marker of sleep-state instability, representing phasic fluctuations between transient activation (A phases) and stable sleep (B phases) during NREM sleep (Parrino et al., 2012). Increased CAP rate has been consistently reported in insomnia, reflecting greater sleep fragmentation and a higher frequency of microarousals, which are not captured by macrostructural PSG metrics (Parrino et al., 2012).

A study by Parrino et al. (2009) focused specifically on insomnia, analyzing 10-channel PSG recordings in 20 patients with paradoxical

insomnia (i.e., normal sleep structure with persistent misperception of poor sleep) and 20 good sleepers. Both the arousal index and CAP rate were significantly elevated in the insomnia group, with a selective increase in CAP during NREM Stage 1 and 2, and a predominance of CAP A2 subtype. These findings supported the view of insomnia as a disorder of disrupted sleep continuity, rather than of reduced sleep duration, due to the recognition of frequent CAP-related arousals, which may hinder the attainment of sustained, restorative sleep.

Within this framework, CAP scoring may offer a neurophysiological bridge between subjective and objective sleep assessments, serving as a granular marker of sleep misperception in insomnia. This perspective is further reinforced by additional evidence discussed in the next section, regarding CAP modulation in response to hypnotic treatment (Terzano et al., 2003).

Nonetheless, despite these promising findings, research on CAP in insomnia has slowed in the past decade, and further studies with larger samples, standardized scoring protocols, and comprehensive clinical assessments are needed to establish its role as a clinically relevant biomarker for diagnosis and treatment monitoring.

4.4. REM sleep instability and its role in insomnia

Recent research increasingly highlighted REM sleep as a crucial target in insomnia pathophysiology, building on both empirical evidence and theoretical advancements in the understanding of REM sleep dynamics and functions (Hong et al., 2023; Simor et al., 2020). Alongside the previously discussed ERP findings by Feige et al. (2021), which demonstrated heightened sensory processing during REM sleep, studies have continued to emphasize the link between REM sleep instability and sleep misperception, particularly in relation to its established role in emotional processing and stress regulation (Tempesta et al., 2018).

REM sleep instability has been operationally defined as an increased number of arousals occurring specifically during REM sleep, leading to selective sleep-stage fragmentation (Feige et al., 2023; Riemann et al., 2024). Given that REM sleep exhibits an EEG pattern closely resembling wakefulness, it appears to be the sleep stage most susceptible to misperception as wakefulness. In this context, a landmark study examined subjective sleep ratings and PSG recordings (14-channel) in a large sample of 100 medication-free patients with primary insomnia and 100 matched controls (Feige et al., 2008). While the insomnia group exhibited a significantly elevated arousal index, this increase was primarily attributable to heightened arousal frequency within REM sleep. Furthermore, while insomnia patients reported more subjective wake time throughout the night, subjective wakefulness was predicted not only by PSG-measured wake time but also by REM sleep duration, suggesting that perceptions of disturbed, fragmented sleep may be closely linked to REM sleep processes—which were indeed disrupted in insomnia.

Building on these findings, subsequent experimental studies manipulated sleep stage-specific awakenings to further explore the relationship between REM sleep alteration and sleep perception (Benz et al., 2020; Feige et al., 2018). Feige et al. (2018) conducted four-night PSG (24-channel) recordings in 27 insomnia patients and 27 controls, with three awakenings from either stage 2 of NREM sleep or REM sleep occurring on the last two nights to assess both objective awakening thresholds and subjective sleep perception. While awakening thresholds did not differ between groups, insomnia patients were more likely to report feeling awake when awakened from REM sleep, but not from stage 2 of NREM sleep, reinforcing the notion that REM sleep in insomnia may represent a hybrid sleep-wake state, characterized by persistent hyperarousal.

A follow-up study by Benz, Riemann, and Feige (2020) extracted a subset of participants from the previous study, specifically those who reported mentation during REM sleep, to examine associations between mentation characteristics and PSG-derived physiological parameters in 22 insomnia patients and 23 controls. Although no significant group differences emerged, the authors found that increased perceived wakefulness correlated with lower delta, theta, and alpha power in the minute preceding REM sleep awakenings. These findings align with prior research suggesting that REM sleep plays a crucial role in silencing the locus coeruleus and promoting the reorganization of limbic circuits. Disrupted REM sleep consolidation, leading to REM instability, may impair sleep-dependent plasticity within the limbic system (Grafe et al., 2024; Wassing et al., 2019).

The overactivation of the locus coeruleus in insomnia, marked by higher noradrenergic tone, may contribute to distress and impaired emotional memory integration, further exacerbating sleep-dependent emotional dysregulation (Riemann et al., 2023a; Van Someren, 2021). Taken together, evidence on REM instability presents a suggestive pathophysiological link between insomnia and its associated 24-hour emotional disturbances (Baglioni et al., 2010; Riemann et al., 2024), and the results reviewed so far underscore the importance of investigating tonic, phasic, and microstructural REM features as potential biomarkers of the sleep-stress relationship, which may provide useful hints about the mechanisms underlying insomnia and its broader psychological consequences.

5. Sleep EEG as a marker of insomnia treatment

Based on the evidence discussed here, key questions arise regarding the clinical utility of EEG markers in the diagnosis and treatment of insomnia, particularly in their effectiveness for capturing treatment-related changes and guiding personalized interventions. Traditionally, clinical trials of insomnia treatments relied on objective PSG measures of macrostructural sleep parameters, despite their limited sensitivity in detecting core symptoms of ID and their weak association with key pathophysiological mechanisms, such as cognitive-emotional and cortical hyperarousal (Frase et al., 2023; Pollmächer, 2023). This limitation is particularly evident in individuals with pronounced sleep misperception and subjective distress, where standard PSG outcomes may fail to reflect clinical symptomatology accurately.

With the notable exception of insomnia cases characterized by objective short sleep duration (Fernandez-Mendoza, 2017), an increase in total sleep time and sleep efficiency alone may not serve as a reliable marker of treatment effectiveness (nor as an adequate clinical trial outcome). Instead, certain EEG microstructural features warrant deeper investigation to determine their clinical relevance in monitoring insomnia treatment response.

Pharmaco-EEG studies have long explored the effects of hypnotic and psychotropic medications on sleep EEG activity, with extensive evidence showing that benzodiazepines (long-, intermediate-, and short-acting) and non-benzodiazepine hypnotics (Z-drugs) can induce reductions in delta power along with increases in sigma and beta power in both healthy adults and insomnia patients (Borbély et al., 1985; Feinberg et al., 2000; Hartmann et al., 2023; Lundahl et al., 2012; Tan et al., 2003, 1998). Notably, one study tackled a critical clinical issue by investigating the long-term effects of benzodiazepine use on sleep EEG in older adults with chronic insomnia. Bastien et al. (2003) recruited a balanced sample of 15 elderly benzodiazepine users with insomnia, 15 drug-free individuals with insomnia, and 16 matched good sleepers, using PSG recordings with four EEG channels. While no significant spectral differences emerged between the drug-free insomnia group and healthy controls, benzodiazepine users exhibited reduced delta and theta power throughout the night, along with increased beta power in the latter part of the sleep period (second and third sleep cycles). This evidence opens the clinical debate and points to criticalities in the prolonged prescription of benzodiazepines as hypnotics for insomnia, especially in the elderly, where these drugs appear to enhance a nocturnal EEG pattern that expresses features similar to the cortical hyperarousal observed in ID.

Again with respect to EEG modulation in response to benzodiazepines and Z-drugs, a seminal study by Terzano et al. (2003) provided a

relevant contribution through CAP scoring. The authors analyzed full-night PSG recordings (10 EEG electrodes) from 47 patients diagnosed with primary insomnia (DSM-IV-TR criteria; American Psychiatric Association, 2000) and 25 matched healthy controls. Following an adaptation night, patients underwent two randomized, double-blind PSG recordings—one under placebo condition and one following the administration of a commonly prescribed hypnotic (zolpidem, triazolam, zopiclone, or brotizolam). Under placebo, insomnia patients exhibited significantly higher CAP rates, particularly in A1 and A2 subtypes, as well as increased EEG arousals, greater wake time after sleep onset, elevated stage 1 of NREM sleep, reduced total sleep time, and reduced SWS. Moreover, pharmacological treatment not only improved these macrostructural parameters but also significantly reduced CAP rate, especially for A1 and A2 subtypes, with only marginal effects on EEG arousals and A3 subtypes, which were not elevated in the insomnia group. Most notably, CAP rate was the strongest objective correlate of subjective sleep quality ($r = -0.5$), highlighting its potential as a treatment-responsive neurophysiological marker that bridges sleep instability and subjective sleep perception.

Among newer pharmacological treatments, dual orexin receptor antagonists (DORAs) recently emerged as a promising option for ID, and some studies investigated their effects on EEG microstructure. In a post-hoc analysis of two phase 3 randomized clinical trials, Di Marco et al. (2024) examined the effects of three-month administration of daridorexant in a large group of patients with chronic ID (total $n = 1,466$; $n = 586$ placebo, $n = 584$ receiving 25 mg, $n = 296$ receiving 50 mg). Notably, daridorexant increased the probability of transitioning from wakefulness to sleep stages, decreased relative alpha power and increased relative delta power during wakefulness, reflecting a shift toward a reduced hyperarousal state. Furthermore, the drug lowered wake EEG similarity to sleep EEG, suggesting a progressive neurophysiological disengagement from wake-like activity.

A systematic review, aggregating studies on the effects of DORAs on sleep in both clinical and non-clinical samples (Clark et al., 2020), further supported the hypothesis that the increase in total sleep time due to DORAs may be driven by REM sleep enhancement. This finding is particularly intriguing, as it suggests that DORAs may exert a REM-stabilizing effect, aligning with the putative role of orexin system dysregulation in insomnia pathophysiology (Mogavero et al., 2023; Palagini et al., 2023).

Compelling EEG evidence also comes from studies investigating the neurophysiological effects of cognitive-behavioral therapy for insomnia (CBT-I)—the gold-standard, non-pharmacological treatment for ID (Edinger et al., 2021; Edinger and Carney, 2015). Sleep restriction therapy (a core CBT-I component) is considered the most effective behavioral intervention, as it progressively increases sleep efficiency by restricting time in bed, thereby amplifying homeostatic sleep pressure and reducing hyperarousal (Angelillo et al., 2025; Furukawa et al., 2024). However, the precise neurophysiological mechanisms underlying its effectiveness remain scantily investigated (Maurer et al., 2018). Nevertheless, several investigations have sought to examine EEG changes associated with CBT-I response. In a landmark single-arm study, Cervena et al. (2004) conducted PSG recordings (two-channel EEG) in nine drug-free patients with psychophysiological insomnia, reporting increased stage 2 of NREM sleep, REM sleep, and SWS following CBT-I. QEEG analysis revealed augmented slow-wave activity (SWA), a faster decline in SWA across the night, and reduced beta and sigma power, suggesting that successful CBT-I treatment is associated with enhanced sleep depth and more efficient homeostatic sleep regulation.

Further supporting these findings, Krystal and Edinger (2010) conducted a two-arm study comparing CBT-I ($n = 16$) with a placebo intervention (a credible desensitization protocol). Their results showed that CBT-I led to a steeper decline in delta power throughout the night compared to placebo, and that increased daytime wakefulness (a known effect of sleep restriction therapy) was associated with both subjective sleep improvement and a steeper delta power slope. Moreover, a lower pre-treatment EEG delta peak during the first NREM cycle and a slower decline in delta power were predictive of better CBT-I response, highlighting the potential for electrophysiological markers to serve as indicators of treatment fit for behavioral interventions.

Another study exploring the effects of CBT-I on EEG spectral power was conducted on a larger sample of 93 older adults with insomnia, utilizing laboratory PSG with four-channel EEG recordings (Hogan et al., 2020). The authors examined broadband EEG spectral power, ranging from 0.5–1 Hz slow oscillations to 16–32 Hz beta activity, and found that CBT-I led to a significant reduction in both sigma and beta power. Prior to treatment, these high-frequency EEG components were elevated in the insomnia group compared to a matched control group of 71 good sleepers, consistent with the core assumptions of the hyperarousal model. The post-treatment reduction in sigma and beta power suggested that CBT-I may act directly on cortical hyperexcitability, facilitating a normalization of sleep-related neural activity.

Again with the goal of objectifying EEG markers of CBT-I responsiveness, Dang-Vu et al. (2017) investigated whether pre-treatment sleep spindle density could predict treatment outcomes. Their study was based on the assumption that sleep spindles reflect a sleep-protective mechanism, and that disruptions in spindle activity may indicate vulnerability to insomnia and perceived sleep discontinuity. PSG recordings obtained prior to treatment from 24 chronic insomnia patients revealed that lower spindle density during stage 2 and 3 of NREM sleep predicted poorer improvements in sleep diary measures and lower self-reported sleep quality at 12-month follow-up. These findings suggest that an insomnia phenotype characterized by disrupted spindle activity may represent a distinct clinical variant, potentially less responsive to CBT-I due to an inherent neurophysiological vulnerability to fragmented sleep.

Similarly, Sforza et al. (2024) examined the homeostatic function of K-complexes and their relationship with CBT-I effectiveness in a multicenter sample of 98 insomnia patients undergoing four to six weeks of in-person CBT-I. Using pre- and post-treatment PSG with six EEG channels, they detected K-complexes during stage 2 of NREM sleep and computed the K-complex slope, an index reflecting the rate of decline in K-complex density over the night. A steeper decline (more negative slope values) reflects stronger sleep pressure buildup and dissipation, a fundamental aspect of homeostatic sleep regulation. Notably, they found that the K-complexes slope predicted treatment response and was also indicative of post-treatment improvement in sleep pressure, as evidenced by the observed decrease in slope magnitude toward negative values.

Finally, a recent mechanistic trial by Maurer et al. (2022) specifically examined the impact of the sleep restriction component of CBT-I on sleep pressure and arousal regulation. In this study, 56 participants diagnosed with ID were randomized to undergo four weeks of sleep restriction therapy or a comparable control intervention (time-in-bed regularization). Among various subjective and objective measures, the authors assessed NREM delta power and beta power as PSG-derived EEG markers of sleep pressure and arousal, respectively, using a six-electrode EEG montage. The results demonstrated that participants receiving sleep restriction therapy exhibited greater self-reported daytime sleepiness and reduced psychomotor vigilance in the early treatment phase compared to those in the control group, consistent with the expected short-term effects of sleep restriction on homeostatic sleep pressure. Notably, delta power increased at both week 1 (early treatment) and week 4 (end of treatment), while beta power decreased by week 4, suggesting that the initial enhancement of sleep pressure was progressively transferred to a reduction in cortical arousal as treatment progressed.

Taken together, the findings reviewed in this section highlight the potential of EEG as a valuable tool in clinical insomnia research, demonstrating how qEEG and sleep microstructural analysis can capture neurophysiological changes associated with effective treatment. Furthermore, the identification of EEG markers predictive of treatment

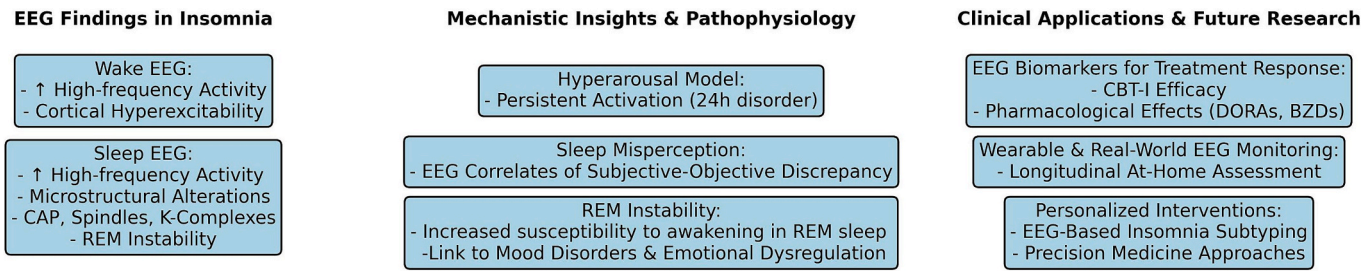

Fig. 3. EEG-based framework for insomnia: findings, mechanisms, and applications. *Legend:* BZDs: benzodiazepines; CBT-I; cognitive behavioral therapy for insomnia; CAP: cyclic alternating pattern; DORAs: dual orexin receptor antagonists; EEG: electroencephalography; REM: rapid eye movement.

response opens promising avenues for refining insomnia phenotyping and guiding personalized therapeutic approaches. Moving forward, greater standardization of EEG-based clinical research protocols and an increased number of mechanistic trials are highly warranted to strengthen the evidence base supporting EEG applications in insomnia treatment research.

6. Concluding remarks and future directions

As demonstrated throughout this review and schematically illustrated in Fig. 3, EEG research significantly contributed to the conceptualization of insomnia as a disorder of the 24-hour cycle, enhancing the understanding of perceived sleep instability and daytime impairment in terms of persistent hyperarousal with identifiable neurophysiological markers. Both wake and sleep EEG studies revealed heightened cortical excitability, increased high-frequency activity, and altered microstructural sleep dynamics (e.g., REM sleep instability) in insomnia, complementing the non-exhaustive evidence obtained from traditional PSG-based measures of sleep architecture.

More specifically, EEG spectral and microstructural markers largely contributed to the characterization of cortical activity, sleep state transitions, and putative mechanisms underlying sleep misperception, suggesting that subjective reports of disrupted sleep may align more closely with fine-grained EEG features rather than overall sleep duration metrics. Beyond these theoretical advancements, EEG research also showed clinical potential for insomnia subtyping and treatment response tracking, with growing evidence suggesting that EEG biomarkers distinguish patients who may benefit more from behavioral interventions (e.g., CBT-I) than pharmacological treatments. Moreover, the quantitative and topographical characterization of EEG patterns in insomnia may serve as a crucial foundation for identifying target neural networks for neuromodulation and non-invasive brain stimulation interventions, a growing area of clinical research that is beyond the scope of this review (Gong et al., 2020; Herrero Babiloni et al., 2023).

Looking ahead, several key research priorities should be addressed to expand the clinical significance and generalizability of EEG-based insomnia research, emphasizing the need for scalable and feasible solutions. Evidence from resting-state EEG studies during wakefulness indicates that even relatively short laboratory recordings with standardized protocols may effectively characterize insomnia-specific electrophysiological patterns. The application of emerging EEG analysis techniques, such as the classification of EEG-based arousal states (Hegerl et al., 2016; Jawinski et al., 2017) and the assessment of aperiodic components of EEG spectra (Donoghue et al., 2020) may further enhance wake EEG recordings by providing evidence on the excitation/inhibition balance, which is likely to represent a key aspect of neurophysiological dysregulation in insomnia.

In addition, high-density short recordings could be integrated with wearable EEG sleep bands and portable EEG monitoring (Levendowski et al., 2017), allowing for longitudinal, real-world assessments of insomnia-related neurophysiological patterns. Such advances would enable continuous monitoring of arousal fluctuations and treatment response patterns over extended periods of time, improving the ecological validity of insomnia research.

From a translational perspective, EEG-based profiling of insomnia phenotypes may provide a useful tool for stratifying participants in future precision-tailored clinical trials designed to mechanistically investigate the action and efficacy of both novel pharmacotherapies and CBT-I in treatment-responsive and treatment-resistant patients (Angelillo et al., 2025; Frase et al., 2023). These efforts could support the standardization of research protocols and the establishment of consensus EEG markers to facilitate their integration into routine insomnia assessment as clinically meaningful diagnostic and treatment monitoring instruments (Paul et al., 2022).

In conclusion, the first century of EEG research demonstrated that clinical neurophysiology can significantly enhance the characterization of the pathophysiology of insomnia, providing key findings on the brain's regulatory mechanisms for sleep and vigilance and attempting to demonstrate the neurophysiological basis of hyperarousal and sleep misperception often presented by patients with ID. Looking forward, it is our hope that the next century will advance our understanding of the dynamics of the "unsleepy" brain and ultimately translate neurophysiological findings into personalized, precision-guided sleep medicine to help clinicians better identify insomnia phenotypes for pharmacological and non-pharmacological treatments.

CRediT authorship contribution statement

Matteo Carpi: Conceptualization, Visualization, Writing – original draft, Writing – review & editing. **Claudio Liguori:** Conceptualization, Supervision, Visualization, Writing – original draft, Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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