



# 台灣睡眠醫學學會 114 年度會員大會暨第 23 屆學術研討會 23<sup>rd</sup> Annual Meeting of Taiwan Society of Sleep Medicine (TSSM)

10/25

## Symposium 1 科技

### 郭博昭教授

**Topic :** Design and Application of an AIoT-Driven Remote Electroencephalogram (EEG) Synchronous Monitoring System

**Abstract :** 心電圖 (Electrocardiography, ECG) 與腦電圖 (Electroencephalography, EEG) 是評估心臟功能與大腦神經活動的非侵入式生理量測工具。但由於傳統儀器體積龐大、價格昂貴且大多設置在醫療院所受限於人力資源，對於臨床上普及造成一定的困難。隨著科技進步，物聯網 (Internet of Things, IoT) 飛速發展，透過無線傳輸與網路儲存架構，可支援生理訊號的連續監測與雲端分析，不僅能降低照護人員的負擔，也有助於提升效率、改善醫療品質，但如何整合人工智慧 (Artificial Intelligence, AI) 和 IoT 技術，建置同步監控、訊號分析與雲端資料處理能力的系統，成為推動智慧醫療應用的關鍵挑戰與發展趨勢。

本 IoT 系統搭配感測器、演算法、軟硬體、物聯網以及臨床介入服務實現資訊和實體的整合。本團隊開發的微型腦波心電儀具備低功耗與長時間監測能力，訊號經由微控制器進行前處理與數位轉換後，透過藍牙模組傳輸至傳輸盒，再經由 Wi-Fi 或 4G 行動網路上傳至雲端伺服器進行儲存與分析，演算法上透過不同生理訊號頻譜分析技術與功率指標計算，提供量化數據。後端架構支援結構化資料庫管理與遠距監控介面，視覺呈現各項生理指標變化，協助醫護人員快速掌握患者狀態進行診斷與決策。

本系統也於精神專科醫院做應用，對居家或住院患者進行長時間的連續監測，探討自律神經、睡眠品質、活動量分析與心腦互動之觀察。系統所建立的生理訊號資料庫可為後續 AI 模型訓練、異常偵測演算法開發與個人化健康預測分析提供重要數據基礎。

未來可進一步擴展至居家照護、亞健康族群監測或是遠距病情追蹤等場景，搭配傳輸盒與雲端平台整合，建立即時回饋、個人化建議與預警的全方位健康管理系統，實現 AIoT 技術在智慧醫療領域的產業化應用與永續發展。

### 陳正文醫師

**Topic :** Recent Advances in Large-Scale Sleep Database Studies and Basic Research on Ultrasound Neuromodulation

**Abstract :** This lecture explores innovations in obstructive sleep apnea (OSA) management, from diagnosis to non-invasive therapeutic strategies.

The first segment will highlight significant progress in large-scale sleep database studies utilizing deep neural networks. A key advantage is the use of unsegmented peripheral oxygen saturation (SpO<sub>2</sub>) and electrocardiography (ECG) signals from extensive public datasets for OSA severity classification and apnea-hypopnea index (AHI) prediction. This approach eliminates the labor-intensive requirement for signal segmentation and annotation, greatly enhancing classification efficiency. SpO<sub>2</sub>-based models have achieved high accuracies, exceeding 91% for two-level classification and reaching up to 81.13% for four-level AHI prediction. ECG-based models have shown up to 59.49% accuracy for four-level classification and a correlation coefficient of 0.83 for AHI prediction.

The second part will focus on basic research in ultrasound neuromodulation, presenting low-intensity pulsed ultrasound (LIPUS) as a promising non-invasive therapeutic method. In vitro studies demonstrate LIPUS's neuroprotective effects by mitigating endoplasmic reticulum (ER) and oxidative stress, preserving



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mitochondrial function, and inhibiting apoptosis. This is mediated by LIPUS-induced calcium influx through mechanosensitive channels, activating critical transcription factors (NFAT, NF- $\kappa$ B) and the AKT pathway, promoting cell survival. In vivo animal studies show LIPUS application to the hypoglossal nerve (HN) significantly enhances genioglossus muscle (GM) activity and improves oxygen saturation. Real-time US imaging confirmed direct tongue movement, and comprehensive safety assessments found no thermal damage or adverse effects on nerve or tissue. These advancements hold potential for more accessible, efficient, and safer OSA diagnostics and treatments.

### 劉文德醫師

**Topic :** Sleep technology in COMISA care: evidence based assessment methods and therapeutic enhancements

**Abstract :** Comorbid insomnia and sleep apnea (COMISA) represents one of the most challenging clinical subtypes of sleep apnea. Because patients suffer from both chronic insomnia and obstructive sleep apnea (OSA), their sleep quality is profoundly impaired. These individuals typically present with **sympathetic overactivation** and **difficulty maintaining sleep**. From a respiratory control perspective, they often demonstrate **increased respiratory drive** and heightened ventilation, which further aggravates upper airway **collapsibility**. Over time, repetitive obstructions and arousals produce **vibration trauma** and **neurogenic inflammation** of the upper airway mucosa, perpetuating a vicious cycle of sleep fragmentation and airway dysfunction.

Assessment in this group is also problematic. Standard in-lab polysomnography (PSG) may not fully capture real-world sleep patterns due to patients' **hyperarousal**. As a result, alternative, less intrusive tools such as **millimeter-wave radar** and **fiber-optic mattress sensors** may provide more ecologically valid measures of **heart rate variability (HRV)** and **respiratory sinus arrhythmia (RSA) coupling**, thereby yielding deeper insight into true sleep quality.

Traditional interventions—**CPAP** or **oral appliances**—often show poor tolerance in COMISA patients, as the insomnia component undermines adherence. This context highlights the potential of novel approaches such as **frequency-specific microcurrent (FSM) stimulation**. By applying targeted microcurrents at specific frequencies, FSM can attenuate sympathetic activity, improve sleep continuity, and stabilize upper airway function. A recent randomized double-blind trial demonstrated that FSM not only enhanced **objective sleep quality** (improved efficiency, reduced WASO, increased N3 sleep) but also reduced indices of **airway instability**. Together, these findings suggest that FSM offers a promising new therapeutic direction for COMISA patients, addressing both hyperarousal and respiratory vulnerability simultaneously.

### 李學禹教授

**Topic :** Revolutionizing Sleep Apnea Diagnosis and Management: Wearable Technology

**Abstract :**

#### **【背景】**

睡眠呼吸中止症(OSA)的診斷與療效追蹤都需要睡眠檢查。然而，睡眠檢查排程曠日持久，檢查時管線甚多影響睡眠，保險給付原則一年內只能在治療前與治療後各作一次，加以檢查費時的不適影響



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病患追蹤檢查的意願。因此居家睡眠檢查如雨後春筍般蓬勃發展，逐漸成為診斷 OSA 的篩檢方式。在眾多穿戴裝置的居家睡眠檢查中，心肺耦合睡眠檢測(CPC)，運算心率與呼吸訊號兩者的耦合與差異，從而判斷出睡眠呼吸異常事件(REI)與睡眠結構，依此診斷 OSA 及反應睡眠品質。CPC 只有餅乾式的胸貼，不需鼻管測氣流也沒有主機及胸腹帶，對睡眠干擾很小，是最舒適的居家睡眠檢查。

### 【目的】

本研究利用 CPC 的高舒適性與病患順從度，對接受氣道手術治療 OSA 的病患，作術後連續密集追蹤檢查。研究目的在於了解氣道手術後初期的安全性(氣道組織水腫導致呼吸惡化血氧下降的時間)與長期的有效性(了解最好療效的月份與復發的時間)。

### 【方法】

本研究針對 10 位接受咽內多部位手術治療 OSA 的病患，分別在術前一週，術後兩週每夜連續檢測，爾後在第 3、4 週以及往後的 11 個月每月一次作持續檢測。本研究的監測指標為睡眠呼吸異常指數(REI)(類似 AHI)與睡眠呼吸中止症特有的缺氧負荷(SASHB)(OSA 病患睡眠期間發生缺氧的嚴重程度與持續時間的總和)。

### 【結果】

手術後的 REI 與 SASHB 兩者有一致性的變化，都在術後第 2~4 天出現呼吸異常與缺氧惡化，在第 5~6 天兩指數緩解後，第 7~9 天再次出現第二波的呼吸異常與缺氧惡化，隨後呼吸與血氧緩解，到第 14 天兩指數呈安全穩定狀態，自此一路減輕到第 2 個月。

### 【結論】

本研究顯示氣道手術治療 OSA 在安全性上，除了證實以往認知術後 2~4 天因氣道傷口水腫，呼吸與血氧可能惡化的現象外，更發現第 7~9 天仍有呼吸異常與缺氧惡化，需密切觀察並輔以姿勢療法，改善鼻塞、減少張口呼吸及服用消炎藥物等來降低氣道阻塞及提高血氧。在療效時間表上，第 2 個月因傷口結疤組織成熟，氣道空間穩定擴大，呼吸異常事件與缺氧狀態都有最大的改善，至於復發時間，則有待更長期的追蹤。

## Symposium 2 技師

### 葉威志醫師

**Topic：**Epilepsy and Sleep

**Abstract：**The relationship between sleep and epilepsy is intricate. Individuals with epilepsy frequently encounter poor sleep quality and disrupted sleep patterns. Research has demonstrated that those with epilepsy experience reduced REM sleep and alterations in the structure of REM sleep. Furthermore, certain antiseizure medications can also impact sleep architecture.

### 蕭慈慧醫師

**Topic：**正壓呼吸器治療

**Abstract：**呼吸道陽壓 (positive airway pressure, PAP) 治療，是在病患睡眠時利用經口或鼻面罩連接呼吸器，允許呼吸器產生的加壓空氣使呼吸道保持通暢，並使患者正常呼吸和入睡，用以治療睡眠



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呼吸障礙。

呼吸道陽壓滴定（PAP titration）檢查，為睡眠技師根據呼吸事件對呼吸道陽壓進行壓力調整，以尋找最佳治療的壓力。

### 賴珮蓁技師

**Topic :** From Struggler to Super User : Empowering Patients in CPAP Therapy

**Abstract :** 至今，多數個案一聽到 CPAP 治療的反應，仍覺得是個麻煩，學習使用的過程更是容易因為干擾原本的睡眠習慣而中斷，此次將透過實例分享，針對 CPAP 使用過程中重點問題進行剖析與解決，提升病人使用舒適度與治療依從性，進一步改善治療成效與生活品質。

### Symposium 3 心理師

### 蕭帆琦助理教授

**Topic :** Basic Mechanisms of Sleep and Circadian Rhythms

**Abstract :** Sleep is regulated by two processes: the circadian rhythm (process C) and the homeostatic system (process S). Circadian rhythm, often described as the body's internal clock, is in the brain and is strongly influenced by light and darkness. It helps determine the timing of when we feel alert during the day and when we become sleepy at night. The sleep drive, regulated by the homeostatic system, increases the longer we remain awake and decreases once we fall asleep. Together, these two systems control the timing, quality, and restorative function of sleep. When circadian rhythm is disrupted, such as by shift work, irregular schedules, or jet lag, sleep often becomes shorter and less refreshing. Over time, these disruptions can negatively affect mental health, physical health, and daily functioning. Understanding these basic principles underscores the importance of maintaining a stable sleep routine and promoting circadian alignment for overall well-being.

### 詹雅雯助理教授

**Topic :** Clinical Intervention Strategies for Circadian Rhythm Disorders

**Abstract :** Disruptions in circadian rhythm can directly impair both nocturnal sleep and daytime functioning. In clinical practice, interviews, sleep diaries, and standardized assessment tools can be used to evaluate an individual's relative sleep phase for diagnostic and treatment purposes. Intervention strategies include light therapy, chronotherapy, and melatonin administration to adjust advanced or delayed rhythms. Beyond jet lag and shift work, clinicians should also pay close attention to patients who present with complaints of "insomnia," as these cases may in fact reflect delayed sleep phase leading to sleep-onset difficulties, or advanced sleep phase resulting in early-morning awakenings. Effective treatment should integrate cognitive-behavioral interventions for insomnia with circadian rhythm adjustments to deliver individualized, evidence-based, and clinically beneficial care.



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呂宗樺醫師

**Topic :** Effects of the Human-Centric Lighting Intervention on Glutamate/GABA Levels and Salivary Melatonin: A 60-Day Pilot Study in Female Adolescents.

**Abstract :**

**Background:**

Light-based interventions may influence the melatonin system; however, their effects on glutamate/GABA balance remain unclear. This pilot quasi-experimental study evaluated three intervention arms: the human-centric lighting (HCL) system, sleep hygiene education (SHE), and a control group.

**Methods:**

A total of 44 female students from a high school were enrolled. Three classes were assigned to one of the following conditions: HCL, SHE, or control. At baseline and after a two-month intervention period, participants underwent overnight polysomnography (PSG) and proton magnetic resonance spectroscopy (<sup>1</sup>H-MRS) to assess glutamate and GABA concentrations in the anterior cingulate cortex.

**Results:**

Nighttime salivary melatonin concentrations increased in the HCL group. A significant change in the excitatory/inhibitory (E/I) ratio was observed between the HCL and control groups. Glutamate levels decreased in the HCL group, while no changes were observed in the SHE or control groups. GABA levels decreased only in the control group. Additionally, the SHE group exhibited prolonged sleep latency.

**Discussion:**

The AloT human-centric lighting system may represent a feasible intervention capable of modulating neurochemical mechanisms related to sleep. Further research is needed to determine its efficacy among individuals with sleep disorders.

## Symposium 4 基礎

張芳嘉教授

**Topic :** Hypocretin in medial prefrontal cortex mediates fear extinction in PTSD

**Abstract :**

**Introduction:**

Post-traumatic stress disorder (PTSD) is characterized by impaired discrimination of trauma-associated fear memories, leading to persistent emotional distress and sleep disruption. The orexin system in the lateral hypothalamus (LH) has been implicated in the recall of extinguished fear memories, while lesions of the medial prefrontal cortex (mPFC)—a major downstream target of the LH—disrupt extinction processes. These findings suggest that orexinergic projections from the LH to the mPFC may contribute to both conditioned fear extinction and sleep regulation.

**Methods:**

Using chemogenetic approaches, we selectively activated or inhibited the LH–mPFC pathway during





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extinction learning. Electrocorticography was applied in parallel to assess sleep states under these manipulations.

### **Results:**

Extinction acquisition was accompanied by heightened activity in both the LH and mPFC. Activation of the LH–mPFC pathway sustained elevated freezing behavior during extinction, whereas silencing this pathway produced an early reduction in freezing that declined rapidly. Pathway manipulation not only altered freezing behavior but also affected extinction memory formation, as confirmed by retrieval and anxiety-related behavioral tasks. Moreover, pathway activation induced insomnia-like phenotypes during the light period.

### **Conclusion:**

These findings indicate that orexinergic projections from the LH to the mPFC play a critical role in the extinction of conditioned fear memories while concurrently modulating REM sleep regulation.

### 蕭逸澤 副教授

**Topic :** Modulation of Fear-Induced Sleep Disturbance through the Lateral Hypothalamus

**Abstract :** A single stressful experience often disrupts subsequent sleep, but the precise mechanisms underlying this phenomenon remain elusive. We hypothesized that a subset of neurons in the lateral hypothalamus (LH), activated during stressful events, contributes to sleep disruption, and that reactivating these neurons is sufficient to induce such disturbances. Using activity-dependent neural tagging in mice, we labeled footshock-activated LH neurons. Reactivation of these neurons reduced total sleep time by more than 9 hours. Further analysis revealed that both corticotropin-releasing factor (CRF)-producing neurons and orexinergic neurons in the LH contribute to sleep loss. Importantly, CRF neurons play a more critical role than orexinergic neurons: reactivation of CRF neurons caused prolonged sleep disruption for over 12 hours, whereas activating orexinergic neurons disrupted sleep for only about 1 hour. These findings suggest that fear-induced reactivation of CRF neurons is a key driver of sleep disruption following stressful events.

## **Symposium 5 內科**

### 鄭婉汝醫師

**Topic :** Endotypes in Patients with Obstructive Sleep Apnea: Clinical Implications and Limitations

**Abstract :** Obstructive sleep apnea (OSA) is a heterogeneous disorder, and understanding its endotypes facilitates both personalized medicine and deeper insight into respiratory physiology. Traditionally, estimating endotypic traits has been labor-intensive (e.g., CPAP drop method) or invasive (e.g., esophageal manometry). More recently, the Phenotyping Using Polysomnography (PUP) method has gained popularity for its ability to derive endotypic traits from standard polysomnography. In recent years, studies have characterized the distribution of these traits in OSA and examined how they vary by age, sex, body mass index, smoking status, symptoms, and polysomnographic features. Certain endotypic traits have also been



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proposed as predictors of treatment outcomes for CPAP and upper airway surgery. Future research should aim to further validate methods for measuring endotypic traits, assess their generalizability across diverse populations, investigate how these traits change with age and treatment, and explore the joint effects of multiple endotypic metrics.

### 王才郁醫師

**Topic :** Additional Medical Treatments for Obstructive Sleep Apnea

**Abstract :** Obstructive sleep apnea (OSA) is a highly prevalent disease. Continuous positive airway pressure ventilator (CPAP) is the gold standard first-line therapy. However, almost 50% patients can not tolerate CPAP treatment. Alternative treatment such as medication is a wonderful dream for those patients. Recently, the identification of endotypes underlying this disease may orient the pharmacological therapy, which means the personalized therapy of OSA. In this speech, OSA pharmacotherapy based on the four main endotypes: anatomy (Pcrit), upper airway muscle power, arousal threshold and ventilatory overshoot (loop gain) will be addressed. Medications for weight loss that modify upper airway anatomy may play a role in the management of OSA, and promising results have been obtained with drugs that increase upper airway muscle power during sleep and/or reduce ventilatory overshoot (loop gain). Ideally, a medication that can effectively increase the arousal threshold but not worsen upper airway muscle power will make this strategy encouraging. Recent studies have demonstrated that the use of certain sedatives do not make OSA severity worse and can improve patients' sleep quality.

## Symposium 6 牙科

### 黃依莉醫師

**Topic :** The correlation between Sleep-Related Breathing Disorders and Temporomandibular joint Disorders

**Abstract :** 本報告檢視了睡眠呼吸障礙 Sleep-Related Breathing Disorders (SDB)，尤其是阻塞型睡眠呼吸中止症 Obstructive sleep apnea (OSA)與顫顎關節障礙 Temporomandibular joint Disorders (TMD)之間的重要關係。除了單純的關聯性之外，最近的證據表明兩者存在因果關係，OSA 是導致 TMD 發展的一個顯著風險因子。我們探討了潛在的機制，包括 OSA 引發的炎症如何導致中樞性疼痛，以及睡眠磨牙症在維持呼吸道暢通的同時，對顫顎關節造成壓力的作用。同時也考量了共同的顫顏特徵。從臨床角度來看，這些發現要求對這兩種疾病進行雙向篩檢。在使用下顎前移裝置 mandibular advancement device (MADs) 治療 OSA 時，評估和監測顫顎關節的健康至關重要，以防止潛在的醫源性損害。本報告主張採用整合性的多學科方法來診斷和治療這些高度相關的疾病，最終目標是改善患者的治療效果。



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許瑛健醫師

**Topic :** Integrated Multidisciplinary Approaches with Weight Management in Obstructive Sleep Apnea Treatment

**Abstract :** Obstructive sleep apnea (OSA) is closely linked to obesity. Recent advances in anti-obesity medications and bariatric/metabolic surgery have enabled more diversified treatment strategies. Studies show that a 10% reduction in body weight is associated with roughly a 25% decrease in the apnea–hypopnea index (AHI). In patients with moderate to severe OSA, weight loss can downstage disease severity, reduce dependence on positive airway pressure (PAP) therapy, and open opportunities for minimally invasive upper-airway surgery or a mandibular advancement oral appliance.

蕭凱元醫師

**Topic :** From A to Z: my first-hand observation of hypoglossal nerve stimulation in USA

**Abstract :** Obstructive sleep apnea (OSA) has long been managed through various non-surgical methods—such as weight loss, oropharyngeal muscle training, and use of adjunct devices like CPAP or mandibular advancement devices (MAD)—as well as surgical approaches (phase I/II surgeries to correct airway anatomy, bariatric surgery, etc.). Despite these options, many patients remain inadequately treated or continue to struggle with their condition. This gap has spurred the development of alternative therapies, such as hypoglossal nerve stimulation (HNS). Following the publication of the landmark, multicenter, prospective STAR trial—which demonstrated the promising clinical efficacy of HNS in treating OSA—the first FDA-approved device, Inspire II, was launched in 2014. Over the subsequent decade, nearly 100,000 patients have benefited from this therapy.

What did we learn from these experiences? Can we further stratify responders and non-responders based on specific endotypes or phenotypes? How can complications be effectively prevented or managed? What device modifications and additional device options have emerged in recent years? Furthermore, what insights have surfaced in U.S. clinical observations, peer discussions, and case studies that are less commonly featured in international conferences?

In light of the fact that hypoglossal nerve stimulation is not yet introduced to Taiwan, this presentation serves as a rapid orientation and checklist for clinicians considering adoption of this new medical device.

**Symposium 7 神經內科**

Prof. Jihwan Myung

**Topic :** Importance of sleep health in shift worker

**Abstract :** The brain is a closed fluid compartment in which total intracranial volume remains constant (Monro-Kellie doctrine), yet its fluid exchange is dynamic. Cerebrospinal fluid (CSF), the principal intracranial fluid, shows daily cycles that likely reflect circadian control by the choroid plexus (CP). The CP harbors a strong molecular clock, but its influence on CSF dynamics remains poorly understood. We show





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that in nocturnal mice, tight junction proteins occludin and claudins reach peak expression around the transition between day and night, which suggests rhythmic closure of the paracellular pathway, whereas NKCC1, which drives blood-to-CSF ionic gradients, increases at night. Evans Blue delivered via the retro-orbital route permeates into CSF more readily at night, and the tracer appears in the contralateral cervical lymph node with minimal delay, consistent with tight balance that preserves intracranial volume. This circadian gating of barrier permeability adds a circadian dimension to metabolite clearance that complements sleep-driven glymphatic drainage from brain parenchyma. Proper temporal alignment of the two processes may optimize clearance of slowly soluble species such as amyloid- $\beta$ , whereas misalignment could impair clearance and accelerate neurodegeneration.

### 林煥然醫師

**Topic :** Importance of sleep health in shift worker

**Abstract :** Shift work is essential in many industries but often comes at the cost of disrupted sleep and circadian misalignment. Irregular schedules reduce total sleep time, impair sleep quality, and cause excessive sleepiness, which in turn affects cognitive performance, vigilance, and mental health.

My speech will explore the health challenges faced by shift workers, focusing on how irregular schedules disrupt sleep and circadian rhythms. I will discuss the consequences of circadian misalignment on metabolic health, highlighting increased risks of obesity, insulin resistance, and type 2 diabetes. Cardiovascular outcomes such as hypertension, arrhythmias, coronary artery disease, and stroke will also be emphasized, along with evidence linking long-term night work to certain cancers. In addition, I will address the psychological impact, including fatigue, reduced vigilance, and mood disorders. Finally, the lecture will present strategies to mitigate these risks, including optimized scheduling, controlled light exposure, lifestyle modification, and selective use of pharmacological aids.

### 陳彥中醫師

**Topic :** Circadian disruptions in neurodegenerative disorders

**Abstract :** Circadian regulation plays a pivotal role in maintaining the integrity of sleep–wake cycles, cognitive functions, and systemic physiology. Increasing evidence indicates that disturbances of circadian rhythms are not merely secondary features of neurodegenerative disorders, but rather integral components of their pathophysiology. In Alzheimer's disease, Parkinson's disease, and Huntington's disease, patients frequently present with early alterations in sleep continuity, rhythm fragmentation, and phase instability. In Parkinson's disease, REM sleep behavior disorder often emerges years before motor manifestations, suggesting that circadian and sleep disturbances may serve as prodromal markers.

At the molecular level, dysfunction of the core clock machinery—including altered expression of CLOCK, BMAL1, PER, and CRY genes—has been reported in both central pacemakers and peripheral oscillators. Impairments in the suprachiasmatic nucleus, melatonin secretion, and light-input pathways such as intrinsically photosensitive retinal ganglion cells further compromise circadian alignment. These



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abnormalities are compounded by neuroinflammatory cascades, oxidative stress, and protein misfolding, which appear to interact bidirectionally with circadian dysregulation, accelerating neuronal vulnerability. From a clinical standpoint, circadian biomarkers including actigraphy-derived rest–activity patterns, body temperature rhythms, hormone secretion profiles, and gene expression signatures provide objective measures that correlate with disease progression and cognitive decline. Recognition of these biomarkers underscores the importance of circadian health as both a clinical outcome and a potential therapeutic target.

Interventions aiming to restore circadian synchrony—ranging from bright light therapy and exogenous melatonin to structured behavioral and pharmacological schedules—demonstrate varying degrees of efficacy. More experimental strategies, such as chronopharmacology and time-restricted feeding, are under investigation in preclinical and early clinical studies.

Taken together, circadian disruption emerges as a unifying theme across neurodegenerative disorders, influencing symptom burden, disease trajectory, and quality of life. Incorporating circadian assessment and chronotherapeutic approaches into clinical practice holds promise for enhancing outcomes and delaying disease progression, yet requires further longitudinal validation and individualized application.

### Symposium 8 外科

#### 康焜泰醫師

**Topic :** Pediatric Obstructive Sleep Apnea: Impact on behavior, growth and learning to cardiovascular and craniofacial development, and future treatment perspective

**Abstract :** Obstructive sleep apnea (OSA) is marked by recurrent upper airway obstruction during sleep, resulting in disrupted airflow and adverse health effects. If left untreated, OSA in children is associated with cardiovascular complications, behavioral issues, impaired neurocognitive development, metabolic abnormalities, and other growth-related problems. Hypertrophy of the adenoid and tonsil that narrows the upper airway is the most common cause of OSA in children, and adenotonsillectomy is the first-line treatment for these children. This section provides a comprehensive overview addressing impacts of pediatric OSA and future perspectives in treatment.

#### 林婉妮醫師

**Topic :** Application of ultrasonography in the diagnosis and treatment of OSA

**Abstract :** 超音波技術近年在阻塞型睡眠呼吸中止症（OSA）患者的臨床評估上，從單純結構影像擴展到功能性分析。透過動態上氣道成像與組織質地評估，醫師能夠更精準地判斷阻塞部位，並協助預測手術成效，提供個人化治療規劃。本演講將探討超音波在臨床診斷、手術治療預測及與藥物誘導睡眠內視鏡（DISE）等工具整合的最新實證與應用，並討論未來在臨床應用上的發展可能性。



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李立昂醫師

**Topic :** Physical activity and its association with cardiometabolic profile in patients with OSA

**Abstract : Introduction:** This study aimed to examine the relationships between physical activity (PA), cardiometabolic profiles, and body composition in adult patients with obstructive sleep apnea (OSA), with and without metabolic syndrome (MetS).

**Methods:** Between September 2021 and August 2023, we conducted a prospective case series at a Taiwanese tertiary medical center, enrolling 44 adult OSA patients. Each participant underwent anthropometric measurements, polysomnography, PA evaluation (via the International Physical Activity Questionnaire-Long Form), one-week heart rate variability (HRV) monitoring (using a wearable electrocardiographic patch), fasting blood tests for lipids, glucose, insulin, and insulin resistance (IR), and body composition analysis via dual-energy X-ray absorptiometry.

**Results:** Among the 44 participants, 20 (46%) had OSA with MetS, and 24 (54%) had OSA without MetS. Compared to those with OSA alone, patients with MetS had higher BMI, waist circumference, 3% oxygen desaturation index (ODI3), triglycerides, total body fat percentage (TBF%), and fat mass, but lower mean SpO<sub>2</sub>, weekend R-R interval, sleep weekday R-R interval, and HDL-C (all  $p < .05$ ). Weekly metabolic equivalent of task-minutes positively correlated with mean SpO<sub>2</sub> and HF power during weekend sleep and inversely with insulin levels, IR, triglycerides, TBF%, fat mass, and LF/HF ratio during both sleep and wakefulness (all  $p < .05$ ). Walking, rather than moderate or vigorous PA, was positively associated with mean SpO<sub>2</sub>, weekend awake R-R interval, and HDL-C, and inversely with neck circumference, AHI, ODI3, insulin levels, IR, total cholesterol, LDL-C, and android-to-gynoid fat ratio (all  $p < .05$ ).

**Conclusions:** Obesity, hypoxemia, and increased heart rate were significantly associated with MetS in patients with OSA. PA, particularly walking, may improve blood oxygenation, cardiometabolic health, and body composition in this population. Further studies are warranted to confirm these findings and explore potential interventions.

徐英碩醫師

**Topic :** The Role and Future Perspectives of GLP-1 Receptor Agonists in the Treatment of Obstructive Sleep Apnea

**Abstract :** 近年來，阻塞性睡眠呼吸中止症（OSA）與肥胖的關聯已被廣泛證實，體重控制不僅影響呼吸道塌陷程度，更決定治療的長期成效。過去我們主要依靠正壓呼吸器、口內裝置與外科手術，但隨著 GLP-1 受體促效劑與雙促效劑（如 GLP-1/GIP）在減重領域的突破，藥物治療開始在 OSA 中展現出全新的角色。2024 年美國 FDA 核准 tirzepatide 用於合併肥胖的中重度 OSA 成人，這是首個針對 OSA 的藥物適應症，象徵治療策略的重大轉折。

從臨床研究來看，SURMOUNT-OSA 隨機對照試驗顯示 tirzepatide 在一年內能使 OSA 嚴重度（AHI）下降近三分之二，並同時改善體重、血壓、低氧負荷與發炎指標，無論是否使用 PAP 效果皆一致。多篇統合分析也陸續支持這些發現，例如 2025 年的 meta-analysis 納入超過千例患者，結果顯示 GLP-1 類藥物平均可降低 AHI 近 10 次/時，體重減輕約 11 公斤，收縮壓下降約 5



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mmHg，且 tirzepatide 效果遠優於 liraglutide。另一篇針對隨機對照試驗的分析則更進一步證實，藥物除了改善呼吸事件外，還能減少低氧負荷與 hs-CRP 等心血管風險因子，而安全性上除了常見的腸胃道副作用外，並無嚴重不良事件增加。整體而言，這些研究讓我們首次看到以藥物方式直接介入 OSA 病程的可能。

然而，PAP 仍然是黃金標準，可以立即消除呼吸事件，而手術治療對於結構性狹窄患者仍不可或缺。GLP-1 類藥物的價值在於提供一個系統性、可持續的體重控制基礎，能降低 PAP 所需壓力、增加病人接受度，也能作為手術前的減重準備，減少麻醉與術後風險，更能在手術後幫助維持療效，避免因體重回升而復發。對於不適合手術或無法長期配合 PAP 的患者，更是多了一條新的治療路徑。

在這樣的發展下，耳鼻喉科與睡眠外科醫師的角色也正在轉變。我們不僅是結構性治療的執行者，更是整體治療策略的設計者與整合者。透過氣道內視鏡與 DISE 評估，我們能判斷結構與體重因素的比例，決定病人是否需要藥物、手術或雙管齊下；透過跨科合作，我們能與新陳代謝科、胸腔科共同建立多專科門診，設計個人化的治療藍圖；在臨床研究上，我們更能推動藥物與外科手術互補的台灣經驗，為未來的治療指引提供證據基礎。

展望未來，仍需要更多長期資料來驗證 GLP-1 類藥物在心血管結局、死亡率與停藥後復發上的影響，也需要頭對頭試驗來比較藥物與減重手術或外科治療的差異。但可以確定的是，GLP-1 類藥物的出現，已經開啟 OSA 治療的新時代。對我們耳鼻喉科與睡眠外科醫師來說，關鍵在於如何把藥物與傳統治療整合，讓病人既能改善氣道結構，又能長期維持體重與代謝健康，真正達到全方位的治療目標。

### Satellite Symposium

#### Dr. Christian Caussé, MD

**Topic :** Pitolisant studies on Narcolepsy and Obstructive Sleep Apnea (OSA)

**Abstract :** Introduction: Obstructive sleep apnoea (OSA) is a common chronic respiratory disease associated with a high burden of disabilities related to sleepiness and reduced quality of life. Despite first-line treatment with continuous positive airway pressure (CPAP) therapy, many patients experience residual EDS. Pharmacological treatment options authorised in Europe and/or the United States are modafinil/armodafinil, solriamfetol, and pitolisant. In the absence of head-to-head trials, the relative efficacy and safety of these agents is largely unknown.

Methods: Randomised controlled trials (RCTs) that compared the efficacy and safety of authorised medications for OSA were analysed using network meta-analysis. The primary efficacy endpoint was combined Epworth Sleepiness Scale (ESS) and Oxford Sleep Resistance (OSLER)/Maintenance of Wakefulness Test (MWT) Z-scores. Quality of life (QoL), overall and cardiovascular safety, and benefit-risk ratios were calculated.

Results: Of 4017 studies identified, a total of 20 RCTs involving 4015 subjects were included. Analysis of combined subjective (ESS) and objective (OSLER/MWT) efficacy outcome Z-scores showed that solriamfetol (150 mg; effect size [ES]=0.66 [95% CI: 0.36, 0.96]), and pitolisant (20 mg; ES=0.66 [95% CI: 0.44, 0.88]), modafinil (200 mg; ES=0.53 [95% CI: 0.33, 0.73]); 400 mg; ES=0.53 [95% CI: 0.42, 0.64]) had a clinically meaningful improvement in efficacy. P-scores ranked placebo, then pitolisant, modafinil 200 mg, modafinil



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400 mg and solriamfetol for overall safety; and pitolisant, then solriamfetol, modafinil 400 mg and modafinil 200 mg for benefit-risk ratio.

Conclusion: Pitolisant, solriamfetol and modafinil had comparable efficacy for maintaining wakefulness in patients with OSA. Pitolisant had a better safety profile and benefit-risk ratio compared with solriamfetol and modafinil. The overall and cardiovascular safety risk ratios suggest that pitolisant might be the best candidate for OSA patients with multiple cardiovascular comorbidities.

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### Keynote 1

**Prof. Hiroki Ueda**

**Topic :** Towards Human Systems Biology of Sleep/Wake Cycles: The Role of Calcium and Phosphorylation in Sleep

**Abstract :** Sleep is one of the great mysteries of life—why do we need it, and how does our brain regulate it? At the Sleep 2012 conference in Boston, we reached to a new way of thinking about **sleep homeostasis**. Instead of relying on the idea that sleep is triggered by specific "**sleep substances**," we hypothesized that sleep homeostasis could be sufficiently explained by the "**wake substances**", such as **calcium**, and integration of their activity over time, such as **calcium-dependent phosphorylation and dephosphorylation**. This idea led us to explore the role of **calcium** and **phosphorylation** in sleep.

Building on pioneering Dr. Setsuro Ebashi's discovery that calcium acts as a key signalling molecule in cells, we hypothesized that calcium might not only activate neurons but also help regulate sleep. To test this, we developed a powerful gene-editing technique called the **Triple-CRISPR** method in 2016, which allowed us to create genetically modified mice with over 95% efficiency(Sunagawa et al. 2016). Using this technique, we studied 25 different genes related to calcium channels and pumps and found that **calcium plays a crucial role in sleep by acting as a brake on brain activity**(Tatsuki et al. 2016).

We also developed **CUBIC**(Susaki et al. 2014; Tainaka et al. 2014), a method that makes brain and other tissues transparent, allowing us to see how calcium affects neurons. Our research further revealed that calcium-dependent kinases, such as **CaMKII $\alpha/\beta$** , store a "**memory**" of **calcium activity** and use it to regulate sleep(Tatsuki et al. 2016). We also identified three types of phosphorylation sites on these proteins that control when sleep begins, how long it lasts, and when it ends(Tone et al. 2022). Additionally, we found that other kinase and phosphatases, such as **PKA, Calcineurin, and PP1**, act as sleep switches in the excitatory post-synapse of excitatory neurons —some (**PKA**) keeping us awake, while others (**PP1 and Calcineurin**) help us sleep(Wang et al. 2024). Interestingly, both sleep-promoting phosphatases, **Calcineurin and PP1, are directly and indirectly calcium-dependent**. We have also discovered that the ryanodine receptor 1, a calcium channel within cells, is a molecular target of inhalational anesthetics(Kanaya et al. 2025), suggesting that anesthesia and sleep may share a common calcium-dependent mechanism.

Our discoveries also led to a new idea of sleep function called **WISE (Wake Inhibition Sleep Enhancement)**





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**mechanism**, where **quiet wakefulness suppresses neuronal connections while deep sleep strengthens them**(Kinoshita et al. 2024), challenging the traditional Synaptic Homeostasis hypothesis. This WISE mechanism also helps explain why chronic sleep deprivation can contribute to depression and why some fast-acting antidepressants increase deep sleep activity. By understanding how calcium and brain activity regulate sleep, we hope to unlock new ways to improve sleep health and develop better treatments for sleep disorders and mental health conditions.

### Keynote 2

#### **Dr. Ariel B. Neikrug**

**Topic** : Behavioral Management of Circadian Function: A Biobehavioral Framework for Health and Resilience

**Abstract** : There is growing recognition of the importance of behavioral modulation of circadian rhythms to improve physical and mental health outcomes. This talk examines how daily behavioral rhythms—particularly those related to sleep, activity, and diet,—can be strategically aligned with circadian physiology to promote resilience and reduce disease vulnerability. Drawing from clinical psychology, circadian science, behavioral medicine, and exercise physiology, I will review mechanisms by which circadian misalignment and dysregulation of the arousal system interact to heighten risk for chronic disease. Emphasis will be placed on practical, evidence-based interventions—including chronobiological techniques and behavioral strategies—that support circadian alignment and attenuate hyperarousal. Framed within a biobehavioral model of resilience, I will highlight how the core pillars of health—sleep, exercise, diet—can be integrated through a behavioral and circadian lens to optimize health and functioning.

### Symposium 9 Circadian Rhythms

#### **Prof. Jihwan Myung**

**Topic** : Peripheral Circadian Clocks Emerge Before the SCN via SNIC in Mouse Embryos

**Abstract** : The mammalian circadian system has traditionally been viewed as hierarchical, with the suprachiasmatic nucleus (SCN) serving as the central pacemaker that synchronizes peripheral clocks throughout the body. This framework has shaped our understanding of how circadian oscillators develop during embryogenesis. However, with PER2::LUC and *Bmal1-ELuc* bioluminescence imaging and circadian time-series qPCR across mouse embryogenesis, we report a different developmental sequence. In the brain, we found that the fourth ventricular choroid plexus (4VCP) exhibits the first detectable circadian oscillations by E11.5 to E12.5, about three days before the SCN clock emerges at E15.5. Similarly, in peripheral tissues, time-differential imaging revealed that the embryonic heart initiates autonomous circadian rhythms prior to SCN development. Oscillations of genes that regulate cardiac excitability are detectable by E13.5, and heart rate rhythms phase-lock to PER2::LUC peaks well before the establishment of sympathetic or parasympathetic innervation. These early peripheral clocks display an abrupt, nonlinear onset pattern consistent with a saddle-node on invariant circle (SNIC) bifurcation, with initial periods that diverge near onset. In the 4VCP, *Bmal1-ELuc* oscillations start at E13.5, coincident with differentiation markers. The earlier PER2::LUC relative to *Bmal1-ELuc* suggests a molecular sequence consistent with SNIC



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and contrasts with the Hopf-type dynamics typical of mature circadian clocks. The SNIC bifurcation pattern supports a developmental model where key peripheral clocks emerge abruptly at defined embryonic stages through autonomous bifurcation events, independent of SCN control. These results provide new insights that may improve clinical care approaches for preterm neonates.

### Prof. Masayuki Ikeda

**Topic :** Sleep-wake rhythms and peripheral clock movements in the diurnal grass rat, *Arvicanthis niloticus*

**Abstract :** Analyzing sleep in laboratory mice or rats allows for pharmacological and genetic approaches and has significantly advanced our knowledge of sleep. However, their circadian behavioral phenotypes are out of phase with our sleep-wake cycles, which limits their use as human models. In this regard, alternative use of diurnal laboratory rodents may be an ideal approach, whereas knowledge regarding their sleep profiles is yet limited. Therefore, we examined EEG and EMG recordings in Nile grass rats and characterized their sleep under 12:12-h light-dark cycles of various lighting intensity. Consequently, we observed bimodal activity patterns coinciding with crepuscular elevation of wakefulness at lower light intensities (10 or 100 lux). Meanwhile, enhancement of wakefulness and a reversal reduction in NREM sleep were observed during the daytime at higher light intensities (300 or 1,000 lux), creating apparent diurnal sleep-wake patterns. The results are consistent with clinical aspects to treat patients with seasonal affective disorders and thus suggest possible use of Nile grass rats as a model of bright light therapy. To further study the peripheral clock movements in Nile grass rats, we established a fibroblast cell line (GrLBmal1-luc) from the lungs of diurnal Nile grass rats stably expressing the *Bmal1-luciferase* reporter gene. The adrenergic stimulation phase-delayed or phase-advanced *Bmal1* transcriptional rhythms, depending on the timing of stimulation as in the human type-0 phase-response-curve. Thus, this cell line may have potential application in modeling human clocks.

### 蔡皇龍教授

**Topic :** BASIC PENTACYSTEINES modulate the circadian clock by repressing the Evening Complex in *Arabidopsis*

**Abstract :** BASIC PENTACYSTEINES (BPCs) are plant-specific transcription factors that play a role in circadian clock regulation. The altered expression levels of target genes in various *bpc* mutant loci combinations suggest that BPC family members can act as repressors, activators, or both, to regulate the transcription of downstream clock genes in *Arabidopsis*. However, the immediate reactions of these genes to BPC ectopic expression don't fully reveal the actual regulatory mechanism. This is most likely because the clock's complex feedback loops are masking the true BPC effects. To investigate this, we enhanced the biological effects of BPC3, a family member with typically low expression, by overexpressing it. Using ChIP-seq, we mapped its genomic binding sites and found that BPC3 targets a range of clock genes with varying binding affinities, offering insight into how BPC proteins modulate the circadian clock. We then simulated the BPC3 binding effects within a publicly available mathematical model. The model's results revealed an action path for BPC3 that aligns with the clock gene expression data observed after BPC3 overexpression. Our simulation



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specifically demonstrates that BPC3's direct repression of *ELF4* within the Evening Complex is the key event leading to the observed clock disruption. This finding positions the evening loop as the central regulatory hub for BPC-mediated clock modulation.

### Lunch Symposium

#### 孫瑜醫師

**Topic :** Resetting the Biological Clock: How Lemborexant Helps Restore Circadian Rhythms and Natural Sleep in Insomnia Patients

**Abstract :** Insomnia is not merely a disruption of sleep—it is often a manifestation of misaligned circadian rhythms. Lemborexant, a dual orexin receptor antagonist (DORA), offers a novel approach to treating insomnia by targeting the neurobiological mechanisms that regulate wakefulness and sleep initiation. This presentation explores how Lemborexant modulates orexin signaling to reduce hyperarousal, thereby facilitating the natural onset and maintenance of sleep.

Recent clinical and mechanistic studies demonstrate that Lemborexant not only improves sleep latency and duration but also contributes to the re-synchronization of circadian rhythms, particularly in patients with delayed sleep phase or fragmented sleep patterns. By promoting sleep that aligns more closely with the body's endogenous biological clock, Lemborexant supports restorative sleep and enhances daytime functioning.

### Symposium 10 精神科

#### 林澂教授

**Topic :** Long-Term Physiological Monitoring for Sleep and Circadian Biomarkers: Towards Individualized Risk-Based Care

**Abstract :** Human behaviors and physiology can now be continuously monitored through a wide range of wearable and mobile technologies. Beyond traditional actigraphy, novel parameters capturing the regularity and variability of minute-to-minute, hourly, and day-to-day patterns have been developed. These measures have been associated with diverse health outcomes, including cancer, cardiovascular disease, and mood disorders. This talk will highlight how long-term physiological and behavioral data streams can be transformed into digital biomarkers of sleep and circadian health, and how these markers may inform individualized, risk-based care. Furthermore, multimodal signals such as photoplethysmography (PPG), electrocardiography (ECG), and smartphone usage data can be integrated to enhance early risk detection and enable more precise, personalized interventions.

#### 金韋志醫師

**Topic :** Prognostic Significance and Severity Stratification Potential of Circadian Rhythm in Myocardial



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### Infarction

**Abstract :** Introduction: Circadian rhythm and myocardial infarction (MI) are closely connected, and monitoring with wearable devices can offer valuable opportunities for deeper insight. We explored the prognostic significance of circadian rhythm and its variations among patients with different Killip classes using actigraphy.

**Methods:** **Patients with acute myocardial infarction (Killip class I–III) were recruited and received continuous actigraphy monitoring during hospitalization.** After discharge, they were followed for assessing prognosis. Actigraphy data were analyzed by both parametric and non-parametric methods to evaluate sleep patterns and circadian rhythms. The Mann-Whitney U test was used for group comparisons between different MI severity, and Spearman correlation was conducted to investigate correlations between actigraphy variables, the Killip classification, and prognosis.

**Results:** We recruited 34 MI patients with MI, comprising 23 in Killip class I (67.6%), 7 in Killip class II (20.6%), and 4 in Killip class III (11.8%). Circadian rhythm parameters were significantly correlated with MI prognosis. Besides, Those with more severe MI (Killip II and III) had significantly lower daytime activity standard deviation ( $142.12 \pm 33.78$  vs.  $105.26 \pm 40.90$ ,  $p=0.017$ ), interdaily stability ( $0.35 \pm 0.12$  vs.  $0.24 \pm 0.11$ ,  $p=0.032$ ), and relative amplitude ( $0.73 \pm 0.11$  vs.  $0.6 \pm 0.12$ ,  $p=0.025$ ) compared to the Killip I group. Significant negative correlations were also found between Killip classes and these three non-parametric factors.

**Conclusion:** Actigraphy monitoring can contribute to the evaluation of MI prognosis, and more severe MI can be linked to more circadian disruption. Non-parametric analysis of actigraphy data may serve as a complementary approach for evaluating and monitoring physical status, contributing to improve MI outcome.

### 阮淳藝醫師

**Topic :** Circadian Rhythm Outcome and Predictive Markers in Patients with Narcolepsy following Modafinil Treatment

**Abstract :** Objective:

Hypersomnolence is a core manifestation of narcolepsy and is often treated with modafinil, but its impacts on circadian rhythm remain unclear. Non-parametric analysis of actigraphy data can provide minor but important features for clinical assessments. Thus, we used actigraphy to track rest-activity patterns in narcolepsy patients before and after modafinil treatment and analyzed the data by non-parametric methods, in order to assess treatment effects and explore the predictor of treatment response.

Methods:

We prospectively recruited participants with narcolepsy type 1 (NT1) and 2 (NT2). After baseline evaluation including polysomnography and multiple sleep latency test, participants received 200–400 mg of modafinil daily for six months. Actigraphy was worn for 7–14 days before and after treatment, accompanied by subjective questionnaires. We used



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paired t-tests for pre-post comparison, and independent t-tests and chi-square tests for between-group analysis. Pearson's correlation was used to examine links between questionnaire scores, REM abnormalities, and circadian data.

### Results:

103 participants (mean age:  $23.95 \pm 10.14$  years; 53.4% male) were recruited. After modafinil treatment, significant increases in daytime activity and the most active 10 consecutive hours (M10,  $p = 0.009$  and  $0.007$ ) were observed, along with an earlier shift in the midpoint time of M10 ( $p = 0.006$ ). NT1 patients showed more improvements than NT2 patients. The children/adolescents subgroup showed an earlier shift in the timing of daytime activity ( $p < 0.001$ ), while the adults exhibited increases in daytime activity and M10 ( $p = 0.019$  and  $0.010$ ). Subjective sleepiness and quality of life (QoL) were associated with circadian parameters, particularly the relative amplitude. Lastly, patients with a higher REM percentage or with nocturnal sleep onset REM period (SOREMP) demonstrated greater improvements in circadian parameters.

### Conclusion:

Modafinil improves circadian rest-activity rhythms in narcolepsy patients, especially those with NT1. The role of REM percentage and nocturnal SOREMP as predictive markers for treatment outcomes warrant further investigation.