Sleep DownUnder 2025 Highlights

From the perspective of Central Disorders of Hypersomnolence

By Michelle Chadwick – Founder & Executive Director, Hypersomnolence Australia

Attending Sleep DownUnder 2025 (SDU) as both a lived-experience representative and as the founder and executive director of Hypersomnolence Australia is always a privilege.

I've attended the APSS's SLEEP conference in the USA, World Sleep in Singapore, and Sleep DownUnder this year, and while our conference may be smaller, its content is absolutely world-class. There were so many brilliant, worthwhile contributions to sleep science and sleep medicine.

This year's program featured more content on Central Disorders of Hypersomnolence (CDoH) than ever before, which was both exciting to see and rewarding to be part of.

I was particularly impressed by the Clinical Symposium "*Hypersomnolence Disorders: Practical Challenges in the Clinic.*" It was, without question, one of the best symposiums I have attended anywhere in the world. The session examined the extremes of Idiopathic Hypersomnia, ie: IH with long sleep, and Narcolepsy, ie: Narcolepsy Type 1 (with cataplexy), delivering an honest, factual, and clinically grounded discussion that did real justice to people living with these debilitating conditions.

Thanks to the generous support of Alkermes, Hypersomnolence Australia was able to bring four lived-experience advocates to SDU this year - Jana Chadd, Sarah Searle, Clare Duncan, and Di Spillane - representing both the Narcolepsy and Idiopathic Hypersomnia communities. Their participation was part of Hypersomnolence Australia's initiative to help lived-experience representatives develop as informed advocates, to learn how research is presented and disseminated, and to gain the knowledge and confidence needed to participate meaningfully in research co-design. The program also aims to bridge the gap between researchers and lived-experience voices by bringing them together in an environment where each can learn from the other.

(More information about this delegate program can be found here: Sleep DownUnder Hypersomnolence Australia Delegate Opportunity.)

Clinical Symposium – *Hypersomnolence Disorders: Practical Challenges in the Clinic*

Symposium Chairs:

Dr Sheila Sivam, Sleep Physician - Woolcock Institute of Medical Research
Prof Brendon Yee, Sleep Physician - Royal Prince Alfred Hospital and Woolcock Institute of Medical Research

This symposium was the highlight of the conference for me. It's rare, especially in Australia, to see such thoughtful attention given to the extremes of Idiopathic Hypersomnia (IH with long sleep) and Narcolepsy (Type 1 - with cataplexy). The session addressed real clinical dilemmas across the central disorders of hypersomnolence with nuance, honesty, and genuine respect for the people who live with these conditions.

Dr Simon Frenkel – *Getting the Diagnosis Right*

Dr Frenkel (Sleep Physician, Western Health) opened by emphasising that current diagnostic tools for hypersomnolence are fallible, except for CSF orexin/hypocretin testing for confirming Narcolepsy Type 1. He stressed that clinicians must understand the limitations of the existing diagnostic paradigm to minimise the risk of misdiagnosis.

He urged caution against the over-reliance on the Multiple Sleep Latency Test (MSLT), noting that it does not reliably distinguish "normal" from "abnormal" sleepiness. For example, at least 22% of healthy controls fall below the <8-minute mean sleep latency threshold, while conversely, roughly two-thirds (≈60–75%) of people with genuine Idiopathic Hypersomnia (IH) record MSLT results above 8 minutes, despite experiencing disabling daytime sleepiness. Similarly, the occurrence of two or more sleep-onset REM periods (SOREMs) - currently required for a narcolepsy diagnosis - is not uncommon in the general population, particularly among shift workers or individuals with prior sleep deprivation, both of which can artificially produce SOREMs.

Dr Frenkel also highlighted circadian misalignment and insufficient sleep as major confounders in the diagnostic process. He advocated strongly for the use of actigraphy and sleep logs (for at least seven days) to distinguish true hypersomnolence from lifestyle or biological rhythm issues.

Importantly, he referenced his recent study: Frenkel S, Amaranayake A, Molesworth C, Orellana L, Southcott AM. *"Allowing ad libitum sleep during overnight polysomnography affects MSLT results in patients being assessed for hypersomnolence."*

- The study looked at 580 consecutive patients who completed an overnight sleep study (PSG) followed by an MSLT - 290 before, and 290 after, a protocol change that allowed participants to sleep as long as they needed before testing (rather than being woken at a set time which is usually the case during an overnight/PSG and daytime/MSLT sleep study).

- After the change, people slept almost an hour longer and woke about an hour later. Their average MSLT sleep latency increased by about 1.3 minutes, and there were

23% fewer results showing a mean sleep latency below 8 minutes.

- The researchers concluded that waking patients at a fixed time before MSLT can cut short their sleep and distort the results, which may lead to over-diagnosing narcolepsy and idiopathic hypersomnia.

During his presentation, Dr Frenkel reinforced the key message from his paper: diagnosing narcolepsy and idiopathic hypersomnia requires much more than an overnight (PSG) and daytime (MSLT) sleep study. Without confirming that patients have had adequate sleep and that their results aren't affected by circadian or lifestyle factors, the risk of misdiagnosis remains significant.

He also underscored the importance of language and lexicon, displaying a slide that drew on the qualitative work of Dr Aaron Schokman et al. (2024, Sleep Medicine). This research illustrated how patients and clinicians often speak different "languages" when describing symptoms such as fatigue, sleepiness, and cataplexy. For instance, patients may use everyday terms like *tiredness* or *sleep attack* to describe experiences that differ from the medical definitions. When clinicians ask about symptom frequency or use standardised questionnaires, these mismatched interpretations can lead to mis-measurement or mis-communication that further complicates diagnosis.

By referencing Dr Schokman's findings, Dr Frenkel emphasised that improving diagnostic accuracy requires not only better physiological tools but also a shared vocabulary between clinicians and patients, ensuring that what patients describe and what clinicians record truly reflect the same experience.

Dr Grace Garden – *Long Sleepers: Why is my patient sleeping so long?*

Dr Garden (Neurologist and Sleep Physician, Macquarie University / Woolcock Institute) gave a very impressive presentation that offered a valuable clinical perspective and a genuine understanding of the challenges faced by people living with idiopathic hypersomnia (IH) with long sleep. What made it particularly powerful was that her discussion acknowledged IH with long sleep as a distinct clinical entity. For people living with this condition, it was deeply validating to hear it described with such accuracy and understanding. The Hypersomnolence Australia IH lived-experience advocates in attendance said they genuinely felt *seen*.

Dr Garden explained that although some individuals naturally sleep longer without impairment, IH with long sleep is different. It is a recognised medical disorder associated with greater symptom severity, earlier onset, and specific biological features.

She described how patients with IH with long sleep experience greater sleep inertia, more severe daytime impairment, and poorer quality of life, often alongside an evening chronotype. Her presentation emphasised the importance of thorough assessment - particularly using actigraphy for at least 7 days and, where possible, extended polysomnography (up to 32 hours), to capture the true sleep need of these patients.

Her slides highlighted that people with idiopathic hypersomnia with long sleep tend to have:

- Longer and deeper sleep durations
- Greater daytime sleepiness
- More pronounced sleep inertia or “sleep drunkenness”
- Higher functional impairment
- Increased depressive symptoms
- Earlier onset and lower body-mass index (BMI)
- A tendency toward an evening chronotype
- Overall lower energy levels

She noted that long sleep in IH includes both night and daytime sleep with total durations of 11 hours or more across 24 hours. She added that some people with IH with long sleep will describe fighting the urge to nap because it does not make them feel better and can even make them feel worse, or because they are unable to predict how long they will sleep.

Her talk also focused on sleep inertia (sleep drunkenness) - the severe, prolonged difficulty transitioning from sleep to wakefulness that can last for hours and often proves more disabling than daytime sleepiness itself. She outlined how patients describe confusion, irritability, poor coordination, and “automatic behaviours” performed without full awareness or memory. These symptoms frequently interfere with education, work, and relationships, often requiring others to help them wake. She noted that these clinical features can help recognise IH and distinguish it from other sleep or circadian disorders (Davilliers et al., 2023).

Long sleep is not always Idiopathic Hypersomnia. It is important to recognise that extended sleep duration can occur in people without any underlying sleep disorder. Some healthy individuals regularly sleep more than nine hours per night and function perfectly well during the day. Similarly, people with circadian rhythm misalignment - such as delayed sleep phase - may also experience very long sleep times. This pattern is especially common in adolescents, whose circadian timing can be naturally delayed, leading many to fall asleep and wake up later than socially expected.

Dr Garden presented a compelling case study of a 17-year-old student who initially appeared to have a hypersomnolence disorder. His family described profound difficulty waking him, and he sometimes slept through entire days, yet all investigations, including metabolic screening, lumbar puncture (CSF testing), MRI, and polysomnography, were normal. Extended actigraphy and detailed sleep-wake documentation eventually revealed a delayed sleep phase with chronic sleep restriction and long “catch-up” sleeps, not idiopathic hypersomnia.

This case reinforced the clear message throughout the symposium that PSG and MSLT alone are not sufficient. She urged clinicians to utilise all available diagnostic tools, including actigraphy, sleep diaries, the Idiopathic Hypersomnia Severity Scale (IHSS), a careful clinical history, and input from the patient’s family, to provide insight into bedtime and sleep routines. In addition, consider the patient’s age and biological rhythm when interpreting the results.

She reminded the audience that teenagers naturally have delayed circadian timing, and overlooking this can lead to serious diagnostic errors. She concluded that doctors are diagnosing people with lifelong disorders and prescribing medications that can affect their health - they owe it to their

patients to do their best to get it right.

Targeted Clinical Questions for Identifying Idiopathic Hypersomnia with Long Sleep and Sleep Inertia

To help differentiate IH with long sleep from other causes of hypersomnolence (excessive daytime sleepiness), Dr Garden recommended clinicians ask detailed, experience-focused questions such as:

- *How long can you sleep - and can you sleep that long every day*
- *What is your ideal sleep duration on weekends or holidays?*
- *How long do you nap for? How do you feel after naps?*
- *What is it like when you wake up in the morning?*
- *How often do you need several alarms or someone else to help you wake up?*
- *After waking, how long does it take before you feel fully functional?*
- *Do you ever act irrationally, say strange things, or feel very clumsy in the moments after waking?*

Dr David Cunnington – *Treating Idiopathic Hypersomnia with long sleep; are stimulants always part of the solution?*

Dr Cunnington (Sunshine Coast Respiratory & Sleep / SleepHub) discussed the clinical realities of managing IH with long sleep, describing it as a seriously debilitating medical disorder for many people. He pointed out that “there’s more to it than sleepiness”.

He outlined a range of symptoms that clinicians should look for in people with IH with long sleep, including:

- Sleep inertia
- Unrefreshing naps
- Brain fog
- Mood disturbance
- Hyperactivity (and other ADHD like symptoms)
- Fatigue
- Autonomic dysfunction

He reminded the audience that stimulants only partially treat sleepiness - they do not address long sleep, fatigue/exhaustion, sleep inertia/sleep drunkenness, brain fog, autonomic dysfunction, or hyperactivity and other ADHD-like symptoms, all of which can be major contributors to disability in IH with long sleep. He also noted that stimulant medications can, in some cases, worsen daytime sleepiness by restricting the prolonged sleep that people with IH with long sleep need.

Dr Cunnington also spoke about the importance of getting the diagnosis right and being honest with patients about the limitations of current testing methods. Echoing Dr Garden’s and Dr Frenkel’s message, he stressed that clinicians have a responsibility to be transparent when diagnostic certainty is lacking - patients deserve clear communication, not misplaced confidence in tests that have clear limitations.

He further emphasised that doctors must also be honest about the limitations of treatment. Stimulant medication is not a cure, and it will not automatically make someone with IH "normal." He noted that Cognitive Behavioural Therapy for Hypersomnia (CBT-H) may be a useful adjunct to help patients develop coping strategies and improve daily functioning. Ultimately, clinicians should help patients understand that successful management often involves substantial lifestyle adjustments and realistic expectations, which may be confronting for some people. This requires sensitivity, empathy, and careful communication from the clinician.

Dr Aaron Schokman – *Narcolepsy: Is It Really Cataplexy?*

Dr Schokman (Research Fellow, University of Sydney) shared his lived experience with cataplexy and also gave a clear and practical presentation on how to identify genuine cataplexy and avoid common diagnostic errors. His talk built on the theme running throughout the symposium - that precision and honesty in diagnosis are essential when dealing with lifelong hypersomnolence disorders.

His slide, adapted from *Dauvilliers, Y., & Barateau, L. (2017). "Narcolepsy and other central hypersomnias." Continuum: Lifelong Learning in Neurology, 23(4), 989–1004* contrasted the key features of typical (genuine) cataplexy with those of atypical or pseudo-cataplexy (not cataplexy).

Typical cataplexy:

- Triggered by a clear, positive emotion such as laughter, telling a joke, or surprise.
- Frequent attacks (multiple per day – per week).
- Brief in duration (less than 30 seconds, unless the trigger persists).
- Consciousness is preserved (people do not 'faint' or 'pass out').
- Generalised or partial, involving the face, head, neck, or knees buckling - with or without falling.

Atypical/pseudo-cataplexy:

- Rare attacks (less than 1 per year, when not treated).
- No further episodes occur despite the absence of treatment.
- Long-lasting episodes (more than 2 minutes).
- Loss or alteration of consciousness.
- Unilateral or asymmetrical localisation, e.g., affecting only one side or one limb.
- No emotional trigger (except occasionally in children)
- Relatives or people nearby do not notice the episodes.
- Only triggered by *negative* stimuli and emotion (e.g., anger, fear, or stress).
- Prodromal symptoms of any kind after the episode, such as feeling warm, sweating, dizziness, tinnitus, visual or auditory impairment, nausea, or tingling of the extremities.

Dr Schokman noted that he does not like the terminology "atypical/pseudo-cataplexy" because the features listed above under this label are evidence that you *do not* have cataplexy, not that it's 'not typical cataplexy'. This distinction is important because mislabeling non-cataplectic phenomena as cataplexy can lead to an incorrect narcolepsy diagnosis.

He emphasised that clinicians must be transparent about diagnostic uncertainty. He noted that objective testing is key; for cataplexy, this means either CSF orexin/hypocretin testing or video evidence of a cataplexy event triggered by strong emotion. Without such evidence, it is impossible to confirm with confidence that a person has genuine cataplexy.

One of Dr Schokman's strongest messages was about the *profound personal consequences* of diagnostic labelling. He reminded clinicians that a diagnosis of narcolepsy, particularly when cataplexy is involved, often becomes a defining part of a person's identity. People shape their lives, relationships, and communities around it - joining support groups, forming friendships, and finding belonging through shared experience. It can be quite a shock for someone to learn that they do not actually share the same experience with people who have genuine narcolepsy and cataplexy.

He cautioned that when such a diagnosis is later questioned or withdrawn, the emotional and practical impact can be immense. Patients are suddenly faced with having to tell their families, friends, and employers that they no longer have the condition they once believed explained their struggles. Many must also inform agencies such as the NDIS or other support providers that have granted accommodations or assistance based on that diagnosis. He urged clinicians to recognise the gravity of this situation: when diagnosing lifelong neurological conditions, doctors must proceed with care, humility, and honesty about the limitations of current testing.

Poster Highlight: *Evaluating the Importance of 7-Day Actigraphy and Sleep Diaries Prior to MSLT*

Presenter: Dr Lucy Pillay, Sleep Fellow at Flinders Medical Centre

Dr Pillay addressed one of the simplest yet most crucial aspects of diagnostic accuracy: verifying adequate sleep before the MSLT.

Her study demonstrated that combining 7-day actigraphy with a sleep diary improves diagnostic reliability by confirming that patients are neither sleep-deprived nor circadianly misaligned at the time of testing.

Highlights included:

- Actigraphy (wrist-worn devices) offers multi-day, real-world monitoring of sleep/wake patterns, providing greater external validity than a single night's polysomnography and next-day MSLT.

- The requirement of ≥7 days of actigraphy plus a sleep diary before in-lab testing helps ensure patients are not sleep-deprived or have a misaligned circadian phase, thereby improving the accuracy of diagnosis.

- Dr Pillay highlighted that many clinicians still rely solely on the MSLT or a brief sleep-study snapshot, which can increase the risk of misdiagnosis when insufficient sleep or irregular sleep–wake patterns are not taken into account.

Her conclusions reinforced guidelines from the American Academy of Sleep Medicine and the Australasian Sleep Association recommending that actigraphy should precede MSLT for suspected hypersomnolence disorders - a practice still not commonly followed in Australia. Implementing this standard could substantially reduce false-positive or ambiguous MSLT results, especially in younger adults and shift workers.

Neuroscience Symposium – *New Perspectives in Sleepiness: Modern Applications of EEG in Hypersomnolence Research*

This session explored how advanced EEG techniques are deepening our understanding of sleep-wake regulation in hypersomnolence disorders.

Dr Scott Coussens - EEG Signature of Idiopathic Hypersomnia

Dr Coussens (Sleep Laboratory Manager at Women's and Children's Hospital SA), shared interesting evidence from *"EEG Signature of Idiopathic Hypersomnia: Insights from Sleep Microarchitecture and Hypnodensity Metrics." Arthur Le Coz, Isabelle Arnulf, et al. 2025*

People with IH with long sleep experience daytime hypersomnolence despite prolonged sleep time and normal sleep macrostructure. Because many describe their sleep as non-restorative, this study investigated whether subtle abnormalities in sleep architecture might explain their symptoms - and found that, not surprisingly, the sleep in people with IH is not abnormal.

The researchers demonstrated that participants with IH do not exhibit hybrid sleep states.*Hybrid sleep states* refer to situations where the brain simultaneously displays features of two or more vigilance states. For example, this happens in Narcolepsy Type 1. Cataplexy is caused when REM sleep features, ie: muscle atonia (paralysis), suddenly intrude into wakefulness. In contrast, EEG recordings in IH showed clear, well-defined transitions between wake and sleep stages, with no evidence of state mixing. In simple terms, the sleep of people with IH is stable and physiologically normal, not fragmented or dissociated.

Instead, IH appears to reflect an abnormally strong and persistent sleep drive - a problem of sleep pressure regulation, rather than state-boundary instability (the hallmark of narcolepsy). Participants showed normal but intensified markers of deep sleep, including higher slow-wave density, more frequent and clustered sleep spindles, and delayed arousal transitions. Because slow waves and spindles are usually indicators of high-quality sleep, their amplification in IH likely reflects an increased need for sleep and greater difficulty achieving full wakefulness.

This finding reinforces what many of us have long recognised: Idiopathic hypersomnia (with long sleep) is not "narcolepsy without the cataplexy." It represents a fundamentally different dysregulation

- one rooted in excessive, unrelieved sleep pressure, not REM instability.

Dr Julia Chapman – Orexin Agonists: A New Frontier

Dr Chapman (Postdoctoral Research Fellow, Conjoint Lecturer, Woolcock Institute of Medical Research) expanded the session by discussing the neurophysiological and clinical effects of orexin receptor agonists - a drug class now considered potentially *life-changing* for people with narcolepsy and potentially, idiopathic hypersomnia.

She presented EEG data demonstrating that these agents produce measurable, objective changes in brain activity associated with alertness and wakefulness:

- **Takeda TAK-925 (IV, danavorexton):** *Studied exclusively in Narcolepsy Type 1 (NT1)* produced rapid and profound wakefulness in participants with confirmed orexin deficiency (low CSF hypocretin-1). Reduced microsleeps and “probability of sleep”. EEG results showed reduced theta/delta power and increased beta/gamma activity, aligning with both subjective and objective improvements in alertness.

- **Takeda TAK-861 (oral, orepexreton):** Also *studied only in NT1,* reduced microsleep incidence and demonstrated sustained wake promotion and significant improvements in Maintenance of Wakefulness Test (MWT) performance, Epworth Sleepiness Scale (ESS), and improved vigilance measures.

- **Alkermes ALK-2680 (alixorexton)**: This compound, in contrast, is being studied across Narcolepsy Type 1, Narcolepsy Type 2, and Idiopathic Hypersomnia populations. Dr Chapman showed dose-dependent EEG effects - increased beta/gamma power (showing the brain was more active and alert) and decreased theta/delta power (reflecting reduced drowsiness) across all three diagnostic groups.

Dose-Response and Clinical Implications

Across all three studies, the EEG effects were dose-dependent - increasing with higher medication doses and aligning with participants’ self-reported improvements in alertness and daytime functioning.

Dr Chapman showed EEG heat-map images illustrating this clear dose-response pattern with ALK-2680 (alixorexton): higher doses led to stronger brain activity, greater wakefulness, and a lower tendency to fall asleep.

This effect was consistent across all groups studied (Narcolepsy Type 1, Narcolepsy Type 2, and Idiopathic Hypersomnia) demonstrating that stimulation of the orexin system can be beneficial even in individuals without an orexin/hypocretin deficiency. These findings further support the therapeutic potential of orexin pathway modulation, with measurable benefits observed across objective, subjective, and physiological outcomes.

Orexin Agonists in the Pipeline

Dr Chapman provided a comprehensive overview of the clinical pipeline:

Company	Molecule	Clinical Stage & Highlights
Takeda	TAK-861 (Oral orepexreton)	Positive Phase 3 (NEJM, May 2025); submission to FDA/EMA/TGA expected 2026.
	TAK-360	Phase 2 for NT2 & IH is ongoing.
Alkermes	ALK-2680 (Alixorexton)	Positive Phase 2 across NT1, NT2, and IH; presented at *World Sleep 2025.*
Eisai	E2086	Positive Phase 1 (NT1) data presented at *World Sleep 2025.*
Centessa/Orexia	ORX-750	Phase 2a trials underway for NT1, NT2, and IH.
Bioprojet/Harmony Biosciences	B1.15205	Positive preclinical results in NT1; Phase 1 planned.
Jazz Pharmaceuticals	JZP-441 (DSP-0187)	Phase 1b ongoing; earlier NT1 arm paused.
Merck	MK-6552	Program terminated.

> "*All of these companies have multiple orexin-2 receptor agonists in development*," she noted - emphasising how competitive and rapidly evolving this therapeutic class has become.

Looking Ahead

Dr Chapman concluded by noting that the ability to experimentally manipulate the orexin system - using both agonists and antagonists - may provide unique insights into the neurobiological mechanisms that regulate sleep and wakefulness.

This research is also helping define downstream pathways (noradrenergic, dopaminergic, serotonergic, histaminergic) that interact with orexin activity, paving the way for future dual orexin agonists that could deliver even more natural, sustained wakefulness.

Dr Chapman highlighted that research into orexin agonists is advancing our understanding of how the brain regulates wakefulness, not just how to restore it when impaired.

Vibrance-3: Safety and Efficacy of Alixorexton (ALK-2680) in Idiopathic Hypersomnia

Presenter: Prof Ron Grunstein, Head of the Sleep & Circadian Research Group at the Woolcock Institute of Medical Research

Professor Grunstein presented new data and design insights from Vibrance-3, a Phase 2, randomised, double-blind, placebo-controlled trial investigating Alkermes' oral orexin-2 receptor agonist, ALK-2680 (alixorexton), for the treatment of Idiopathic Hypersomnia (IH).

Study Overview

Idiopathic Hypersomnia is characterised by excessive daytime sleepiness, prolonged nocturnal sleep, and sleep inertia that are not relieved by extended sleep. Current treatments act indirectly on alertness pathways; ALK-2680 instead targets the orexin (hypocretin) system, a mechanism central to maintaining wakefulness.

Vibrance-3 aims to assess both efficacy and safety of once-daily alixorexton over eight weeks of treatment.

- **Primary endpoint:** Change in Epworth Sleepiness Scale (ESS) score from baseline to week 8.

- **Secondary endpoints:** Change in Idiopathic Hypersomnia Severity Scale (IHSS) score, clinician- and patient-reported outcomes (CGI-S, PGI-S), Maintenance of Wakefulness Test (MWT), safety and tolerability measures (vital signs, ECG, adverse-event monitoring), and exploratory EEG-based sleep-stage analyses.

Design and Population

- **Randomisation:** Participants are assigned 1 : 1 : 1 : 1 to 10 mg, 14 mg, or 18 mg alixorexton or placebo.

- **Treatment period:** Eight weeks, preceded by a ≤ 2-week screening and wash-out.

- **Planned enrolment:** ≈ 96 adults (≤ 70 years; BMI 18–40 kg/m²) meeting ICSD-3 criteria for IH and with residual sleepiness (ESS > 12).

- **Exclusions:** Significant comorbid sleep, cardiovascular, or psychiatric disorders.

Participants completing the trial may roll over into a long-term, open-label extension (Vibrance-3-LTS; NCT06767683) to evaluate sustained benefit and tolerability.

Significance

This is one of the first controlled trials to directly evaluate an orexin-2 receptor agonist in IH. Phase 1 and 2 data from earlier Vibrance studies in narcolepsy have already demonstrated robust improvements in wake maintenance and reductions in microsleeps.

Recruitment for the Vibrance-3 IH arm has commenced at the Woolcock Institute (Sydney) for participants in NSW and QLD, Monash University (Melbourne), and the Adelaide Institute of Sleep Health.

Professor Grunstein emphasised that if results replicate prior findings, ALK-2680 could become the first oral therapy to restore orexin-driven wakefulness in IH, addressing the disorder's underlying neurochemical imbalance rather than compensating for it symptomatically.

This development marks a turning point for people living with IH - introducing, for the first time, a medication designed to act on the same pathway that naturally sustains alertness and stabilises the sleep–wake cycle.

Those living in NSW or QLD, email: hypersomnolence@woolcock.org.au if you are interested in participating in this study.

If you're in South Australia, you can contact Alison Teare at alison.teare@flinders.edu.au.

And, if you're in Victoria, reach out to: trials@monashhealth.org

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Poster Highlight – *A Novel Dietary Protocol to Manage Symptoms of Hypersomnolence*

Presenter: Dr Elizabeth Machan, Woolcock Institute of Medical Research / University of Sydney

Dr Machan presented a poster highlighting a new clinical study investigating the feasibility and tolerability of a Whole Food Ketogenic Diet (WFKD) as a potential way to improve symptoms in people living with Narcolepsy Type 1 (NT1), Narcolepsy Type 2 (NT2), and Idiopathic Hypersomnia (IH).

Study Background and Rationale

The study explores how nutritional interventions targeting inflammation and metabolic regulation may influence daytime alertness and energy stability in hypersomnolence disorders. The ketogenic diet limits daily carbohydrate intake to 30–50 grams, inducing nutritional ketosis, with macronutrient distribution of 5–10% carbohydrates, 5–20% protein, and 70–80% fat.

Previous research (Field et al., *Nutritional Research Reviews*, 2021) showed that low-carbohydrate or ketogenic diets led to an 83% improvement in neurological outcomes and a 71% reduction in inflammation, outcomes highly relevant to disorders characterised by fatigue, inflammation, and altered energy metabolism.

The comparator group follows a Whole Food Diet (WFD) aligned with the Australian Guide to Healthy Eating, consisting of 45–65% carbohydrates, 20–35% fat, and 15–25% protein. Whole food diets have a higher glycaemic load and can lead to blood glucose spikes, which may exacerbate fatigue and sleepiness in those with central hypersomnolence disorders.

Study Design and Methods

This 12-week feasibility trial includes adults with NT1, NT2, or IH. Following screening and baseline assessments, participants first complete 1–3 weeks on a standardised Whole Food Diet before being randomised to continue on the Whole Food Diet or transition to the Whole Food Ketogenic Diet for the remaining 9 weeks.

The structured protocol includes:

- Comprehensive baseline testing: PSG, MWT, actigraphy, metabolic profiling, pathology, and quality-of-life (QOL) surveys.
- Five consultations with a nutritionist, incorporating both in-person and telehealth sessions (weeks 3, 6, 8, 10, and 12).
- Nutritional education and removal of ultra-processed foods.
- Ketosis monitoring twice weekly using urinary and capillary ketone testing.
- Post-intervention evaluation at 12 weeks, repeating baseline measures and semi-structured interviews.

Study Aims and Implications

The trial aims to evaluate the feasibility, adherence, and symptom impact of ketogenic versus whole food diets in people with hypersomnolence disorders. By integrating metabolic and sleep physiology data, researchers hope to better understand how energy metabolism and inflammation contribute to persistent sleepiness.

Dr Machan noted that hypersomnolence conditions may involve not only disrupted sleep–wake regulation (as seen in narcolepsy) but also impaired energy utilisation at a cellular level. Nutritional strategies that stabilise glucose and reduce inflammation could therefore provide a meaningful new avenue of symptom management - one that aligns with patient interest in non-pharmacological interventions.

The presentation closed by recognising the project's collaborative, multidisciplinary design spanning sleep medicine, dietetics, pharmacology, neuroscience, and lived experience advocacy.

If you live in Sydney and are interested in participating in this study, please reach out to Dr Rowena Field - rowena.field@sydney.edu.au or Francis Cheong - francis.cheong@woolcock.org.au

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REM Intruder: Sleep-Wake Instability in Narcolepsy.

Presenter: Dr Sheila Sivam, Sleep Physician, Woolcock Institute of Medical Research

Dr Sivam explained how REM intrusion underpins hallmark symptoms of narcolepsy such as cataplexy, sleep paralysis, and hypnagogic hallucinations. She highlighted ongoing research at the Woolcock Institute mapping the neural networks involved in REM transitions. She emphasised the critical role of orexin deficiency in destabilising boundaries between sleep and wake.

Clinical Year in Review

Dr Sivam also delivered a concise, thoughtful overview of the year's advances in narcolepsy and IH research, integrating new neuroimaging and pharmacologic findings. Her talk elegantly tied together what the conference as a whole demonstrated - that the field is moving toward precision medicine informed by both biomarkers and lived experience.

Conclusion

This year's symposium reinforced many of the key principles I've long advocated for through Hypersomnolence Australia (HA), particularly the need for better communication between clinicians and patients, and more thoughtful, accurate diagnostic practices.

I echo the conversations around lexicon - the language used between doctors and patients. For years, I've wanted HA to collaborate with clinicians to develop a diagnostic checklist and question guide designed to help doctors ask the right questions in ways that patients can understand. This tool would not only guide clinicians toward more accurate diagnoses but also include examples of how patients may describe their experiences and what those responses might actually indicate. I hope the momentum from this symposium helps make that collaboration possible.

It is also vital for clinicians to recognise that people living with idiopathic hypersomnia and narcolepsy are often cognitively impaired when they attend medical appointments. Many experience brain fog, word-finding difficulty, and at times may still be in a state of sleep drunkenness or on the verge of sleep during consultations. Doctors need to understand that this impaired cognitive state can affect how patients describe their experiences. What might sound vague or inconsistent is often the result of impaired alertness, not a lack of insight or reliability. It's crucial that clinicians do not inadvertently invalidate a patient's lived experience simply because it doesn't align neatly with textbook definitions or their own expectations.

I strongly support the use of all available diagnostic tools, including actigraphy, sleep diaries, thorough clinical history, HLA testing, validated scales such as the Idiopathic Hypersomnia Severity Scale, and objective measures such as CSF analysis. The consequences of misdiagnosis are enormous. As highlighted throughout the hypersomnolence symposium, people often build their entire lives around their diagnosis - joining support groups, forming friendships, and shaping their identity around what they've been told is a lifelong neurological condition.

For some, discovering that they never had narcolepsy (with or without cataplexy) or idiopathic hypersomnia in the first place can be deeply distressing, confusing, embarrassing, and destabilising. This underscores how important it is for doctors to be transparent about diagnostic limitations and honest about uncertainty. When doctors fail to do this, it often falls to patient organisations to explain what the diagnosis means, clarify the limitations of current diagnostic tools, and help patients understand when their diagnosis changes, conversations that should be taking place within a clinical setting.

It is not the purpose of organisations like Hypersomnolence Australia to manage this kind of emotional fallout, yet it's something we are increasingly faced with. What is often overlooked is that this distress is not limited to patients - it also affects the volunteers within HA, who are left carrying the emotional burden of conversations that, ideally, should be had between the patient and their treating doctor, and in many cases involve professional psychological intervention and support. It's an extremely heavy responsibility for volunteers to have to explain diagnostic uncertainty, correct misinformation, and provide reassurance that should be delivered through appropriate professional channels. Greater transparency, consistency, and access to appropriate professional support could prevent much of this distress, helping to safeguard the wellbeing of both patients and lived experience volunteers.

I was also impressed by the broader content of the conference, particularly the advances shared in the orexin agonist trials, which offer real hope for people living with narcolepsy and idiopathic hypersomnia. Equally impressive was the innovative EEG research that is deepening our understanding of how these conditions affect the brain. Seeing such high-quality science in the idiopathic hypersomnia and narcolepsy space, and seeing it happening here in Australia, is genuinely exciting. I hope we continue to see even more of this calibre of research and discussion featured at Sleep DownUnder in the future.

As I often say, we still have a long way to go - but we've also come a very long way from where we were when I founded Hypersomnolence Australia in 2013. I would like to acknowledge and thank the few dedicated doctors who have remained committed to central disorders of hypersomnolence over the years, as well as those who have joined the journey along the way. Their continued focus on these complex and often overlooked conditions, when it would have been far easier to devote their efforts to more common sleep disorders, is something I deeply appreciate.

Ultimately, this symposium gave me hope that we are moving toward a more person-centred, transparent, and evidence-driven approach, one that values lived experience alongside clinical expertise. I hope that these discussions will inspire collaborative efforts to improve diagnostic clarity, communication, and, most importantly, the care and understanding of those living with narcolepsy and idiopathic hypersomnia.