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National Drug &
Alcohol Research Centre
The Difference is Research

An exploratory analysis of actigraphy and sleep diaries in a methamphetamine withdrawal clinical trial

Liam S Acheson^{1,2,3}, Christopher Gordon⁴, Nadine Ezard^{1,2,3,5}, Nicholas Lintzeris^{5,6,7}, Adrian Dunlop^{5,8,9}, Jonathan Brett^{10,11}, Craig Rodgers², Anthony Gill², Michael Christmass^{12,13}, Rebecca McKetin¹, Michael Farrell¹, Steve Shoptaw¹⁴, Krista J Siefried^{1,2,3}

¹ The National Drug and Alcohol Research Centre (NDARC), the University of New South Wales, Sydney, Australia; ² Alcohol and Drug Service, St Vincent's Hospital Sydney, Sydney, Australia; ³ The National Centre for Clinical Research on Emerging Drugs (NCCRED), c/o the University of New South Wales, Sydney, Australia; ⁴ The Woolcock Institute, Sydney, Australia; ⁵ New South Wales Drug and Alcohol Clinical Research and Improvement Network (DACRIN), NSW, Australia; ⁶ The Langton Centre, South East Sydney Local Health District, Sydney, Australia; ⁷ Discipline of Addiction Medicine, the University of Sydney, Sydney, Australia; ⁸ Drug and Alcohol Clinical Services, Hunter New England Local Health District, Newcastle, Australia; ⁹ School of Medicine and Public Health, the University of Newcastle, Newcastle, Australia; ¹⁰ Clinical Pharmacology and Toxicology, St Vincent's Hospital Sydney, Sydney, Australia; ¹¹ St. Vincent's Clinical School, the University of New South Wales, Sydney, Australia; ¹² Next Step Drug and Alcohol Services, Perth, Australia; ¹³ National Drug Research Institute, Curtin University, Perth, Australia; ¹⁴ Department of Family Medicine, The University of California Los Angeles, Los Angeles, USA

Acknowledgements

The work presented here was conducted on Gadigal land, and I would like to pay my respects to elders past, present and emerging and extend that to any Aboriginal and Torres Strait Islander peoples here today.

I would also like to acknowledge and thank the community of people who have generously participated in this research, and the clinical staff at St. Vincent's Hospital Sydney.

Conflicts of interest

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Sleep and Methamphetamine

- **Regular MA use → lasting sleep disturbances**
- During MA withdrawal
 - **Hypersomnia** prevalent and extreme during “crash”
 - Both **insomnia and hypersomnia** apparent during withdrawal
- Sleep changes identified as **some of the most undesirable symptoms of withdrawal**
- Disturbed sleep is considered a **universal risk factor for relapse**

Current approaches to assessing sleep

- Questionnaires
 - E.g. Insomnia Severity Index, Pittsburgh Sleep Questionnaire
- **Not fit for purpose**
 - **Not validated** in substance using populations
 - Questions regarding satisfaction may **incorrectly imply healthy sleep**
- **Quantitative sleep assessment rare**
 - Only used in pre-clinical, observational studies
- **Can we measure sleep better?**



Actigraphy and daily sleep diaries

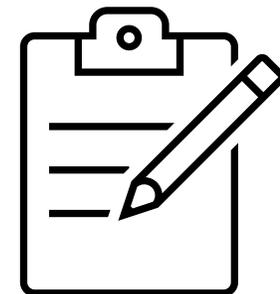
Actigraphy

- **Wrist worn device**
- Accelerometer to estimate sleep-wake
- **Comparable accuracy** to polysomnography (PSG)
- Worn over **days to weeks**



Consensus Sleep Diary

- **Daily reporting** of subjective sleep duration and quality
- **Developed in collaboration** with experts and consumers



Why this approach?

Advantages

- **Non-invasive**, low participant burden
- **Continuous monitoring** through whole sleep-wake cycle
- Can **compare subjective and objective** sleep
- **Cost-effective** when compared to PSG

Disadvantages

- **Does not include neurological measures**, commenting on sleep architecture difficult
- Requires **more financial resources than surveys**

Study Design

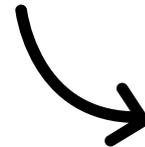
Primary Aim: To examine the **feasibility and utility** of **actigraphy and sleep diaries** during a clinical trial of lisdexamfetamine for the treatment of acute methamphetamine withdrawal

Setting: Inpatient withdrawal management unit,
St Vincent's Hospital Sydney, Australia

Trial protocol

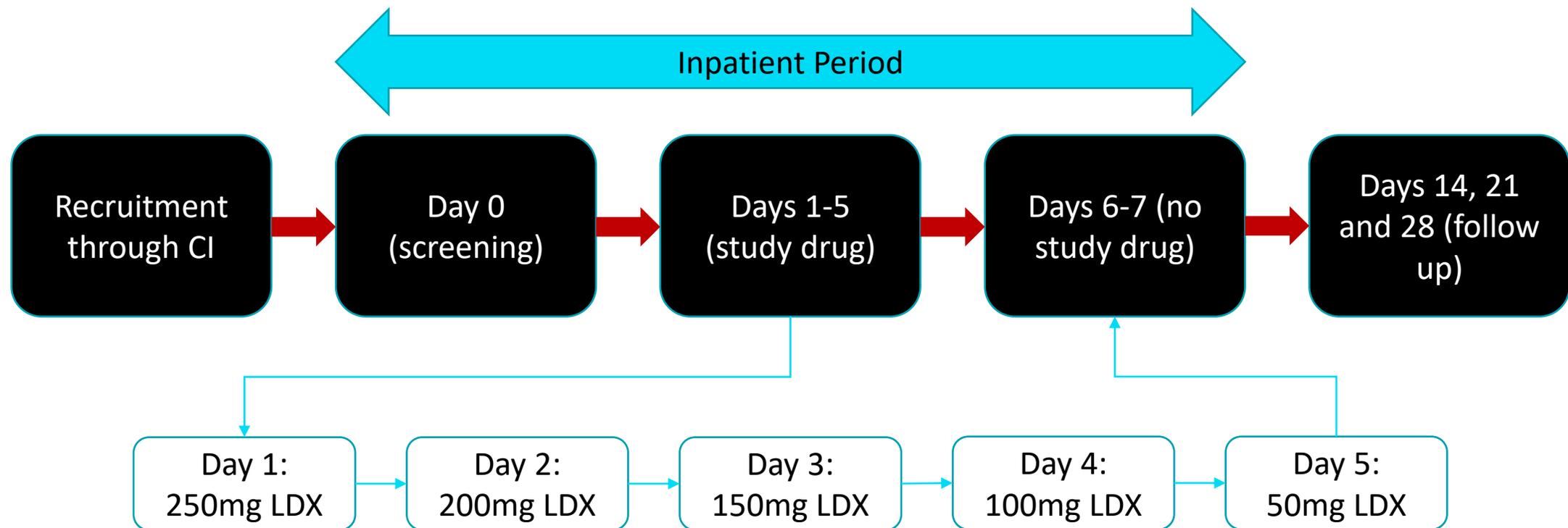


Clinical trial
results



Procedure – intervention

- LDX formulated in 50mg capsules
- Dispensed each morning under supervision
- All participants could also receive treatment as usual (symptom management, supportive care)



Procedure – sleep measures

Actigraphy

- Participants received the device **on admission**
- **Trained** in function and purpose
- Instructed to **wear constantly** through admission (could remove to shower)
- Returned device on discharge

Sleep Diary

- Modified Consensus Sleep Diary (removed items on work, exercise and medication)
- Self completed each morning during admission
- **~ 5 minutes per day**

Outcomes and measures

Feasibility and utility

- Proportion of available actigraphy data and completed sleep diary entries
- Participant experiences via semi-structured interviews

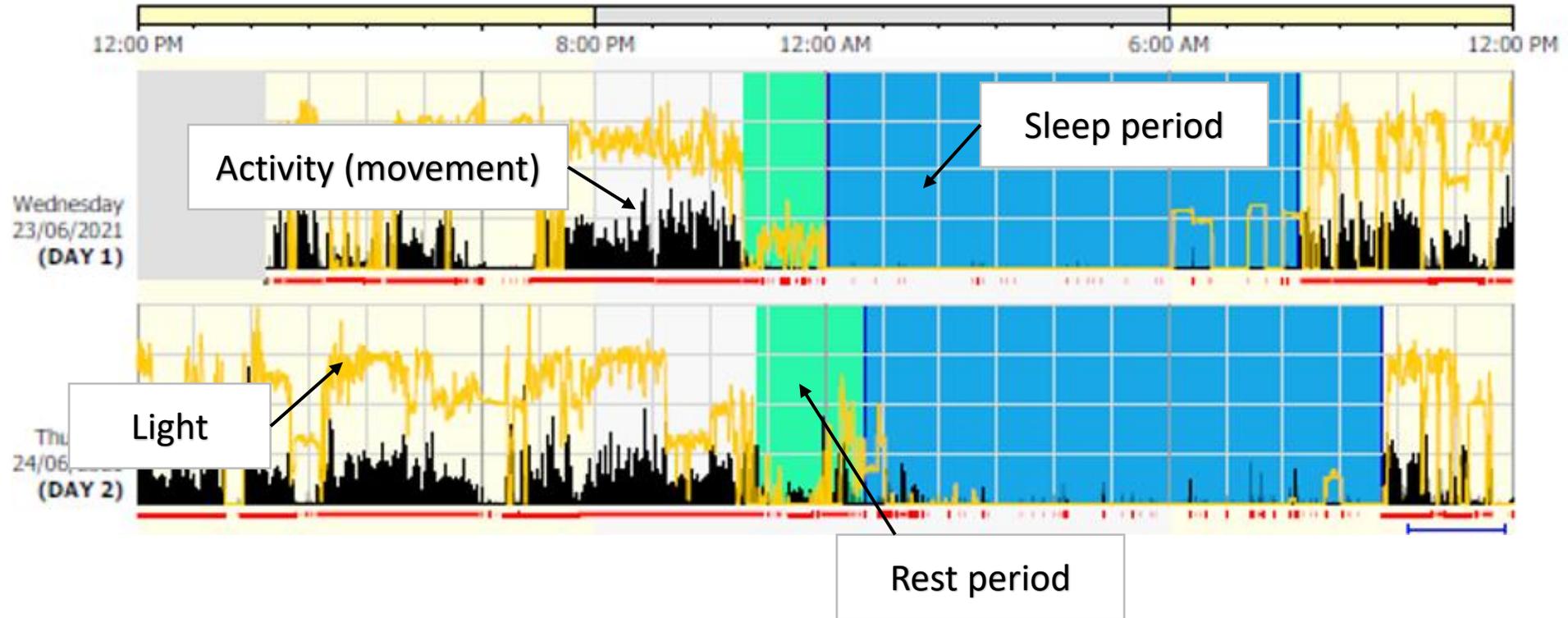
Differences in sleep outcomes between actigraphy and diaries

- Total sleep time, sleep onset latency, wake after sleep onset, sleep efficiency and subjective sleep quality

Sleep definitions

Term	Definition
Total Sleep Time (TST)	The total amount of sleep time scored during the total recording time, in minutes
Sleep Onset Latency (SOL)	The duration of time from attempting to fall asleep to falling asleep in minutes
Wake After Sleep Onset (WASO)	The total duration of wakefulness periods between initially falling asleep and finally waking in the morning in minutes
Sleep Efficiency	The ratio of total time asleep to the total rest interval expressed as a percentage
Sleep Quality	9-point Likert Scale (diary only)

Example actogram



Results: Demographics

n=10 participants recruited

- **37.1 (IQR 31.7-41.9) years old**
- 4 = heterosexual male, 5 = homosexual male, 1 = heterosexual female
- Had been **using MA for 13.6 years** prior to admission
- Over the 28 days prior to admission, our participants **used on 23/28 days**, and on a typical day would use **0.6g of MA per day**
- Mixed smoking and injecting
- Recent other substance use included **GHB (50%)** and **cannabis (50%)**. **No recent opioid use** was reported

Feasibility and utility

- 7/10 participants **wore the actigraph for the entire duration of their admission**
- 3/10 removed the device at some point
 - Once each
 - Average 21 minutes off-wrist (maximum time off-wrist 31 minutes)
 - **>99% on-wrist time**
- **All participants completed the CSD** each morning (no missing data)
- 8/10 participants completed qualitative interviews
 - **No participant** indicated the device was distracting or difficult to wear
 - Devices **did not impact ability to sleep** or receive medical care
 - Daily sleep diaries were **not considered onerous**

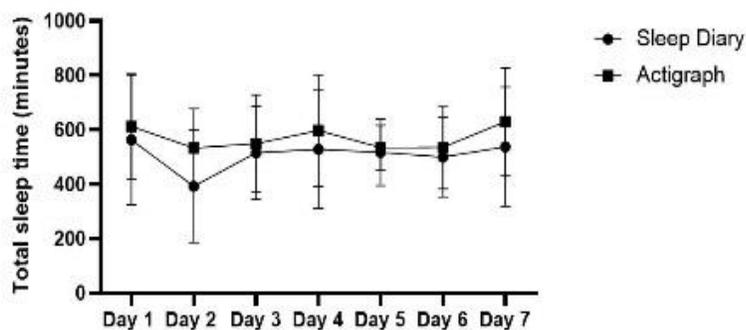
Mean summary sleep statistics across 7-day admission

	Sleep Diary (mean (SD))	Actigraph (mean (SD))	Effect size (mean difference (95% CI))	p-value
Total Sleep Time (min)	509.1 (184.3)	567.6 (162.1)	-58.5 (-101.4 to -15.7)	0.008
Sleep Onset Latency (min)	28.1 (53.3)	22.4 (29.4)	5.7 (-8.1 to 19.4)	0.410
Wake After Sleep Onset (min)	28.5 (43.3)	75.2 (53.9)	-46.6 (-59.3 to -33.9)	<0.001
Efficiency (%)	83.6 (16.0)	83.6 (9.6)	0.04 (-4.9 to 4.9)	0.986
Quality (1-9, lower = better)	4.4 (1.8)	*		

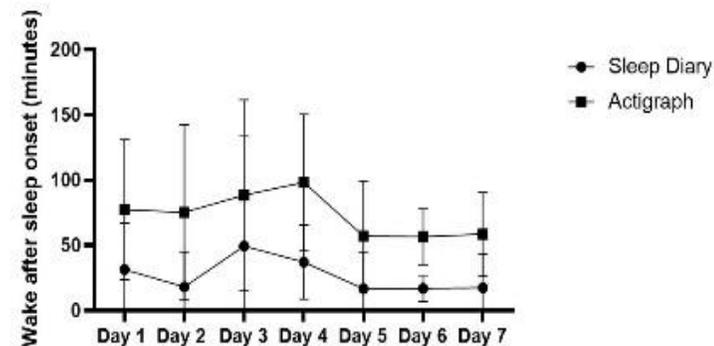
*; not available via actigraphy

Daily actigraphic and sleep diary data

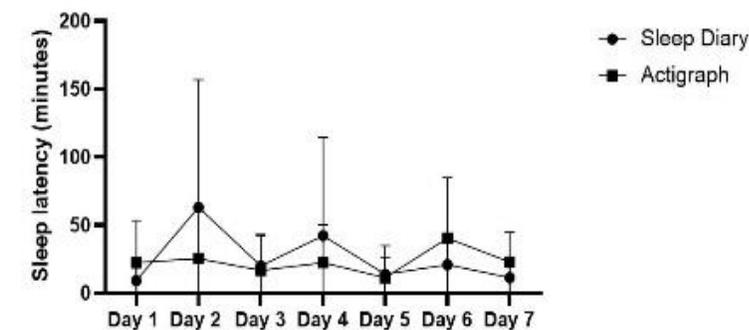
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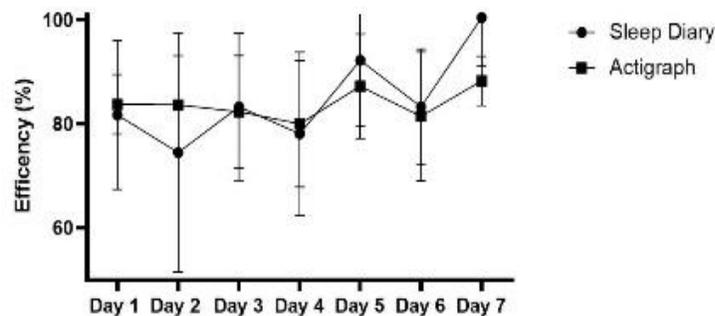
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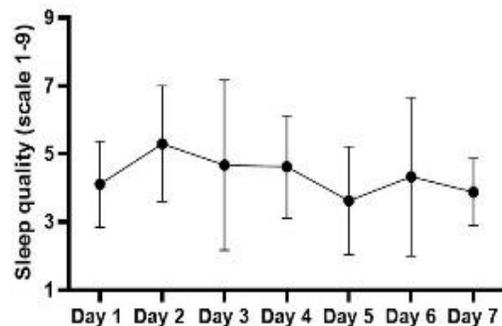
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2d.



2e.



Discussion

- Actigraphy and daily sleep diaries allows for **acceptable measurement of sleep-wake parameters, without impacting the delivery of therapeutic intervention or participant well-being**
- Limitations
 - **Investigational product** and **concomitant medications**
 - Lack of neurological measures
 - More expensive than questionnaires
- Methodology **acceptable** by participants
- Actigraphy appropriate for up to **30 days of continuous monitoring**
 - Scalable to **outpatient** and **community** applications

Discussion

- Participants **underestimated total sleep time and wake after sleep onset**
 - Expected and important
 - **“Paradoxical sleep”**
 - Subjectively perceived and objectively measured sleep are different
 - May indicate **reduced slow-wave sleep**
- Methodology allows for evaluation of sleep related treatment outcomes and longitudinal data collection
- Future studies should consider actigraphy and sleep diaries for monitoring of sleep wake outcomes

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Thank you!

For more information:

krista.siefried@svha.org.au

liam.acheson@svha.org.au