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# **Lisdexamfetamine for the management of acute methamphetamine withdrawal: Protocol for an open-label safety and feasibility study**

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## Background



- Australasia has the highest rate of amphetamine dependence worldwide
- In people who use methamphetamine (MA), daily and weekly use has increased from 9.3% in 2010 to 17% in 2019
- MA second most common drug of concern in Australian treatment settings, accounting for 26% of treatment episodes
- Abrupt cessation of MA → characteristic withdrawal symptoms

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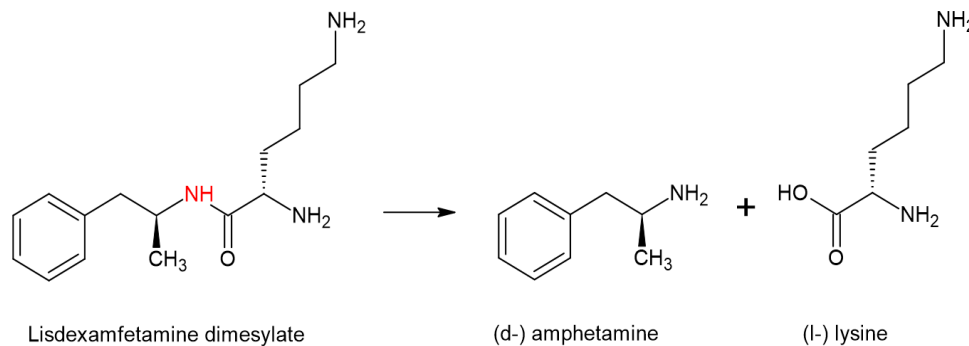
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## Rationale

- Ineffective treatment of withdrawal symptoms → high rates of relapse to use
- Reduction in withdrawal / craving severity → better treatment outcomes
- There is no evidence-based pharmacotherapy for the management of MA withdrawal
- Agonist-like therapies have shown promise
  - i.e. dexamphetamine
- Lacked efficacy

## Why lisdexamfetamine?

- Traded under Vyvanse® for ADHD / binge eating disorder
- Lisdexamfetamine (LDX) is an inactive prodrug of dexamphetamine, hydrolysed into dexamphetamine in whole blood
- LDX has slower onset and lower peak dopamine concentrations
- Lower abuse liability, less positive reinforcing effects compared to dexamphetamine
- Cannot be diverted



*Hydrolysis of lisdexamfetamine dimesylate to (d-)amphetamine and (l-)lysine*

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## Study Design and Aims

Open label, single arm clinical trial of a tapering dose regimen of LDX for management of acute MA withdrawal

Primary Aim:

To determine the **safety and feasibility** of delivering a five-day tapering dose regimen of LDX for the inpatient treatment of acute MA withdrawal

Secondary Aims:

- Acceptability
- Retention in care
- Changes in withdrawal / craving
- Sleep quality

Study design and procedures developed with **consumer consultation**

## Participants

n=15 adults presenting for admission for management of acute methamphetamine withdrawal at SVHS

Inclusion Criteria	Exclusion Criteria
<ul style="list-style-type: none"><li>• Adults over the age of 18 years</li><li>• Presenting to inpatient drug treatment services seeking treatment for acute MA withdrawal</li><li>• Methamphetamine use disorder as determined by an addiction medicine specialist according to DSM-5 criteria</li><li>• Last MA use within 72 hours of planned first study drug dose</li><li>• Have a positive urine drug screen for methamphetamines</li><li>• Willing and able to provide written informed consent</li></ul>	<ul style="list-style-type: none"><li>• Women lactating, pregnant or of childbearing potential who are not willing to avoid becoming pregnant during the study</li><li>• Expected concurrent withdrawal from alcohol, opioids, benzodiazepines, gamma-hydroxybutyrate or other gabapentinoids</li><li>• Known contradictions to lisdexamfetamine</li><li>• Medically significant condition which in the opinion of a study medical officer renders a patient unsuitable for the study</li><li>• Involuntary patients</li></ul>

Recruitment: Opportunistic - through Centralised Intake, treatment services or on admission

## Intervention

Lisdexamfetamine dimesylate

- Tapering dose starting at 250mg
  - Equivalent to approximately 74mg of dexamphetamine
- Once daily dosing

Study day (inpatient)	Lisdexamfetamine dose
Day 1	250mg OD
Day 2	200mg OD
Day 3	150mg OD
Day 4	100mg OD
Day 5	50mg OD

## Procedure



**Day 0:** Screening and baseline assessment

**Day 1 to Day 5:** Inpatient period, participants receive medication and undergo daily assessment of adverse events, treatment satisfaction, withdrawal and craving severity and sleep

**Day 6 to Day 7:** Inpatient period, participants receive no medication and undergo assessment of adverse events, treatment satisfaction, withdrawal and craving severity and sleep

Rescue medication: diaz/olanz available days 1-7

**Days 14, 21 and 28:** Outpatient telephone follow up to assess adverse events, access to wrap around health services, substance use



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# Novel Sleep Measures

- Sleep is poorly investigated in substance use related research
  - Point surveys
- Gold standard sleep measurement requires objective and subjective measurement over time
- No study to date has investigated sleep in this was in people who use or are withdrawing from stimulants
- In this study:
  - Continuous actigraphy
  - Daily sleep diary
- Proof of concept only

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## Conclusions

- First study to investigate LDX for the management of acute MA withdrawal
- If safe and feasible will inform development of a fully powered RCT
  - Consumer input
  - Novel sleep measures
- If effective, LDX has the potential to be the first pharmacotherapy for MA withdrawal

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# Thank You

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