CRACKS IN THE ICE

WELCOME TO THE CRACKS IN THE ICE WEBINAR SERIES
Current and promising treatment options for ice dependence

Professor Maarten van den Buuse, Professor Frances Kay-Lambkin and Dr Shalini Arunogiri

23rd July 2019
Overview

1. Effects of ice on the brain
2. Psychosocial and e-health treatment approaches
3. Innovations in Pharmacotherapies for Methamphetamine Use Disorder
4. Q&A
Part 1: Effects of ice on the brain

Professor Maarten van den Buuse
La Trobe University,
School of Psychology and Public Health, Melbourne
The human brain

- weighs about 1.5 kilograms.
- volume is 1.1 - 1.3 cm³ = 1.1 - 1.3 litre
- makes up about 2 percent of a human's body weight.
- uses 20-25% of your oxygen and glucose supply.
- consistency is similar to tofu.
- contains about 100 billion nerve cells (neurons) - the ”gray matter“ → 100,000,000,000 (15x global population)
- Each neuron may be connected to as many as 10,000 other neurons.
- contains billions of nerve fibers - the “white matter”

(www.livescience.com & www.bioscience.com)
Neurons communicate

- Communication between neurons is via electrical impulses and chemical transmission.
- Communication between neurons is done via the release of chemicals (neurotransmitters) into the gap between nerve cells (synapse).
- Neurotransmitters diffuse across the synapse to activate response sites (receptors) on the next cell.
- There are many different neurotransmitters, including dopamine, noradrenaline and serotonin.
Neurotransmitters

Pleasure
Reward
Motivation/Drive
DOPAMINE
Mood
Cognitive function
Attention
Apetite
Sex
Aggression
Alertness
Concentration
Energy
Anxiety
Impulse
Irritability
NORADRENALINE
Obsessions
Compulsions
Memory
SEROTONIN
Pleasure
Reward
Motivation/Drive
www.deplin.com/LifeWith Depression/Causes
Drugs as ‘imposters’ of neurotransmitters

- Dopamine
- Noradrenaline
- Amphetamine
- Methamphetamine
Drugs as ‘imposters’ of neurotransmitters

Metamphetamine
Acts on several neurotransmitter systems:
• Dopamine
• Noradrenaline
• Serotonin
Methamphetamine in the brain

To watch a video about this topic, please use the link below.

https://youtu.be/T-duk-PiIXo
Methamphetamine reaches many parts of the brain and lingers there for a long time

(Fowler and others, NeuroImage 2008)

Methamphetamine peaks fast but clears slower than cocaine
Chronic use of methamphetamine

- Decreased number of neurons in several parts of the brain
- Reduced numbers of connections between neurons
- Decreased levels of dopamine and serotonin transporters

- Cognitive effects
  - Attention
  - Judgement
  - Problem solving
  - Memory
  - Psychotic symptoms
Methamphetamine effects recover with prolonged abstinence (Volkow and other, 2001)

Methamphetamine effects recover with prolonged abstinence

(Volkow and other, 2001)
Meth effects are variable

- **Biological:** Changes in the brain’s pleasure/reward system are modulated by multiple other systems and proteins in the brain.

- **Genetics:** Individuals with a first-degree relative, such as a parent or sibling, who are addicted to a substance such as meth, are at higher risk for developing addictions later in life.

- **Age:** Individuals who begin to abuse drugs at earlier ages are at a greater risk.

- **Environmental:** Stress (housing, family, life events) contribute to risk for developing addictions.
Research into methamphetamine effects in the brain: genes, proteins

Proteomics and bio-informatics
Meth effects are variable: questions

- **Biological**: can treatments that affect other neurotransmitter systems reduce the harm associated with meth in the brain?

- **Genetics**: can we predict that some individuals are more sensitive to the harmful effects of meth than other?

- **Age**: can we understand what it is in the adolescent/young adult brain that increase vulnerability to the harmful effects of meth?

- **Environmental**: how do stress and other environmental factors exacerbate the harmful effects of meth?
Part 2: Psychosocial and e-health treatment approaches

Professor Frances Kay-Lambkin
Crystal Methamphetamine

• Effects of crystal methamphetamine directly.
• Crystal methamphetamine acts to increase psychiatric symptoms
  • Psychostimulants are somewhat unique, because they are more likely to induce psychosis than other illicit drugs.
  • Depression, anxiety, suicidal ideation, dysphoria and cognitive deficits are commonly reported.
• People with mental health problems may continue to use crystal methamphetamine to attenuate psychiatric symptoms
• Active use of substances can substantially interfere with psychiatric pharmacotherapies
• Act to negatively affect treatment engagement.

Treatment approaches

- Pharmacotherapies have typically been used in combination with psychosocial treatments for methamphetamine use.
  - Aim of increasing treatment engagement and retention, managing withdrawal, maintenance or relapse prevention treatment.

- Psychosocial treatments show promise.
  - Psychotherapy, psychoeducation and relapse prevention.
  - Focus on abstinence and reducing comorbid problems.
  - Treatment retention can be difficult.

Psychological treatment

- To date, strongest evidence for efficacy for people using methamphetamine, and is the primary treatment available.
  - Contingency management to increase abstinence and decrease crystal methamphetamine-related risk behaviours.
  - Cognitive behavior therapy to reduce crystal methamphetamine use and manage comorbid mental health symptoms
  - Motivation enhancement training to encourage treatment engagement and motivation for change.

CBT/MI for Stimulants

Baker et al. (2005), Addiction, 100, 367-378

- First study of psychosocial treatment for methamphetamine (stimulant) use – N=214.

- Control: self-help booklet

- 2-sessions: motivational interview, behavioural self monitoring and case formulation (session 1) + coping with cravings and lapses (session 2)

- 4-sessions: session 1 + session 2 + controlling thoughts about use (behavioural activation, cognitive restructuring, session 3) and relapse prevention (including refusal skills, session 4).

CBT/MI for Stimulants

Abstinence rates

Control: 17.6%
1-session: 21.6%
2-sessions: 33.8%**
3-4-sessions: 37.9%**

• Significantly higher abstinence rate (p<.01) among treatment group (verified by random urine screens)

Baker et al. (2005), Addiction, 100, 367-378
But…

At 6-month follow-up, 53.6% of the sample were still using at least weekly.

Baker et al. (2005), Addiction, 100, 367-378
Offers unprecedented opportunities to increase translation of health (and mental health) behaviour change interventions into real world settings...including 24/7 access to interventions
Breaking the Ice

- Funded by the Commonwealth Department of Health and Ageing (AUSTRALIA)
- Adapt face-to-face interventions
- Randomised controlled trial
A randomised controlled trial of a web-based intervention for users of amphetamine-type stimulants: Six month outcomes

Robert J Tait¹,2, B.Sc (Hons), Ph.D; Rebecca McKetin³, Ph.D; Frances Kay-Lambkin⁴,⁵, Ph.D; Bradley Carron-Arthur², BPsysch (Hons); Anthony Bennett², BAppSc; Kylie Bennett², BSc, BA (Hons); Helen Christensen²,⁶, PhD; Kathleen M Griffiths², PhD.

¹National Drug Research Institute, Faculty of Health Sciences, Curtin University, Perth, Australia
²National Institute for Mental Health Research, The Australian National University, Canberra, Australia
³Centre for Research on Ageing, Health and Wellbeing, The Australian National University, Canberra, Australia
⁴National Drug and Alcohol Research Centre, University of New South Wales, Sydney, Australia
⁵Centre for Translational Neuroscience and Mental Health, University of Newcastle, Newcastle, Australia
⁶Black Dog Institute, University of New South Wales and Prince of Wales Hospital, Sydney, Australia
Weighing it all up – Changing your drug use

Now have a look at your list of positives and negatives about changing your drug use.

How important are each of these reasons and negatives to you personally?
If '0' was 'not important at all' and '10' was 'very important' what number would you give them?

Use the sliders to rate how important each item is to you:

<table>
<thead>
<tr>
<th>Good things about change</th>
<th>Importance (0-10)</th>
<th>Not so good things about change</th>
<th>Importance (0-10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I would have more money</td>
<td>9</td>
<td>It would be hard to cope with withdrawal</td>
<td>5</td>
</tr>
<tr>
<td>I would feel healthier</td>
<td>9</td>
<td>I would feel low all the time</td>
<td>5</td>
</tr>
<tr>
<td>I would be proud of myself</td>
<td>5</td>
<td></td>
<td>5</td>
</tr>
<tr>
<td>I could get in control of my life again</td>
<td>5</td>
<td></td>
<td>5</td>
</tr>
</tbody>
</table>
Practical steps you can do now

Next, what might have to happen in your life so that making a change to your stimulant use becomes a top priority? If you had a magic wand, what would you wave away in your life right now, to make it easier for you to change your using habits?

Might you have to keep yourself away from the temptation of parties and social events for a while? Might you have to clean out your stash of drugs or gear so that you do not have any left at home to tempt you? Maybe you can start to remove temptation from your life right now?

So, take a few minutes to think about what some of these things might be and type them in the space below.

Practical things I can do right now
What are some practical things you could do?

Jess took on board a lot of suggestions that the psychologist discussed with her about her quit attempt. She made contact with some of her friends and planned some things in the week ahead to keep her occupied like going to the movies and starting Zumba classes.
Results…

ASSIST ATS score

- BTI
- Control

<table>
<thead>
<tr>
<th>Months</th>
<th>0</th>
<th>3</th>
<th>6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Score</td>
<td>18</td>
<td>16</td>
<td>14</td>
</tr>
</tbody>
</table>

- Months 0
- Months 3
- Months 6
Results...

‘Exposure’ completing ≥ 1 modules (n=51): 0 modules (n=30): control (n=79)

- Intended help-seeking ($p=.014$)
- Actual help-seeking ($p=.034$)
- Days out of role ($p=.007$)
I mainly smoke ice with friends when we party at the weekend. I think that the scare campaign about ice is just media lies – my experiences have been completely different. Me and my friends would never become the “scabby, on the verge of crazy, violent meth heads” that you see on television. The first time I used it was great and I've only had good experiences since then. We just want to have fun on the weekends.
“If we can provide support to people from a young age we can help...”
...BUT THE IMPACT CAN BE MUCH GREATER

https://cracksintheice.org.au
Do you think YOU could be helped in this situation?

“It would have been nice to have someone to talk to about what was going on. Someone who could give me strategies to help cope and to help the person with the addiction.”

“Easier to access support services.”

“I think an online support group would be good as could be anonymous and share strategies. It's hard to talk about your son’s ice addiction to family friends and colleagues or explain the exhaustion and grief you feel.”
www.ffsp.org.au
Access code XJ91

DASHBOARD

The Family and Friend Support Program

Other peoples stories  My results  About me  Toolbox  Cracks in the ice
People using crystal methamphetamine can and will engage in psychological treatment.

Psychological treatment needs to target common comorbidities associated with crystal methamphetamine use.

Brief CBT/MI and eHealth interventions are effective in this population.
  - Can improve readiness to change AND treatment engagement
  - 24/7 access, repeated visits over time.

Support programs for family members and friends are critical and available.
Collaborators

Robert Tait (Curtin University)
Rebecca McKetin (Curtin University)
Amanda Baker (the University of Newcastle)
Nicole Lee (360Edge)
Richard & Gill Velleman (Velleman Consultancy & University of Bath)
Maree Teesson (University of Sydney)
Nicola Newton (University of Sydney)

Jenny Geddes (the University of Newcastle)

The Cracks in the Ice team

Funders: Commonwealth Department of Health + NSW Ministry of Health
Part 3: Innovations in Pharmacotherapies for Methamphetamine Use Disorder

Dr Shalini Arunogiri
<table>
<thead>
<tr>
<th>PHYSICAL SYMPTOMS</th>
<th>COMEDOWN</th>
<th>WITHDRAWAL</th>
<th>REMAINING SYMPTOMS</th>
<th>PSYCHOLOGICAL SYMPTOMS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exhaustion / low energy</td>
<td>Depression / anxiety</td>
<td>Strong urges to use</td>
<td>Strong urges to use</td>
<td></td>
</tr>
<tr>
<td>Increased sleep</td>
<td>Irritability</td>
<td>Mood swings</td>
<td>Mood swings</td>
<td></td>
</tr>
<tr>
<td>Increased appetite</td>
<td>Paranoia</td>
<td>Anxiety</td>
<td>Anxiety</td>
<td></td>
</tr>
<tr>
<td>Restlessness</td>
<td>Amotivation</td>
<td>Boredom</td>
<td>Boredom</td>
<td></td>
</tr>
<tr>
<td>Strong cravings</td>
<td>Anhedonia</td>
<td>Cravings</td>
<td>Urges to use</td>
<td></td>
</tr>
<tr>
<td>Sleep difficulties</td>
<td>Suicidal ideation / behaviour</td>
<td>Sleep returns to normal</td>
<td>Mood improves</td>
<td></td>
</tr>
<tr>
<td>Nightmares</td>
<td></td>
<td>Activity level returns to normal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aches, pains and stiffness</td>
<td></td>
<td>General health improves</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headaches</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Pharmacotherapy for amphetamine dependence: A systematic review

Nicole K. Lee, Linda Jenner, Angela Harney, Jacqui Cameron

Results: A total of 49 studies investigating 20 potential pharmacotherapies were eligible for inclusion. Of these, 35 studies related to 33 level II quality randomized controlled trials (RCTs). Five medications were subject to multiple RCTs. Four of these medicines demonstrated some limited evidence of benefit for reducing amphetamine use: methylphenidate (as reported in three studies), buprenorphine (in three studies), modafinil (two studies), and naltrexone (one study). Four RCTs of dexamphetamine suggest its benefit on secondary outcomes such as treatment retention, but not for reducing amphetamine use. Six other medicines indicate the potential for efficacy, but the number of studies is too small to draw conclusions.
Medication Treatment - MA Dependence

- Medication
  - No evidence for medication treatments for MA withdrawal or dependence
    (Lee et al, 2018; Morley et al, 2017)

- 33 Level II quality RCTs--- overall no medication consistently effective
Medication Treatment - MA Dependence

- Following four medications suggest limited evidence of benefit
  - Methylphenidate
  - Modafinil
  - Bupropion
  - Naltrexone

- Many other medications may have a role in managing symptoms on a case by case basis
  e.g. mirtazapine; dexamphetamine
  (retention, not reducing use)

- Current Phase III multisite trial - Lisdexamfetamine

- Caution re: side-effects
- Caution re: risks of misuse and diversion
  esp. stimulants
Table 6. Pharmacological management of methamphetamine dependence

<table>
<thead>
<tr>
<th>MEDICATION</th>
<th>NUMBER OF TRIALS</th>
<th>DOSE RANGE</th>
<th>ABSTINENCE</th>
<th>REDUCED USE</th>
<th>CRAVING</th>
<th>TREATMENT RETENTION</th>
<th>COMMENTS</th>
<th>REFERENCES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antidepressants</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bupropion</td>
<td>5</td>
<td>150mg twice daily</td>
<td>?</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>Low treatment adherence; significantly higher abstinence in adherent versus non-adherent participants, particularly in people using methamphetamine less frequently.</td>
<td>[146, 159-160]</td>
</tr>
<tr>
<td>Mirtazapine</td>
<td>1</td>
<td>30mg</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>Reduction in use, and lower sexual risk behaviours found in a group of men who have sex with men.</td>
<td>[118]</td>
</tr>
<tr>
<td>Sertraline</td>
<td>2</td>
<td></td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>May increase use, worsen craving.</td>
<td>[163, 164]</td>
</tr>
<tr>
<td>Imipramine</td>
<td>1</td>
<td>150mg</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>No placebo controlled trials; the only trial compared 150mg versus 10mg dose. Retention in treatment was significantly longer for subjects who were treated with 160mg compared to 10mg dose.</td>
<td>[163, 164]</td>
</tr>
<tr>
<td>Stimulants</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dexamphetamine sustained release</td>
<td>2</td>
<td>60-110mg</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>Limited evidence for reducing severity of dependence, craving, and improving retention; but not for reducing use.</td>
<td>[101, 122]</td>
</tr>
<tr>
<td>Methylphenidate sustained release</td>
<td>3</td>
<td>18-54mg</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>Limited but conflicting evidence for reducing use and reducing craving.</td>
<td>[153, 164, 167]</td>
</tr>
<tr>
<td>Modafinil</td>
<td>5</td>
<td>200-400mg</td>
<td>x</td>
<td>?</td>
<td>x</td>
<td>x</td>
<td>One trial suggested lower methamphetamine use with higher (400mg) compared to lower (200mg) dose modafinil, in those who had higher medication adherence.</td>
<td>[118, 146-171]</td>
</tr>
</tbody>
</table>

**DURATION**
Most trials <14 weeks

**DOSE**
Dose not high enough

**DROP-OUT**
Dropouts in placebo RCTs 40-50%
Innovative Pharmacological Treatments
Shout out to our clinical trial team
The N-ICE Trial is a world first clinical trial for methamphetamine dependence.

The N-ICE Trial will establish if N-Acetyl-Cysteine (NAC) can reduce craving for ice and help people stop using ice.
What is NAC?

- **Listed by WHO as an essential medicine**
  - Paracetamol overdose
  - Mucolytic therapy for cystic fibrosis / COPD
  - Kidney disease

- **A range of other potential uses**
  - Influenza
  - Fertility treatment
  - Psychiatric disorders
    - Alzheimer's, bipolar, MDD, OCD, schizophrenia
    - Addictions

- **Sold as supplement online / OTC** (not approved in Australia)
  - Safely used as a supplement (not a natural substance!)
  - Few side-effects (nausea, GI irritation)
Cysteine has 2 key metabolic roles:

1. **Antioxidant activities**  
   (glutathione - precursor)
2. **Modulation of the glutamate system**  
   (reward / reinforcement pathway)

Addresses 2 types of psychiatric disorders

1. **Oxidative stress**  
   (schizophrenia, bipolar disorder, depression, anxiety)
2. **Impulsivity / compulsivity**  
   (SUDs, gambling)

NAC is an amino acid precursor for cysteine
1. **Relieves craving for MA**  
   (small cross over trial in Iran)  
   – Reduced use?  
   – Reduced severity of dependence?

2. **Protects against neurotoxic effects of MA**  
   (antioxidant effects)  
   – Ameliorates MA-related neuropsychiatric sequelae?  
     • Depression  
     • Psychosis  
     • Hostility/agitation  
   – Trialled for depression, bipolar disorder, schizophrenia/psychosis
To test whether 2400mg daily oral NAC will:

1. Reduce methamphetamine use relative to placebo (primary objective)
2. Reduce methamphetamine dependence, craving and withdrawal
3. Reduce psychiatric symptoms

**NAC group** 12-week supply 2,400mg oral NAC/day

**COMPARED TO**

**Placebo group** 12-week supply of oral placebo/day
STUDY TYPE: Phase II double-blind placebo controlled
SETTING: Community (Melbourne, Wollongong, Geelong)
DURATION: ~18-month recruitment (3 month follow-up)
PARTICIPANTS: n=180 (60 participants per site)
DATA COLLECTION: Initial screen, baseline survey + 12 x weekly follow-ups

ADJUNCTIVE CARE:
• All participants receive a copy of the “On Ice” self-help brochure
• All get referral information
• Participants are free to get other help/treatment during the trial
# ELIGIBILITY CRITERIA

<table>
<thead>
<tr>
<th>INCLUSION</th>
<th>EXCLUSION</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Dependent on MA</td>
<td>• Enrolled in drug treatment</td>
</tr>
<tr>
<td>• 18 – 60 years old</td>
<td>• In need of acute psychiatric / health care</td>
</tr>
<tr>
<td>• Want to reduce MA use</td>
<td>• Contraindications for NAC</td>
</tr>
<tr>
<td>• Willing to comply with trial protocol</td>
<td>• NAC hypersensitivity</td>
</tr>
<tr>
<td></td>
<td>• Pregnant</td>
</tr>
<tr>
<td></td>
<td>• Unwilling to use contraception</td>
</tr>
<tr>
<td></td>
<td>• Taking contraindicated medications (e.g. nitroglycerin)</td>
</tr>
<tr>
<td></td>
<td>• Known / suspected systemic disorder</td>
</tr>
<tr>
<td></td>
<td>• Cancer</td>
</tr>
<tr>
<td></td>
<td>• Epilepsy / Seizures</td>
</tr>
<tr>
<td></td>
<td>• GI ulcers / stones</td>
</tr>
<tr>
<td></td>
<td>• Asthma</td>
</tr>
</tbody>
</table>
## STUDY ENDPOINTS

### PRIMARY ENDPOINT

**Methamphetamine use**
- Days of use – TLFB calendar system
- Number of positive weekly saliva tests

#### Timeline Followback Calendar

<table>
<thead>
<tr>
<th>Year</th>
<th>2018</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sun</td>
<td>Mon</td>
</tr>
<tr>
<td>J</td>
<td>A</td>
</tr>
<tr>
<td>14</td>
<td>15</td>
</tr>
<tr>
<td>22</td>
<td>23</td>
</tr>
<tr>
<td>29</td>
<td>30</td>
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<tr>
<td>5</td>
<td>6</td>
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<tr>
<td>12</td>
<td>13</td>
</tr>
<tr>
<td>19</td>
<td>20</td>
</tr>
<tr>
<td>26</td>
<td>27</td>
</tr>
</tbody>
</table>

### N-ICE

[Image: N-ICE logo]
STUDY ENDPOINTS

SECONDARY ENDPOINTS

• Methamphetamine craving *(Craving Experience Questionnaire)*
• Methamphetamine dependence *(Severity of Dependence Scale)*
• Methamphetamine withdrawal *(Amphetamine Withdrawal Questionnaire)*
• Depression *(Montgomery Asberg Depression Rating Scale - MADRS)*
• Positive psychotic symptoms and hostility *(Brief Psychiatric Rating Scale BPRS)*

OTHER

• Tolerability *(Treatment Satisfaction Questionnaire for Medication)*
• Safety *(AEs, SAEs using REDCap)*
• Adherence *(eCAP)*
• Data for costing
Recovering ice addicts treated with ADHD medication in Australian trials

By state political reporter Richard Wittingham
Updated 29 May 2014, 10:00pm

A drug used to help inattentive and impulsive children could be a key to turning addicts off the deadly drug, research shows.

Researchers were recently involved in Australia's Pharmaceutical Benefits Scheme, treating 500 million of their patients for ADHD (attention deficit hyperactivity disorder). However, it was observed that younger children seemed to respond well to the drug.

"People can take this drug, a day. It has a slow onset, across the whole day," she said.

"This is a drug, it can work. It might help more symptoms of excitement that bring a craving to use methamphetamine,"

St Vincent's hospital recently offers a small number of patients a new drug to reduce cravings.

"We're not simply hooking people with daily doses and we're not descending because you're not going to get bigger doses. But we're not sure why the research worked. It is because of the way it converts to demethylamphetamine in the blood,"

So even if you brush it up and inject it, it's not going to work quicker, you're not going to get higher quicker.

"As well as keeping it in your pocket, it's easy to swallow."
THE LIMA STUDY

BACKGROUND

Initial pilot study
NHMRC grant for multisite study

Ezard et al, 2016 BMC Psychiatry

Sydney (St Vincent’s, Western Sydney LHD, RPA), Newcastle (HNELHD) and Adelaide (DASSA), Melbourne (Turning Point)
The aim of The LiMA Study is to test if lisdexamfetamine is effective in reducing methamphetamine use, cravings and withdrawal symptoms.

This is a randomised double-blind placebo-controlled study.

One group will receive lisdexamfetamine and another will receive a placebo, in addition to counselling. The participants, clinicians and researchers involved in the study will not know to which group they have been allocated. The two groups will be compared and the findings will contribute to evidence for the future use of lisdexamfetamine in the treatment of methamphetamine dependence.

180 PEOPLE will be recruited to the LiMA Study being conducted in specialist treatment centres in Sydney, Newcastle, Adelaide and Melbourne.
Stimulant agonist treatments have not been shown to be effective in trials for methamphetamine dependence (e.g. dexamphetamine).

A range of features of lisdexamfetamine suggest it could provide a more effective alternative as a long-acting stimulant:

- **Slower** onset of action and **longer** duration of action (compared to dexamphetamine)
- **Less diversion / abuse liability**
  - Crushing / extraction does not release dexamphetamine
  - Snorting, smoking or injecting does not affect time / concentration of dexamphetamine
lisdexamfetamine

- Dexamphetamine pro-drug
- Converted ‘in vivo’ (in the body)
  - Within red blood cells
  - To dexamphetamine
- Peak concentration
  - 3.5 hrs after dose
- Duration of action
  - Approx 10-12h
  - Therefore can be once daily medication
Most common side effects are also seen with methamphetamine and other stimulant use:

- Loss of appetite
- Dry mouth
- Headache
- Insomnia
- Diarrhoea
- Agitation
- Irritability
- Nausea
- Weight loss
- Increase in heart rate
- Increase in blood pressure
**EXCLUSION CRITERIA**

- Unstable other substance use
- No significant (unstable) psychiatric illness *(as judged by trial psychiatrist)*
- A range of cardiovascular illnesses

**INCLUSION CRITERIA**

- Adults with methamphetamine dependence
- Other treatments haven’t worked
A study of *lisdexamfetamine* for the treatment of *methamphetamine* dependence
Conclusion

- Psychosocial treatment approaches are effective for most individuals if they access treatment and are retained
- Still no medication treatments with proven effectiveness on use outcomes
  - Off label use associated with risks (individual and prescriber)
  - Innovative options being trialled across Australia
- Watch this space!
Q & A
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