CRACKS IN THE ICE

WELCOME TO THE CRACKS IN THE ICE WEBINAR SERIES

Australian Government
Department of Health

THE UNIVERSITY OF SYDNEY
Matilda Centre

cracksintheice.org.au

Current and promising treatment options for ice dependence

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

23rd July 2019

Australian Government
Department of Health

THE UNIVERSITY OF SYDNEY
Matilda Centre

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

cracksintheice.org.au

Part 1: Effects of ice on the brain

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

Australian Government
Department of Health

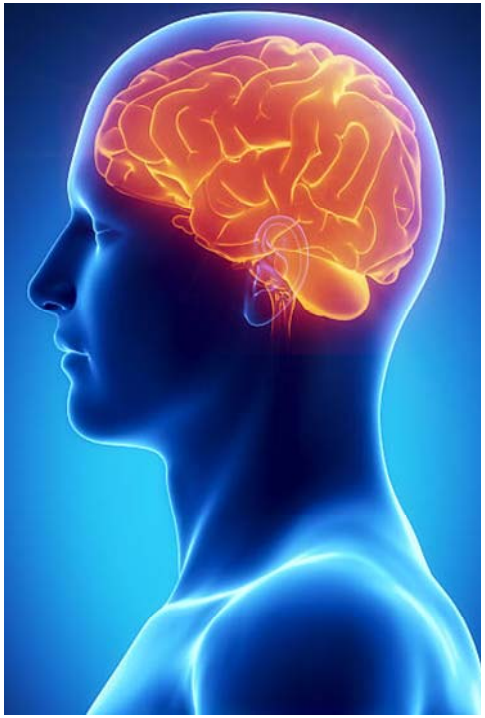
THE UNIVERSITY OF SYDNEY
Matilda Centre

LA TROBE UNIVERSITY

The human brain

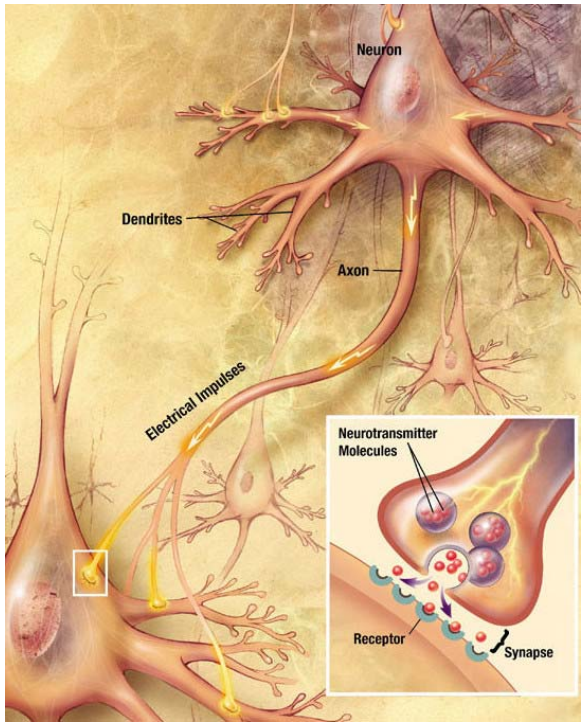
- weighs about 1.5 kilograms.
- volume is 1.1 - 1.3 cm^3 = 1.1 - 1.3 litre
- makes up about 2 percent of a human's body weight.
- uses 20-25% of your oxygen and glucose supply.
- consistency is similar to tofu.
- contains about 100 billion nerve cells (neurons) - the "gray matter“ --> 100,000,000,000 (15x global population)
- Each neuron may be connected to as many as 10,000 other neurons.
- contains billions of nerve fibers - the “white matter”

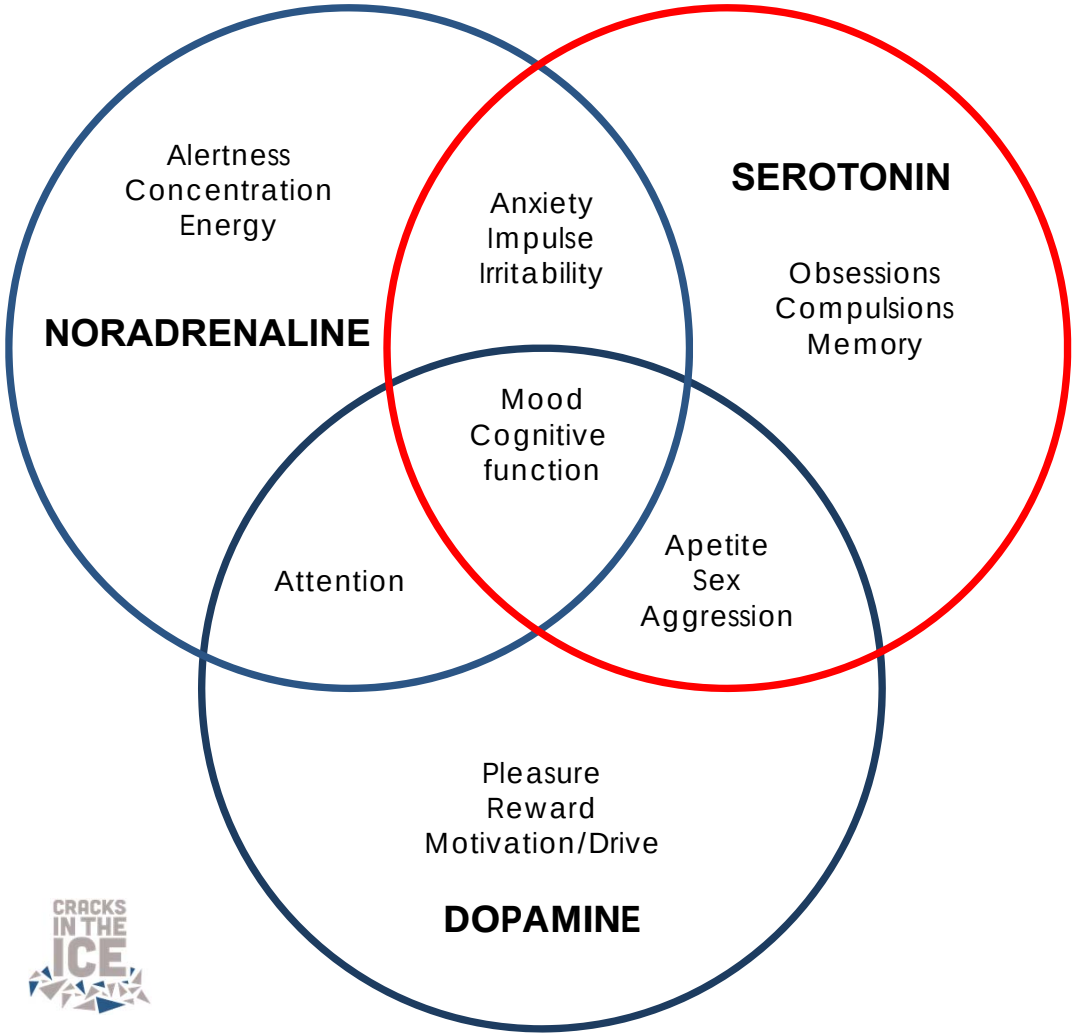
(www.livescience.com & www.bioscience.com)



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*

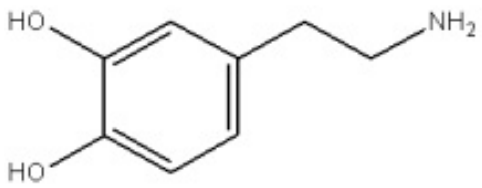




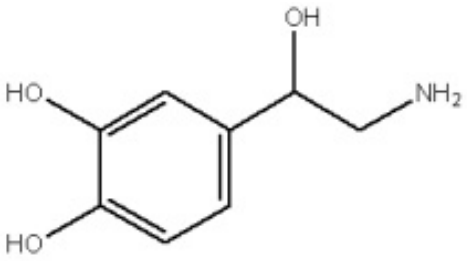
Neurotransmitters

www.deplin.com/LifeWith Depression/Causes

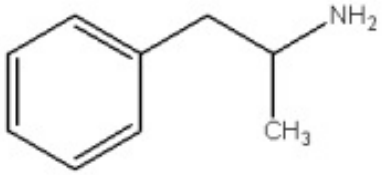
Drugs as ‘imposters’ of neurotransmitters



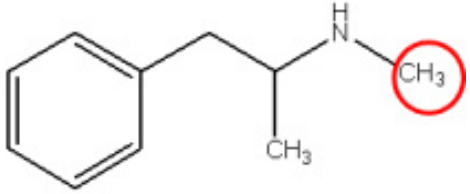
dopamine



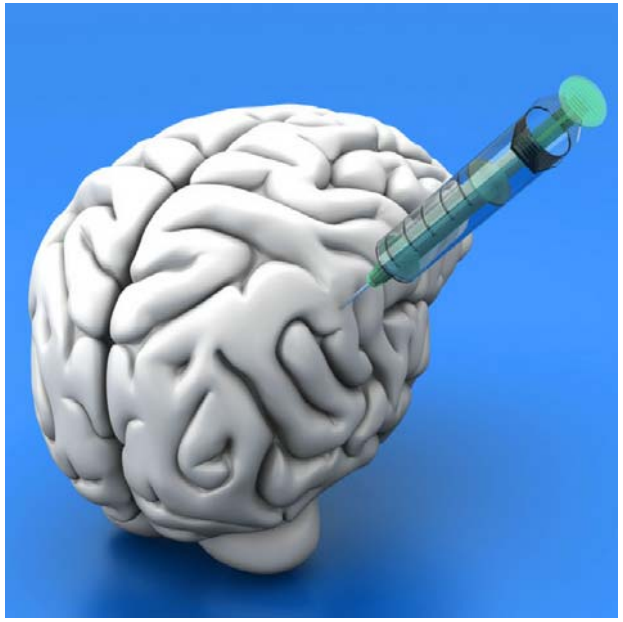
noradrenaline



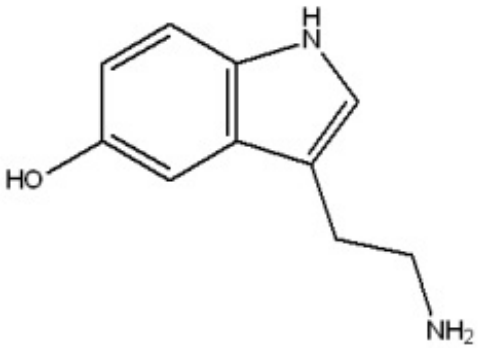
amphetamine



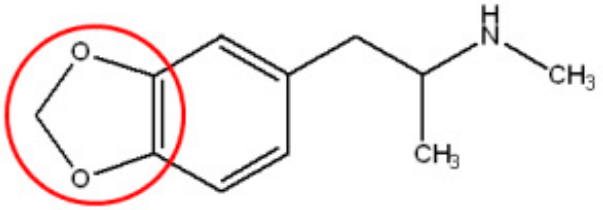
methamphetamine



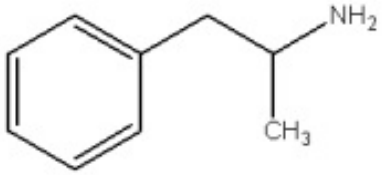
Drugs as ‘imposters’ of neurotransmitters



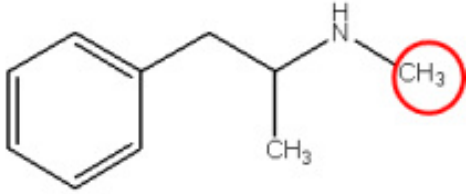
serotonin



methylenedioxymethamphetamine



amphetamine



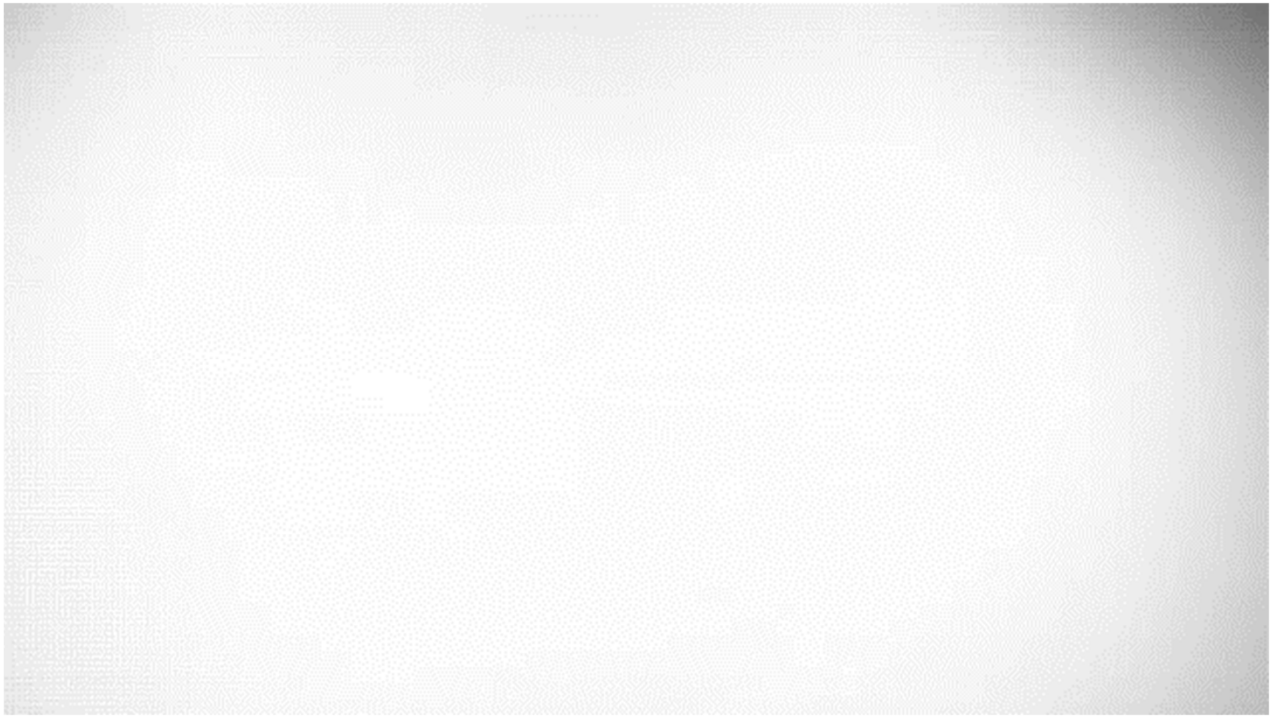
methamphetamine

Metamphetamine

Acts on several neurotransmitter systems:

- Dopamine
- Noradrenaline
- Serotonin

Methamphetamine in the brain



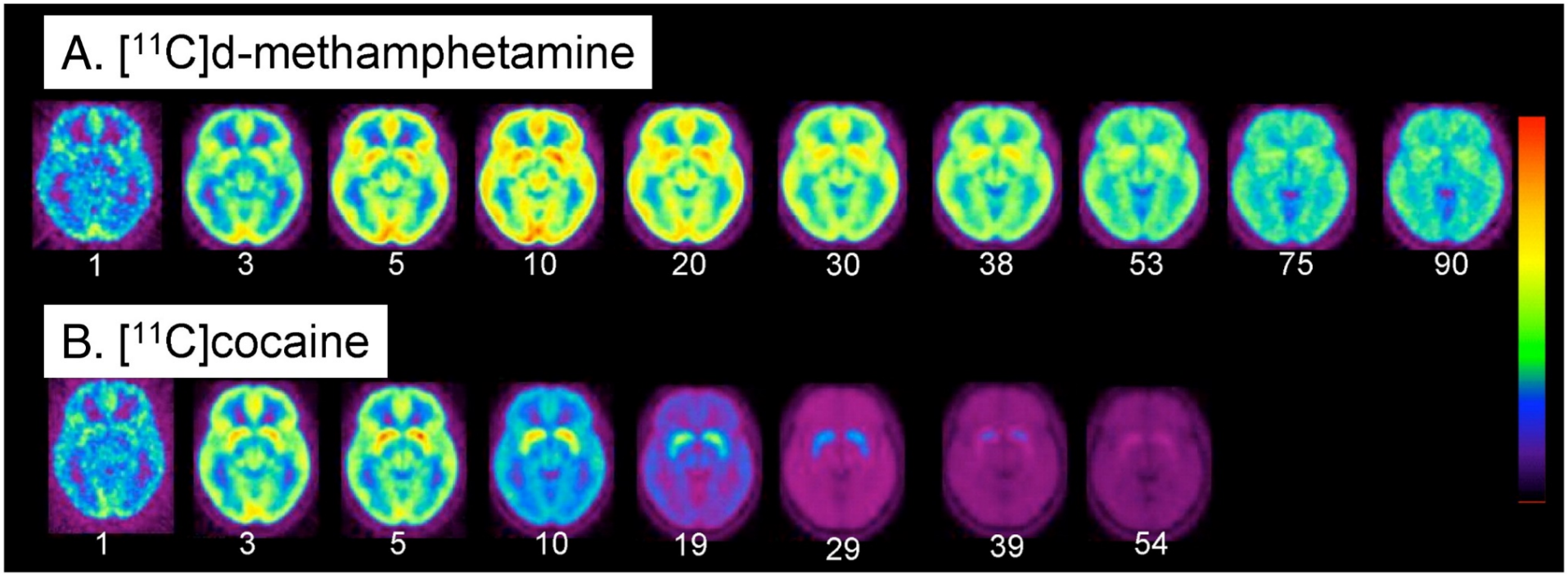
To watch a video about this topic, please use the link below.

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)

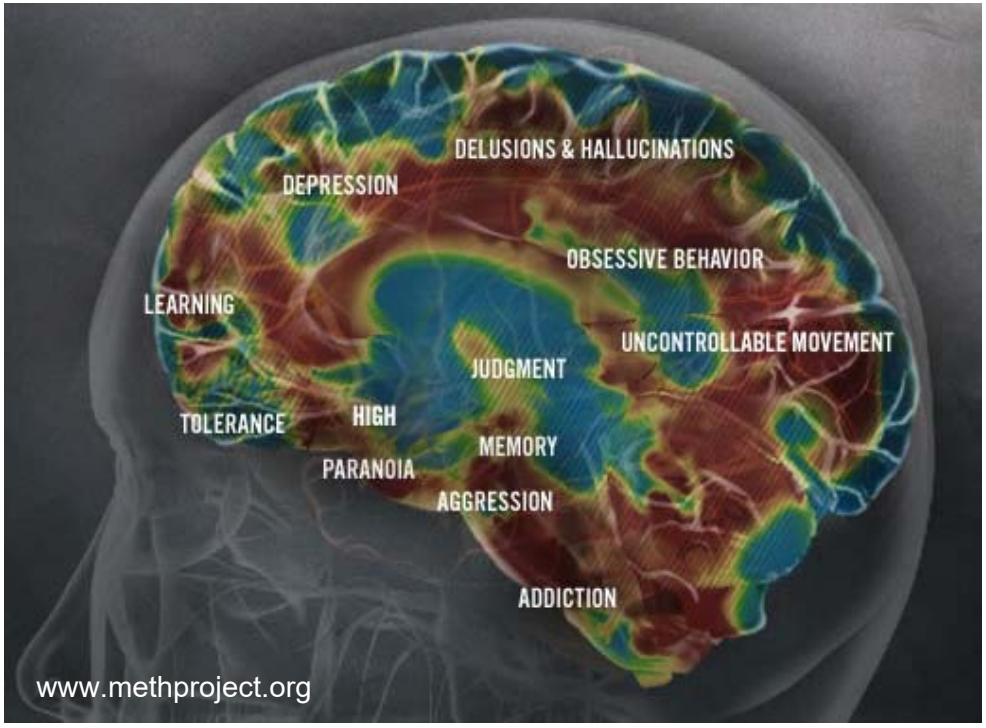
Methamphetamine peaks fast but clears slower than cocaine

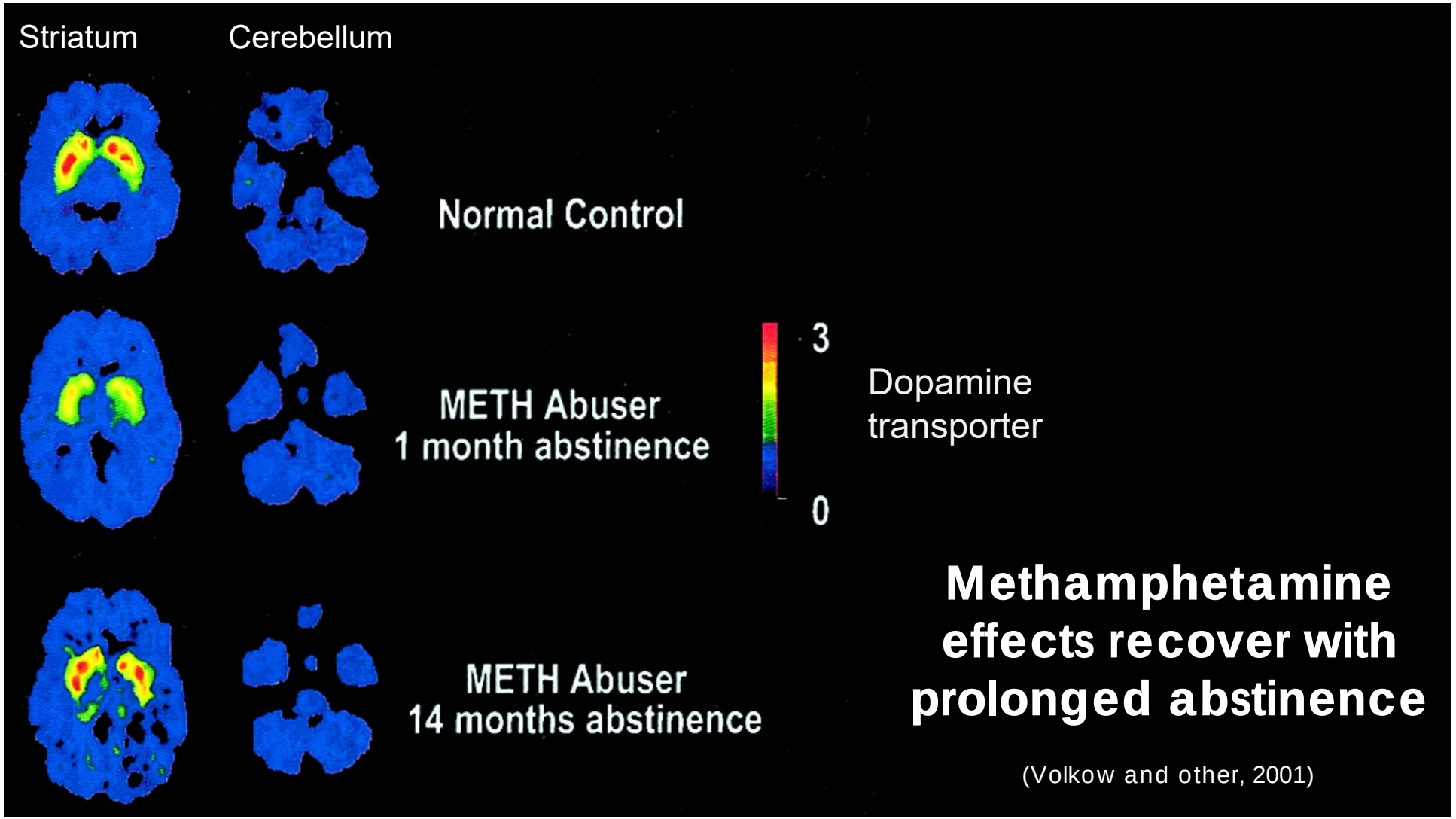


Chronic use of methamphetamine

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

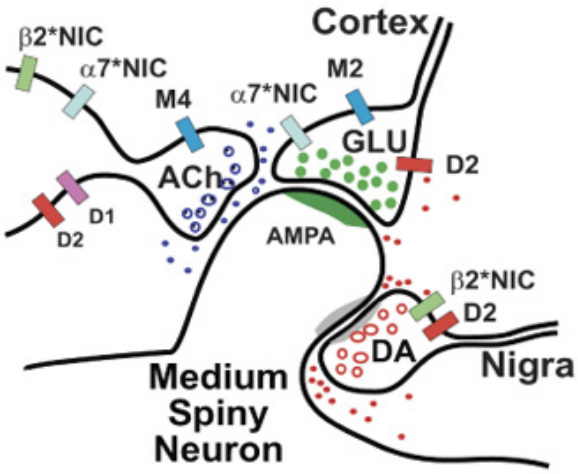
- Cognitive effects
  - Attention
  - Judgement
  - Problem solving
  - Memory
  - Psychotic symptoms



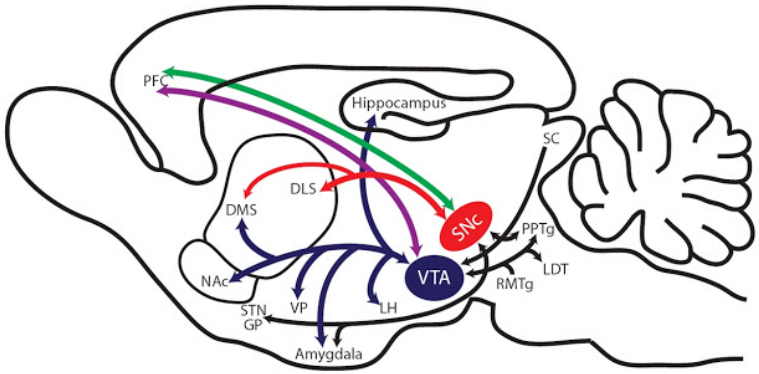

Striatum
Cerebellum
Normal Control
METH Abuser
1 month abstinence
3
0
Dopamine
transporter
METH Abuser
14 months abstinence
Methamphetamine effects recover with prolonged abstinence
(Volkow and other, 2001)

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.

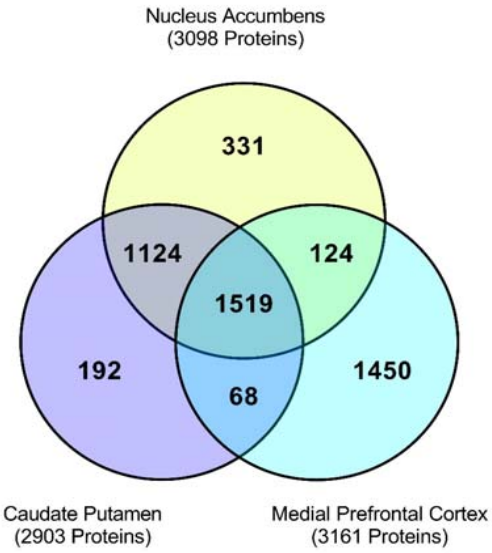


Research into methamphetamine effects in the brain: genes, proteins



LA TROBE UNIVERSITY

CRACKS IN THE ICE



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?

Predict, prevent, reverse

cracksintheice.org.au

Part 2: Psychosocial and e-health treatment approaches

Professor Frances Kay-Lambkin

Australian Government
Department of Health

THE UNIVERSITY OF SYDNEY
Matilda Centre

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.

Frei & Clarke (2011). Medical J Aust 195(3): S5-S6.
Darke S, et al. Drug Alcohol Rev. 2008 May; 27(3):253-62.
Glasner-Edwards S, et al. Drug Alcohol Rev. 2010 Jan; 29(1):12-20.
Newton TF, et al. Am J Addict. 2009 Jul-Aug; 18(4):294-300.

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.

Ciketic S, et al. J Subst Use 2012;17:363–83.

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.

Rawson RA, et al. Addiction. 2004 Jun; 99(6):708-17.
Ciketic S, et al. J Subst Use 2012;17:363–83.

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).

https://www1.health.gov.au/internet/publications/publishing.nsf/Content/drugtreat-pubs-cogamph-toc

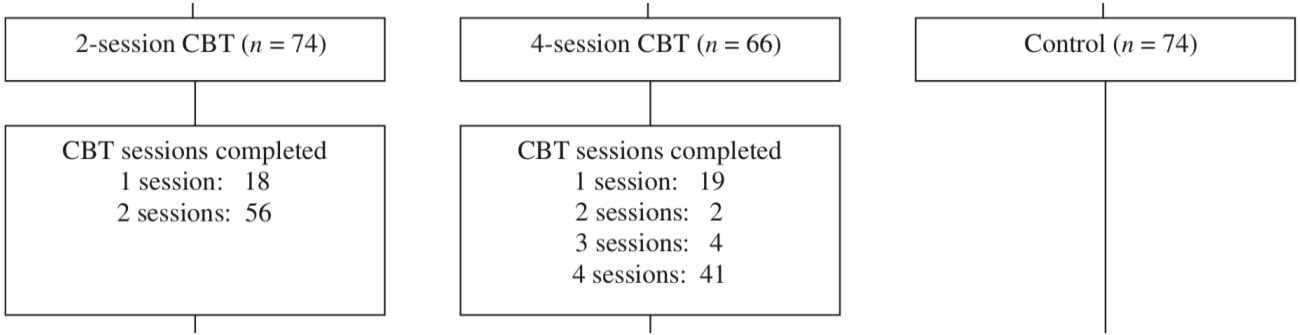
CBT/MI for Stimulants

Abstinence rates

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

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

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



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

cracksintheice.org.au

Breaking the Ice

- Funded by the Commonwealth Department of Health and Ageing (AUSTRALIA)
- Adapt face-to-face interventions
- Randomised controlled trial

BREAKING THE ICE

Original Paper

A randomised controlled trial of a web-based intervention for users of amphetamine-type stimulants: Six month outcomes

Robert J Tait[1,2], B.Sc (Hons), Ph.D; Rebecca McKetin[3], Ph.D; Frances Kay-Lambkin[4,5], Ph.D; Bradley Carron-Arthur[2], BPsych (Hons); Anthony Bennett[2], BAppSc; Kylie Bennett[2], BSc, BA (Hons); Helen Christensen[2,6], PhD.; Kathleen M Griffiths[2], PhD.

[1]National Drug Research Institute, Faculty of Health Sciences, Curtin University, Perth, Australia

[2]National Institute for Mental Health Research, The Australian National University, Canberra, Australia

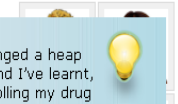
[3]Centre for Research on Ageing, Health and Wellbeing, The Australian National University, Canberra, Australia

[4]National Drug and Alcohol Research Centre, University of New South Wales, Sydney, Australia

[5]Centre for Translational Neuroscience and Mental Health, University of Newcastle, Newcastle, Australia

[6]Black Dog Institute, University of New South Wales and Prince of Wales Hospital, Sydney, Australia

Weighing it all up – Changing your drug use



"I've changed a heap myself, and I've learnt, I'm controlling my drug use at the moment, as in I think I've used 4 or 5 times in 2 months. I'm not even smoking pot very regularly any more, like I used to be a big bong head."

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

How important are each of these reasons and negetives 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:

Good things about change	Importance (0-10)	Not so good things about change	Importance (0-10)
I would have more money	9	It would be hard to cope with withdrawal	5
I would feel healthier	9	I would feel low all the time	5
I would be proud of myself	5		
I could get in control of my life again	5		

SAVE MY RESPONSES

BREAKING THE ICE

FACT SHEETS

Introduction | Reasons for change | Setting goals | Support crew | Positive results | Change plan | What works | Practical steps | The next step

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?

SAVE MY RESPONSES

Click on a character to follow their story

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.

Module 1 | Module 2 | Module 3

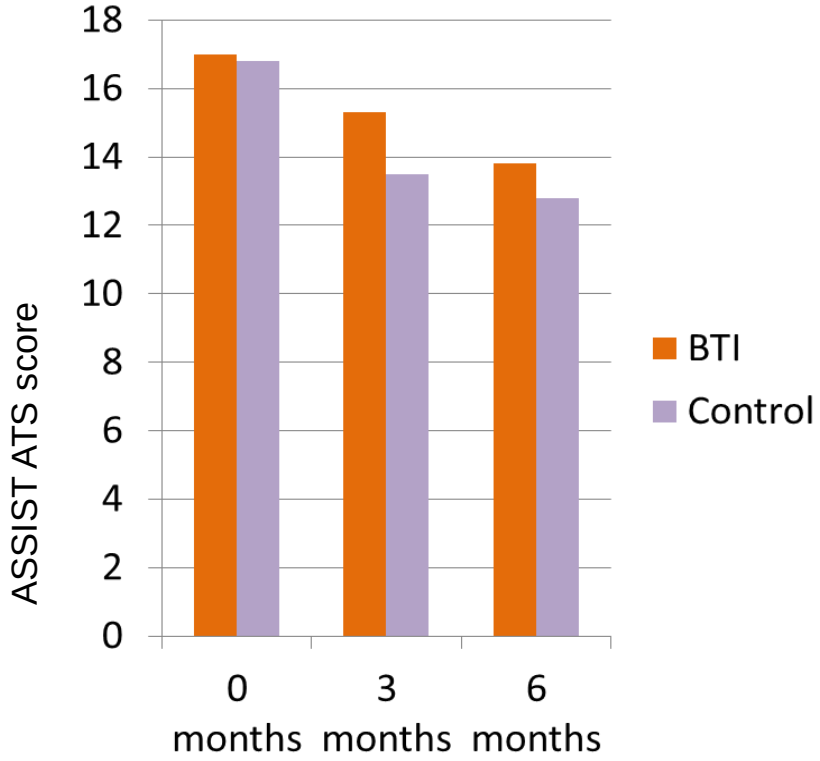
BACK

NEXT

Log out | Change password

cracksintheice.org.au

Results…

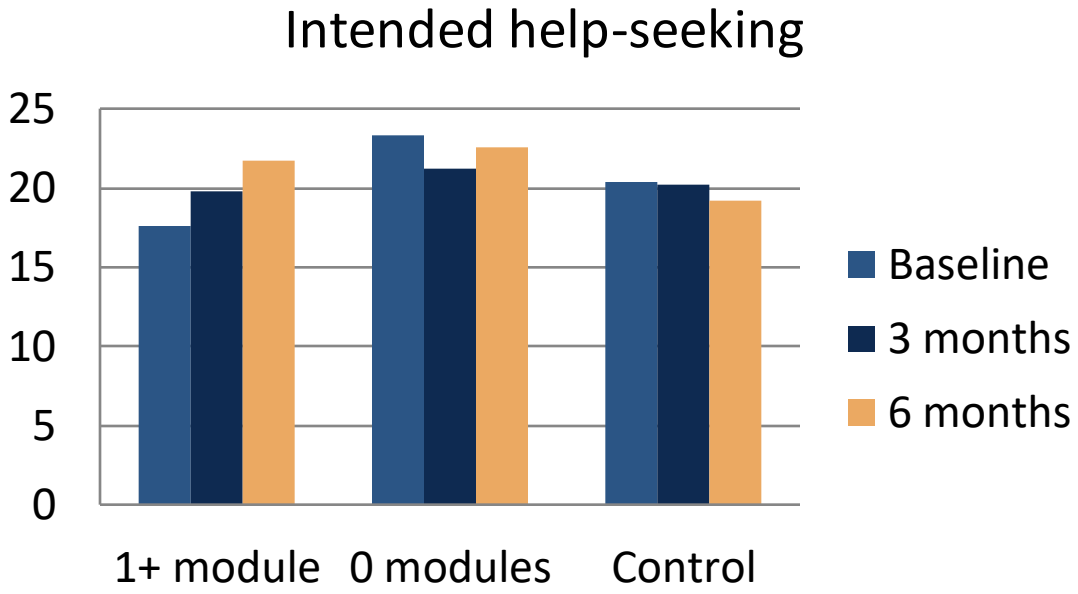


cracksintheice.org.au

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)

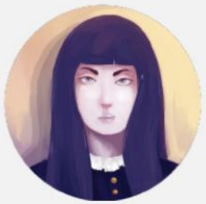


1 WHAT'S IN IT FOR ME?

Explores what's happening in your life at the moment

2 WEIGHING IT ALL UP

Will help you to weigh up the important isuues that you have identified



Ryan | Jess | Ash | Josh

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.

1 WHAT'S IN IT FOR ME?

- Introduction
- Relationships
- Money
- Health
- Work/Study
- Legal Issues
- Mental Health
- Ice Use
- What Now?
- My Summary
- Summary - Stories

0 % COMPLETE

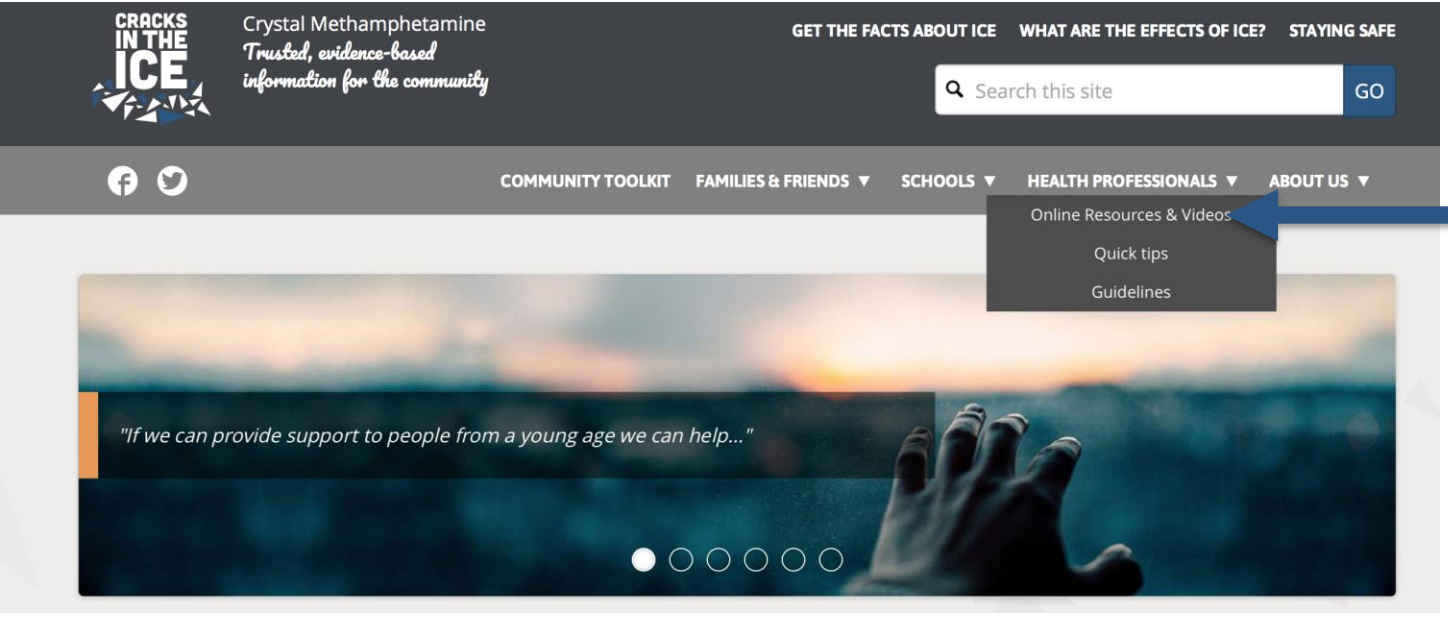
2 WEIGHING IT ALL UP

2 WEIGHING IT ALL UP

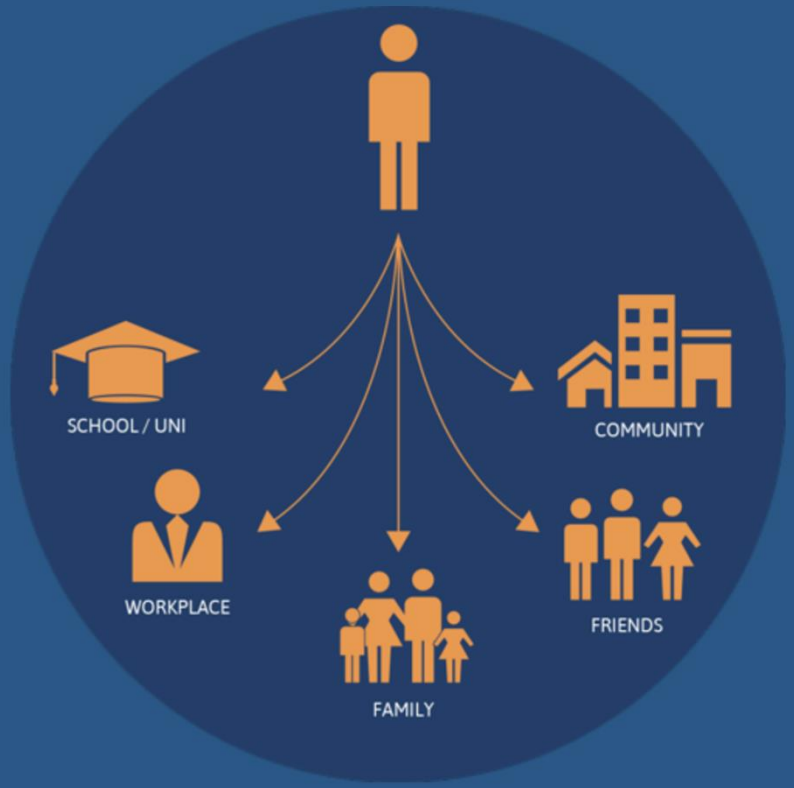
- Introduction
- Good Things About Drugs
- Not So Good Things About Drugs
- Weighing It All Up - Using Drugs
- Good Things About Change
- Not So Good Things About Change
- Weighing It All Up - Changing Your Drug Use
- Summary
- My Summary
- What Now?

0 % COMPLETE

cracksintheice.org.au



BREAKING THE ICE: AN INTERNET-BASED BRIEF EARLY INTERVENTION



...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."

cracksintheice.org.au

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

cracksintheice.org.au

Crystal Methamphetamine
Trusted, evidence-based information for the community

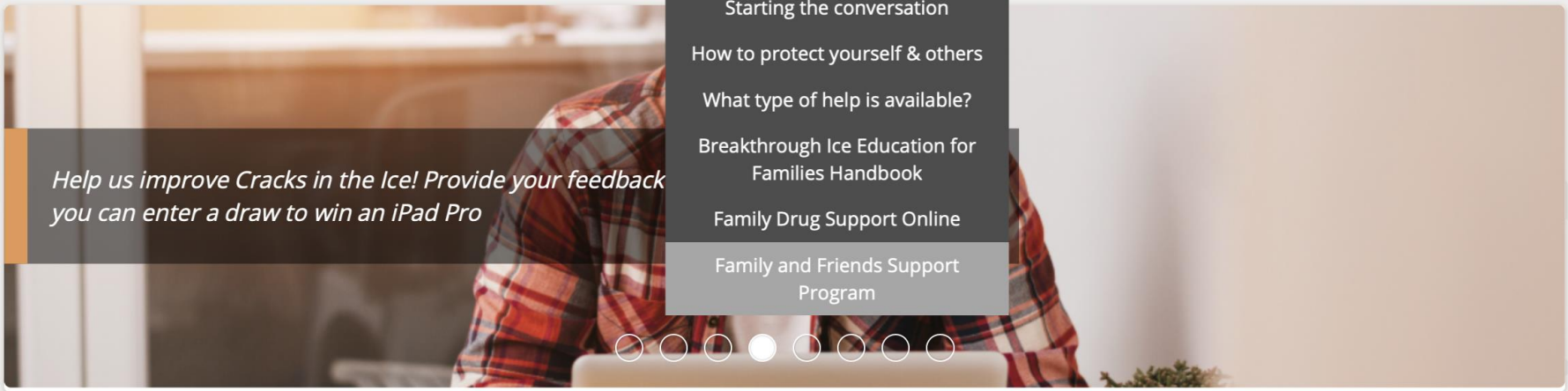
GET THE FACTS ABOUT ICE | WHAT ARE THE EFFECTS OF ICE? | STAYING SAFE

Search this site GO

ORDER FREE RESOURCES HERE

COMMUNITY TOOLKIT | FAMILIES & FRIENDS ▼ | SCHOOLS ▼ | HEALTH PROFESSIONALS ▼ | ABOUT US ▼

- Concerned about someone using ice?
- Starting the conversation
- How to protect yourself & others
- What type of help is available?
- Breakthrough Ice Education for Families Handbook
- Family Drug Support Online
- Family and Friends Support Program



cracksintheice.org.au

Summary

- 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.

cracksintheice.org.au

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

cracksintheice.org.au

Part 3: Innovations in Pharmacotherapies for Methamphetamine Use Disorder

Dr Shalini Arunogiri

Australian Government
Department of Health

THE UNIVERSITY OF SYDNEY
Matilda Centre

METHAMPHETAMINE TREATMENT GUIDELINES

Turning Point
TREATMENT · RESEARCH · EDUCATION

www.turningpoint.org.au

METHAMPHETAMINE

WITHDRAWAL IS MORE PROTRACTED THAN WITHDRAWAL FROM OTHER DRUGS LASTING APPROX

10-15 DAYS

	PHYSICAL SYMPTOMS		PSYCHOLOGICAL SYMPTOMS
COMEDOWN 1-3 DAYS	Exhaustion / low energy Increased sleep Increased appetite Restlessness		Depression / anxiety Irritability Paranoia Amotivation Anhedonia Suicidal ideation / behaviour
WITHDRAWAL 2-10 DAYS	Strong cravings Sleep difficulties Nightmares Aches, pains and stiffness Headaches Increased appetite		Strong urges to use Depression / anxiety Mood swings Poor concentration and confusion Paranoia Easily upset
REMAINING SYMPTOMS 7-28 DAYS	Strong cravings Sleep difficulties Nightmares		Strong urges to use Mood swings Anxiety Boredom
1-3 MONTHS	Cravings Sleep returns to normal Activity level returns to normal General health improves		Urges to use Mood improves

Drug and Alcohol Dependence
Volume 191, 1 October 2018, Pages 309-337

Pharmacotherapy for amphetamine dependence: A systematic review

Nicole K. Lee [a, b], Linda Jenner [b], Angela Harney [b], Jacqui Cameron [b, c]

Show more

https://doi.org/10.1016/j.drugalcdep.2018.06.038

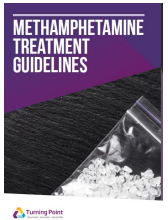
Get rights and content

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



ELSEVIER

Drug and Alcohol Dependence
Volume 191, 1 October 2018, Pages 309-337

Pharmacotherapy for amphetamine dependence: A systematic review

Nicole K. Lee [a, b], Linda Jenner [b], Angela Harney [b], Jacqui Cameron [b, c]

Show more

https://doi.org/10.1016/j.drugalcdep.2018.06.038

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**

MEDICATION	NUMBER OF TRIALS	DOSE RANGE	OUTCOMES: ABSTINENCE	OUTCOMES: REDUCED USE	OUTCOMES: CRAVING	OUTCOMES: TREATMENT RETENTION	COMMENTS	REFERENCES
ANTIDEPRESSANTS								
Bupropion	5	150mg twice daily	?	×	×	×	Low treatment adherence; significantly higher abstinence in adherent versus non-adherent participants, particularly in people using methamphetamine less frequently.	[148, 159-162]
Mirtazapine	1	30mg	×	✓	×	×	Reduction in use, and lower sexual risk behaviours found in a group of men who have sex with men.	[115]
Sertraline	2	–	×	×	×	×	May increase use, worsen craving.	[163, 164]
Imipramine	1	150mg	×	×	×	✓	No placebo controlled trials; the only trial compared 150mg versus 10mg dose. Retention in treatment was significantly longer for subjects who were treated with 150mg compared to 10mg dose.	[163, 164]
STIMULANTS								
Dexamphetamine sustained release	2	60-110mg	×	×	✓	✓	Limited evidence for reducing severity of dependence, craving, and improving retention; but not for reducing use.	[121, 122]
Methylphenidate sustained release	3	18-54mg	×	✓	✓	✓	Limited but conflicting evidence for reducing use and reducing craving.	[153, 166, 167]
Modafinil	5	200-400mg	×	?	×	×	One trial suggested lower methamphetamine use with higher (400mg) compared to lower (200mg) dose modafinil, in those who had higher medication adherence.	[118, 168-171]

DOSE
Dose ?not high enough

DROP-OUT
Dropouts in placebo RCTs 40-50%

DURATION
Most trials <14 weeks

CRACKS IN THE ICE

Innovative Pharmacological Treatments

Shout out to our clinical trial team

Turning Point
TREATMENT · RESEARCH · EDUCATION

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.

Drug and Alcohol Review (2016)
DOI: 10.1111/dar.12414

COMMENTARY

A potential role for N-acetylcysteine in the management of methamphetamine dependence

REBECCA McKETIN[1], OLIVIA M. DEAN[2,3,4], AMANDA L. BAKER[5], GREG CARTER[5], ALYNA TURNER[2,4,5], PETER J. KELLY[6] & MICHAEL BERK[2,3,4]

CRACKS IN THE ICE

A study protocol for the N-ICE trial: A randomised double-blind placebo-controlled study of the safety and efficacy of *N*-acetyl-cysteine (NAC) as a pharmacotherapy for methamphetamine ("ice") dependence

Rebecca McKetin, Olivia M. Dean, Alyna Turner, Peter J. Kelly, Brendan Quinn, Dan I. Lubman, Paul Dietze, Gregory Carter, Peter Higgs, Amanda L. Baker, Barbara Sinclair, David Reid, Victoria Manning, Nina te Pas, Wenbin Liang, Tamsin Thomas, Ramez Bathish, Margaret Kent, Dayle Raftery, Shalini Arunogiri, Frank Cordaro, Harry Hill and Michael Berk

Trials 2019 **20**:325
https://doi.org/10.1186/s13063-019-3450-0
Received: 9 November 2018 | **Accepted:** 16 May 2019 | **Published:** 4 June 2019

National Drug Research Institute, Curtin University

Perth, WA

Rebecca McKetin (Coordinating Investigator)

Nina te Pas (Trial Coordinator)

Wenbin Liang (Statistician)

Nicole Edwards (Trial Coordinator)

Barwon Health, Deakin University

Geelong, VIC

Olivia Dean (Site Lead Investigator)

Alyna Turner (Site Coordinator)

Michael Berk

Turning Point/Eastern Health, Monash University; Burnet Institute

Melbourne, VIC

Dan Lubman (TP) (Site Lead Investigator)

Brendan Quinn (BI) (Site Coordinator)

Victoria Manning (TP)

Paul Dietze (BI)

University of Wollongong

NSW

Peter Kelly (Site Lead Investigator and Site Coordinator)

Dayle Raftery (PhD Candidate)

Illawarra Drug and Alcohol Service, Illawarra Shoalhaven Local Health District (ISLHD), Wollongong, NSW

Barbara Sinclair (Medical Director D&A Service ISLHD)

David Reid (director D&A service ISLHD)

University of Newcastle

NSW

Amanda Baker

Gregory Carter

La Trobe University, Melbourne, VIC

Peter Higgs

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)

How does NAC work?

NAC is an amino acid precursor for cysteine

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)*

Trialling NAC in MA Use Disorder

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

STUDY OBJECTIVES

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

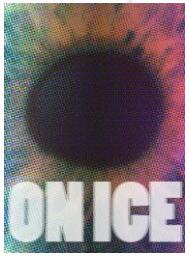
NAC group 12-week supply 2,400mg oral NAC/day

COMPARED TO

Placebo group 12-week supply of oral placebo/day

STUDY DESIGN

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

INCLUSION	EXCLUSION
• Dependent on MA	• Enrolled in drug treatment
• 18 – 60 years old	• In need of acute psychiatric / health care
• Want to reduce MA use	• Contraindications for NAC

• Willing to comply with trial protocol	• NAC hypersensitivity
	• Pregnant
	• Unwilling to use contraception
	• Taking contraindicated medications (e.g. nitroglycerin)
	• Known / suspected systemic disorder
	  • Cancer
	  • Epilepsy / Seizures
	  • GI ulcers / stones
	  • Asthma

STUDY ENDPOINTS

PRIMARY ENDPOINT

Methamphetamine use

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

TIMELINE FOLLOWBACK CALENDAR

2018	SUN	MON	TUES	WED	THURS	FRI	SAT
		1 New Year's day	2	3	4	5	6
J	7	8	9	10	11	12	13
A	14	15	16	17	18	19	20
N	21	22	23	24	25	26	27
	28	29	30	31	1	2	3
F	4	5	6	7	8	9	10
E	11	12	13	14 Valentines day	15	16 Chinese new yr	17
B	18	19	20	21	22	23	24
	25	26	27	28	1	2	3
M	4	5	6	7	8	9	10
A	11	12 Labour day	13	14	15	16	17 St. Patrick
R	18	19	20	21	22	23	24
	25	26	27	28	29	30 Good Friday	31 Day/LS end
A	1 Easter Sunday	2 Easter Monday	3	4	5	6	7
P	8	9	10	11	12	13	14
R	15	16	17	18	19	20	21
	22	23	24	25 Anzac day	26	27	28
	29	30	1	2	3	4	5
M	6	7	8	9	10	11	12
A	13 Mother's Day	14	15	16	17	18	19
Y	20	21	22	23	24	25	26
	27	28	29	30	31		

CRACKS IN THE ICE

N-ICE

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

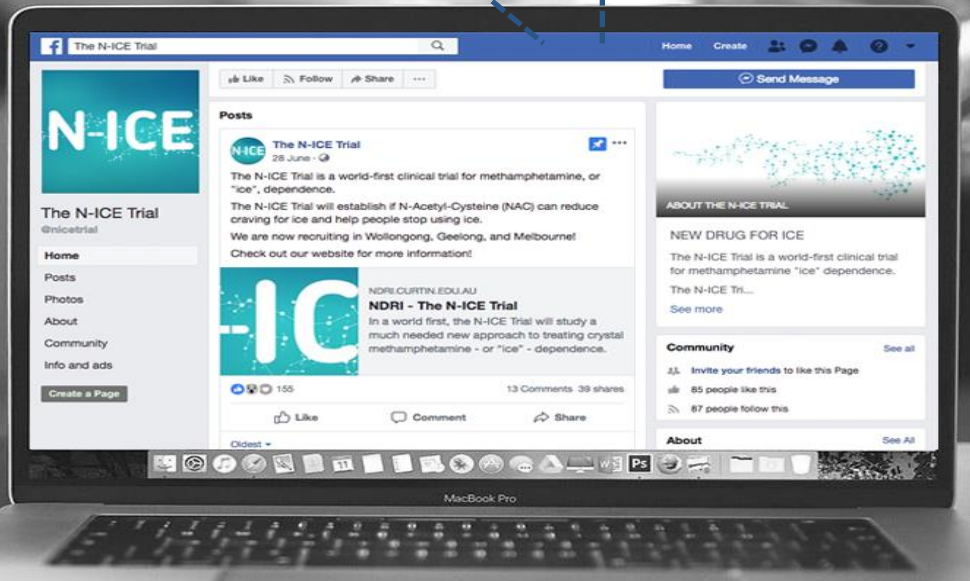
- Tolerability *(Treatment Satisfaction Questionnaire for Medication)*
- Safety *(AEs, SAEs using REDCap)*
- Adherence *(eCAP)*
- Data for costing

CRACKS IN THE ICE

N-ICE

www.facebook.com/nicetrial

http://www.nicetrial.info



0434 960 033 (Ramez – Research Officer)
nicetrial.melb@monash.edu

ABC NEWS

Just In | Politics | World | Business | Sport | Science | Health | Arts | Analysis

Qld bushfires | See all current bushfire warnings from Fire and Emergency Services.

Print | Email | Facebook | Twitter | More

Recovering ice addicts treated with ADHD medication in Australian trials

By state political reporter Richard Willingham

Updated 25 Sep 2018, 10:03pm

PHOTO: Researchers hope the ADHD medication will decrease cravings in recovering ice addicts. (NSW Police: AAP)

ABC NEWS

Just In | Politics | World | Business | Sport | Science | Health | Arts | Analysis | Fa

Qld bushfires | See all current bushfire warnings from Fire and Emergency Services.

Print | Email | Facebook | Twitter | More

ADHD treatment trialled in bid to help ice addicts kick deadly habit

By Mark Doman

Updated 14 Oct 2014, 12:14pm

A drug used to treat inattentive and impulsive children could be the key to weaning addicts off the deadly drug ice, researchers say.

PHOTO: Researchers hope a new treatment could help reduce the withdrawal symptoms from ice addicts. (NSW Police: AAP)

Lisdexamfetamine was recently listed on Australia's Pharmaceutical Benefits Scheme for the treatment of attention deficit hyperactivity disorder (ADHD) in children between the age of six and 18 years old.

But researchers at Sydney's St Vincent's Hospital are hoping higher doses of the drug could help serious ice users control cravings.

Associate Professor Nadine Ezard will explain the trial at the Australian Drugs Conference in Melbourne today.

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

"The idea is that, if it works, it might help those symptoms of withdrawal that trigger a desire to use methamphetamine."

St Vincent's Hospital currently offers dexamphetamine as a treatment for a small number ice users as a last resort measure.

Users must attend the hospital for daily doses and must be monitored because improper use can give people ice-like highs.

But lisdexamfetamine has researchers excited because of the way it converts to dexamphetamine in red blood cells.

> "So even if you crush it up and inject it, it's not going to work quicker, you're not going to get higher quicker"
>
> Nadine Ezard, St Vincent's Hospital

THE LIMA STUDY

BACKGROUND

Ezard et al,
2016 BMC Psychiatry

Initial **pilot study**
NHMRC grant for **multisite** study

ANZCTR
Australian New Zealand Clinical Trials Registry

Sydney (*St Vincent's, Western Sydney LHD, RPA*), **Newcastle** (*HNELHD*) and **Adelaide** (*DASSA*), **Melbourne** (Turning Point)

AIM

The aim of The LiMA Study is to test if **lisdexamfetamine** is effective in reducing **methamphetamine use, cravings and withdrawal symptoms**.

STUDY DESIGN

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

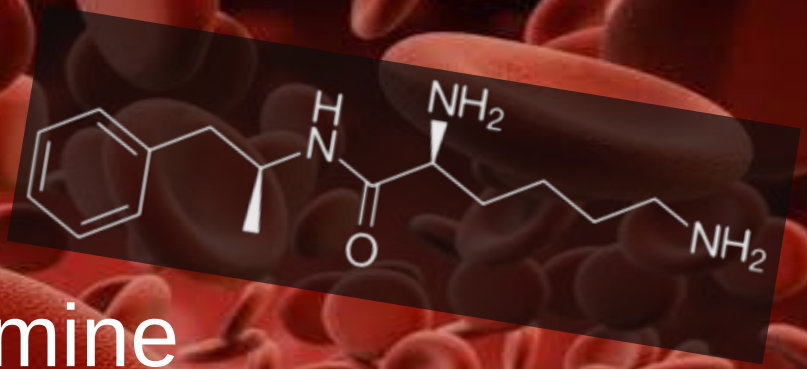
To the **LiMA Study** being conducted in specialist treatment centres in **Sydney, Newcastle, Adelaide and Melbourne.**

WHY LISDEXAMFETAMINE?

Stimulant agonist treatments have not been shown to be effective in trials for methamphetamine dependence (e.g. dexamphetamine)

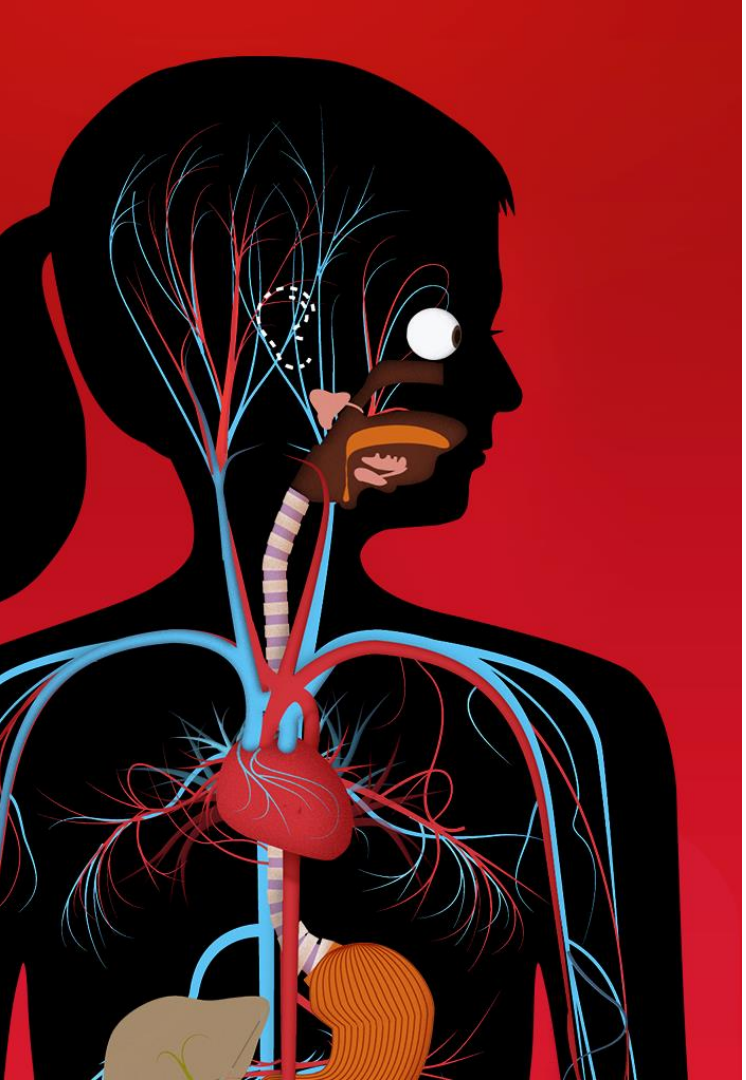
A range of features of **lisdexamfetamine** suggest it could provide a more effective alternative as a long-acting stimulant

- **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



lisdexamfetamine

POTENTIAL SIDE EFFECTS & ADVERSE EFFECTS

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

Table 1

Lisdexamfetamine: Fast facts

Brand name: Vyvanse
Class: CNS stimulant
Indication: Moderate and severe binge eating disorder
FDA approval date: January 30, 2015
Manufacturer: Shire
Dosage forms: 10, 20, 30, 40, 50, 60, and 70 mg capsules
Recommended dosage: 30 mg/d in the morning, titrated by 20 mg/d per week to 50 to 70 mg/d

EXCLUSION CRITERIA

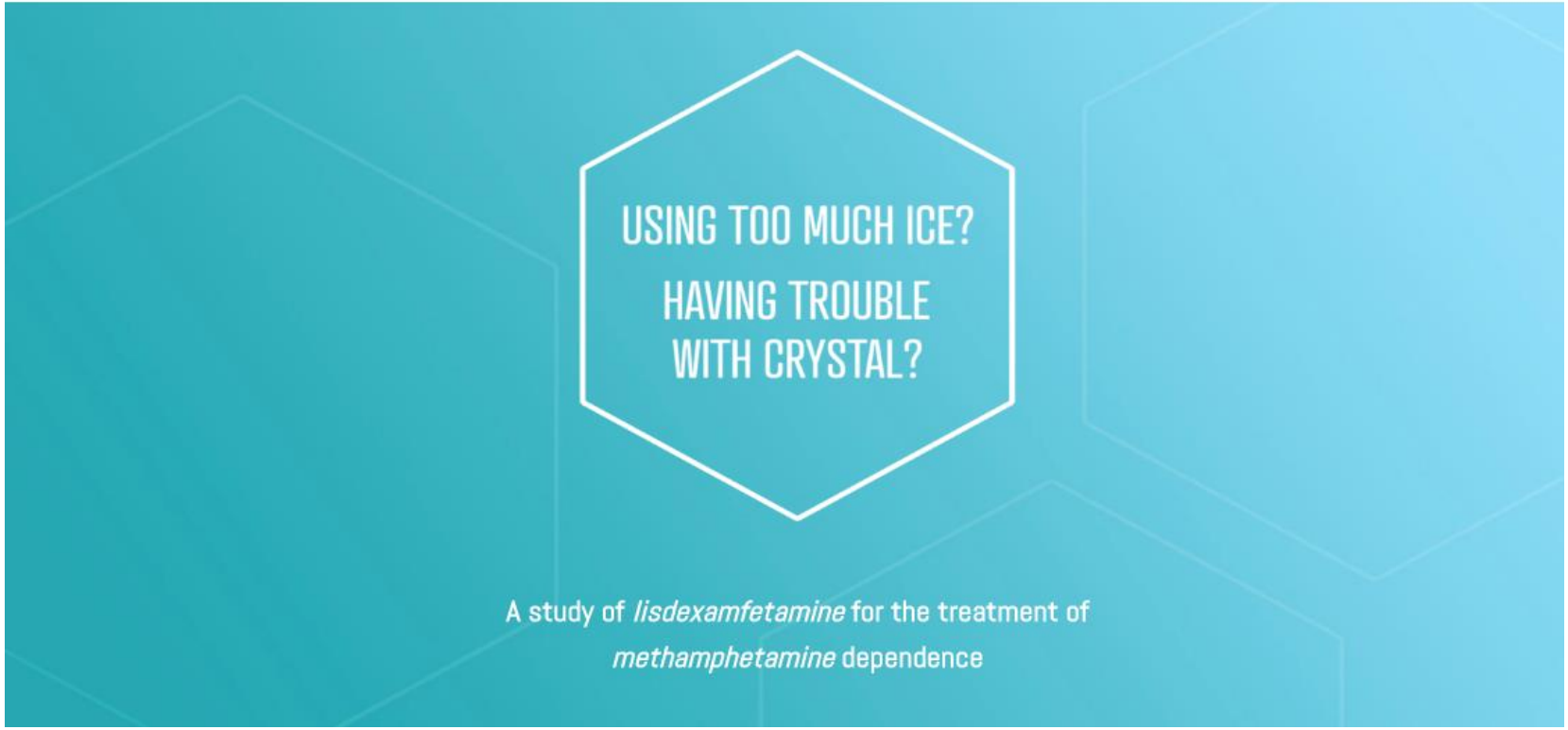
- Unstable other substance use
- No significant (unstable) psychiatric illness *(as judged by trial psychiatrist)*
- A range of cardiovascular illnesses

INCLUSION CRITERIA

- Adults with methamphetamine dependence
- Other treatments haven't worked

CRACKS IN THE ICE

THE LIMA STUDY



limastudy.info

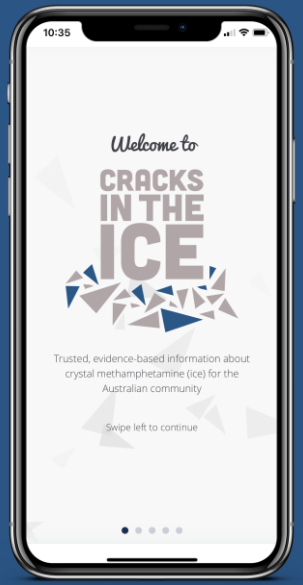
CRACKS IN THE ICE

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

Download the app today



Download on the App Store

GET IT ON Google Play

Search for “Cracks in the Ice” and download for FREE

Follow us on social

@cracksintheice

twitter.com/cracksintheice
facebook.com/cracksintheice

CRACKS IN THE ICE

THANK YOU

info@cracksintheice.org.au

Find out more at:

www.cracksintheice.org.au

Australian Government
Department of Health

THE UNIVERSITY OF SYDNEY
Matilda Centre