Methamphetamine: The Science of Addiction

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Department of Health and Human Services

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Methamphetamine

Speed

Ice

Crank

Crypto

Chalk

Fire

Glass
Methamphetamine

“Meth”, “Speed”, “Ice”, “Glass”, “Crystal”, “Crank”

Stimulant – potential neurotoxin associated with long-lasting effects on the dopamine and serotonin systems.
Who uses methamphetamine?
Tools to Monitor National Drug Trends

- NIDA’s Community Epidemiology Workgroup
- SAMHSA’s National Survey on Drug Use & Health
- NIDA’s Monitoring the Future
- SAMHSA’s Drug Abuse Warning Network
- SAMHSA’s Treatment Episode Data Set
- NIJ’s Arrestee Drug Abuse Monitoring
• Timely information on use patterns
• Identify emerging trends
• Identify who is actually using and vulnerable populations
• Identify risk factors

WHY MONITOR?
Early 80s - outlaw biker gangs
Use was concentrated in the West, Southwest and Hawaii in the mid and late-80’s
Early to mid-90s spread to Midwest and South
Now at epidemic proportions in many regions of the country
Majority of users 18-34 years old
Use increasing in rural and suburban communities
According to surveys and estimates by WHO and UNDCP, methamphetamine is the most widely used illicit drug in the world except for cannabis.

Worldwide it is estimated there are over 42 million regular users of methamphetamine, as compared to approximately 15 million heroin users and 10 million cocaine users.
The Emerging Epidemic

WAVE 1: 1982-85
The Methamphetamine Epidemic in Philadelphia

1984 DAWN Monitors
Clandestine labs operated by bikers and/or local gangs
The Emerging Epidemic

WAVE 2: 1986-94
The Early Spread of Methamphetamine
The Emerging Epidemic

WAVE 3: 1995-96
The Spread of Methamphetamine Eastward
Methamphetamine Lab Seizures: 1999 and 2004

Total of All Methamphetamine Laboratories Including Labs Only, Meth Only Calendar Year 1999

Total of All Meth Clandestine Laboratory Incidents Including Labs, Dumpsites, Chem/Glass/Equipment Calendar Year 2004

Source: National Clandestine Laboratory Database
Total: 6,781 / 43 States Reporting Dates: 01/01/99 to 12/31/99

Source: National Clandestine Laboratory Database
Total: 15,994 / 49 States Reporting Dates: 01/01/04 to 12/31/04
Primary Methamphetamine/amphetamine admission rates
(per 100,000 population aged 12 and over)

NOTES: See Chapter 2.
SOURCE: Office of Applied Studies, Substance Abuse and Mental Health Services Administration, Treatment Episode Data Set (TEDS) – 3.01.04.
The spread (geographically and into new user groups) of methamphetamine abuse was identified as an issue of great concern by CEWG members.

Abuse indicator remain high in Hawaii, west coast and southwest areas AND, notably,

Methamphetamine abuse is spreading eastward.
CEWG: Monitoring Methamphetamine Abuse

One of the Data Sources (DAWN ED Mentions)

1983

- Miami: 9
- St. Louis: 2
- Denver: 4
- Chicago: 4
- Atlanta: 9
- Washington, DC: 0
- Baltimore: 3
- Philadelphia: 187
- Minneapolis: 7
- Phoenix: 7
- San Diego: 47
- Los Angeles: 22
- Seattle: 3
- San Francisco: 36
- Dallas: 18
- Boston: 1
CEWG: Monitoring Methamphetamine Abuse

One of the Data Sources (DAWN ED Mentions)

1983, 1994

- San Francisco: 1,301 (1983), 36 (1994)
- Phoenix: 802 (1983), 7 (1994)
In 2003, over 12.3 million people age 12 or older reported having used methamphetamine at least once in their lifetime.

BUT

Is methamphetamine abuse increasing?

Source: 2003 NSDUH, SAMHSA
According to the Monitoring the Future Study, methamphetamine is not increasing.

Percent of students reporting use of methamphetamine in past year, by grade.

Legend:
- Red diamond: 8th Grade
- Yellow square: 10th Grade
- Green triangle: 12th Grade

* P < .05
Primary Methamphetamine Treatment Admissions

Treatment Episode Data Set (TEDS)
What is methamphetamine?
METHAMPHETAMINE

\[ \text{CH}_2\text{CH} \cdot \text{NH} \cdot \text{CH}_3 \]
Amphetamine Drugs

Amphetamine

Methamphetamine

Methylenedioxymethamphetamine (Ecstasy, MDMA)

Transmitters

Dopamine

Serotonin
• Schedule II drug
• High potential for abuse
• Limited therapeutic use:
  • Narcolepsy
  • Ritalin resistant ADD
  • Extreme obesity

WHAT IS METHAMPHETAMINE?
Ice

High purity methamphetamine crystals or coarse powder ranging from translucent to white, sometimes with a green, blue, or pink tinge.
Speed

- It is methamphetamine powder ranging in color from white, yellow, orange, pink, or brown.
- Color variations are due to differences in chemicals used to produce it and the expertise of the cooker.
- Other names: shabu, crystal, crystal meth, crank, tina, yaba
What is Yaba?

- Combination of methamphetamine and caffeine
- Means crazy medicine in Thai
- Produced in Southeast and East Asia
- Popular in Asian communities in the U.S.
- Increasingly available at raves and techno parties
- Sold as small, brightly colored green or orange-red tablets
- Sometimes flavored like candy, appealing to youth
- Sometimes heated and vapors inhaled (chasing the dragon) or crushed into powder and snorted or injected

National Drug Intelligence Center, DOJ
• Synthetic stimulant
• Pills, capsules, powder, and chunks
• Can be made from easily available OTC drugs containing ephedrine, pseudoephedrine, etc.
• “Cookers” in clandestine labs
• Recipe on internet
• Intranasal snorting: 5 min. to onset
• Oral ingestion: 20 min. to onset
• Smoked: seconds to onset (euphoric rush)
• IV Injection: seconds to onset (euphoric rush)
Rapid input dominates!

- Immediate euphoric “rush”
- Produces 8 to 24 hr high

Snorting: 46%
Smoking: 31%
IV: 19%
Other: 3%

Pennell, 1999
• Intranasal snorting: 2-4 hours
• Oral ingestion: 3-5 hours
• Smoked: 1-3 hours
• IV Injection: 1-3 hours; may last 6-12 hours, depending on tolerance and dosage
2002 Methamphetamine Price Ranges

Powdered Meth:
• $3,000-$13,000/pound
• $300-$1,700/ounce
• $40-$125/gram

Ice:
• $1,200-$70,000/pound
• $350-$2,300/ounce
• $120-$500/gram

HOW MUCH DOES METH COST?
What are the effects of methamphetamine?
Concerns with Methamphetamine

- Neurotoxic in animal models of drug self-administration
- Highly addictive
- Intoxication associated with behaviors that increase risks for infection with HIV and HCV
- Can be easily manufactured by small clandestine laboratories
Does methamphetamine affect the way you function?

- speed and motor coordination
- attention and alertness
- cognitive function
- mood
- motivation
• Increased motor activity
• Increased attention
• Decreased fatigue
• Appetite suppression
• Euphoria/Rush
• Increased respiration
• Hyperthermia
• Irregular heartbeat
• Irritability
• Tremors
• Convulsions
• Stroke
• Brain hemorrhage
• Shortness of breath
• Nausea/vomiting

ACUTE EFFECTS OF METH USE
LONG TERM EFFECTS OF METH USE

- Addiction
- Psychosis/paranoia
- Hallucinations
- Anxiety
- Depression
- Anorexia/malnutrition
- Aggression/violence
- Formication & skin infections
METHAMPHETAMINE WITHDRAWAL SYNDROME

- Drug craving
- Depression
- Sleep disturbances
- Hunger
• Sores/abscess at injection site
• Infection of heart valves and lining
• HIV/AIDS
• HEP C & other infectious diseases
METH Use Leads to Severe Tooth Decay


“METH Mouth”

Meth and AIDS
What is the Role of Methamphetamine in the HIV Epidemic?

- Does it disrupt immunological function?
- What is the neurobiology that underlies the risky sexual behavior that occurs during METH intoxication?
- What physiological changes resulting from METH use may increase level of infectivity (e.g., erosion of normal protective epithelial layer)?
Methamphetamine and Sex
I am more likely to have sex when using ...

Percent Responding "Yes"

Primary Drug of Abuse

<table>
<thead>
<tr>
<th>Drug</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>opiates</td>
<td>7.4</td>
<td>11.4</td>
</tr>
<tr>
<td>alcohol</td>
<td>41.5</td>
<td>50.0</td>
</tr>
<tr>
<td>cocaine</td>
<td>65.8</td>
<td>27.8</td>
</tr>
<tr>
<td>meth</td>
<td>79.4</td>
<td>61.1</td>
</tr>
</tbody>
</table>

(Rawson et al., 2002)
My sexual drive is increased by the use of …

(Rawson et al., 2002)
My sexual pleasure is enhanced by the use of …

![Bar chart showing the percent responding "Yes" to the use of different drugs by gender.]

(Rawson et al., 2002)
My sexual *performance* is improved by the use of …

(Rawson et al., 2002)
Methamphetamine Impacts the Spread and Course of HIV/AIDS:

- Increases risky sexual behavior, especially among men who have sex with men (MSM)
- Reduces medication adherence to HAART
- Increases replication of FIV in brain cells (the feline equivalent of HIV)
- Meth dependence increases the risk of HIV-related cognitive problems
Methamphetamine Dependence Increases Risk of Neuropsychological Impairment in HIV+ Persons

HIV+/METH+, HIV-/METH+, HIV+/METH- > HIV-/METH-

- HIV+/METH+ (n=43): 58%
- HIV-/METH+ (n=47): 40%
- HIV+/METH- (n=50): 38%
- HIV-/METH- (n=60): 18%

p < 0.005

Grant et al, J Intl Neuropsychological Society V 10, pg 1, 2004
What about prenatal exposure to methamphetamine?
Animal Studies

• Limited studies of prenatal exposure to methamphetamine

• Variable results: Some decreases in neurotransmitters; some increases; different sites

• May result from differing dose levels, variable gestational exposure, and postnatal ages at which offspring are assessed.

• More studies needed.
Infant Development, Environment, And Lifestyle Study (IDEAL)
Multi-Site Study of Prenatal Methamphetamine Use

- “Hotbeds” of Methamphetamine Use
  - Iowa
  - Oklahoma
  - Southern California
  - Hawaii

- Over 13,000 deliveries screened
- Subjects: 200 Meth exposed and 200 control infants
- Three-year longitudinal study
- Preliminary data available for newborn and one month
Multisite Study of Prenatal Methamphetamine

- Child Outcomes
  - Arousal regulation
  - Cognition
  - Social relationships
  - Neuromotor development
  - Neuroendocrine function
  - Medical status

- Overall goal: To determine how drug effects and effects of psychosocial risk characteristics of the environment combine to affect child outcome
Fetal Effects of Methamphetamine

Preliminary evidence suggests that prenatal methamphetamine exposure is associated with subtle physical and neurobehavioral effects including:

• Lower arousal
• Poorer self-regulation
• Poorer quality of movement
• Increased central nervous system stress
• Small for gestational age
• Long-term consequences???
Clinical observations suggest that prenatal Methamphetamine exposure is associated with increased incidence of:

**Short-term effects**
- Abnormal sleep patterns
- Poor feeding
- Tremors

**Delayed Effects**
- Attention deficit disorder
- Poor School Performance
- Language delays
So...
Why Do People Take Methamphetamine In The First Place?
Why do people take drugs?

**To feel good**
- To have novel:
  - Feelings
  - Sensations
  - Experiences
- AND
- To share them

**To feel better**
- To lessen:
  - Anxiety
  - Worries
  - Fears
  - Depression
  - Hopelessness
WHY DO PEOPLE TAKE METH?

• Sense of well-being, euphoria
• Increased energy
• Release of social inhibitions
• Feelings of cleverness/competence
• Magnification of pleasurable sensations
• Appetite suppression
People Take Methamphetamine Because They Like What it Does to Their Brains
How does Methamphetamine exert its behavioral effects?

We Know That Despite Their Many Differences, most Abused Substances Enhance the Dopamine and Serotonin Pathways
**Dopamine Pathways**

- Functions
  - Reward (motivation)
  - Pleasure, euphoria
  - Motor function (fine tuning)
  - Compulsion
  - Perseveration

**Serotonin Pathways**

- Functions
  - Mood
  - Memory processing
  - Sleep
  - Cognition

Locations:
- Nucleus accumbens
- Frontal cortex
- Hippocampus
- Striatum
- Substantia nigra/VTA
- Raphe
Vmat, Action potential, transporter, dopamine/serotonin, DA/5HT receptor
• Release DA from vesicles and reverse transporter

Drug Types:
• Amphetamines
  - methamphetamine
  - MDMA (Ecstasy)
Natural Rewards Elevate Dopamine Levels

**FOOD**

- **NAc shell**
- % of Basal DA Output vs. Time (min)
- Empty Box Feeding

**SEX**

- DA Concentration (% Baseline) vs. Time (min)
- Mounts, Intromissions, Ejaculations

Sample Number 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17

**Source:** Di Chiara et al.

**Source:** Fiorino and Phillips

Natural Rewards Elevate Dopamine Levels
Effects of Drugs on Dopamine Levels

**AMPHEXTAMINE**

<table>
<thead>
<tr>
<th>Time After Amphetamine</th>
<th>% of Basal Release</th>
</tr>
</thead>
<tbody>
<tr>
<td>DA</td>
<td>DOPAC</td>
</tr>
<tr>
<td>HVA</td>
<td></td>
</tr>
</tbody>
</table>

**COCAINE**

<table>
<thead>
<tr>
<th>Time After Cocaine</th>
<th>% of Basal Release</th>
</tr>
</thead>
<tbody>
<tr>
<td>DA</td>
<td>DOPAC</td>
</tr>
<tr>
<td>HVA</td>
<td></td>
</tr>
</tbody>
</table>

**NICOTINE**

<table>
<thead>
<tr>
<th>Time After Nicotine</th>
<th>% of Basal Release</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accumbens</td>
<td>Caudate</td>
</tr>
<tr>
<td>Dose (mg/kg)</td>
<td></td>
</tr>
</tbody>
</table>

**MORPHINE**

<table>
<thead>
<tr>
<th>Time After Morphine</th>
<th>% of Basal Release</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose (mg/kg)</td>
<td></td>
</tr>
</tbody>
</table>

*Source: Di Chiara and Imperato*
Chronic methamphetamine abuse has long lasting effects on the brain....
Dopamine D2 Receptors are Lower in Addiction
Striatal FDOPA Activity

Pre-Amphetamine/Control

Post-Chronic Amphetamine (10 days)

Superior  Inferior
METH can be toxic to brain DA cells in laboratory animals. It is therefore important to determine if METH induces similar changes in DA cells in humans and to assess their functional significance and degree of recovery.
Dopamine Transporter Loss After Heavy Methamphetamine Use

Comparison Subject       METH Abuser

Methamphetamine Decreases Dopamine Receptors In the Human Brain

Source: Volkow, et al.
Dopamine Transporters ([\(^{11}\text{C}\)d-threo-MP])

Dopamine Receptors ([\(^{11}\text{C}\)raclopride])

Glucose Metabolism ([\(^{18}\text{FDG}\)])
Gray Matter Reductions in Methamphetamine Users

Infralimbic Cortex Even Has Structural Deficits

Methamphetamine users show Gray Matter Loss

Methamphetamine Abusers have Hippocampal Volume Deficits

Implication:

Brain changes resulting from prolonged use of psychostimulants, such as methamphetamine may be reflected in compromised emotional, cognitive, and motor functioning.
### Subjects

Detoxification in METH abusers

<table>
<thead>
<tr>
<th></th>
<th>Early (n = 12)</th>
<th>Late* (n = 13)</th>
<th>Controls (n = 21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age range (years)</td>
<td>21 - 47</td>
<td>26 - 38</td>
<td>21 - 43</td>
</tr>
<tr>
<td>Age mean (years)</td>
<td>32 ± 8</td>
<td>33 ± 5</td>
<td>32 ± 8</td>
</tr>
<tr>
<td>Gender</td>
<td>7 F, 5 M</td>
<td>9 F, 4 M</td>
<td>6 F, 15 M</td>
</tr>
<tr>
<td>Years of METH use (range)</td>
<td>2 - 20</td>
<td>2 - 20</td>
<td>0</td>
</tr>
<tr>
<td>Years of METH use (mean)</td>
<td>11 ± 7</td>
<td>12 ± 6</td>
<td>0</td>
</tr>
<tr>
<td>Amount of METH use (g/day)</td>
<td>3 ± 5</td>
<td>3 ± 4</td>
<td>0</td>
</tr>
<tr>
<td>Last day of METH use (range in months)</td>
<td>0.5 - 6</td>
<td>6 - 36</td>
<td>0</td>
</tr>
<tr>
<td>Last day of METH use (mean in months)</td>
<td>2.1 ± 1.4</td>
<td>14 ± 7</td>
<td>0</td>
</tr>
</tbody>
</table>

* 5 METH abusers were tested both in early and late detoxification

@ Only 11 controls underwent DAT measures

@ Controls
Subjects

**METH Abusers:**

- **Inclusion Criteria:**
  - DSM IV criteria for METH-dependence
  - METH use of at least: 0.5 g/day, 5 days a week and 2 years 2 weeks or more of abstinence

- **Exclusion criteria:**
  - seropositive for HIV,
  - co-morbid psychiatric illness and/or neurological disease,
  - drug-dependence other than METH and nicotine.

**Controls:**

- **Exclusion criteria:**
  - as for METH abusers except for the exclusion on dependence or abuse of METH.
Scanner: CTI 931 (15 slices, 6x6x6.5 mm FWHM).

Tracers: DAT: 4-8 mCi of $[^{11}C]d$-threo-methylphenidate
Dynamic scans obtained for a total of 84 min.
Metabolism: 4-8 mCi of FDG.
Twenty min emission scan started 35 after injection

Model: DAT: The ratio of DV in striatum to that of DV in CB corresponds to $(B_{\text{max}}/K_d) + 1$ and was used as model parameter of DAT availability.
Metabolism: Sokoloff model
Methamphetamine abusers have significant reductions in dopamine transporters.

\( \text{BNL - UCLA - SUNY} \)
\( \text{NIDA - ONDCP - DOE} \)
Motor Task
Loss of dopamine transporters in the meth abusers may result in slowing of motor reactions.

Memory Task
Loss of dopamine transporters in the meth abusers may result in memory impairment.
Dopamine Transporter Loss After Heavy Methamphetamine Use

Dependence of Motor Speed on Striatal DAT

**Gross Motor Function**

- Timed gait (seconds)
  - Graph showing a negative correlation:
    - $r = 0.53$
    - $p < 0.05$

- Dopamine transporter ($B_{\text{max}}/K_d$)

**Fine Motor Function**

- Pegboard (seconds)
  - Graph showing a negative correlation:
    - $R = 0.57$
    - $p < 0.05$

- Dopamine transporter ($B_{\text{max}}/K_d$)

*Volkow et al, AJP (in press)*
Dependence of Verbal Memory on Striatal DAT

**Interference recall**

- Number of words vs. Dopamine transporter (Bmax/Kd)
- \( R = 0.70 \)
- \( p < 0.005 \)

**Delayed recall**

- Number of words vs. Dopamine transporter (Bmax/Kd)
- \( R = 0.64 \)
- \( p < 0.01 \)

*Volkow et al, AJP (in press)*
Summary

- Significant DAT loss in METH abusers tested at early detoxification that is larger in caudate than putamen.

- Decreases in DAT are associated with motor slowing and impaired memory.

- DAT losses recover significantly with protracted detoxification but the recovery of NP function does not.
Conclusion

- DAT recovery with detoxification could reflect
  Recovery of damaged terminals
  Compensation by viable terminals
  or
  Decreases in expression of the DAT
  Decreases DAT trafficking and internalization

DAT recovery while beneficial was insufficient for complete recovery of NP function suggesting that other systems are involved in the NP abnormalities.
Recovery?

What do we know?
Chronic Amphetamine Causes Lasting Changes
We Have Generated A Lot of Evidence Showing That...

Prolonged Use of Methamphetamine Can Change the Brain In Fundamental and Long-Lasting Ways

Is there recovery?
DAT Recovery with prolonged abstinence from methamphetamine

Effects of METH Detoxification on DAT

<table>
<thead>
<tr>
<th></th>
<th>Caudate</th>
<th>Putamen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bmax/Kd (Early)</td>
<td>1.5</td>
<td>2.3</td>
</tr>
<tr>
<td>Bmax/Kd (Late)</td>
<td>1.9</td>
<td>2.1</td>
</tr>
</tbody>
</table>

Significance: $p < 0.003$, $p < 0.05$
Neuropsychological Function in METH Abusers During Early and Late Detoxification

**Motor**

- **Timed gate**
  - Time (seconds)
  - Early: 6, 7, 8, 9, 10, 11, 12, 13
  - Late: 6, 7, 8, 9, 10, 11, 12, 13
  - \( p = 0.14 \)

- **Pegboard**
  - Time (seconds)
  - Early: 45, 50, 55, 60, 65, 70, 75, 80
  - Late: 45, 50, 55, 60, 65, 70, 75, 80
  - \( p = 0.73 \)

**Memory**

- **Immediate Recall**
  - Number of words
  - Early: 6, 8, 10, 12, 14, 16
  - Late: 6, 8, 10, 12, 14, 16
  - \( p = 0.47 \)

- **Delayed Recall**
  - Number of words
  - Early: 6, 8, 10, 12, 14, 16
  - Late: 6, 8, 10, 12, 14, 16
  - \( p = 0.11 \)
DAT in Methamphetamine Abusers Tested During Early or During Late Detoxification

Caudate

<table>
<thead>
<tr>
<th></th>
<th>Controls</th>
<th>Early</th>
<th>Late</th>
</tr>
</thead>
<tbody>
<tr>
<td>DA (Bmax/Kd)</td>
<td>(n =11)</td>
<td>(n =12)</td>
<td>(n =11)</td>
</tr>
<tr>
<td>p</td>
<td>&lt;0.001</td>
<td>&lt;0.01</td>
<td></td>
</tr>
</tbody>
</table>

Putamen

<table>
<thead>
<tr>
<th></th>
<th>Controls</th>
<th>Early</th>
<th>Late</th>
</tr>
</thead>
<tbody>
<tr>
<td>DA (Bmax/Kd)</td>
<td>(n =11)</td>
<td>(n =12)</td>
<td>(n =11)</td>
</tr>
<tr>
<td>p</td>
<td>&lt;0.01</td>
<td>&lt;0.05</td>
<td></td>
</tr>
</tbody>
</table>
Partial Recovery of Brain Dopamine Transporters in Methamphetamine (METH) Abuser After Protracted Abstinence

Brain Metabolism in METH Abusers with Abstinence

**Thalamus**

+12 ±9%, \( p \leq 0.015 \)

**Striatum**

+2.7 ±6.7%, \( p = 0.34 \)
Partial Recovery of Brain Metabolism in Methamphetamine (METH) Abuser after Protracted Abstinence

Control Subject (30 y/o, Female)
METH Abuser (27 y/o, Female) 3 months detox
METH Abuser (27 y/o, Female) 13 months detox

Thalamic and Striatal Metabolism in METH Abusers During Early and Late Detoxification

<table>
<thead>
<tr>
<th>Ratio</th>
<th>Thalamus</th>
<th>Striatum</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.05</td>
<td>1.1</td>
<td>1.3</td>
</tr>
<tr>
<td>1.1</td>
<td>1.15</td>
<td>1.3</td>
</tr>
<tr>
<td>1.15</td>
<td>1.2</td>
<td>1.3</td>
</tr>
<tr>
<td>1.2</td>
<td>1.25</td>
<td>1.3</td>
</tr>
<tr>
<td>1.25</td>
<td>1.3</td>
<td>1.3</td>
</tr>
</tbody>
</table>

+12 ± 9%, p < 0.015
+2.7 ± 6.7%, p = 0.34
DAT in Methamphetamine Abusers Tested During Early or During Late Detoxification

**Caudate**

- Controls (n=11)
- Early (n=12)
- Late (n=11)

**Putamen**

- Controls (n=11)
- Early (n=12)
- Late (n=11)

- DA transporters (Bmax/kd)

- p < 0.001
- p < 0.01
- p < 0.05
Summary

Increases in Metabolism
  Early: posterior parietal cortex (precuneus)
  Late: posterior parietal cortex (precuneus)

Decreases in Metabolism
  Early: caudate, NAc, insula, thalamus, mesencephalum
  Late: caudate, NAc, insula

Recovery in thalamic metabolism associated with recovery in NP tests linked to dopaminergic activity.
We Have A Variety Of Effective Treatment Options In The Clinical Toolbox

...And We Are Trying To Improve Existing And Develop New Options
In Order to Develop Effective Treatments

What Do We Need to Do To...

• Counteract neuroadaptations that underlie the addictive process?

• Reverse METH’s Neurotoxic Effects?
Treatments for Methamphetamine

- Cognitive Behavioral Therapies
- Contingency Management
- MATRIX Model
- New Medications (treatment and overdose) are being developed
## Methamphetamine Addiction Pharmacotherapies in Clinical Trials

<table>
<thead>
<tr>
<th>Phase I</th>
<th>Phase II</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aripiprazole</td>
<td>Baclofen</td>
</tr>
<tr>
<td>Atomoxetine</td>
<td>Bupropion</td>
</tr>
<tr>
<td>Bupropion</td>
<td>Gabapentin</td>
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<tr>
<td>Carvedilol</td>
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<td>Clonidine</td>
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<tr>
<td>Lobeline</td>
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<td>Modafinil</td>
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<tr>
<td>Perindopril</td>
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</tr>
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<td>Prazosin</td>
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<tr>
<td>Rivastigmine</td>
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<tr>
<td>Sertraline</td>
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<tr>
<td>Topiramate</td>
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Clinical Challenges for Treatment of Methamphetamine Addiction

- Poor treatment engagement rates
- High dropout rates
- Severe paranoia
- High relapse rates
- Ongoing episodes of psychosis
- Severe craving
- Protracted dysphoria

Many patients may require medical/psychiatric supervision and need ongoing treatment with antipsychotic medications
Self-report of MA use at enrollment, discharge, and 6 month follow-up following Matrix treatment

Rawson et al, Addiction, 99, p 708, 2004
The Goal of Treatment is to help the brain and the person recover normal function.
What We Need To Know – Future Plans

• Demographics - who is using meth and why
• Brain mechanisms of meth action and addiction
• Improved Prevention
• Genetic/environmental factors in vulnerability to meth addiction
• Progression from meth use to addiction
• Better Treatments: Behavioral and Pharmacotherapies
• Prenatal effects