

Methamphetamine: Effects on the Brain and Challenges in Reunification

Wendy Wright, MD
Rady Children's Hospital of San Diego
January 23, 2012

- **Prenatal Effects.** Infants exposed to methamphetamine prenatally may experience developmental and learning delays (Rawson, Anglin, et al., 2002), research in this area is ongoing. Children with these effects may need specific treatment to address these issues.

Household safety. Exposure to environmental toxins (arsenic, lye, mercury, lead) during the manufacture process is especially risky for young children (USDOJ, 2003). A complete assessment of household safety must be conducted with a specific eye to potential household hazards associated with methamphetamine manufacture and use.

Childhood supervision and neglect.

Parents may sleep for excessive periods of time following drug binges and during periods of withdrawal. This may lead to a lack of supervision and to other forms of child neglect. Because methamphetamine use suppresses appetite, users may not regularly purchase or prepare food leaving children at risk of nutritional neglect (Rawson, Anglin, et al., 2002).

- **Physical abuse.** Agitation and violent behavior associated with withdrawal may increase risk for physical abuse.

Sexual abuse. When parents are using methamphetamine, children may be exposed to sexualized behavior in adults which may also put them at risk for sexual abuse

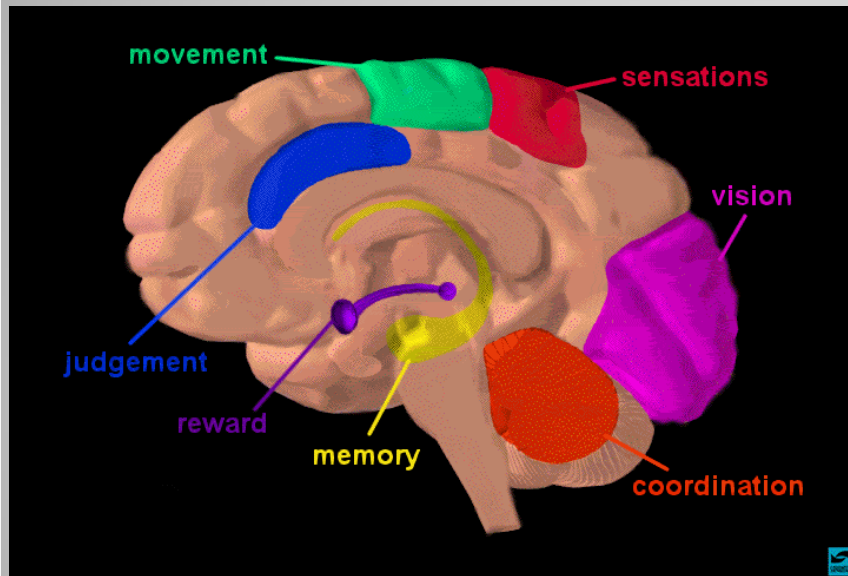
Lack of positive social support systems. Parents involved with methamphetamine may have few positive support systems and only be associated with others involved with methamphetamine. These conditions increase concern for child safety, and make it more difficult to change negative behaviors

- SL – 17 yr old and her 4th time at Polinsky
- LL – 13 yr old and 4th time at Polinsky
- HL – 13 yr old not with her twin – in a group home for behavior problems
- TL – 10 yr old not at Polinsky with her sibs and whereabouts unknown to her sibs
- BL – 2 yr old with medical issues and at Polinsky with sibs
- All there as mom going to rehab “again” and can’t have kids with her.

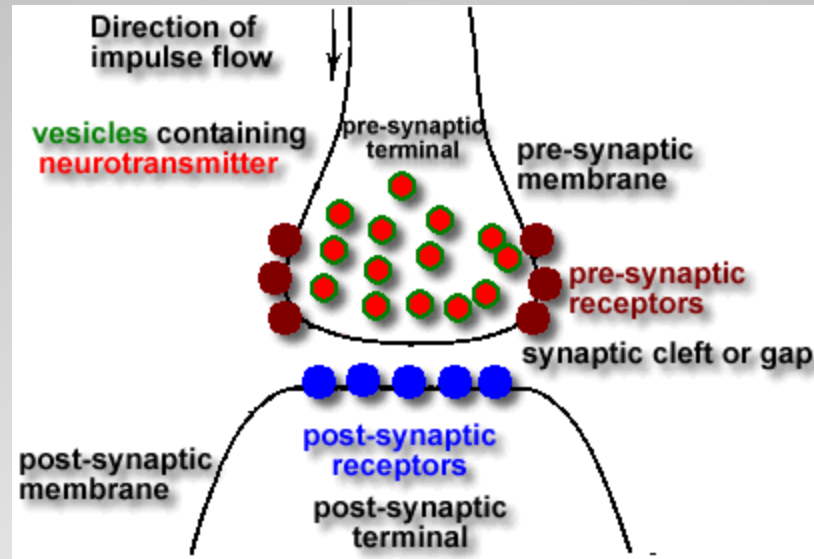
- 2 sibs admitted to Polinsky as mom missing for 2 days and they were found in a garage with a known drug and sex offender
- Oldest – 11 has been in 6 schools from K to 6th grade
- Second mad and scared because the first day mom gone was her 9th birthday
- Mom with long history of off and on drug abuse

- Neurotransmitters
- Methamphetamine
 - Acute Affects
 - Chronic Affects
- Research

Dopamine System:



- *Every* substance of abuse has some effect on the limbic (dopamine) reward system
- Dopamine, one of many neurotransmitters, is found in several regions of the brain; is involved in pleasurable feelings, activity reinforcement, movement, motivation, & emotions



- Synthesized in neuron
- Stored in synaptic vesicles
- Released into synapse after excitatory changes in the pre-synaptic nerve
- Binds to post-synaptic receptor
- Opens channels allowing ionic changes in post receptor propagating impulse

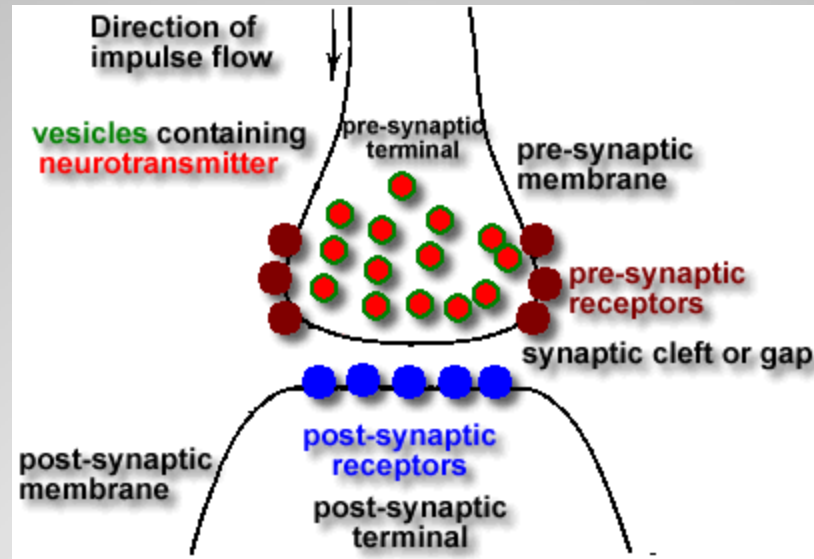
Physiology of Neurotransmitters

- Cellular Action
- Methods of Usage
- Clinical Effects
- Acute Affects
- Chronic Effects

Methamphetamine

- Enters nerve terminals via cell membranes
- Transported in via transporter molecules
- In terminal enters DA vesicles
 - Releases DA
- Blocks intracellular destruction of DA
- All leads to ↑ amount of DA in synapse

Cellular Action



- DA in the cytoplasm then undergoes auto-oxidation which generates toxic oxygen radicals and other chemicals
- Excess dopamine itself causes the toxicity
- MA itself is not toxic – It just gets the process started

Cellular Action

Lukas SE et al: Nat'l Consensus Meeting on Use, Abuse & Squeal of MA with Implications for Prevention, Research, & Research 1996

- Smoked, orally ingested, or injected
- Euphoria, alertness and confidence, reduced fatigue and appetite
- Massive release of DA = High
- Plasma half-life= 4-12 hrs; effects last 4-24 hours (depending on age and other co-morbid conditions)

Methods of Usage

Lukas SE et al: Nat'l Consensus Meeting on Use, Abuse & Sequelae of MA with Implications for Prevention, Research, & Research 1996

Methamphetamine – Acute Clinical Effects

- Related to ↑ DA in synapse
- ↑ Fight or Flight responses
- Pleasure and euphoric feelings
- Influences emotions of:
 - Aggression
 - Defensive behaviors
 - Social behaviors
 - Sexual behaviors
- Movement disorders

Acute Effects

- Temperature
- Blood Pressure
- Heart Rate
- Pupils

Acute Effects

- Irritability
- Impulsivity
- Impaired judgment
- Insomnia
- Psychotic behaviors
 - Hallucinations
 - Paranoia
- Acute toxic psychosis

Methamphetamine

Chronic Effects

- Weight Loss
- Skin Problems
- Dental Issues
- Cardiac Disabilities
- Central Nervous System

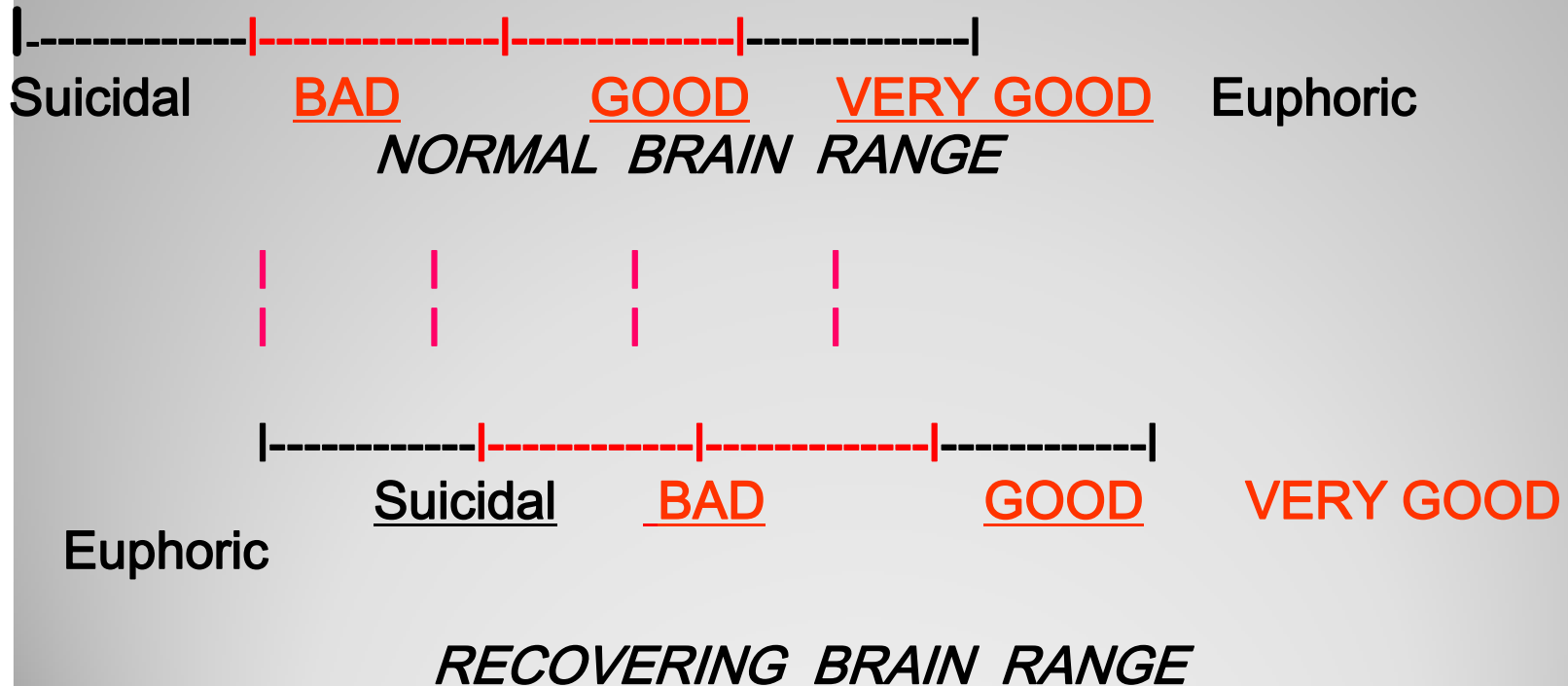
- Drugs of abuse activate DA system
- DA system connected to brain controlling memory, emotion, motivation
- Non-drug pleasurable activity also activates these centers
- Re-enforces the drug behavior to mimic other pleasures

Chronic Use

Chronic Use

- Eventually, the dopamine circuit becomes blunted
- Tolerance = re-set of the circuit to a new normal
- The user is thus no longer depressed but is not euphoric
- “Drinking to feel normal”

Brain's Limited Range & Duration of "Emotional" Experience



- A Japanese study noted that after an average use of 5 years the risk of psychosis was significantly greater.
- The distinguishing feature from schizophrenia is its visual or tactile hallucinations, as opposed to generally auditory hallucinations in the former.

Chronic Central Effects in Users

- Tolerance: The chronic user will progressively increase the dose to obtain desired effects
- Methamphetamine abusers may increase their dose 50 to 100 times the initial amount over time: up to several hundred milligrams/day, which would be fatal to the non-user

Chronic Use

- Compulsive or repetitive behaviors are manifestations of chronic use.
- Long term use in humans has resulted in delusional, paranoid behavior and violence.
- Severe neurological and psychiatric conditions such as hemorrhagic and ischemic infarcts, subarachnoid hemorrhages and memory loss may be seen.

Chronic Central Effects in Users

A Few Studies

Chronic Central Effects in Users

- Subjects: N=26 with a history of MA dependence; 24 age-matched controls
- Regular MA use for at least 12 months, at least 5 days/wk, 0.5g/d
- Last MA use more than 2 weeks earlier
- Mean period of abstinence of 4.25 months (0.5-21 mos)

Chronic Central Effects in Users

- Proton MRS measurements of N-acetylaspartate (NAA); a putative marker of neuronal integrity, which is reduced along with neuronal damage or loss.
- Reduced NAA has been reported in many conditions such as hypoxia, cerebral infarction, closed head trauma, dementias, HIV brain diseases and brain tumors.

Chronic Central Effects in Users

- Three brain regions studied: Midfrontal gray matter, right frontal white matter, right basal ganglia
- NAA reduced by 6% in the frontal lobe and by 5% in the basal ganglia of MA users
- White frontal matter decrease is dose-dependent
- These findings suggest neuronal loss or persistent neuronal damage

Chronic Central Effects in Users

- The persistence of these abnormalities may be related to persistent abnormal behaviors such as violence, psychoses and personality changes seen in some individuals months or even years after their last drug use.

Recovery of DA Transporters with Protracted MA Abstinence

- 12 methamphetamine abusers were enrolled in a California drug-court monitoring program and were drug-free during the study
- First assessment: within 6 months of last using methamphetamine
- Second assessment: at least 9 months later

Volkow ND, Chang L et al Am J Psychiatry 21 (23) p 9414-8 Dec 2001

Recovery of DA Transporters with Protracted MA Abstinence

- After 9 month's abstinence, the participants' DAT levels had increased to almost near non-users, yet they performed no better on tests of gross and fine motor skills and memory.
- However, the sample size was small.
- Those who used meth for less time and in smaller quantities recovered more DA transporter molecules

Chronic Central Effects in Users

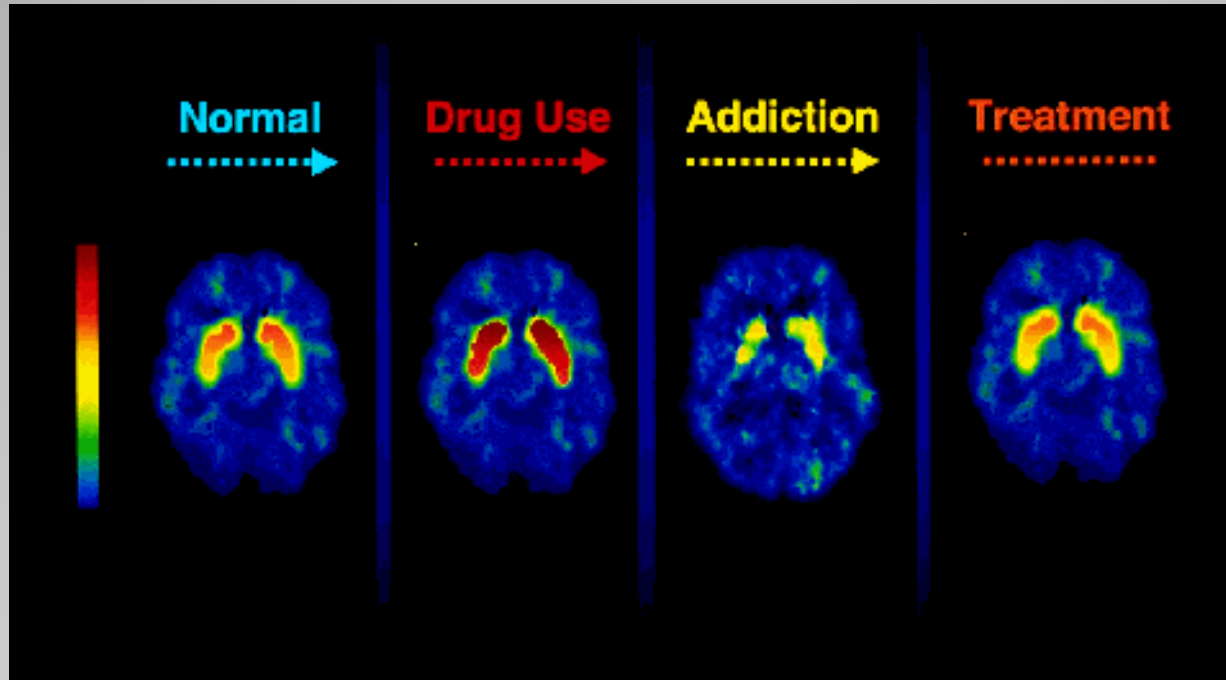
- The longer the period between the 1st & 2nd evaluation, the greater the amount of recovery of DA transporter levels.
- The relationship between impaired function and DAT loss and recovery is still unclear. Longer follow-up is needed.

Chronic Central Effects in Users

- PET scans of 15 methamphetamine abusers and 20 non-drug users
- Meth users had a lower rate of glucose metabolism and lower levels of dopamine D2 receptors in the orbitofrontal cortex: the part of the brain associated with compulsive disorders

Volkow & Chang, Am J. of Psychiatry, Dec 2001

Brain changes with Meth Use



•PET scans show loss of dopamine transporters with meth use/addiction, and improvement after long-term sobriety

-Volkow 2001

Chronic Central Effects in Users

- Disruption of this metabolism may contribute to compulsive drug intake in addicted people
- This association between DA receptors and the orbitofrontal cortex metabolism has been previously reported in cocaine addicts and alcoholics

Volkow & Chang, Am J. of Psychiatry, Dec 2001

More Meth Brain Damage

- Perfusion MRI: measure blood flow in key brain regions
- Methamphetamine abuse is related to changes in blood flow in the same regions that PET scans have shown increased glucose usage
- 20 nonusers and 20 methamphetamine users who had used >2.8 gm/day for average of 6.5 days/week for approximately 8 years BUT had been abstinent for an average of 8 months

More Meth Brain Damage

- The increased blood flow was found in the parietal regions, which are involved in receiving and processing information from sensory receptors in the skin, muscles and joints as well as in the integration of auditory, visual and somatic information
- Dr. Chang theorizes the increased flow represents an increase in activity by glial cells due to their higher metabolic rate. These try to repair damaged nerve cells.

- **Methamphetamine Abusers Have Slower Reaction Times on Computerized Cognition Tests**

- Computer-task sequential reaction time tests require subjects to press a key when they see a number appear twice in a row (one-back target) or when a number repeats after one intervening number (two-back target). On the one-back test, methamphetamine abusers' average response time was 21.5 percent slower than that of the nonusers; on the two-back test, their average response time was 18 percent slower.

More Meth Brain Damage

- Methamphetamine users had decreased blood flow in other areas of the parietal region and in the frontal & basal ganglia region
- These areas control response speed and attention span and coordinate motor functions and psychomotor speed
- The decreased blood flow may indicate that the nerve cells are damaged beyond the point of repair by the glial cells

What does this mean?

- A battery of 9 computerized tests designed to assess subtle signs of cognitive decline were administered
- Testing revealed consistently slower response times for methamphetamine abusers
- Particularly on tasks that required working memory, the immediate storage of information, and mental coordination

What Does this All Mean?

- Parenting
 - How, When, Quality
- Long term Skills
- Permanency for the kids