

Psychiatric Comorbidity in Methamphetamine-Dependent Patients



Suzette Glasner-Edwards, Ph.D.
UCLA Integrated Substance Abuse Programs
August 11th, 2010



Overview

- Comorbidity in substance users
- Risk factors for depression and suicidality in meth users
- Anxiety in meth users
- Psychosis in meth users
- Conclusions and future directions

Addiction and Psychiatric Comorbidity

- What is comorbidity?
- Comorbidity is common in addiction.
- Comorbidity is observed in at least 48% of adults with meth addiction.
- In meth users, the most common comorbid psychiatric diagnoses are mood, anxiety, and psychotic disorders.
- Understanding who is at greatest risk can inform the plan of care.

Clinical Challenges in the Treatment of Psychiatric Disorders and Addiction

- Although abstinence helps, it does not resolve the underlying psychiatric disorder.
- Confrontational approaches typical in addiction treatment settings may exacerbate mood and anxiety disorders.
- 12-step models often do not acknowledge the need for pharmacological treatments.
- Treatment programs do not often offer integrated treatment for substance and psychiatric disorders.

Possible Relationships Between Addiction and Psychiatric Illness

- Psychiatric illness causes addiction
 - Self-medication
 - Psychiatric illness alters brain reaction to substances
 - Addiction may take on a life of its own
- Addiction causes psychiatric illness
 - Intoxication/withdrawal effects
 - Addiction causes brain changes that result in psychiatric illness
 - Psychiatric illness may take on a life of its own
- Independent illnesses

Possible Relationships Between Addiction and Psychiatric Illness (cont'd)

- Psychiatric comorbidity worsens prognosis
 - Interferes with treatment process
 - Conditions fuel each other, making it difficult to achieve treatment goals
- Addiction+psychiatric illness become related over time
 - Psychiatric symptoms become conditioned cues that trigger drug use
- Common risk factors underlying both disorders
 - E.g., stress, trauma, genetics

Comorbidity and Outcomes

- Psychiatric diagnoses are associated with poorer outcomes in drug abuse treatment settings.
- In meth users, this has been found for a range of psychiatric illnesses including mood, anxiety, psychotic, and eating disorders.
- Depressive disorders (but not symptoms), whether or not they are substance-induced, predict relapse and/or failure to remit from alcohol and drug use disorders (Hasin et al., 2002; Greenfield et al., 1998)

Clinical Implications

- Comorbidity is common and worsens prognosis
- Depression is easiest to identify due to the high prevalence of this illness
- Other less prevalent disorders (e.g., bipolar disorder, panic disorder, schizophrenia) are strongly associated with substance use disorders
- If you see depression + substance abuse, look for other disorders

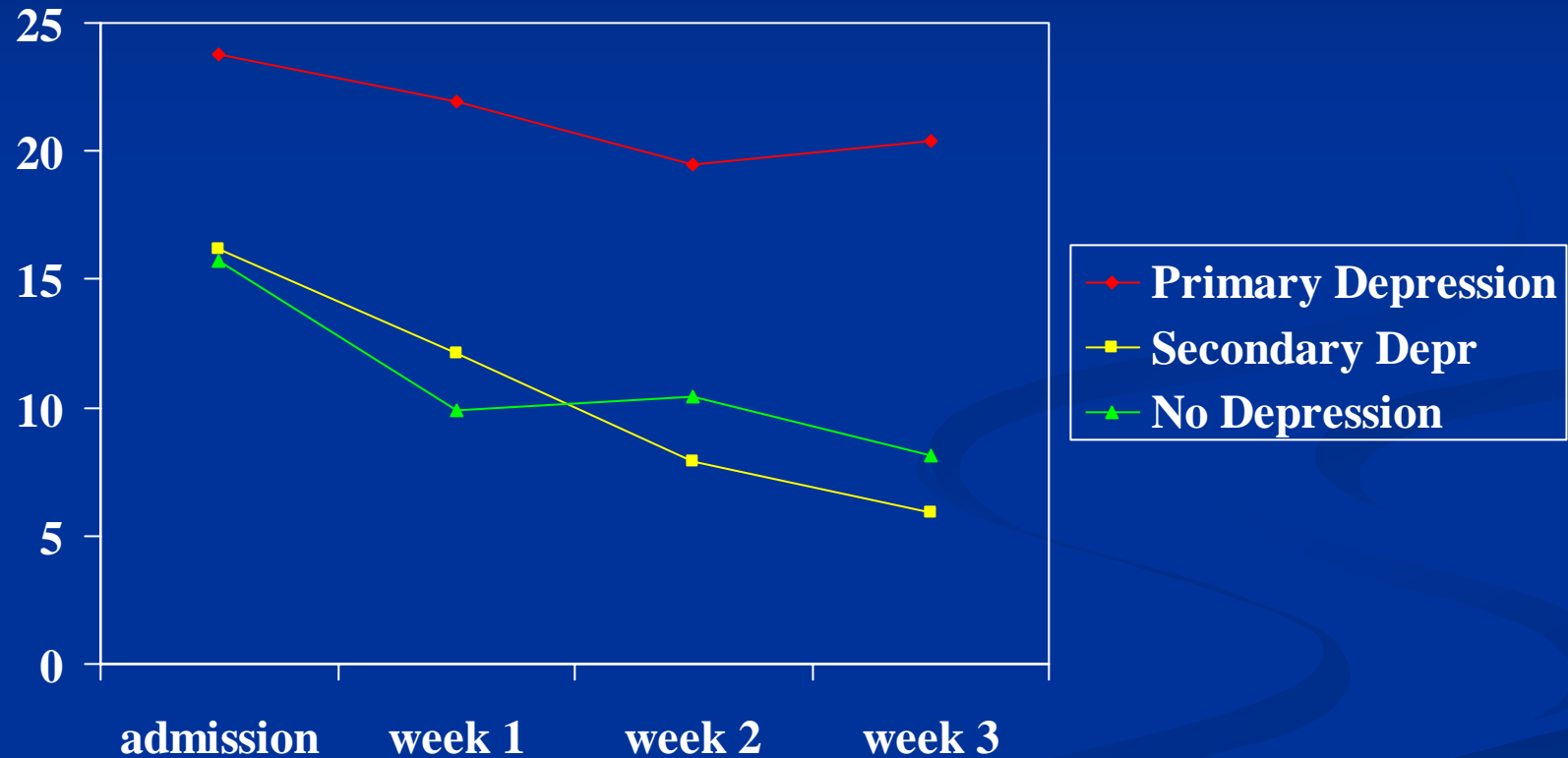
Diagnosing Comorbidity

- Diagnostic confusion is common
 - Substance intoxication, withdrawal, chronic use can produce anxiety, depression, and psychosis
 - Alcohol and stimulant use are strongly associated with these symptoms
- Likely to resolve with abstinence
 - Treat the substance use disorder
- May be difficult for clients to achieve sufficient abstinence to determine the cause
- How do we know which psychiatric conditions to treat?

Primary vs. Secondary Depression

Example from Inpatient Studies of Alcoholism

(Brown & Schuckit, 1995)



Diagnosing Comorbidity using DSM-IV-TR

- Primary (i.e., independent) depression:
 - Temporally independent; preceded drug abuse or persisted in abstinence
 - Ideally abstinence is current, directly observed
- Substance-induced depression:
 - Overlaps with periods of substance use
 - Exceeds what would be expected from usual toxic or withdrawal effects of substances
- Usual effects of substances
 - See DSM-IV intoxication and withdrawal criteria

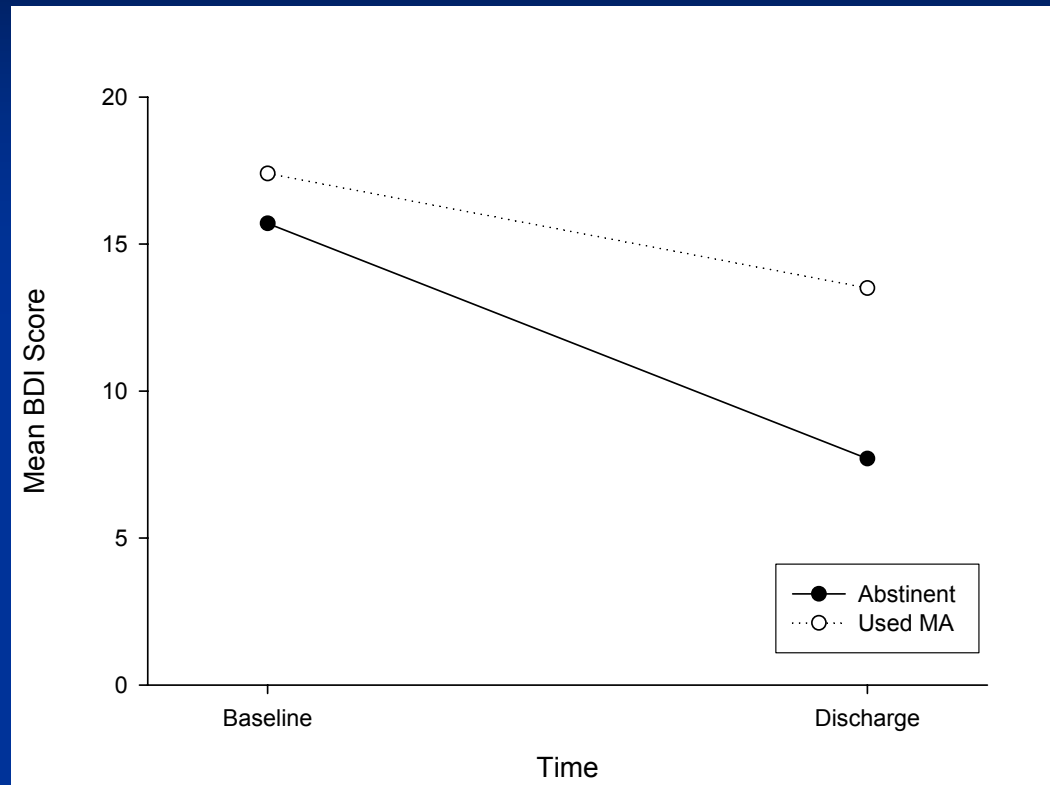
Diagnosing Comorbidity

- Establish ages at onset of regular substance use
- Establish periods of abstinence during the history
- Examine whether MDD, or other syndromes antedate substance use or persist during abstinence
 - Construct a timeline

Depression in MA Users

- Depression is one of the most common psychiatric symptoms reported in MA dependent patients (Zweben et al., 2004)
- 51% lifetime history of depression and 23.5% lifetime history of dysthymia found in amphetamine-dependent individuals (NESARC, 2006)
- Psychiatric and SUD comorbidity worsens prognosis and treatment outcomes (McKay et al., 2002; Ritsher et al., 2002)
- Predictors of depression in MA users unknown
- MDD risk factors in general population: female gender, family hx, abuse hx, prior suicide attempts, alcohol use

Depressive Symptoms and MA Use



Those who remained abstinent from MA showed a greater reduction in depressive symptoms as compared to those who used within 30 days prior to treatment discharge.

Suicidality in MA Users

- MA use associated with high rates of suicidal behaviors
- In recent study of treatment-seeking MA users, 28% of women and 13% of men reported lifetime SA history (Zweben et al., 2004)
- Risk factors for suicidal behaviors in substance abusers include: affective disorders, polysubstance dependence, nicotine use, low education, and sexual abuse history
- In cocaine dependent patients, trauma history, physical illness, MDD, alcohol and opioid comorbidity were significantly associated with lifetime SAs (Roy, 2001)
- No studies to date of SA risk factors in MA users

MAT-SS Study Design

- Post-treatment follow-up of 526 MTP participants
- In-person assessments conducted by trained interviewers
- Risk factors for depression and SAs measured at baseline (tx entry)
- Depression diagnoses assessed at follow-up (average of 3.1 years post-tx)

Participants

- Inclusion criteria: 18+ yrs old, MA dependence dx at entry, use within 30 days prior to tx
- Exclusion criteria: Severe medical or psychiatric conditions, need for detox, recent drug treatment
- Characteristics: average age of 36.2, majority female (60%), Caucasian (68%), employed (60%), high-school educated (76%), and unmarried (84%)
- At baseline (pre-tx): average MA use 12 days out of 30, preferred route smoking (62%), followed by IV (28%) and intranasal (9%) use

Assessments

- Addiction Severity Index given at baseline to assess:
 - MDD risk factors:
 - prior EtOH tx
 - family psych hx
 - SA hx
 - abuse hx
 - SA risk factors:
 - prior SUD tx
 - family psych hx
 - abuse hx
 - depression hx
 - prior psych admissions
 - chronic medical problems
 - MA use hx: lifetime years of use and preferred route

Assessments (cont'd)

- Beck Depression Inventory (Beck, 1961) given at baseline to assess depressive symptom severity; total score > 20 was examined as a potential risk factor for a post-treatment diagnosis of MDD.
- Mini International Neuropsychiatric Interview (MINI) (Sheehan et al., 1998) given by trained interviewers at 3-year follow-up to determine:
 - Major Depressive Disorder diagnoses
 - Lifetime history of suicide attempts

Results

- 15.2% (n=80) met criteria for MDD at follow-up
- Family psych hx, abuse hx and chronic medical problems did not predict MDD
- Two significant risk factors for MDD were found:
 - lifetime history of SA
 - BDI>20

MDD Risk Factors

Risk Factor	Odds Ratio	95% C.I.	p
BDI>20	2.21	1.23-3.99	*0.008
Gender (%women)	1.30	0.79-2.40	0.398
Route of administration (% IV)	1.20	0.66-2.18	0.531
EtOH treatment hx	1.56	0.84-2.90	0.151
SAs (lifetime)	2.42	1.32-4.44	*0.004
Depression (lifetime)	1.49	0.78-2.84	0.221

Predictors of SA

- 28.7% (n=151) of MA dependent patients at follow-up had attempted suicide in their lifetime
- Lifetime years of MA use, cigarette smoking, and prior drug tx were not associated with SAs
- Five risk factors for lifetime SA were identified:
 - BDI>20
 - Female gender
 - IV use
 - Psychiatric admission hx
 - Serious depression hx

Discussion

- This study identified clinical, demographic, and substance use predictors of MDD and SAs in MA users
- Results are consistent with prior work demonstrating relationship between depression and female gender, EtOH use, and IV methamphetamine use
- BDI moderate severity cutoff in MA users is clinically useful
- Psychiatric history is a better indicator of suicide risk in MA users than drug use history/characteristics

Clinical Implications

- MDD and SA risk factors may be easily identified in clinical settings
- Screening for these clinical indicators will facilitate identification of MA users for whom psychiatric intervention may be warranted
- Abstinence promotes depressive symptom recovery
- Proper assessment of comorbid psychopathology may have important implications for optimizing treatment and outcomes in MA users

Anxiety in Methamphetamine Users

- Anxiety symptoms are among the most frequent psychiatric complaints of MA users.
- Anxiety symptoms commonly emerge both during MA intoxication and withdrawal.
- Likely related to MA-induced activation of the sympathetic nervous system.
- Over 26% of the MA users have an anxiety disorder (current or past).

Anxiety Disorders in MA Users

- The most common anxiety disorder is Generalized Anxiety Disorder, observed in over 12% of MA dependent adults, followed by Social Anxiety Disorder (8%) and Post-Traumatic Stress Disorder (6%).
- Those with anxiety disorders report greater MA use frequency after tx compared to those without an anxiety disorder.
- Those with anxiety disorders are more likely to be hospitalized after tx than those without a diagnosis and have triple the risk of attempting suicide in their lifetimes compared to those without anxiety disorders.
- MA users with anxiety disorders have poorer treatment adherence and exhibit declining functioning over time after treatment.

Glasner-Edwards, S., Mooney, L.J., Marinelli-Casey, P., Hillhouse, M., Ang, A., Rawson, R.A. (in press). Anxiety disorders among methamphetamine dependent adults: association with posttreatment outcomes. *American Journal on Addictions*.

Clinical Implications

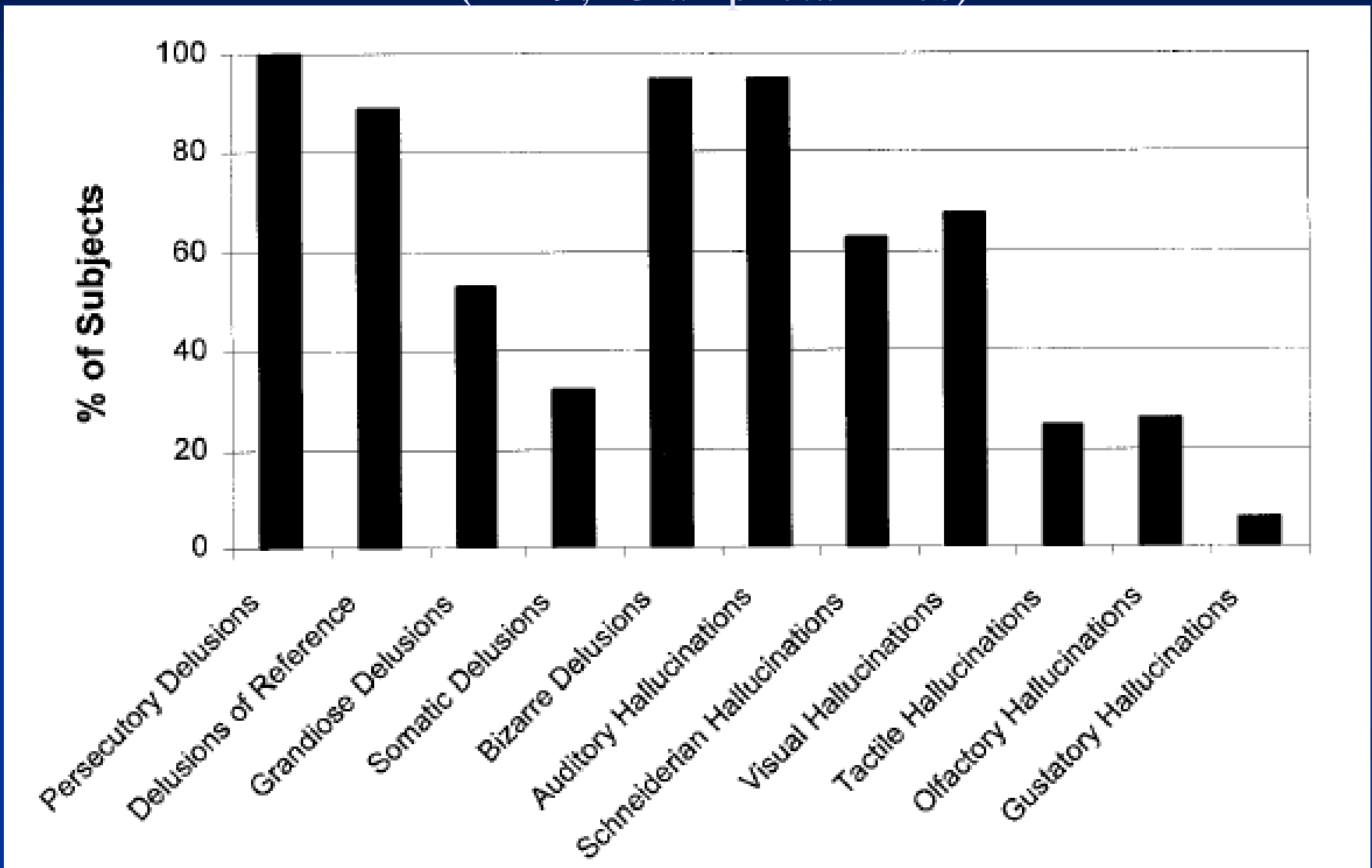
- Screening for anxiety disorders and closely monitoring symptoms and treatment progress in MA users with these problems is warranted.
- Awareness of elevated suicide risk in these patients is cause for careful assessment of suicidality.
- Anxiety and stress reduction techniques (e.g., cognitive behavioral therapy and mindfulness-based stress reduction) may be helpful for anxious MA users, though no studies yet to inform optimal approach.

Methamphetamine Psychosis

- Persecutory delusions
- Ideas of reference
- Hallucinations (visual > auditory; olfactory, tactile)
- Stereotyped and compulsive acts
- Anhedonia and depression
- Blunted affect
- Poverty of speech
- Prone to delirium and violence

Stimulant-Induced Psychosis

(n=19; 13 amphetamines)



Harris & Batki, 2000

MA Psychosis Inpatients from 4 Countries: Thailand, Japan, Philippines, Australia

No. of patients having
symptoms (%)

Psychotic symptom	Lifetime	Current
Persecutory delusion	130 (77.4)	35 (20.8)
Auditory hallucinations	122 (72.6)	75 (44.6)
Strange or unusual beliefs	98 (58.3)	39 (23.2)
Thought reading	89 (53.0)	27 (16.1)
Visual hallucinations	64 (38.1)	38 (22.6)
Delusion of reference	64 (38.1)	20 (11.9)
Thought insertion or made act	56 (33.3)	18 (10.7)
Negative psychotic symptoms ^a		36 (21.4)
Disorganized speech ^a		19 (11.3)
Disorganized or catatonic behaviour ^a		14 (8.3)

Methamphetamine Psychosis

- Occurs after single use and brief exposure
- Total “dose” more critical than duration of use
- Symptoms similar in naïve & experienced users
- Full range of “schizophrenic” symptoms
- Symptoms recur with “stress,” without drugs
- Persistent psychosis (?)

MA Psychosis and Schizophrenia

- Latent schizophrenia made manifest by low dose MA
- Schizophrenia prolongs duration of psychosis
- Schizophrenic symptoms recur after stress in MA abusers
- *MA Psychosis is NOT Schizophrenia. However, the greater the familial loading for schizophrenia, the more likely the MA user is to develop psychosis, and the longer that psychosis is likely to last (Chen et al Am J Med Genetics (2005) 136B:87-91)*

Persistent MA Psychosis

- Japanese literature has since the 1960s recognized a persistent psychotic syndrome in chronic meth addicts even after months to years of abstinence that is distinct from Schizophrenia.
- A recent review of acute Meth psychosis studies from 1956, 1982, and 2003 showed that in acutely psychotic meth abusers 190 of 326 (58%) had resolution of their psychosis within 10 days of admission.
- However, 31% of these patients had psychotic syndromes persisting >1 month, with 28% (50 of 170) in 1 study having psychosis lasting >6 months.
Ujike and Sato *Ann NY Acad Sci* 1025:279-287 2004

Psychosis and Treatment Outcomes

- In a recent study of 526 MA users 3 years after treatment, 12.9% of the sample was diagnosed with a psychotic disorder (current or past).
- Those with psychotic illness were more likely to have been hospitalized within the year prior to FU than those without a diagnosis (OR=2.4, 95% C.I., 1.2-4.3) and reported more episodes ($\beta=0.33$, SE=0.11, $p<0.01$).
- Those with psychotic illness evidenced declining functional outcomes in several domains (medical, employment, legal) and worsening psychological impairment over time from baseline to follow-up.
- No difference in MA use frequency among those with and without psychotic disorders during FU (M=12.5 \pm 1.6 versus 14.3 \pm 0.6 months); no difference in tx adherence.

Treatment of MA Psychosis

- For acute MA psychosis, treatment of choice is a combination of benzodiazepines and antipsychotic medications.

Battaglia J et al Am J Emerg Med (1997) 15 (4):335-341

- For persistent psychosis, treatment with a small dose of haldol may be an effective means of preventing subsequent relapse to psychosis.

Sato M et al 1983 Biolog Psychiatry 18: 429-440

Summary of MA Psychosis

- Methamphetamine psychosis remains an important clinical and public health issue.
- Genetics play a role in the persistence of methamphetamine psychosis.
- Further research needs to address the acute and long term effects of therapeutic agents relating to both acute and persistent MA psychosis and the diverse patient populations affected.

Conclusions

- Rates of psychiatric disorders in MA users are notably higher than prevalence estimates of such syndromes in the general population.
- Poorer functional outcomes are associated with psychiatric illness in MA users.
- MA use outcomes are poorer among MA users with psychiatric comorbidity.
- Abstinence promotes psychiatric symptom recovery.
- Screening for risk factors and addressing psychiatric symptoms may optimize outcomes in this population.

Thank you!

Suzette Glasner-Edwards, Ph.D.

sglasner@ucla.edu

310-267-5206