Co-occurring Disorders and Meth Abuse

Explore Aspects of Co-occurring Mental Illness

Consider Pre-existing Mental Illness as a Risk Factor for Addiction

Discuss Drug Induced Psychiatric Symptoms

Understand the relationship between methamphetamine and several common mental illnesses

Consider Screening and Assessment for Co-occurring Disorders

No Wrong Door

Many substance abusing patients do not desire addiction treatment, or even consider themselves addicts, but rather present for mental health care related to other problems such as depression or anxiety. Additionally increasing numbers of addicts, particularly methamphetamine addicts, have severe mental illnesses resulting from their substance abuse (Zweben 2004). The resulting confusion has resulting in a stalemate in some instances, in which substance abuse treatment is refused because of significant mental health issues (we don’t have the staff for that), and mental health care is refused because of substance abuse issues (he needs to get clean first and then we will see him).

Thus the necessity of the ‘no wrong door’ approach, which recognizes the need for concurrent treatment of both mental health and substance abuse problems. We have now recognized that is it unrealistic to expect the substance abusing mental health patient to quit using in order to see the doctor. Substance abuse treatment is also unlikely to be effective while concurrent mental illnesses are left untreated, impairing the patient’s ability to cooperate with therapy. Mental health professionals may live in compartmentalized worlds, but most addicts do not. Both problems must be addressed simultaneously, which will frequently require that psychoactive medications be given to people who are still using illicit psychoactive substances.

The potential for untoward medication interactions, overdose - intentional or otherwise, diversion or manipulation of prescribed medications is greatly increased in the case of active addiction to a psychoactive drug, particularly methamphetamine. Interpretation of signs and symptoms is greatly complicated by the presence of methamphetamine abuse and often a drug test is needed to distinguish between acute intoxication and symptoms of co-occurring major mental illness. Significant drug related symptoms can persist for months into withdrawal from methamphetamine, and are sometimes seen indefinitely. In those cases, there is always the question of whether the illness was actually preexisting to the addiction or developed as a result of drug use.
Pre-existing mental illness can be a precipitating factor in the development of the addiction – the self-treatment model. Pre-existing mental illness can also be exacerbated by concurrent drug use, with a subclinical trait morphing into a full blown syndrome under the influence of methamphetamine. The complications in diagnosis and treatment are increased exponentially when there are co-occurring substance abuse and mental illness, particularly in the case of methamphetamine abuse. A clear understanding of the interaction between mental illness and methamphetamine addiction is essential to successful treatment of both the mental illness and the addiction. (Torrens 2006)

A Overview of Methamphetamine Addiction

Methamphetamine is a powerful CNS stimulant, with differing pharmacokinetics depending on dose and route of administration. Low dose oral use has minimal effects on mental status other than increased alertness and mental focus. It is commonly prescribed for narcolepsy and other indications. Low dose and closely monitored oral methamphetamine is used by the military for long aerial missions with good results.

High dose, smoked or injected methamphetamine is far more potent in its effects on the brain’s function and even structural integrity. Different preparations of methamphetamine have varying degrees of potency. The most powerful form of the drug is the HCl salt of methamphetamine, commonly known as Ice. This discussion is focused on the effects of the high dose, smoked or injected Ice form of methamphetamine.

1. Effects on mood

The initial euphoric effect of methamphetamine is related to its actions in the CNS at the transmission points for mono-amine neurotransmitters, including dopamine, serotonin, and norepinephrine. All three of these neurotransmitters are released in large amounts with the acute administration of methamphetamine. A high energy state, alertness and endurance, are associated with the methamphetamine high, as are feelings of power, invincibility, and loss of appetite. The extremely high levels of these neurotransmitters result in prolonged states of agitation and wakefulness, mood swings, and increase in sexual desire.

Longer term use however leads to depletion of these same neurotransmitters, resulting in worsening of the withdrawal symptoms after a high. Withdrawal symptoms persist for up to three weeks and include sleep disturbances, lethargy, depressed mood, anxiety, and diminished sexual responsiveness. (McGregor 2005, Newton 2004) These aversive feelings contribute to the development of repetitive and compulsive use of the drug to maintain normal activity levels.

2. Psychotic features

Long term and high dose use of methamphetamine, particularly in vulnerable individuals, leads to para normal experiences and sensations that are hallucinatory in nature. They may be in any sensory modality, including muttering voices, threatening images, and tactile sensations (McKetin 2006). Hallucinations usually follow a period of prolonged wakefulness, perhaps days long, and usually resolve with rest and abstinence from methamphetamine.
In some individuals, however, the hallucinations generalize to a psychotic state with delusional thought patterns and persistent hallucinations even months after withdrawal from methamphetamine.

3. Effects on cognition

Acute methamphetamine intoxication is associated with improvements in cognitive function, particularly in high functioning individuals who are sensitized to methamphetamine. (Kirkpatrick 2008) Alertness and attention are improved as an acute effect of the drug, and next day performance is not impaired. (Perez 2007)

Prolonged methamphetamine use however is associated with cytotoxicity to several frontal and temporal lobe areas associated with complex reasoning, judgment and executive function. (Paulus 2002) Memory is significantly impaired due to injury to the hippocampus and surrounding cortical and association areas. (Thompson 2004) These changes can progress to the level of dementia in some patients, and can interfere with effective cognitive behavioral treatment.

B Co-occurring Illnesses Associated with Methamphetamine

Given the significant physiologic and anatomic changes associated with methamphetamine use, it is likely that a preexisting, perhaps sub clinical, mental illness could be exacerbated by methamphetamine use. Because of the potency of the current methamphetamine preparations found on the street, even healthy individuals could experience symptoms of major mental illness in conditions of intoxication or withdrawal.

We will review some of the common co-occurring mental illnesses associated with methamphetamine abuse with an eye to identify the effect methamphetamine has in exacerbating or precipitating mental illness in methamphetamine addicts.

1. PTSD

Some studies have estimated that 75% of female and >50% male methamphetamine addicts have clinical PTSD, commonly related to childhood sexual or physical abuse. Symptoms of anxiety and depression are acutely relieved by the use of stimulants, and feelings of powerlessness are reduced under the influence of methamphetamine. The patient has finally found something that works, makes him feel confident and powerful. Even subclinical PTSD symptoms that do not meet the full criteria for PTSD, can precipitate drug addiction in vulnerable persons. (Reynolds 2005)

Conversely, PTSD symptoms are often exacerbated by methamphetamine use because of the stressful nature of the drug culture – with rapes and beatings and threats being commonplace. The hyperarousal and anxiety symptoms are often worsened by continued methamphetamine use, precipitating full blown PTSD in patients who previously had only scattered or occasional symptoms related to their history of abuse.

Neuroanatomy of PTSD sufferers is marked by a reduced ability of the prefrontal cortex and anterior cingulate cortex to control the heightened emotional output from the
amygdala (Nutt 2004, Semple 2003). The hyperarousal and anxiety symptoms are difficult to control even with maximal mental effort.

PTSD is associated with abnormalities in several areas of the brain including the hippocampus, anterior cingulate cortex and insular cortex (Yamasue 2003, Chen 2006). These are the same cortical areas that are impaired in methamphetamine addiction and are associated with poor impulse control and compulsive drug use. The neurologic changes associated with PTSD are similar in some respects to the changes associated with addiction, especially those found in methamphetamine addicts.

Methamphetamine users showed significantly reduced cerebral blood flow in the anterior cingulate gyrus, with a significant persistent reduction even after six months abstinence. This suggests a structural change, not just a functional neurotransmitter mediated effect, in the anterior cingulate gyrus, an important area for control of impulses and behavior (Huang 2006). Multiple studies have demonstrated reduced task related activation of the anterior cingulate gyrus in methamphetamine users. Paulus in 2005 showed that those addicts who eventually relapsed had markedly reduced activation of the dorsolateral prefrontal cortex and anterior cingulate gyrus compared to addicts who did not subsequently relapse.

Preexisting PTSD changes may predispose patients to more rapid onset and severe course onset of addiction due to inherent weakness in these same control areas of the brain, prefrontal cortex and anterior cingulate gyrus. PTSD patients may be more difficult to treat and more likely to relapse because of the underlying abnormalities in brain function that serve to maintain addiction (Najavits 1998).

Treatment of both conditions concurrently is preferred since improvement in PTSD symptoms is associated with reduced drug intake. Concurrent therapy was preferred by most patients as both conditions are treated in a complementary way, with cognitive behavioral therapy and pharmacologic intervention (Back 2006).

2. Depression

Depression commonly co-occurs with substance abuse, and particularly methamphetamine abuse, both as a preexisting condition and as a consequence of methamphetamine use (Kosten 1998). The chronically depressed person who stumbles upon methamphetamine will find an incredibly effective ‘treatment’ for his depressed mood and lack of energy. The alertness and attention associated with methamphetamine use relieve his depressive symptoms and allow him to become normally active again. His new drug ‘works’ a lot better than anything they have at the doctor’s office.

But methamphetamine use over a prolonged period of time depletes neurotransmitter concentrations, contributing to a worsening of his symptoms, consistent with the ‘crash.’ Drug use accelerates, further compounding the depletion of his neurotransmitter reserves. Numerous studies have demonstrated the long lasting reduction in serotonin transmission even months after discontinuing methamphetamine use (Sekine 2006). This study showed markedly reduced serotonin transmission many months after withdrawal from methamphetamine, particularly in the anterior cingulate and orbitofrontal areas. In acute withdrawal, depressive symptoms were strongly correlated with reduced blood flow in
these same areas, the anterior cingulate and orbitofrontal areas, as well as amygdala (London 2004).

Long term depression following methamphetamine use has been noted, with studies showing reduced metabolic activity in the striatum and nucleus accumbens following protracted (nine months) abstinence (Wang 2004). Persistent depression for up to 5 years had been reported in up to 65% of recovering methamphetamine addicts.

These prolonged depressive symptoms contribute significantly to relapse and poor treatment outcome. Even with competent psychiatric help, some patients are not able to find relief from their depressive symptoms, and are vulnerable to relapse to drug use. Suicide is a significant risk in these patients (Glassner-Edwards 2008).

3. Anxiety

Anxiety is a disabling symptom in recovering methamphetamine addicts. Anxiety impairs the patient’s participation in group therapy which is a major component of most rehabilitation programs.

Two neuropeptides linked to anxiety that are increased by methamphetamine use are DBI (diazepam binding inhibitor) and CART (cocaine amphetamine related transcript). CART is an endogenous neuropeptide that is markedly increased by stimulant drugs including methamphetamine. It is concentrated in hypothalamic appetite areas, and also in the ventral tegmental area, nucleus accumbens, hippocampus and amygdala suggesting an effect on emotional and reward systems (Stanek 2006). CART has been found to be a potent endogenous anxiogenic neuropeptide linked to increased anxiety behaviors in rodents, which is also found in high concentrations in autopsy studies of the human meth abusing brain (Hurd 2000).

DBI (diazepam binding inhibitor) is another endogenous anxiogenic neuropeptide that has been linked to alcohol, opioid and nicotine withdrawal. Levels are increased in users of these drugs, and those levels skyrocket in withdrawal. (Kastura 2004) Since the majority of methamphetamine addicts also smoke and drink, DBI would certainly contribute to the anxiety symptoms seen in withdrawal.

Anxiety in methamphetamine withdrawal has also been linked to anatomic changes in glucose metabolism through the midbrain. London (2004) correlated anxiety symptoms in early abstinence with reduced glucose metabolism in the anterior cingulate cortex, orbitofrontal cortex and insula, and with increased metabolism in the amygdala. These findings were also related to craving scores and depression.

Methamphetamine causes an enormous release of norepinephrine in the CNS, and high levels are noted for months after withdrawal (Rothman 2001, Yui 2003). This long term hypersensitivity of the noradrenergic system is a major cause of the heightened anxiety seen in both active users, and recovering addicts. The normal inhibitory relationship between serotonin and norepinephrine is uncoupled, resulting in uncontrolled surges of norepinephrine even long after discontinuation of methamphetamine (Salomon 2006).
In addition to the generalized anxiety state characteristic of drug withdrawal, many methamphetamine addicts also have significant delusion and hallucinations that are also anxiety provoking. The content of these hallucinations commonly revolves around guns and narcs and dealers, all of which are threatening to the patient. But biochemically, norepinephrine levels have been noted to skyrocket during these psychotic episodes, even in the absence of anxiety provoking stimuli, and even when appropriate antipsychotic medications are given (Yui 2003).

4. ADHD

ADHD presents special challenges to the clinician because it commonly co-occurs with methamphetamine addiction, and treatment frequently requires the use of stimulant medications. The obvious risk of manipulation and diversion, as well as dosing questions make these patients challenging. Accurate diagnosis is essential and is often overlooked. Pediatricians who ask normal nine-year-olds six loaded questions in five minutes and then place them on stimulants contribute to the confusion. Anyone taking low dose stimulants will notice an improvement in focus and attention. That is the effect low dose stimulants have on normal people, which is why truck drivers like them so much. The diagnosis on ADHD is not made by putting a child on stimulants and seeing if he ‘does better.’ There are psychometric tests than can more adequately confirm the diagnosis of ADHD than the six loaded questions in the pediatrician’s office.

But real biochemical ADHD, properly diagnosed, is a risk factor for the development of a methamphetamine addiction because low doses of amphetamines are therapeutic. The ADHD brain is deficient in dopamine and norepinephrine, and so low dose stimulants increase focus and attention and improve performance in many areas. When untreated or inadequately treated ADHD patients are offered methamphetamine, they are sure they have found ‘their drug.’ As these patients abuse methamphetamine, the resulting depletion of dopamine and norepinephrine produces a worsening of their symptoms, and so they take more methamphetamine to correct the problem. The result is a rapidly escalating addiction.

The appropriate use of low dose stimulants in childhood ADHD is not a risk factor for methamphetamine addiction. Treated children are 50% less likely to become addicted to methamphetamine than ADHD children who are not treated (Willens 2003). It is not the Ritalin that causes the addiction, but rather the ADHD, uncontrolled in young adulthood, that can precipitate methamphetamine addiction.

Methamphetamine using ADHD patients are harder to treat and have more relapses than non ADHD addicts. Meth users with ADHD have more cognitive deficits (Sim 2002) The good news is that treatment of concurrent ADHD, even with stimulant medications, does not impair recovery from addiction, (Wilens 2005) and may enhance it as symptoms are controlled (Waxmonskey 2005) and relapse prevented (Schubiner 2005). Non-stimulant therapies are available and are preferred, but low dose oral stimulants with proper monitoring are appropriate when needed.

Somehow giving a patient Ritalin while they are still using methamphetamine seems counterproductive at best and unethical at worst. Still, the tiny doses of amphetamine and oral route of administration make the impact of Ritalin negligible in the face of smoking
a pipe of ice. And the potential benefit in reducing illicit drug use is substantial when underlying ADHD symptoms are controlled with medications.

5. Bipolar Spectrum

The Mother of all Co-occurring Disorders associated with methamphetamine is Bipolar Disorder. Virtually every methamphetamine addict exhibits some of the clinical symptoms of Bipolar Disorder in either intoxication or withdrawal. In some cases those symptoms persist indefinitely after withdrawal, even if the pre-addiction personality was normal. A majority of the methamphetamine addicts diagnosed with bipolar did not have any symptoms of the disorder prior to their addiction, and in fact are exhibiting symptoms of meth intoxication and withdrawal.

The relationship between methamphetamine abuse and bipolar symptoms can be described in 3 categories:

Bipolar Constellation- Bipolar symptoms related solely to methamphetamine intoxication and withdrawal that resolve in detoxification and recur with repeated use. These symptoms represent normal methamphetamine intoxication of an otherwise healthy individual. These self-limited symptoms do not generally require pharmacologic intervention. These are the patients most often seen in primary care settings in which the use of methamphetamine is not acknowledged by the patient or detected by the provider, and a mis-diagnosis of bipolar is quite likely.

Bipolar Stimulant Spectrum - sub threshold symptoms that preceded the first use of methamphetamine, exacerbated by the use of methamphetamine, and do not resolve with simple or prolonged detoxification. These patients may not have been diagnosed prior to their addiction, but had a strong family history and various hypo manic tendencies and characteristics. These characteristics may actually predispose patients to addiction as they seek to maintain the manic and avoid the depressive states. Adequate treatment of the underlying mood disturbance can significantly enhance recovery and quality of life (Camacho 2003).

Preexisting Bipolar Disorder, while much less common, is also seen; the previously diagnosed Bipolar Disorder patient who abuses stimulants, often in an attempt to maintain a manic phase, resulting in severe psychotic reactions in association with methamphetamine use.

The effectiveness of concurrent medical treatment of Bipolar Disorder in the face of ongoing stimulant addiction has been demonstrated, showing both improvement in bipolar symptoms and reduction in drug use (Salloum 2007). The mood stabilizing anticonvulsants are our first line treatment, while Lithium is less popular because of its higher toxicity in the hands of an unreliable patient. Atypical anti-psychotics are also used with good results.

6. Psychosis
Methamphetamine use causes mild psychotic symptoms in a majority of people who use it in high doses regardless of their genetic propensity for psychosis (Ujika 2006). Psychotic symptoms are 11X more frequent in recreational meth users than in non users, regardless of whether they met criteria for dependence or not. Only a small portion of the variability in symptom severity was related to a clinical diagnosis of dependence (McKetin 2006).

Reported symptoms of methamphetamine psychosis include persecutory delusions in 77% of psychotic patients, auditory hallucinations in 45%, and strange or unusual beliefs or thought reading were also common. Negative symptoms including psychomotor retardation, poverty of speech, and flattened affect are also seen in methamphetamine psychosis, though not while acutely intoxicated (Srisurapanont 2003).

The progression of symptoms begins with occasional hallucinations associated with sleep deprivation under the influence of meth. These symptoms are extremely common with 90% of IV meth users experiencing at least one hallucination. Patients then progress to a pre-psychotic phase in which transient delusions and hallucinations are seen only when intoxicated. In the pre-psychotic state patients have insight; they realize their hallucinations are not real, and often ascribe them to their drug use. Symptoms can then generalize into a delusional state with no insight, and persistent hallucinations in the absence of intoxication (Ujike 2004). These psychotic symptoms can persist despite treatment for months in abstinent methamphetamine users (Akiyama 2006).

Adrenaline surges have been noted in persistently psychotic patients in prolonged withdrawal with methamphetamine psychosis. Surges of 4X normal control levels of plasma nor-epinephrine levels have been reported during recurrent psychotic episodes, and baseline levels of 2X normal controls with no identifiable external stressor to explain the surge of norepinephrine (Yui 2003). The extreme anxiety associated with these psychotic episodes is attributed to this adrenaline surge.

Biochemically, dopamine transporter density is significantly reduced in the nucleus accumbens and caudate of methamphetamine users, and the degree of reduction correlates with the severity of psychotic symptoms (Iyo 2004). In endogenous schizophrenia, serotonin receptor binding is dramatically increased. However, serotonin receptor binding is markedly decreased in methamphetamine users (Tauscher 2002). This may form the biochemical basis of the neuroleptic dysphoric state we often see. “That stuff made the voices go away, but I feel lousy.” Compliance with neuroleptic medications is often poor. Combination with a SSRI improves clinical effect and compliance. Kaneko 2006

Anatomically, psychotic symptoms are associated with a high incidence of multiple patchy deficits in cerebral blood flow among the abstinent users seen in SPECT scans. Severity of symptoms was also related to and elevation in the creatine/phosphocreatine ratio on MRS scanning suggesting cellular damage (Iyo 2004). Severe persistent psychosis more common in patients with variant of superoxide dismutase enzyme that results in higher levels of oxygen free radicals leading to increased cellular damage (Nakamura 2006).
The same atypical antipsychotic medications that are effective in endogenous schizophrenia are used in methamphetamine psychosis, with good results in most cases. The majority of cases of methamphetamine psychosis resolve within 6 months of abstinence, and so long term treatment is not usually necessary. Management of methamphetamine psychosis is complicated by the fact that many patients relapse into addiction while on potent psychotropic medications, and compliance and efficacy are difficult to evaluate.

7. Dementia

There is abundant evidence that abstinent methamphetamine addicts have significant frontal lobe dysfunction that contributes to impaired judgment, reasoning, impulse control and decision making (Paulus 2002). Dysfunction in the cingulate and insular cortices contributes to attention deficits. London (2005) and Thompson (2004) demonstrated significant loss of hippocampal tissue correlated with memory loss and cognitive deficits. These cognitive deficits contribute to the difficulties in applying classic cognitive behavioral therapy to methamphetamine rehabilitation. Patients are thought to be unmotivated and non-compliant, when they are often just overwhelmed by the mental demands made by classical CBT.

The cognitive deficits associated with methamphetamine are due to a combination of biochemical and anatomic changes. While there is significant cellular damage associated with methamphetamine use (Ernst 2000, Thompson 2004) there are also reversible biochemical changes that are long lasting, but not necessarily permanent (McCann 2007). Prolonged abstinence from methamphetamine, on the order of 12-18 months is necessary to permit the evaluation of cognitive impairment in any one individual.

C Screening and Assessment of Co-occurring Illnesses

Numerous assessment tools are available from a variety of sources and each has its strengths and weaknesses. The CAAPE (Comprehensive Addictions and Psychological Evaluation) is a combined substance abuse scale and mental health assessment. They assess for personality disorders as well as the above co-occurring disorders. The SA 45 (Symptom Assessment – 45) or MINI plus (MINI International Neuropsychiatric Interview) is a quick assessment of global psychiatric function, and can be administered along with the SSI-SA (Simple Screening Instrument for Substance Abuse) or ASI (Addiction Severity Index) assessments of substance abuse. Any of these scales can be followed sequentially to evaluate progress in treatment.

As professionals, we separate early in our clinical careers into either substance abuse or mental health as our field of choice. The realities of patient care, however, no longer permit us to pick and choose who we will care for. Cross training and dual certification are fast becoming the standard of care in mental health. Economic realities will make that progression more rapid and complete with time.

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