

Editors Corner

Drug dependence: Some Clinical Issues

By

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*** Dramatic increase in Methylphenidate Consumption:**

Methylphenidate is a CNS stimulant whose pharmacological properties are essentially the same as those of amphetamines. These substance were widely abused in the 1960s and national and international controls were strengthened accordingly, although some substances continued to be manufactured illicitly. It was classified under the 1971 convention on psychotropic substances in schedule II as having high abuse potential, its manufacture, consumption and abuse subsequently decreased considerably. Since the beginning of the 1990s, however the world wide medical use of Methylphenidate has increased sharply. According to the reports of the International Narcotics Control Board, the global licit manufacture of Methylphenidate rose rapidly a five fold increase in just 7 years .(Ghodse, 1999)

*** Drug Abuse and Psychiatric Comorbidity:**

The association between drug abuse and psychiatric comorbidity; described as dual diagnosis; has become an increasing source of clinical concern and has generated research interest in the addiction and general psychiatric communities. In the past years there have been a number of review articles looking at areas of this problem. Mueser, et al (1998) Suggested that there is some evidence for the common factor models (particularly with antisocial personality disorders) and the model (biological vulnerability to psychiatric disorder resulting in sensitivity to small amounts of alcohol or drugs). They found little evidence for the self- medication model.

Epidemiology

Regier, et al. (1998) gave Figures of 34% mood disorder comorbid with substance misuse and 17% for those with anxiety disorder with substance misuse. Farrell et al. (1998) reported 50% drug use 'ever' for a household sample, 13% for an institutional samples and 28% for a homeless sample in U.K. Bobo, et al. (1998) suggested that high depression scores were a risk at 12 month follow up for relapse to alcohol or marihuana but not cocaine. Troisi, et al. (1998) found an increased risk of psychiatric disorder with an increased level of cannabis use.

In papers focusing on psychotic diagnosis and inpatients, Kirchner, et al. identified a subgroup of schizophrenic patients who had substance use disorder. Alcohol was the most commonly abused drug (86%), followed by cocaine (12) and Cannabis (12%). Addington and Duchak (1997) look at the

reasons for substance use in schizophrenia and found patients reporting use for pleasure or to get high.

Looking at psychotic patients presenting at an emergency room and screening them for their substance use, Claassen, et al. (1997) found that 21% had used alcohol or an illegal substance before visiting the E.R. Lin, et al. (1998) from Taiwan examined the prevalence of substance use disorders among inpatients with bipolar and major depressive disorder in a hospitalized population. They found that 18% of their mood patients screened positive for substance misuse. Benzodiazepines were the most commonly found substance(10%) followed by alcohol (6%).

Weiss, et al. (1998) looked at medication compliance in a retrospective study amongst patients with bipolar and substance use disorder. They found greater compliance with sodium valproate than with lithium. They also noted that some patients particularly on benzodiazepines and tricyclic antidepressants, may use more medication than prescribed.

Substance Abuse and psychiatric comorbidity in children and Adolescents:

Both conduct disorders and ADHD have been associated with enhanced risk for substance use disorders.

Early onset substance abuse disorders have been shown to be associated with higher levels of psychopathology in male samples.

Early onset male alcoholics have been found to have more antisocial characteristics than late onset alcoholics (Mogue, et al. 1997).

High rates of psychopathology particularly conduct disorder associated with major depression have been reported in adolescents with alcohol dependence (Clark, 1997).

Adult men with adolescent onset of substance misuse have been found to have higher rates of comorbid conduct disorder and attention-deficit disorder than patients with an early or late adult onset of substance abuse (Clark, et al. 1998). The area of attention deficit hyperactivity disorder and psychiatric substance abuse is an area of growing interest. Biederman, et al. (1998) found a two fold increase risk of psychiatric substance misuse among adults with ADHD. They also commented that those patients were more likely to make the transition from alcohol use disorder to a drug use disorder. There is a potential therapeutic role for nicotine for attention-deficit hyperactivity (Conners, 1996).

The association of conduct disorders with high rates of

substance use disorders is well established; rates of substance use disorders of 65% in boys and 94% in girls have been reported for subjects whose childhood conduct problems extend into adulthood (Disney, et al. 1999).

The adolescent onset group have also been found to have higher rates of major depressive disorder (with an onset before the age of 18 years) and a short time between first substance use and the development of dependence.

A specific association between the incidence of childhood misbehavior (i.e. conduct disorder) and the development of injecting drug use has been established.

Brack, et al. (1998) found that depressive disorder rates were significantly related to the level of use of tobacco, alcohol, marijuana and other illicit drugs with tobacco having the greatest significance. Miller-Johnson, et al. (1998) reported that the highest substance misuse levels were found in the conduct disorder groups.

* **The Relationship between Tobacco use and Mental Disorders:**

Nicotine affects virtually all of the major neurotransmitter systems by its actions at nicotine cholinergic receptors which are widely distributed in the brain. Patients suffering from disorders such as schizophrenia, depression and eating disorders are particularly prone to smoking, and there is now good evidence that tobacco use and abstinence can have a clinically significant impact on such patients. Spring, et al. (2003) found that schizophrenic and depressed smokers recognize many drawbacks associated with smoking, but compared to nonpatients who smoke as heavily, they also perceive more benefits and find cigarettes more appealing than alternative rewards. The heightened reward value of smoking warrants attention in tailoring tobacco control interventions for schizophrenic and depressed smokers.

- **Neuropharmacology of tobacco use**

The psychoactive effects of nicotine stem largely from its molecular similarity to acetylcholine. Nicotine cholinergic receptors are widely distributed in the brain and there is a clear evidence for their role in modulation of the release of a number of neurotransmitters including the catecholamines and 5-hydroxytryptamine (5HT). It also decreases the level of monoamine oxidase B which has important role in the breakdown of dopamine, and so smoking may enhance dopamine activity not only by enhanced release, but also by dopamine breakdown. There is also considerable evidence to suggest that nicotine has complex effects on the serotonergic system. Acute nicotine enhances serotonin release. However chronic administration produces a decrease in serotonin concentration and synthesis in the hippocampus.

Functional magnetic resonance imaging identified dose-dependent increases in neuronal activity in brain regions

including the nucleus accumbens, amygdala and frontal lobes following I.V. Nicotine injections in smokers. Rose, et al. (2003) using PET to study the influence of nicotine on neuronal systems in cigarette smokers indicated that nicotine affects brain regions involved in arousal and reward, and suggested that it may be linked to motivationally significant aspects of tobacco dependence.

So it is not so surprising that tobacco use is associated in various ways with a number of mental disorders.

- **Tobacco and Schizophrenia**

Recent studies have confirmed earlier reports of substantially increased smoking prevalence in patient suffering from schizophrenia (generally more than 70%) compared with other psychiatric (40%-70%) and normal control individuals (30%-40%) (Chang & Choo, 1996, Diwan, et al. 1998).

Dalack and colleagues (1998) reviewed the clinical and preclinical links between smoking and schizophrenia and supported the commonly held view that smoking in schizophrenia may represent an attempt to self-medicate symptoms of illness (particularly negative symptoms). However, among the studies they reviewed are a number which found increased ratings of both positive and negative symptoms in smokers compared with non-smokers (Ziedonis, et al. 1994- Hall, et al. 1995). The causal direction here is not clear but it remains possible that smoking and nicotine can exacerbate psychotic symptoms under certain conditions. A general finding from the preclinical literature is that acute nicotine administration (against a low background level) increases dopamine activity, whereas chronic exposure produces desensitization (Pidoplichko, et al. 1997).

Given the considerable evidence suggesting that positive schizophrenic symptoms are related to over activity in the mesolimbic dopamine system (Gray, et al. 1991) this suggests that chronic regular smoking may "medicate" positive symptoms through desensitization, but that intermittent smoking (or relapse after a brief abstinence) might worsen positive psychotic symptoms. (Foulds & Toone, 1995).

Adler and colleagues (1998) suggested a pathogenic role of the gene for the α -7-nicotinic receptor in schizophrenia which produces an auditory sensory gating deficit in schizophrenia which is improved by nicotine. Following smoking cessation there will be increased blood levels of anti-psychotic medication caused by reduced metabolism (Solokangas, et al. 1997).

Although patients with schizophrenia should clearly be encouraged to stop smoking for the benefit of their health, the difficulty in achieving this and the potential effects on mental health should not be underestimated.

- **Tobacco and Depression**

There is an important link between tobacco use and depression, such that people with a history of depression are

more likely to smoke, more likely to find it difficult to stop and are at increased risk of suffering significant mood disturbance or full blown depression if they succeed in stopping smoking (Covey, et al. 1998). There is some evidence that nicotine itself has an antidepressant effect both in animals (Semba, et al. 1998) and humans (Salin-Pascual, et al. 1998).

Of particular interest is the increasing evidence for the efficacy of various types of antidepressant medication in helping smokers to stop smoking as nortriptyline and fluoxetine have shown promise in clinical trials and bupropion has been recently approved by the US-FDA as a prescription drug for smoking cessation (Prochazka, et al. 1998, Nioura, et al. 1995, Hurt, et al. 1997). Although these antidepressants are thought to work through differing mechanisms, one possible common effect is that they inhibit neuronal catechamine or serotonin uptake. It has been suggested that the resulting increased synaptic levels of these neurotransmitters could reverse the withdrawal symptoms stemming from the absence of nicotine-mediated neurotransmitter release (Benowitz, 1997).

Patients with a history of a major depressive episode after smoking cessation should be monitored closely during a cessation attempt and should be advised to use an adequate dose of nicotine replacement to offset withdrawal symptoms.

- Smoking and other mental disorders

There is some evidence of tobacco use for weight control in young people with body-image concerns (Wiseman, et al. 1998).

* Drugs and violence

Some drugs are reported to be more commonly associated with aggressive behavior and violence than others. Smart, et al. (1997) concluded that students who reported violent delinquency also reported the most frequent use of amphetamines and cocaine

There is a reason to suspect that abuse of anabolic — androgenic steroids (used by athletes) increases the risk of violent outbursts among susceptible individuals (Isacsson, et al. 1998).

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