Comorbid Tobacco Dependence and Psychiatric Disorders

by Andrea H. Weinberger, Ph.D., M.A., Kristi A. Sacco, Psy.D., M.A., and Tony P. George, M.D.

In the United States, smoking is the leading preventable cause of disease and death and it is estimated that over 440,000 people die from smoking-related causes annually (U.S. Department of Health and Human Services, 2004). Adverse health consequences of smoking include lung cancer, cardiovascular disease and stroke.

Although the overall prevalence of smoking has been decreasing to 23% in 2000 (Centers for Disease Control and Prevention, 2004), current smokers seem to have more difficulty quitting despite combining U.S. Food and Drug Administration-approved pharmacological treatments (nicotine replacement therapies, sustained-release bupropion [Zyban]) with behavioral therapies. A large proportion of these difficult-to-treat smokers may have comorbid psychiatric and substance use disorders (Kalman et al., in press). Determining the usefulness of current smoking cessation treatments can guide clinicians. Advances in our understanding of biological explanations for the high rates of comorbid nicotine addiction and mental disorders may lead to the development of more targeted and effective treatment.

Epidemiology

Large population-based studies in the United States report the current rate of smoking to be approximately 22% to 28% (CDC, 2004; Grant et al., 2004; Lasser et al., 2000). Smokers with current psychiatric disorders have significantly higher rates of smoking (41% on average), and it has been estimated that patients with mental illness consume 44.3% of all cigarettes in the United States (Lasser et al., 2000). The highest smoking prevalences were found for people with bipolar (68.8%), psychotic (49.4%) and substance use disorders (49.0%) (Lasser et al., 2000).

According to the DSM-IV, nicotine dependence is determined by daily smoking (typically 10 to 40 cigarettes/day), resulting in tolerance and the presence of withdrawal symptoms after smoking cessation. While the general rate of nicotine dependence has been reported at 12.8%, much higher rates have been found for smokers with psychiatric disorders (Figure) (Grant et al., 2004).

Rates of dependence in psychotic populations also appear to be high (Dalack et al., 1998; Kalman et al., in press). Smokers with comorbid psychiatric or substance use disorders are less likely to attempt quitting (Lasser et al., 2000) and have higher risk of developing smoking-related illnesses (Hurt et al., 1996; Lichtermann et al., 2001).

There have been several hypotheses to explain the high rates of smoking among people with psychiatric and substance use disorders. One hypothesis is that genetic factors influence vulnerability to both smoking and these disorders (Kendler et al., 1993). Second, certain environmental factors (e.g., stress, poverty) are associated with increased smoking and the onset of symptoms of psychiatric disorders. Third, people with psychiatric or substance use disorders use smoking as a way to self-medicate clinical symptoms, side effects of psychiatric medication or cognitive deficits (Chambers et al., 2001; Sacco et al., 2004).

Biologic and Genetic Contributors

Nicotine stimulates the release of several neurotransmitter systems, including dopamine, norepinephrine, 5-hydroxytryptamine (5-HT), glutamate, γ-aminobutyric acid (GABA) and endogenous opioid peptides, and acts as an agonist on presynaptic nicotinic acetylcholine receptors (nAChRs), which are stimulated endogenously by acetylcholine (Mansvelder and McGehee, 2002; Picciotto, 2003). Although chronic exposure of agonists typically produces receptor downregulation, chronic nicotine administration causes a paradoxical upregulation of nAChRs through rapid desensitization followed by receptor inactivation (Gentry and Lukas, 2002). After a short period of abstinence (e.g., overnight), nAChRs are resensitized and once again responsive to nicotine. This may explain why many smokers tend to report the first cigarette of the morning as their most satisfying.

The dopamine reward system is associated with addiction to drugs of abuse, including nicotine (Volkow et al., 2002a). Nicotine is thought to be reinforced by stimulating nAChRs in the ventral tegmental area of the midbrain that project to the nucleus accumbens, an important limbic area thought to be involved in drug reinforcement and reward. Further, these neurons project to the prefrontal cortex, which is thought to directly influence cognitive states, such as arousal and cognitive functioning.

Nicotine administration has been shown to improve neurocognitive deficits observed in neuropsychiatric disorders such as schizophrenia (George et al., 2002a; Sacco et al., 2005; Smith et al., 2002), attention-deficit/hyperactivity disorder (Conners et al., 1996; Levin et al., 1996) and Alzheimer’s disease (Newhouse et al., 2002).
1. Identify smokers
   • Ask whether each patient is a smoker.
   • Assess self-report and objective measures of smoking (e.g., timeline follow-back methods, CO levels, plasma cotinine levels).
   • Assess level of nicotine dependence (e.g., Fagerstrom Test for Nicotine Dependence).

2. Assess motivation to quit smoking
   • Assess the patient’s current level of motivation to quit smoking (e.g., on a scale from 1 to 10).
   • Ask patient about the negative and positive aspects of quitting (e.g., decision balance).
   • Ask patient about perceived barriers to quitting.
   • Be optimistic and encouraging about the possibility of changing to nonsmoking status.

3. Increase access to smoking cessation treatment
   • Explain options for pharmacological and behavioral treatment. Consider use of pharmacotherapies that target pathophysiological links between tobacco use and psychiatric disorder (e.g., atypical antipsychotics in schizophrenia).
   • Involve the patient in integrated nicotine and psychiatric/substance abuse treatment, if possible, or make available referrals for treatment.

4. Follow-up after quit attempt
   • Monitor changes in psychiatric symptoms and medication side effects after quit attempt.
   • Reassess smoking status (e.g., CO levels) and give feedback.
   • Focus on relapse prevention by asking about cravings and difficult situations.
   • Assess motivation to quit if there has been a relapse, and encourage repeat attempts at cessation.

Patients treated with atypical antipsychotic agents, especially clozapine (Clozaril), smoke less (George et al., 1995; McEvoy et al., 1999, 1995) and have an easier time quitting (George et al., 2002b, 2000) than those treated with typical antipsychotic medications. However, smoking cessation can cause a change in plasma concentrations of psychotropic agents due to a decrease in the induction of cytochrome P450 1A2. Monitoring medication side effects may be required within the first month after quitting (Kalman et al., in press; Ziedonis and George, 1997).

Mood Disorders

Major depression. Smokers with depression have a more difficult time quitting (Glassman et al., 1988; Lasser et al., 2000; Niaura et al., 2001) and require more attempts to quit (Glassman et al., 1993, 1990) than smokers without depression. However, a past history of major depression does not appear to influence tobacco treatment outcomes (Hayford et al., 1999). Although some research has reported that smoking cessation can lead to a reemergence of depressive symptoms (Covey et al., 1997; Glassman et al., 1990), other studies have questioned this relationship (Thorsteinsson et al., 2001; Tsah et al., 2000).

Pharmacotherapies for smoking cessation have not been extensively evaluated in patients with current major depression. One open-label trial of bupropion SR (300 mg/day) suggested that this medication was well tolerated in smokers taking selective serotonin reuptake inhibitor and enhanced short-term (three-month) cessation success in about one-third of patients (Chengappa et al., 2001). Additional research on smokers with a history of depression suggested the usefulness of NTP (Thorsteinsson et al., 2001) and nicotine gum (Kinnunen et al., 1996) for short-term smoking cessation.

In addition, some antidepressant medications appear to be useful agents. Nortriptyline (Aventyl, Pamelor) (Hall et al., 1998) and bupropion (Hayford et al., 1999) have shown promise as smoking cessation aids while SSRIs do not appear to enhance smoking abstinence (Dalack et al., 1995; Niaura et al., 2002). Behavioral therapies such as CBT should be strongly considered, as smokers with depression are likely to fail with more minimal interventions (Brown et al., 2001). Improved cessation outcomes with the addition of CBT have been reported for nortriptyline and nicotine gum (Hall et al., 1998, 1994).

Bipolar disorder. Glassman et al. (1993) found that patients with bipolar disorder (BD) may also be at risk for recurrence of depressive symptoms during smoking cessation. No empirically based treatments have been published for smokers with BD. Our group is currently conducting a double-blind, placebo-controlled trial of bupropion SR for the treatment of nicotine dependence in smokers with BD.

Anxiety Disorders

Cinciripini and colleagues (1995) found that smokers with high levels of trait anxiety taking buspirone (BuSpaR) versus placebo were more likely to be abstinent at trial end point but not at follow-up. A placebo-controlled study of bupropion SR for smokers with post-traumatic stress disorder reported that bupropion was well tolerated and resulted in higher rates of smoking cessation (60%), as compared to placebo (20%) (Hertzberg et al., 2001). Interestingly, a study by McFall and colleagues (2005) found that smokers who received tobacco treatment integrated with their psychiatric care were five times more likely than smokers who received separate treatment to report abstinence from smoking nine months after the study.

Table 1

Steps to Aid Smoking Cessation in Psychiatric and Substance-Abusing Patients

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Source: Weinsberger BH et al. (2008)
Tobacco Dependence

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