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Review

Negative affective states and cognitive impairments in nicotine dependence

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ABSTRACT

Smokers have substantial individual differences in quit success in response to current treatments for nicotine dependence. This observation may suggest that different underlying motivations for continued tobacco use across individuals and nicotine cessation may require different treatments in different individuals. Although most animal models of nicotine dependence emphasize the positive reinforcing effects of nicotine as the major motivational force behind nicotine use, smokers generally report that other consequences of nicotine use, including the ability of nicotine to alleviate negative affective states or cognitive impairments, as reasons for continued smoking. These states could result from nicotine withdrawal, but also may be associated with premorbid differences in affective and/or cognitive function. Effects of nicotine on cognition and affect may alleviate these impairments regardless of their premorbid or postmorbid origin (e.g., before or after the development of nicotine dependence). The ability of nicotine to alleviate these symptoms would thus negatively reinforce behavior, and thus maintain subsequent nicotine use, contributing to the initiation of smoking, the progression to dependence and relapse during quit attempts. The human and animal studies reviewed here support the idea that self-medication for pre-morbid and withdrawal-induced impairments may be more important factors in nicotine addiction and relapse than has been previously appreciated in preclinical research into nicotine dependence. Given the diverse beneficial effects of nicotine under these conditions, individuals might smoke for quite different reasons. This review suggests that inter-individual differences in the diverse effects of nicotine associated with self-medication and negative reinforcement are an important consideration in studies attempting to understand the causes of nicotine addiction, as well as in the development of effective, individualized nicotine cessation treatments.

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1. Introduction

Although the positively reinforcing effects of nicotine certainly play an important part in nicotine dependence, an accumulating literature implicates a role for negative reinforcement in nicotine dependence as well. Indeed, the most common responses of individuals when asked why they smoke usually involves some effect of nicotine that alleviates some negative state, either of cognition or affect. In many cases these negative states are certainly the result of nicotine dependence and acute withdrawal, but there is substantial evidence that in many cases these states may predate initial nicotine use. This possibility is rather difficult to determine in individual cases because smoking is initiated so early in life, often in early to mid-adolescence. However, the high degree of comorbidity of smoking with psychiatric disorders suggests that at least some portion of this self-medication may be true for premorbid conditions.

Nicotine addiction and dependence has a much higher prevalence in individuals with a psychiatric diagnosis and is associated with higher levels of smoking compared to psychiatrically healthy individuals (Lawrence et al., 2009). This relationship has been noted for numerous psychiatric disorders, including schizophrenia (de Leon et al., 1995), attention deficit hyperactivity disorder (ADHD) (Chen et al., 2012; McClernon and Kollins, 2008; Pomerleau et al., 1995), major depression (Breslau et al., 1991; Chen et al., 2012; Glassman et al., 1988), bipolar disorder (Waxmonsky et al., 2005), anxiety disorders (Breslau et al., 1991; Chen et al., 2012; Dickerson et al., 2009), post-traumatic stress disorder (PTSD) (Beckham et al., 1995; Chen et al., 2012; Dickerson et al., 2009; Koenen et al., 2005; Roberts et al., 2008), antisocial personality disorder (Chen et al., 2012; Dickerson et al., 2009), and obsessive-compulsive disorder (Grabe et al., 2001), as well as addiction to other substances (Chen et al., 2012; Dickerson et al., 2009; Grabe et al., 2001). These associations could be interpreted as support for the premise that psychological and neurobiological attributes that predispose individuals to nicotine addiction also predispose them to these other disorders (Paterson and Markou, 2007). While some nicotine use may reflect self-treatment for pre-existing psychiatric symptoms on the part of these individuals, other nicotine use could involve self-treatment for symptoms that emerge during, or are exacerbated by, nicotine withdrawal (Markou et al., 1998). The ability of nicotine to alleviate stress and anxiety, improve mood and cognition, promote wakefulness, etc., may account for higher rates of smoking in individuals with psychiatric diagnoses, the so-called self-medication hypothesis (Markou et al., 1998).

Self-treatment effects may also contribute to smoking in individuals without a psychiatric diagnosis, but with less extreme, sub-clinical alterations in mood, affect, or cognition. Indeed, a sample of smokers had a much higher lifetime incidence for mood, anxiety, and substance abuse disorders than non-smokers (Keuthen et al., 2000), prompting those authors to conclude that "subsyndromal" psychiatric symptoms may contribute substantially to the risk for nicotine dependence. Consistent with this idea, nicotine use is increased in non-psychotic siblings of individuals with schizophrenia (Smith et al., 2008). Moreover, greater anhedonia severity or cognitive dysfunction in individuals without a current diagnosis of major depression predicts increased risk for relapse to smoking (Cook et al., 2010; Leventhal et al., 2009; Patterson et al., 2010). The diversity of symptoms in these disorders, and the multitude of effects of nicotine, suggest that there is substantial heterogeneity in the underlying reasons for smoking across individuals.

Despite the evidence for self-medication in smokers, the vast majority of preclinical and clinical research into the biological basis of nicotine addiction has emphasized positive reinforcement (see Table 1 for a glossary of terms relevant to this review) as the major determinant of nicotine addiction liability (Glautier, 2004; Watkins et al., 2000a). Theoretical perspectives have been proposed that emphasize negative reinforcement at later stages of the addiction process (Koob, 2013; Koob and Le Moal, 2008; Watkins et al., 2000a). The pattern of psychiatric comorbidities discussed above however, and the early onset of smoking in most individuals, suggest that self-medication and negative reinforcement may also be important at earlier stages in some individuals. This review will discuss such premorbid possibilities, highlighting studies from both a clinical and preclincial modeling perspective.

2. Premorbid conditions that may predispose individuals to nicotine dependence: clinical findings

The relationship of psychiatric disorders to nicotine dependence suggests a potential mechanism – or mechanisms given the number of psychiatric conditions that are highly comorbid with smoking – that might underlie addiction liability for nicotine dependence. Understanding these processes may contribute substantially to the treatment of comorbid psychiatric conditions, as well as smoking, as the prognosis is poorer for psychiatric patients with comorbid addictions (Batel, 2000). For instance, individuals with a dual diagnosis of addiction and a psychotic disorder have more severe symptoms (Margolese et al., 2004), which may relate to both their poorer prognosis and greater use of addictive substances if those are taken in part for reasons of self-medication. However, one of the most fundamental questions surrounding these issues is the extent to which these psychiatric conditions are premorbid in origin, or develop after extended nicotine use. A prospective longitudinal study observed that teenage smoking was associated with an increased incidence of a range of psychiatric diagnoses (Sorensen et al., 2011). Of course, although smoking in this study predated the diagnoses of psychiatric disorders, this finding does not necessarily mean that psychiatric symptoms were not present prior to the actual diagnoses. It remains to be seen whether teenage smoking reflected self-medication prior to full onset of psychiatric conditions or if teenage smoking may have accelerated the development of those psychiatric conditions. Again, there need not be a single answer to this question; smoking, or subsequent withdrawal experiences, may exacerbate the development of some conditions but not others. As an indication of this sort of heterogeneity, it has been shown that smoking topography (total puffs, puffs per cigarette, inter-puff intervals and puff volumes) are quite different between equally dependent smokers with, or without, a concurrent diagnosis of schizophrenia (Tidey et al., 2005).