

Nicotine and Nonnicotine Factors in Cigarette Addiction

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- Co-invented the transdermal nicotine patch
- Leader in IV nicotine technique
- Takes Philip Morris money

Overview

- Smoking kills >400,000 Americans/year.
- Nicotine, as a reinforcer in humans, plays a role in cigarette addiction
- Nicotine replacement therapy (NRT) does help smokers quit, but success rates are low.
- NRT does not address nonnicotine components
- Introductory topics include: Clinical evidence for nicotine reinforcement and withdrawal, nicotine is not enough, disassociating nicotine from nonnicotine components, which nonnicotine component is most important, implications for treatment.

Clinical evidence for nicotine reinforcement

- Nicotine is a reinforcer in humans
 - Robust self-administration of pure nicotine and tobacco-delivered nicotine.
- Withdrawal syndrome:
 - includes symptoms of urge to smoke, irritability, difficulty concentrating
 - can reduce the likelihood of a quit attempt and decrease chances of long-term cessation.
- Pharmacologically pure nicotine (nicotine replacement therapy--NRT): Gum, transdermal patch, lozenge, inhaler, and nasal spray
 - Efficacious--approximately doubles long-term cessation rates
 - Thought to work, at least in part, via withdrawal suppression

Nicotine is not enough

- If smokers are smoking primarily for nicotine, then easy transition from cigarettes to NRT and then weaning off NRT
- Smoking cessation success rates with NRT, while double that of placebo, remain low
 - Aversive stimuli associated with NRT
 - Absence of rapid bolus delivery mimicking series of puffs

Dissociating Nicotine from Nonnicotine components of Smoking

- IV nicotine
 - Delivers nicotine independently from cigarette smoke
 - Results are mixed on whether IV nicotine has subjective rewarding effects
 - Extremely rapid/high doses work best (up to 3 mg in 10 s)
 - Does relieve craving

Dissociating Nicotine from Nonnicotine components of Smoking

- Denicotinized cigarettes
 - Deliver sensory and motor components of smoking without delivering nicotine
 - Provides positive subjective effects (e.g. relieves craving, negative affect)
- Effect of “denics” on craving varies across studies
 - Higher FTND scores, better craving relief, suggesting smokers are more dependent on nonnicotine smoke components as well as nicotine
- “Denic” cigarettes satiates smokers more than IV nicotine when smokers are allowed to concurrently ad libitum smoke their cigarettes

Denic Cigarettes and IV nicotine

- Study that compared the ability of cigarette smoke and IV nicotine to satiate smokers who were allowed concurrent access to their usual brand of cigarettes
- Controlled puffs of reg/denic cig, followed by IV infusion of nic/saline for 1 hr; ad libitum smoking for next 3 hours
- “Denic” cigarettes satiates smokers more than IV nicotine when smokers are allowed to concurrently ad libitum smoke their cigarettes
- Combination of both “denic” cigarettes and IV nicotine recaptured same satiating effect of usual-brand cigarettes

Which nonnicotine component is most important?

- Motoric components
 - handling, puffing, inhaling
 - solely motoric components do not elicit satisfaction (sham smoking)
- Sensory components
 - taste, aroma, tracheobronchial sensations
 - sensory components important for satisfaction (especially for women)
 - menthol, flavoring, nicotine contribute to sensory qualities

Implications for Smoking Cessation Treatment

- Rapid smoking
 - Smoke cues become aversive with rapid puffing
- Supplemental nicotine administration during smoking
 - Wear 21 mg TN while smoking ad libitum for 2 weeks
 - TN makes cigs less rewarding, indirectly diminishes rewarding effects of sensorimotor cues
 - Great success rates
 - Nicotine intake remains constant so nicotine toxicity not an issue

Implications for Smoking Cessation Treatment

- Nicotinic antagonist administration
 - Mecamylamine: non-competitive antagonist at nicotinic receptors
 - Acute administration leads to increased smoking; effect is transient
 - Continued administration leads to reduced smoking, reduced rewarding effects associated with cues
 - Use of concurrent nicotine/mecamylamine for 2 weeks prior to quit dates leads to 30% quit rates
 - Rationale for nic/mec treatment is both agents bind to different sites on the nicotinic receptor, attenuate reinforcing effects of cigs and achieve greater effect than either drug alone

Implications for Smoking Cessation Treatment

- Use of very low-nicotine-content cigarettes
 - Removes nicotine vs. attempting to block the reinforcing effects in inhaled nicotine
 - Actual low nicotine content vs. vent holes (compensatory behavior)
 - Used in conjunction with NRT (wean off nicotine; cues less reinforcing)

Treatment Approaches—Replacing Sensorimotor Cues

- Temporary substitutes to alleviate craving/withdrawal
 - Inhaled citric/ascorbic acid, stimulates respiratory tract sensations that accompany cigarette smoking
 - Delivery of pepper constituents (e.g. capsaicin)
 - “Denics” and low nicotine cigarettes help cope with early craving and devalue cues by removal of contingent nicotine reinforcement

Future Research Directions

- Clarify the relative importance of nicotine and nonnicotine factors
 - Use paradigms to manipulate each factor selectively
- Analyze importance of smoke components in subpopulations
 - Females respond to sensory cues more than males
 - Schizophrenics respond more to nicotine's direct effects on the central nervous system
 - Gene variants (people with DRD4 gene have increased cessation rates with NRT)