Physiology of Tobacco Addiction and Effective Medications

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Neurochemical Effects of Nicotine

Nicotine

- Dopamine → Pleasure
- Norepinephrine → Appetite Suppression
- Acetylcholine → Arousal, Cognitive Enhancement
- Vasopressin → Memory
- Serotonin → Mood Modulation
- β-endorphin → Anxiety Reduction

Benowitz NL. *Primary Care*. 1999; 26: 619.
The Addictive Nature of Nicotine

- The addictive characteristics of nicotine are believed to be a result of its rapid, intense and short-acting effects on dopamine release in the brain.
  - When inhaled, nicotine reaches the brain within 10 seconds
  - Nicotine’s half-life is approximately 2 hours

- Similar to addictions associated with cocaine, amphetamines and opiates, nicotine addiction is a chronic, relapsing medical condition and warrants clinical intervention.
  - Nicotine, cocaine, amphetamines and morphine act on different areas in the dopamine reward system that encompasses the mesolimbic portion of the brain.
  - Among users of alcohol, tobacco, cannabis, and cocaine, tobacco users were more likely to be nicotine dependent (28%) than alcohol (5.2%), cannabis (8.2%) or cocaine (11.6%) users.

Nicotine binds predominantly to nicotinic acetylcholine (nACh) receptors in the CNS; the primary is the α4β2 nicotinic receptor in the Ventral Tegmental Area (VTA).

After nicotine binds to the α4β2 nicotinic receptor in the VTA, it results in a release of dopamine in the Nucleus Accumbens (nAcc) which is believed to be linked to reward.
The Cycle of Nicotine Addiction

- The half-life of nicotine is only 2 hours. This, along with its rapid clearance from the CNS, results in withdrawal symptoms occurring quickly. Withdrawal symptoms, combined with cravings for tobacco, result in relapses that reinforce the reward and satisfaction from nicotine—starting the addiction cycle over again.

<table>
<thead>
<tr>
<th>Nicotine Withdrawal Symptoms</th>
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<tr>
<td>Irritability</td>
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<td>Difficulty concentrating</td>
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<td>Restlessness</td>
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<td>Depressed mood</td>
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<td>Anxiety</td>
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<td>Insomnia</td>
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<td>Increased appetite</td>
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<td>Decreased heart rate</td>
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Three Facets of Nicotine Addiction
Approaches to Therapy of Tobacco Dependence

Components of Tobacco Dependence

- Physiological
- Psychological
- Behavioral*

Treatment Approaches to Therapy

- Pharmacotherapy
- Pharmacotherapy/Behavioral Counseling
- Behavioral Counseling

* Behavioral components include triggers and stressors such as alcohol, prior severe withdrawal symptoms, work and family issues, driving, living with another smoker, etc.
FDA Approved Smoking Cessation Medications

- **Nicotine Replacement Therapy**
  - Patch (21, 14 and 7mg)
  - Gum (2 and 4mg)
  - Lozenge (2 and 4mg)
  - Inhaler
  - Nasal Spray

- **Bupropion SR (150mg bid)**

- **Varenicline (1mg bid)**

- **The Guidelines* recommend using pharmacotherapy on every quit attempt for adults unless contraindicated**

Meta analyses of clinical trials show that NRT, bupropion and varenicline can double or triple the chances of successfully quitting smoking when compared to placebo.

Most trials included behavioral counseling—an important component for achieving the highest possible quit smoking rates.
Tobacco use is an addiction

Like other addictions it can be a chronic relapsing disorder

Treatments that combine behavioral counseling with FDA approved medications offer smokers their best chance to quit