Menthol Sensory Properties and Possible Effects on Topography

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What is Topography?

• “Puffing behavior”

• Quantifiable
  – Number of puffs per cigarette
  – Puff volume (ml: mean & total)
  – Puff duration (seconds)
  – Puff flow (ml/sec)
  – Inter-puff interval (seconds)
Topography

Photo provided by Dr. Pamela Clark 2010
Overview

• What are menthol’s sensory properties?

• Do these properties contribute to the smoking experience?

• Does menthol alter topography?
Published Literature

• 343 articles in the NCI Bibliography of Literature on Menthol and Tobacco (2009) + 23 recent additions

  → Not directly relevant
  → Reviews (mostly relied on primary sources)

26 articles

Note: Red and * denotes tobacco industry-funded study
Sensory Qualities and Smoking Topography

• Reviews have been published on menthol’s pharmacology and sensory qualities$^{1,2,3,4*}$

• Small number of published smoking topography studies comparing menthol & nonmenthol smokers. Variability:
  – Differences in study design and protocols
  – Differences in *ad lib* (as desired) smoking versus rapid-smoking procedures
  – Only one study varied menthol content$^5$

Sensory Properties of Menthol
Sensory Properties: Flavor

• Natural menthol is primarily found in peppermint and cornmint

• Menthol stimulates olfactory and taste receptors\(^1\)
  – Mint-like flavor and smell

• Menthol smokers (\(n=473\))^2:
  – 60% would pay more money for a menthol cigarette than for a nonmenthol cigarette
  – Taste was one of the 3 main reasons for smoking menthol cigarettes

Sensory Properties: Cooling & Warming

• When applied to skin or mucosal surface causes a sensation of coolness or warmth\(^1\)

• Affects thermoreceptors---Transient receptor potential (TRP) receptors\(^2\)
  – Activates TRPM8 (“cold activated”) receptors
  – Activates TRPM3 (“warm activated”) receptors
  – May also activate TRPM8 pain receptors causing a painful sensation.

Cooling & Warming (cont.)

- Inhalation of menthol produces cooling sensation\(^1\)

- Menthol inhalation stimulates trigeminal cold receptors, resulting in cool sensation without a change in physiological temperature

- Menthol can increase sensation of cold in oral cavity, but can either enhance or attenuate feelings of warmth

1. Eccles 1994
Sensory Properties: Respiration

- Menthol often used as a nasal decongestant and gives users sensation of increased airflow and respiratory ease, without physical decongestant activity\(^1,2,3\)

- Menthol inhibited ventilation in *in vivo*\(^4\) experiments & increase breath hold time in humans\(^5\)

- Menthol acts as a cough suppressant\(^6,7\)

- In animal models menthol has been demonstrated to:
  - Promote mucus clearance\(^3\)
  - Produce bronchodilation (*in vitro* and *in vivo*)\(^8\)

Sensory Properties: Analgesia

• Menthol has both analgesic and local anesthetic effects

• Analgesic effects likely due to¹
  – Activation of TRPM8
  – Inhibition of pain-sensitive TRP1
  – Activation of κ-opioid system (when given orally to rodents)²

• Menthol is an irritant; however desensitization develops with repeated exposure³

• Menthol reduces nicotine’s irritant properties through cooling and cross-desensitization³

¹ Harris 2006; ² Galeotti 2002; ³ Dessirier et al. 2001
Sensory Properties: Perceived Strength

• Menthol can produce varying degrees of irritation and temperature sensations\(^1\)
  – Trigeminal nerve endings in mouth and throat
  – Seems directly related to menthol’s cooling effect

• Menthol may be added to increase perceived strength and smoke-like sensations in low-yield cigarettes\(^2\)
  – Menthol content was greater in “ultralight” or “light” menthol cigs compared with regular or medium/mild menthol cigs (48-brands)\(^3\)

• Menthol smokers believe menthol cigarettes are more soothing to the throat than nonmenthol\(^4\)

Tobacco Documents-Based Research on Menthol & Topography
Tobacco Industry Documents-Based Research: Changing Menthol Levels

• Publicly available tobacco industry docs showed different properties associated with different levels of menthol\(^1\):
  – Low-content menthol cigarettes to mask the taste of tobacco/reduce throat scratch
  – Higher menthol cigarettes for increased impact and menthol flavor

1. Kreslake et al. 2008
Tobacco Industry Documents-Based Research: Consumer Preference

• Publicly available tobacco industry docs showed smoking status was associated with overall liking of menthol concentrations\(^1\)
  – Heavy smokers (>20 cpd) preferred higher levels of menthol (0.80%)
  – Moderate smokers (≤20 cpd) preferred moderate concentrations (0.52%)

\(^1\) Kreslake, et al 2008
# Tobacco Industry Documents-Based Research: Properties & Function

<table>
<thead>
<tr>
<th>Property</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cooling</td>
<td>Mask irritation of smoke&lt;br&gt;Enable initiation and increased uptake&lt;br&gt;Substitute perceived smoke effect</td>
</tr>
<tr>
<td>Anesthetic (Analgesic)</td>
<td>Counter- or anti-irritant; Reduce pain sensations&lt;br&gt;Mask irritation of smoke; enable initiation &amp; increased uptake</td>
</tr>
<tr>
<td>Impact</td>
<td>Increased bite or strength&lt;br&gt;Substitute for nicotine in low-tar cigarette</td>
</tr>
<tr>
<td>Sensory</td>
<td>Increase smoothness; Reduce harshness&lt;br&gt;Enable deeper inhalation and uptake&lt;br&gt;“Smoke soothing”</td>
</tr>
</tbody>
</table>

1. Wayne & Connolly 2004 (modification of Table 4)
Interim Summary
Sensory Properties of Menthol

- Convergent data on sensory properties of menthol

- Flavor, cooling, analgesia, sensation of ease of respiration
  - Could result in larger puff volumes, increased frequency, deeper inhalation, greater intensity of smoking
  - Increased breath hold time may alter inhalation patterns
Role of Menthol’s Sensory Qualities on Topography
# Does Mentholation Result in Larger Puff Volumes and Increased Frequency?

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>Participants</th>
<th>Methods</th>
</tr>
</thead>
<tbody>
<tr>
<td>1993 Caskey et al.</td>
<td>28</td>
<td>Men only</td>
<td>Three rapid-smoking; Jarvik <em>ad lib</em> (smoke as desired)</td>
</tr>
<tr>
<td>1994 Jarvik et al.</td>
<td>20</td>
<td></td>
<td></td>
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<tr>
<td>1994 Miller et al.</td>
<td>12</td>
<td></td>
<td>Commercially available cigarettes</td>
</tr>
<tr>
<td>1995 McCarthy et al.</td>
<td>29</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1996 Ahijevych et al.</td>
<td>37</td>
<td>Women only</td>
<td>Smoke <em>ad lib</em></td>
</tr>
<tr>
<td>1999 Ahijevych &amp; Parsley</td>
<td>95</td>
<td></td>
<td>Smoked preferred brand of commercially available cigarettes</td>
</tr>
</tbody>
</table>
## Menthol’s Effect on Puff Volume Compared to Nonmenthol Cigarettes

<table>
<thead>
<tr>
<th>Decreased volume</th>
<th>No significant effect</th>
<th>Increased volume</th>
</tr>
</thead>
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<td>1994 Jarvik et al.</td>
<td>1995 Miller et al.</td>
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<td>1996 Ahijevych et al.</td>
<td></td>
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</table>
Menthol’s Effect on Puffs per Cigarette Compared to Nonmenthol Cigarettes

<table>
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<tr>
<th>Fewer Puffs</th>
<th>No Significant Effect</th>
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<td>1995 McCarthy et al.</td>
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</table>
Other Topography Measures

• Jarvik et al.¹ (men, n=20)
  – Decreased puff volume, fewer puffs
  – AND puff flow rate significantly lower during menthol cigarette smoking
  – BUT no significant differences in peak puff flow and puff duration

• Ahijevych and Parsley ² (women, n=95)
  – Significantly larger puff volume among menthol smokers
  – BUT no significant differences in mean puff duration, inter-puff interval or total puff duration between cigarette types

Self-Reported Topography

• Prospective cohort (n=29,037) menthol and nonmenthol smokers reported similar puff frequencies, depths of inhalation and length of cigarettes smoked\(^1\)

• No difference in ratings of harshness between menthol and nonmenthol smokers\(^2\)

• Menthol smokers (n=473) gave “ease of inhalation” as one of the 3 main reasons for smoking menthol cigarettes\(^3\)

Limitations of Topography Studies

• Small sample sizes
  – Majority of the comparative studies (5/6) under 40 participants
  – Largest was 95 participants
  – Small studies do not account for inter- and intra-individual differences in smoking behavior

• Gender-specific: 2 women-only; 4 men-only

• External validity: 3 studies drew participants from drug and alcohol treatment center
Summary

• Sensory properties of menthol
  – Well-documented: taste, cooling/warming, respiratory, analgesic/anesthetic
  – Component of perceived strength

• Studies do not give consistent topography results:
  – Puff volume: 4 - depressive or no effect; 1 – increase (women)
  – Puff frequency: 2 - fewer puffs; 3 - no significant effect
  – No effect found with variation in menthol content
  – Self-reported assessments not consistent
Clarifying Questions?

References are listed in subsequent slides
References


References


