Cigarette Mentholation Increases Smokers’ Exhaled Carbon Monoxide Levels

Gregory E. Miller, Murray E. Jarvik, Nicholas H. Caskey, Suzanne C. Segerstrom, Martin R. Rosenblatt, and William J. McCarthy

Male smokers (N = 12) participated in 3 controlled-dose smoking sessions spaced 1 week apart. In each session, Ss inhaled 1,200 cc of cigarette smoke. Menthol dosage varied across sessions, such that Ss smoked experimental cigarettes that had been injected with 0 mg, 4 mg, or 8 mg of menthol. Exhaled carbon monoxide levels increased concomitantly with menthol dosage. There were no differences in smoking topography across the 3 conditions. The ability of menthol to increase the toxicity of cigarette smoke by raising carbon monoxide levels is discussed. Results suggest that menthol cigarette preference may account for some of the racial differences in smoking behavior and smoking-related outcomes found in past literature.

Mentholated cigarettes have gained in popularity in the United States during the last 20 years such that 75% of African-American smokers and 23% of Caucasian smokers prefer menthol to regular cigarettes (Cummings et al., 1987; Sidney, Tekawa, & Friedman, 1989). The reasons for this preference are not clear. One property of menthol is that it produces a sensation of coolness by stimulating cold receptors (Green, 1986, 1992; Orani, Anderson, Sant’Ambrogio, & Sant’Ambrogio, 1991; Sant’Ambrogio, Anderson, & Sant’Ambrogio, 1991), and this property has been exploited in promotional advertising for mentholated cigarettes.

African-American smokers have a higher incidence of tobacco-related cancer than Caucasian smokers, despite their lower rates of daily cigarette consumption (Satariano & Swanson, 1988). Sidney et al. (1989) suggested that the differences in cancer incidence between African Americans and Caucasians might be accounted for by the higher rate of menthol cigarette smoking among African Americans.

The goal of the present research was to explore several mechanisms by which mentholated cigarettes may be linked to an increased vulnerability to tobacco-related cancer. By systematically adding menthol to cigarettes, we attempted to discover whether mentholation would influence the smoking topography and the carbon monoxide exposure of our subjects.

Subjects participated in three menthol-controlled-dose smoking sessions spaced 1 week apart. Menthol dosage varied across sessions, so that subjects smoked experimental cigarettes injected with 0 mg, 4 mg, or 8 mg of menthol. We hypothesized that, as the menthol dosage was increased, subjects would show concomitant increases in exhaled carbon monoxide levels. We hypothesized further that increases in exhaled carbon monoxide

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would be accounted for by alterations in smoking topography. That is, we expected that menthol's anesthetic effects (Budvari, O’Neill, Smith, & Heckelman, 1989) would allow subjects to take larger puffs from our smoking apparatus and thus expose them to greater per-puff quantities of smoke constituents.

### Method

**Subjects**

Subjects were recruited from the inpatient substance abuse ward at the Veterans Administration Medical Center, West Los Angeles. To participate in the study, subjects had to be free of pulmonary and respiratory disease, smoke a minimum of 15 cigarettes per day, and be free of psychotropic medication. Participants were required to attend three separate experimental sessions, with an interval of at least 5 days between sessions. Because subjects were enrolled in a 21-day drug treatment program, most of them (26) were discharged from the hospital before completing all three sessions. An additional 2 subjects reported to research assistants that they had decided to quit smoking and thus no longer wished to participate in the study. A total of 40 subjects participated in at least one experimental session, only 12 of whom completed all three sessions. The 28 subjects who failed to complete all three experimental sessions did not differ from the 12 subjects with respect to smoking history measures (e.g., Fagerstrom Tolerance Scale [FTS], Fagerstrom & Schneider, 1989; self-reported depth of inhalation, all $r < 1.00$).

The final sample comprised 12 African-American male inpatients. At the time of the investigation, all subjects were undergoing treatment for alcohol or drug dependence. Drug and alcohol abstinence was confirmed through urine and breath testing, which are weekly requirements for patients on substance abuse wards. Subjects were paid $10 per hour in hospital cafeteria coupon booklets for their participation.

Six subjects characterized themselves as primarily menthol cigarette smokers. The remaining 6 subjects were primarily regular cigarette smokers. No significant differences were found between menthol and regular cigarette smokers on demographic or smoking history variables (see Table 1). Subjects’ mean age was 42.0 years ($SD = 6.7$). Subjects had been smoking for an average of 19.5 years ($SD = 10.4$) and smoked 16.2 cigarettes daily ($SD = 7.5$). Subjects reported an average of 2.8 quit attempts ($SD = 3.7$); the mean number of

### Table 1

**Descriptive Statistics for Demographics and Smoking History Measures**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Menthol smokers ($n = 6$)</th>
<th>Regular smokers ($n = 6$)</th>
<th>All subjects ($N = 12$)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$M$</td>
<td>$SD$</td>
<td>$M$</td>
</tr>
<tr>
<td>Age</td>
<td>39.83</td>
<td>6.79</td>
<td>44.16</td>
</tr>
<tr>
<td>Year of school</td>
<td>13.83</td>
<td>2.56</td>
<td>13.33</td>
</tr>
<tr>
<td>Number of others sharing residence who smoke</td>
<td>1.67</td>
<td>1.21</td>
<td>1.33</td>
</tr>
<tr>
<td>Cigarettes per day</td>
<td>16.50</td>
<td>7.84</td>
<td>15.83</td>
</tr>
<tr>
<td>Depth of inhalation</td>
<td>2.33</td>
<td>0.52</td>
<td>2.66</td>
</tr>
<tr>
<td>Fagerstrom Dependence Score</td>
<td>7.16</td>
<td>1.33</td>
<td>6.67</td>
</tr>
<tr>
<td>Years smoked</td>
<td>15.50</td>
<td>10.35</td>
<td>23.50</td>
</tr>
<tr>
<td>Quit attempts</td>
<td>1.50</td>
<td>2.07</td>
<td>4.16</td>
</tr>
<tr>
<td>Number of quit programs attended</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>Longest number of days without smoking</td>
<td>60.33</td>
<td>94.12</td>
<td>98.00</td>
</tr>
<tr>
<td>Percentage currently married</td>
<td>33.33</td>
<td>—</td>
<td>66.66</td>
</tr>
</tbody>
</table>

*Note. All data are from self-reports. Dashes indicate not applicable.*
days the longest quit attempt had lasted was 79.2 (SD = 137.0). Mean self-reported depth of usual smoke inhalation was 2.5 on a 4-point scale ranging from not at all (1) to very deeply (4), SD = 0.5. The mean score on the FTS was 6.9 (SD = 1.7). Scores on the FTS range from 0 to 11, with higher scores indicating greater nicotine dependence (Fagerstrom & Schneider, 1989).

Of the subjects tested, 6 had never been married, 4 were divorced, 1 was married, and 1 was widowed. Subjects lived with a mean of 2.5 other people (SD = 0.5). All subjects had at least a high school education; the mean number of years of education was 13.6 (SD = 1.9).

Procedure

We used a repeated measures design in which subjects participated in three controlled-dose smoking sessions. Menthol dosage varied across sessions, so that subjects smoked experimental cigarettes containing 0 mg, 4 mg, or 8 mg of menthol. Pre- and postexperiment measures of exhaled carbon monoxide, blood pressure, and pulse were collected at each session.

The experimental cigarettes were regular Marlboros (1992 Federal Trade Commission ratings: nicotine delivery = 1.10 mg, tar = 16 mg, carbon monoxide = 14 mg), which had been injected with 40 μl of an alcohol-based solution that delivered 0 mg, 4 mg, or 8 mg of menthol. All cigarettes were allowed to dry for 30 min before they were used in experimental trials. Biochemical analyses indicated that the 4- and 8-mg menthol cigarettes corresponded to the range of menthol contained in popular commercial cigarettes (Jarvik, 1993).

Subjects reported to the laboratory at 8:30 p.m. the evening before each of the experimental sessions. Subjects first completed an informed consent form. Breath samples were then collected to determine levels of exhaled carbon monoxide. We asked subjects to inhale deeply, hold their breath for 30 s, and then exhale 500 cc into a Travenol intravenous bag. Exhaled carbon monoxide levels were then determined by feeding the breath sample into an Ecolyzer (Model 5001, Energetics Science, New York, NY). After breath samples had been collected, subjects were scheduled for an appointment the following morning and instructed not to smoke until after that appointment.

Subjects returned to the laboratory the follow-

ing morning for the experimental session. At the first session, subjects completed questionnaires regarding smoking history, smoking habits, and demographics. Breath samples were then collected to determine baseline levels that could be compared with both the night-before and postexperiment levels. Subjects were required to show a 70% overnight drop in exhaled carbon monoxide level as a criterion for abstinence. Subjects who did not show a sufficient overnight decrease were not allowed to participate in experimental trials on that day and were rescheduled. All 12 subjects in the final sample showed sufficient overnight carbon monoxide decreases at each of the three experimental sessions.

Baseline cardiovascular measures of systolic blood pressure, diastolic blood pressure, and heart rate were also taken; these were taken three times to increase the reliability of the measures. Measurements were taken at 30-s intervals.

Subjects were then seated at a desk facing a controlled-dose smoking apparatus that has been described in detail elsewhere (Jarvik, Rosenblatt, Carpenter, Caskey, & McCarthy, 1992). After an experimental cigarette was placed in the apparatus and lit, subjects drew puffs through the apparatus at 30-s intervals until they had drawn a total of 600 cc of smoke. The apparatus was constructed so that subjects could draw a maximum of 100 cc of smoke per puff. To confirm that they had inhaled the smoke rather than simply drawing it out of the apparatus, subjects exhaled at least 700 cc of air into a spirometer.

After subjects had drawn and inhaled a total of 600 cc of smoke from the apparatus, we again collected breath samples. Subjects then repeated the smoking protocol described previously, drawing puffs from the apparatus at 30-s intervals until they had drawn another 600 cc of smoke, for a cumulative total of 1,200 cc of smoke. Postexperiment measures of systolic blood pressure, diastolic blood pressure, and heart rate were then repeated; we also collected final breath samples. Subjects were paid at the end of each experimental session. Subjects who did not complete the protocol were scheduled for an appointment 1 week later. The order in which the 12 subjects participated in the 0-mg, 4-mg, and 8-mg menthol trials was random and counterbalanced.
Results

Smoking Topography

Repeated measures analyses of variance were used to determine whether there were any topographic differences between menthol and regular smokers at any menthol dose. Menthol and regular smokers did not differ significantly on the quantity, $F(1, 10) = 1.38, ns$, or the volume, $F(1, 10) = 0.74, ns$, of the puffs they took. Similarly, menthol dosage did not influence the quantity, $F(2, 9) = 1.36, ns$, or volume, $F(2, 9) = 0.95, ns$, of subjects' puffs. It took subjects an average of 17.7 puffs ($SD = 3.23$) to inhale 1,200 cc of smoke from the apparatus. The mean per-puff volume was 71.5 cc ($SD = 11.30$).

Exhaled Carbon Monoxide

After 1,200-cc intake. We analyzed carbon monoxide data using a repeated measures analysis of covariance (ANCOVA) in which the covariate was the baseline carbon monoxide value taken after overnight abstinence and immediately before the experimental procedure. The dependent variable was carbon monoxide boost (post- minus pre-carbon monoxide value) after inhaling 1,200 cc of smoke. Independent variables were dose (0 mg, 4 mg, or 8 mg of menthol) and cigarette preference.

There was a significant effect for the repeated variable, menthol dose, $F(2, 19) = 9.37, p < .002$. An analysis of trend revealed that carbon monoxide levels increased concomitantly with menthol dosage in a linear fashion, $F(1, 9) = 10.43, p < .01$. Figure 1 illustrates this trend. In the no-menthol condition, mean carbon monoxide boost was 5.6 parts per million (ppm); in the 4-mg menthol condition, 6.1 ppm; in the 8-mg menthol condition, 8.1 ppm. Planned comparisons revealed that carbon monoxide boosts in the 8-mg condition were significantly greater than carbon monoxide boosts in either the 0-mg menthol condition, $F(1, 9) = 10.43, p < .01$, or the 4-mg menthol condition, $F(1, 9) = 14.91, p < .004$. Carbon monoxide boosts in the 0-mg menthol condition did not differ significantly from carbon monoxide boosts in the 4-mg menthol condition, $F(1, 9) = 2.78, ns$.

There was also a significant main effect for cigarette preference, $F(1, 9) = 5.08, p < .05$, such that subjects who stated that they preferred menthol cigarettes had greater carbon monoxide boosts than those who stated they preferred regular cigarettes (menthol, 7.6 ppm; regular, 5.6 ppm). The interaction between menthol dose and cigarette preference did not reach statistical significance.

After 600-cc intake. We also performed a repeated measures ANCOVA using carbon monox-
ide boosts after 600 cc of smoke as the dependent variable. The covariate was the baseline carbon monoxide value taken after overnight abstinence and immediately before the experimental procedure, and the independent variables were menthol dosage and cigarette preference.

There was a nonsignificant main effect of cigarette preference, $F(1, 9) = 2.73$, $ns$. Menthol smokers had a mean carbon monoxide boost of 3.78 ppm, whereas regular smokers had a mean carbon monoxide boost of 3.0 ppm. There was also a nonsignificant effect for the repeated variable of menthol dosage, although differences were in the expected directions, $F(2, 19) = 2.38$, $ns$. In the no-menthol condition, subjects had a mean carbon monoxide boost of 2.9 ppm; in the 4-mg menthol condition, 2.9 ppm; in the 8-mg menthol condition, 4.3 ppm. There were no significant differences in carbon monoxide boosts across the three menthol dosages.

When analyses were redone excluding cigarette preference as an independent variable, the effect of the repeated variable (menthol dosage) increased, $F(2, 21) = 2.58$, $ns$. The interaction between cigarette preference and menthol dosage did not reach statistical significance.

**Cardiovascular Variables**

Reliability of the repeated blood pressure and heart rate measurements was assessed by calculating the mean intertrial correlation across all measurements of a particular type. The mean correlation for diastolic blood pressure measurements was 0.69 ($SD = 0.15$); for systolic blood pressure measurements, 0.70 ($SD = 0.23$); for heart rate, 0.87 ($SD = 0.10$). Because measurements were highly reliable, averages across the three measurements were used in these analyses. Two subjects, one menthol cigarette smoker and one regular cigarette smoker, had missing data across all three trials on at least one visit and were thus excluded from the analyses.

As in the carbon monoxide analyses, we performed a repeated measures ANCOVA using the baseline values taken immediately before the experimental procedure as covariates. The dependent variables were change in blood pressure and heart rate (post- minus prevalue) after inhaling 1,200 cc of smoke. Independent variables were dose (0 mg, 4 mg, or 8 mg of menthol) and cigarette preference. There were no significant differences between menthol and regular cigarette smokers or across menthol dose on any of the cardiovascular variables—systolic blood pressure, diastolic blood pressure, or heart rate—nor were there any significant interactions.

**Discussion**

This study demonstrates that adding menthol to cigarettes causes a significant increase in exhaled carbon monoxide despite a constant volume of smoke exposure. The mechanism responsible for this effect remains to be clarified. The results of this investigation allow us to rule out topographic explanations; across the three menthol dosages, subjects did not differ in the number or the size of the puffs they took. It may be an interaction with menthol in the combustion of the cigarette or a physiological effect of menthol on the smoker. We favor the possibility that increased carbon monoxide is secondary to a physiological effect of menthol on the smoker.

Menthol is an ingredient found in certain mint plants such as spearmint and peppermint, but most commercial menthol is synthetic. Menthol is categorized as Generally Regarded As Safe by the U.S. Food and Drug Administration, and as such it is used as an additive in a large variety of food and pharmaceutical preparations to which it imparts a distinctive flavor and aroma. Furthermore, menthol has been shown to stimulate cold receptors, producing a sensation of coolness (San't Ambrogio et al., 1991). This property has been exploited in some brands of cigarettes to counteract the perceived burning sensation from tobacco smoke.

One of the most plentiful toxic ingredients of cigarette smoke is carbon monoxide (U.S. Department of Health and Human Services, 1990). Mainstream smoke usually delivers between 10 and 20 mg of carbon monoxide per cigarette (U.S. Department of Health and Human Services, 1988). Whether carbon monoxide levels in smokers are high enough to cause behavioral changes is a matter of dispute (U.S. Department of Health and Human Services, 1988).

Possible links between carbon monoxide in cigarette smoke and increased risk of disease have been studied in the natural environment and in the laboratory (Stewart, 1975). Cigarette smoke contains carbon monoxide in quantities large enough
to cause significant polycythemia. Inhalation results in the formation of carboxyhemoglobin, which displaces oxyhemoglobin and decreases the oxygen-carrying capacity of blood (Collier, 1976). Smokers typically have carboxyhemoglobin levels ranging from 3.2% to 6.2% (Stewart et al., 1974). Thus, carbon monoxide exacerbates conditions in which oxygen needs are compromised, such as emphysema and myocardial insufficiency.

In recent years, other cellular functions of carbon monoxide have been demonstrated, and it is likely that perturbations of these functions by abnormally high concentrations of carbon monoxide could impair such functions (Barinaga, 1993; Verma, Hirsch, Glatt, Ronnett, & Snyder, 1993). The present research demonstrated that menthol influences the absorption of one constituent of cigarette smoke: exhaled carbon monoxide. It is possible, however, that menthol's physiological influence extends beyond exhaled carbon monoxide. Wagenknecht et al. (1990) reported that African-American smokers had higher levels of serum cotinine than did Caucasian smokers, after controlling for the number of cigarettes smoked per day. Given the pronounced racial difference in menthol preference noted previously, it is possible that menthol preference may partially account for the racial differences in serum cotinine reported by Wagenknecht et al. Other factors (e.g., diet, genetics, metabolic differences) may also be responsible for this effect.

It is also possible that mentholation of cigarettes results in increased absorption of other tobacco smoke constituents (e.g., nicotine, total particulate matter), which could help to explain the observed racial differences in tobacco-related cancer. However, further research is needed to evaluate that possibility.

References


P&C Board Appoints Editor for New Journal: 

*Journal of Experimental Psychology: Applied*

In 1995, APA will begin publishing a new journal, the *Journal of Experimental Psychology: Applied*. Raymond S. Nickerson, PhD, has been appointed as editor. Starting immediately, manuscripts should be submitted to

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The *Journal of Experimental Psychology: Applied* will publish original empirical investigations in experimental psychology that bridge practically oriented problems and psychological theory. The journal also will publish research aimed at developing and testing of models of cognitive processing or behavior in applied situations, including laboratory and field settings. Review articles will be considered for publication if they contribute significantly to important topics within applied experimental psychology.

Areas of interest include applications of perception, attention, decision making, reasoning, information processing, learning, and performance. Settings may be industrial (such as human–computer interface design), academic (such as intelligent computer-aided instruction), or consumer oriented (such as applications of text comprehension theory to the development or evaluation of product instructions).