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Review

Review

Why We Must Continue to Investigate Menthol's Role in the African American Smoking Paradox

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Abstract

Background: The disproportionate burden of tobacco use among African Americans is largely unexplained. The unexplained disparities, referred to as the African American smoking paradox, includes several phenomena. Despite their social disadvantage, African American youth have lower smoking prevalence rates, initiate smoking at older ages, and during adulthood, smoking rates are comparable to whites. Smoking frequency and intensity among African American youth and adults are lower compared to whites and American Indian and Alaska Natives, but tobacco-caused morbidity and mortality rates are disproportionately higher. Disease prediction models have not explained disease causal pathways in African Americans. It has been hypothesized that menthol cigarette smoking, which is disproportionately high among African Americans, may help to explain several components of the African American smoking paradox.

Purpose: This article provides an overview of the potential role that menthol plays in the African American smoking paradox. We also discuss the research needed to better understand this unresolved puzzle.

Methods: We examined prior synthesis reports and reviewed the literature in PubMed on the menthol compound and menthol cigarette smoking in African Americans.

Results: The pharmacological and physiological effects of menthol and their interaction with biological and genetic factors may indirectly contribute to the disproportionate burden of cigarette use and diseases among African Americans.

Conclusions: Future studies that examine taste sensitivity, the menthol compound, and their effects on smoking and chronic disease would provide valuable information on how to reduce the tobacco burden among African Americans.

Implications: Our study highlights four counterintuitive observations related to the smoking risk profiles and chronic disease outcomes among African Americans. The extant literature provides strong evidence of their existence and shows that long-standing paradoxes have been largely unaffected by changes in the social environment. African Americans smoke menthols disproportionately, and menthol's role in the African American smoking paradox has not been thoroughly

explored. We propose discrete hypotheses that will help to explain the phenomena and encourage researchers to empirically test menthol's role in smoking initiation, transitions to regular smoking and chronic disease outcomes in African Americans.

Introduction

Blacks/African Americans, the second largest minority group in the United States,[1] have historically had worse health outcomes and greater social disadvantage than any other racial/ethnic group.[2] The risk factors, incidence, morbidity, and mortality rates for the leading causes of death in United States are often greater among blacks/African Americans[2] and life expectancy is 3.8 years lower than that of the whites.[3] Cigarette smoking is a major cause of diseases and deaths among blacks/African Americans, but the disproportionate burden of smoking during adulthood and disease outcomes among blacks/African Americans is largely unexplained by empirical investigations.[4–6]

The term "smoker's paradox" has been used to describe counterintuitive observations related to cigarette smoking patterns and/or smoking-related disease patterns in different groups.[7,8] The "Black/African American smoking paradox" encompasses a number of phenomena related to cigarette smoking behavior in youth and young adulthood and the disproportionate disease outcomes observed in black/African American adult smokers in the United States.

The first paradox is that social disadvantage among black/African American youth does not result in earlier initiation of cigarettes compared to other racial/ethnic groups. For example, poverty rates have been at least three times higher among black/African American than white youth since 1976.[9] Despite their disadvantage, compared to other racial/ethnic groups, blacks/African Americans are more likely to initiate cigarette smoking[10–12] and overall tobacco use[10] later in life with more than 50% initiating after age 18.[12]

The second paradox is that social disadvantage among black/African American youth does not result in higher cigarette smoking prevalence rates than that of white youth. Blacks/African Americans, irrespective of gender, are more likely than whites to be placed in juvenile system facilities,[13] but black/African American youth in the justice system have lower substance use,[14] cigarette smoking,[15] daily smoking,[15] and smoke fewer cigarettes per day compared to white youth.[14] Despite their social disadvantage, data consistently show lower cigarette smoking prevalence rates among noninstitutionalized black/African American youth compared to white, Hispanic, and American Indian/Alaska Native youth.[16–20] In 1977, 36.7% of black/African American compared with 38.3% of white 12th graders smoked in the past 30 days.[19] In 1987, 14.2% versus 32.1%; in 1997, 14.3% versus 40.7%; in 2007, 10.8% versus 24.9%; and by 2014, 9.0% of black/African American compared with 17% of white 12th graders reported smoking in the past 30 days.[19] Furthermore, data show that the use of any tobacco product,[18] concurrent use of tobacco products,[18,20] and concurrent use of cigarettes and cigars are lower among black/African American compared with white high school students.[19]

The third paradox is that low cigarette smoking prevalence rates among black/African American youth do not result in low rates of smoking in the past 30 days in young adulthood. Blacks/African Americans lose their advantage relative to whites in young adulthood, and one study shows that achieved socioeconomic status and life transitions do not explain these observations.[21] Data from the 2012 Surgeon General's Report show that among 18–25 year olds, 26.3% of all blacks/African Americans, 31.7% of black/African American males, and 21.4% of black/African American females smoked cigarettes in the past 30 days in 2010.[10] Black young adults are more than twice as likely than white young adults to report increases from nondaily to daily smoking.[22]

The fourth paradox is that lower prevalence rates of smoking, frequency (daily vs. nondaily smoking) and intensity of smoking (the number of cigarettes smoked per day) do not result in a lower burden of tobacco-caused diseases. Over the past 20 years, smoking prevalence rates have not greatly differed between black/African American and white adults,[23] and their smoking profiles do not explain the disproportionate burden of chronic diseases. Smoking rates among black/African American adults declined from 27.2% in 1994[24] to 18.3% in 2013[25] and among whites from 26.3%[24] to 19.4%.[25] Although blacks/African Americans have lower smoking frequency and intensity compared to whites and American Indians and Alaska Natives, they have higher disease risk.[11] Historical trends and recent data show that black/African American youth[17] and adults smoke fewer cigarettes per day compared with whites[11,26] and are more likely to smoke nondaily compared to whites, Asians, and American Indians and Alaska Natives.[10] However, blacks/African Americans and Native Hawaiians who smoke 10 or fewer cigarette per day have disproportionately higher lung cancer risk compared with whites and Japanese.[5]

Blacks/African Americans have the highest overall cancer incidence and mortality rates and the highest lung cancer incidence and death rates in the United States compared to other racial/ethnic groups.[27] Blacks/African Americans have similar chronic obstructive pulmonary disease (COPD) rates as whites,[28] but black/African American men with COPD have a sixfold increased risk for lung cancer compared with whites.[4] Blacks/African Americans are almost twice as likely as whites to have a first stroke and die following a stroke.[29] From 2006 to 2010, the prevalence of strokes among blacks/African Americans increased,[30] while trends among whites and Hispanics showed no changes.[30] Deaths from heart disease, stroke, and hypertension combined are higher among blacks/African Americans compared to all other ethnic groups and almost twice that of white adults.[31]

Several researchers have hypothesized that menthol cigarette smoking may help to explain the African American smoking paradox,[32–34] but the causal pathways are unclear.[35,36] Menthol is a flavor additive in cigarettes that is found naturally in peppermint (*Mentha piperita*)[37] and corn mint plant oils (*M arvensis* and *M canadensis*).[38] The L-menthol is the most widely used isomer as a flavorant because it has greater cooling properties than other menthol isomers.[39] Menthol has been used as a local anesthetic, antiseptic, antifungal,[39] antibacterial, and antipruritic agent and is commonly used in toothpaste, mouthwash, and topical rubs.[38,40–42] It is also used to reduce respiratory discomfort that leads to coughing[43] and to treat digestive disorders.[44,45] The physiological and pharmacological properties of menthol that are enjoyed through food and health products are the same properties that can cause harm when menthol is used as a flavor additive in cigarettes.

National data show that 74%–88% of black/African American adult smokers report smoking menthol-flavored cigarettes.[46,47] About 95% of black/African American smokers aged 12–17, 94% aged 18–25, 92% aged 26–34, 90% aged 35–49, and 81% aged 50 and over smoked menthol cigarettes in the past 30 days. In contrast, 26% of all whites, 51% of whites aged 12–17, 36% aged 18–25, 24% aged 26–34, 20% aged 35–49, and 21% aged 50 and over reported menthol cigarette smoking in the past 30 days.[46] Thus, menthol cigarette smoking is popular among blacks/African American smokers irrespective of age, whereas among whites, the popularity of menthol smoking declines as age increases.[46]

The goal of this article is to provide an overview of the potential role that menthol cigarettes play in the black/African American smoking paradox and why this deserves further investigation in future research. We also discuss specific categories of research needed to better understand this unresolved puzzle. We recognize that there are other factors such as discrimination, acculturation, socioeconomic status, peer influences, and neighborhood deprivation that may influence the smoking paradox, smoking in general, and tobacco-related health disparities. Several articles published in this special issue provide empirical data to elucidate different components of the "Black/African American smoking paradox". We have narrowly focused this article on menthol as one potential factor that influences the smoking paradox. Our review is designed to generate a series of hypotheses that can be tested in future research and ultimately inform tobacco regulatory policy, prevention, and cessation interventions.

Methods

Our configurative review is largely designed to interpret and understand the observed paradoxes rather than to aggregate empirical data and make empirical statements about the paradoxes as done with traditional systematic aggregate reviews.[48] Few empirical studies have sought to explain the specific role of menthol in the African American smoking paradox, and therefore we offer concepts for future investigation based on the existing evidence. We first examined synthesis reports of the literature on menthol cigarette smoking including the Food and Drug Administration's (FDA) Tobacco Products Scientific Advisory Committee (TPSAC) report on menthol in cigarettes[35] and the FDA's report on menthol in cigarettes.[36] However, it was not our goal to replicate or redo existing syntheses. We examined multiple data sources and publications to help us understand trends in smoking, current cigarette smoking prevalence rates, and menthol smoking among black/African American youth and young adults. These data sources included Monitoring the Future, the National Survey on Drug Use and Health, National Youth Tobacco Survey, the Youth Risk Behavioral Survey, National Health Interview Survey, National Adult Tobacco Survey, Surgeon General's Reports, the Census Bureau data, and other federal reports. We searched for additional literature in PubMed on the menthol compound and menthol cigarettes. We used the following search terms and combination of search terms to conduct our PubMed search: African American or black; smoking; menthol; menthol compound; initiation; quitting or cessation; nicotine dependence; nicotine metabolism; nicotine; disease; adolescents or youth; young adults; discrimination; social disadvantage; neighborhood deprivation; parental disapproval; marketing; policy; secondhand smoke exposure; sensory; chemosensory; taste; and smell. We also examined secondary references that were relevant.

Results

The Physiological and Pharmacological Effects of Menthol in Cigarettes

We first discuss the physiological and pharmacological effects of menthol since these factors are important to understanding menthol's role in the African American smoking paradox.

More than 90% of all cigarettes contain menthol,[49] but cigarette characterized as menthol can be detected by smell and taste and are marketed as menthol cigarettes. Menthol is the most popular characterizing flavor in the United States and menthol cigarettes are used by nearly 30% of all smokers.[46] Other characterizing flavors like strawberry, grape, or cherry were banned in 2009 under Section 907 Tobacco Product Standards of the Family Smoking Prevention and Tobacco Control Act, but menthol was excluded. Additional details on the physiological and pharmacological effects of menthol are summarized in two synthesis reports.[35,36]

Menthol is the only flavor additive that at different concentrations acts on the olfactory (smell), gustatory (taste),[50] and trigeminal systems (cooling and pain)[51–53] to produce different sensory effects. Data from the tobacco industry documents suggest that low to moderate levels of menthol (100 to 1000 ppm per tobacco weight) produce fairly weak sensations (eg, flavor, smell, cooling), but can take the edge off of the pain sensations of nicotine and tobacco and make the smoke smoother in cigarettes where menthol is not a characterizing flavor.[54] In menthol cigarettes, the higher levels of menthol (above 1000 ppm per tobacco weight) are evident and menthol dilutes or masks negative tobacco sensations (eg, pain, stinging, bitter taste).[54] At the right concentration, menthol can reduce irritation and sensitivity to nicotine.[55] Data show that 19 ppm of L-menthol can reduce cigarette smoke (9 mg/m^3) induced irritation by 50% in rats.[56] At 300 mg/m^3 of cigarette smoke, irritation is suppressed by 50% with 66 ppm of L-menthol.[56] L-menthol also acts as a counterirritant to acrolein and cyclohexanone, both of which are major irritant toxicants in cigarette smoke.[43,56] Menthol's analgesic, anesthetic, and counterirritant effects[43,56] on the tongue[57] and in the respiratory system may make smoking easier for first time and continued smokers. Menthol cooling can last up to 70 minutes in humans[58] by activating TRPM8 receptors.[55] Furthermore, menthol flavor additives influence the self-administration of nicotine.[59,60] Because menthol reduces nausea[61] and headaches,[61] it may disguise symptoms of nicotine poisoning and further contribute to its abuse liability among first time and continued smokers.

The Potential Role of Menthol in Smoking Among Black/African American Youth and Young Adults

Experimentation and Smoking in Blacks/African Americans

In the next sections, we highlight some of the literature on first time smoking, initiation of smoking, and transitions in smoking among blacks/African Americans, some of which have already been noted in the introduction and summarized in prior synthesis reports.[35,36] As previously stated, black/African American youth initiate smoking later in life than white youth despite their social disadvantage, and transition to regular smoking at older ages than whites.[62,63] Studies show that 34% of black/African American high school students reported that they ever tried cigarette smoking compared to 42.9% of whites and 62.3% of American Indians and Alaska Natives in 2013.[64] Only 6.7% of black/African American high school students reported smoking a whole cigarette before age 13, 4.3% reported ever-daily use, and 1.7% reported current daily use in 2013.[64] One

study shows that on average, blacks/African Americans initiate cigarette smoking 1 year later than whites and transition to regular use 1 year later as well, resulting in a 2-year lag between the time of smoking initiation and transition to regular smoking.[63]

The TPSAC and the FDA synthesis reports both stated that there is sufficient evidence to conclude that the availability of menthol increases experimentation and regular smoking.[35,36] Studies show that among nonestablished smokers, 51.7% initiated with menthol cigarette.[65] It is not clear what percentage of blacks/African Americans initiate smoking with a menthol or nonmenthol cigarette, but it is likely that they experimented first with a menthol flavored cigarette for several reasons. About 94% of black/African American smokers aged 12–17 used a menthol cigarette in the past 30 days[46] and many black/African Americans in this age group may be experimenters. Studies show that switching from menthol to nonmenthol is low and less likely than switching from nonmenthol to menthol.[66,67] One study shows that only 5.3% of black/African American young adults who initiated with menthol switched to nonmenthol cigarettes.[66]

Data also show that the initiation of menthol cigarette smoking in blacks/African Americans is associated with an increased odds of transitioning to regular smoking.[68,69] Conclusions in the TPSAC report specifically indicate that there is sufficient evidence to conclude that the availability of menthol increases the likelihood of experimentation and regular smoking beyond the anticipated prevalence if such cigarettes were not available in the general population and particularly in African Americans.[35] The FDA made a similar conclusion and stated that menthol in cigarettes is likely associated with increased initiation and progression to regular use.[36] Based on the evidence, we postulate that the late onset and transition to regular smoking in blacks/African Americans in older ages combined with the use of menthol cigarettes may increase smoking prevalence at higher rates among blacks/African Americans than other racial/ethnic groups. Other groups are likely to have experienced the transition from initiation to regular smoking at younger ages and have lower rates of menthol cigarette use.

Although we postulate that menthol cigarette smoking in young adulthood explains increases in regular smoking and more dramatic increases in the prevalence of smoking among blacks/African Americans as compared with whites, it does not explain why their experimentation with cigarettes occurs in older versus younger ages. We investigated the literature on taste sensitivity to help address this component of the African American smoking paradox.

Taste Sensitivity and Protection From Early Onset of Smoking Among Blacks/African Americans

It has been hypothesized that the tobacco industry targeted menthol cigarettes to populations with specific chemosensory characteristics[70] because they were aware that some groups are likely to reject the bitter taste of nicotine. Studies suggest that sensitivity to bitter tastes is a genetic trait[71,72] mediated by TAS2R38 gene and possibly 25 other bitter taste receptors expressed on the tongue.[72] TAS2R38 encodes a chemosensory receptor sensitive to phenylthiocarbimide (PTC), 6-*n*-proplythiouracil (PROP), and many other thiourea-containing compounds.[73,74] Thiourea compounds are bitter sulphur containing compounds that are found in foods such as spinach and cruciferous vegetables.

In 1938, not long after menthol cigarettes were patented by Lloyd Spud Hughes in 1925,[75] a researcher discovered that some individuals perceived the bitter taste of PTC, while others did not.[76] PTC and PROP, a less toxic compound, have been used as markers of genetic variability in perceptions of taste[73] and to help distinguish three taster groups. Earlier studies using PTC suggested that taste was bimodal (taster and nontaster), but there is substantial evidence that taste sensitivity is a continuous measure of intensity and can be divided into nontasters, medium tasters, and supertasters.[77–79] Bartoshuk and colleagues[80] have shown that supertasters perceive stronger taste intensities from sweet and bitter compounds including PTC and PROP. Studies suggest that 19%–25% of the world's population are supertasters, 50% are medium tasters, and 25%–31% are PROP nontasters.[78] Thus, people who are likely to reject bitter flavors comprise 70%–75% of the population.[78–80]

Perceptions of taste vary by gender,[81,82] age,[83,84] and ethnicity.[85–87] Studies suggest that 35% of women and 15% of men are supertasters.[88] Studies show that differences in sensitivity to bitter taste is apparent in younger ages such that children in general have lower thresholds for bitter taste than adolescents and adults, and are thus more likely to reject bitter tastes.[84,89,90] In comparison to children who are tasters, children who are nontasters are more likely to accept bitter-tasting vegetables and fruit juices.[91,92] Asians and African Americans are more likely than whites to be supertasters.[85] Studies show that 60% of Indians (from India), 70% of Caucasians, 90% of Southeast Asians, 97% of West Africans,[93] and 63% of members of the Plain American Indian tribe perceive bitter taste.[82]

Nicotine is generally perceived as a bitter taste.[94,95] Studies suggest that PTC/PROP tasters are likely to find cigarettes adversely bitter and taster status may protect against smoking bitter toxic compounds like tobacco.[82,96–99] Since African Americans, like youth, are also more likely to reject bitter flavors, then sensitivity to bitter taste among African American youth may protect African Americans from cigarette smoking in adolescence to a greater extent than whites who are less likely to reject bitter flavors. In addition, one study shows that younger people have a lower threshold for menthol than older people.[100] Menthol at high concentrations can be an irritant like nicotine.[101] The lower threshold for bitter taste among blacks/African Americans combined with the lower threshold for menthol in younger ages may also protect African Americans from initiating smoking at earlier ages to a greater extent than whites.

Age and race/ethnicity related thresholds to bitter taste and age-related thresholds related to menthol may also help to explain transitions to smoking and regular smoking in young adult blacks/African Americans. Although sensitivity to bitter taste decreases with age, declines in sensitivity to bitter taste among African Americans may not be as steep as whites since they are more likely to be supertasters. However, the declines may be sufficient in young adulthood such that smoking is more tolerable. As menthol becomes more tolerable with age, menthol in cigarettes may mask the bitter taste and negative sensory aspects of nicotine experienced by adolescent blacks/African Americans. Studies show that menthol has cross-desensitizing effects on nicotine and these effects are independent of its cooling effects.[101] However, the desensitizing effects last up to 16 minutes and wear off over time.[101] It remains to be tested if desensitizing effects also influence lower intensity of smoking among black/African American youth and young adults. The desensitizing effects may also increase continued use because the sensory effects may become pleasurable.[101] Thus, we postulate that there is an interactive effect of age, race/ethnicity, bitter taste sensitivity, and trigeminal sensitivity related to menthol. These factors together could explain low rates of smoking among adolescent blacks/African Americans and transitions to regular smoking in young adulthood. This hypothesis remains to be

tested and studies among adolescents and young adults in laboratory settings could compliment longitudinal population-based studies to generate empirical evidence related to the smoking paradox.

Smoking Maintenance and Menthol Cigarettes

In this section, we briefly review the existing evidence on how menthol maintains smoking since the continued use of menthol cigarettes may contribute to the disproportionate disease outcomes we observe among blacks/African Americans. We recognize that the lack of access to and affordable cessation resources, low cigarette taxes, advertising, lack of comprehensive smokefree laws, and other social environmental factors play a role in quitting behaviors. Those factors have been highlighted in previous reports.[10,20]

Menthol and Smoking Intensity

In the introduction, we indicate that blacks/African American smoke fewer cigarettes per day than whites, which does not explain the disparities. Their lower intensity of smoking may be due their threshold for tolerating the bitter flavor of nicotine. Studies show that social smokers have a stronger perception of bitter taste compared with regular smokers, and a lower percentage of tasters among smokers consumed 20 or more cigarettes per day than nontasters.[99] Menthol smoking may attenuate the negative sensory effects of nicotine, which results in blacks/African Americans consuming fewer cigarettes per day than white smokers. The TPSAC report indicated that the evidence was mixed on whether menthol smokers smoke fewer cigarettes per day than nonmenthol smokers.[35] More evidence is needed on whether black/African American menthol smokers consume fewer cigarettes per day than blacks/African American nonmenthol smokers. Future studies would need to test how race/ethnicity and taster status influence the number of cigarettes smoked per day.

Menthol and Nicotine Dependence

Smokers with higher levels of nicotine dependence are at increased risk for quitting difficulty. The TPSAC report stated that the evidence is sufficient to conclude that menthol cigarettes increase the likelihood and degree of addiction in youth, but is not sufficient to conclude that it does in adults.[35] However, the FDA report stated that the weight of the evidence supports that menthol in cigarettes is associated with increased dependence.[36] The conclusions were not specific to blacks/African Americans and subsequent studies have not examined nicotine dependence in black/African American menthol and nonmenthol smokers. What is known is that taster status and menthol influence nicotine dependence. One study shows that among African American adults, nontasters are more likely and tasters are less likely to be dependent smokers.[102] This same study showed that being a nontaster was significantly associated with nicotine dependence among African American females.[102] This specific study examined gene polymorphisms related to taster status and did not take menthol cigarette smoking into consideration, which could influence dependence among multiple taster groups. Menthol increases the neural response of taste receptors in a similar manner as alcohol[103] and studies are needed to determine if menthol cigarette smoking mediates the relationship between taster status and nicotine dependence among blacks/African Americans.

Menthol and Quitting Smoking

Quitting smoking before age 35 can significantly reduce tobacco morbidity and mortality,[104] but studies suggest that compared with nonmenthol smokers, menthol smokers experience greater difficulty quitting,[105–107] and are less successful in quitting even when using nicotine replacement therapy.[107,108] The TPSAC and the FDA report stated that the evidence is sufficient to conclude that menthol in cigarettes results in the likelihood of lower smoking cessation success in African American smokers.[35,36] We defer the reader to the reports for discussions on the extant literature and briefly discuss quitting difficulty among African Americans in this section.

National data from 2010 show that 76% of blacks/African Americans compared to 69% of whites, 61% of Hispanics, and 63% of other racial/ethnic groups expressed an interested in quitting smoking. In 2010, nearly 60% of blacks/African Americans reported a quit attempt in the past year, a rate higher than any other racial/ethnic group.[109] However, in 2010, only 3% of blacks/African Americans compared to 6% of whites, 19% of Hispanics, and 10% of other racial/ethnic groups were able to quit for at least 6 months.[109] Menthol can inhibit quitting processes especially among African Americans[35,36] since it reduces irritation in the oral cavity,[110] eases inhalation of smoke, and suppresses respiratory irritation.[43] Other studies also show lower successful quit rates among African Americans compared to other racial/ethnic groups[106,107,111,112] and among African American menthol smokers compared with African American nonmenthol smokers.[106] Lower rates of successful quitting due to menthol smoking alone may not explain the disproportionate morbidity rates among African Americans, but it deserves further investigation.

The Potential Role Menthol Plays in Tobacco-Caused Diseases

Comprehensive evidence reviews conducted by TPSAC[35] and independently by the FDA[36] stated that there was insufficient evidence to conclude that menthol smokers have an increased risk for any chronic disease. The conclusions were based on limited evidence even for lung cancer. In the report, the TPSAC indicated that the high prevalence of menthol cigarette smoking adds to the burden of premature deaths in African Americans. Few studies have been specifically designed to answer whether or not menthol is associated with chronic disease risk. We include a brief discussion on how menthol directly and indirectly through its effects on nicotine influence pathways toward chronic disease.

Menthol as a Pathway to Chronic Disease

Studies show that menthol inhibits nicotinic acetylcholine receptors, and serotonin-gated ion channels, known to contribute to pain signaling.[113,114] If pain signaling is inhibited, the illness symptoms may be blunted among menthol smokers and result in delays in seeking health care. The desensitizing effects of menthol on nicotine wear off over time,[101] but the chronicity of this effect reduces tissue-protective signaling provided by the irritant sensation.[101]

Menthol and Nicotine as Pathways to Chronic Disease

Menthol may influence disease pathways through its effects on nicotine. Prior studies suggest that African Americans,[115–118] Asians,[115,118,119] Hispanics,[115–117] and persons of mixed ethnicity have slower nicotine metabolism compared to whites.[115] Several studies also show slower metabolism among menthol compared with nonmenthol smokers.[117–120] Some studies show slower nicotine metabolism among menthol smokers, but the differences between menthol and nonmenthol smokers were not significant.[121–123] One study conducted

by the tobacco industry showed that nicotine metabolism was higher among nonmenthol smokers compared with menthol smokers, but the differences were not statistically significant.[124] One study showed that blood cotinine levels were 1.5 times higher in animals exposed to L-menthol plus smoking than those exposed to smoke alone.[56] It is possible that greater exposure of menthol smokers to nicotine can trigger coronary events through various pathways.[20]

Cardiovascular Disease

Death rates due to heart disease, stroke, and hypertension combined are higher among African Americans compared to all other ethnic groups and almost twice that of white adults.[31] Cross-sectional studies show that former menthol smokers have higher body mass index compared with former nonmenthol smokers,[125] and that current menthol cigarette smokers have significantly higher Framingham 10-year risk scores (FRS), higher body mass index, a 40% increased risk in abdominal obesity, and are more likely to have hypertension compared with nonmenthol smokers.[126] Another study found that menthol smokers have higher systolic blood pressure and aortic stiffness index than nonmenthol smokers.[127] These studies were cross-sectional in nature and therefore, we cannot make conclusions about the temporal relationship between menthol smoking and cardiovascular disease (CVD). However, future studies are needed to investigate the mediation role of nicotine in the relationship between menthol cigarette smoking and CVD and intermediate disease outcomes such as obesity. Nicotine is an independent risk factor for CVD and accelerates atherosclerosis.[20,128]

Cancer

Studies do not show that nicotine[20] or menthol[35,36] cause cancer in humans, but nicotine can bioactivate carcinogenic pathways as indicated in the 2014 Surgeon General Report. Nicotine can inhibit apotosis in the lung cells; activate Ras-Raf ERK cascade; and stimulate fibronectin production activating ERK, P13-K, mTOR, and PPAR-ß/δ.[20] Nicotine could potentially promote metastases.[20] Higher doses of nicotine in cells have also induced cytoxicity.[20] Furthermore, there is some evidence of nicotine's potential risk in oral, esophageal, and pancreatic cancer.[20] Studies are needed to investigate how nicotine may mediate the relationship between menthol smoking and carcinogenic pathways.

Chronic Obstructive Pulmonary Disease

Studies on the relationship between COPD and menthol smoking are limited. One study did not show differences between menthol and nonmenthol smokers in COPD and comorbidities like CVD, peripheral vascular disease, hypertension, diabetes, osteoporosis, cerebral vascular disease, and gastro-oesophageal reflux. However, the longitudinal results show that menthol smokers experience more severe exacerbations of COPD compared with nonmenthol smokers.[129] The results did not stratify the data by race/ethnicity. Studies are needed to better understand how menthol exacerbates COPD and whether or not this pathway increases the risk for lung cancer.

Discussion

This article provides an overview of the potential role that menthol cigarettes play in the black/African American smoking paradox. Based on our review, this topic is an under-investigated area of research. Menthol cigarette smoking is high among African Americans and we postulate that menthol influences the paradox through several pathways. Menthol's interaction with taster status and age-related thresholds may protect blacks/African Americans from smoking in adolescence, but facilitate smoking in older age since sensitivity to bitter taste declines with age. As blacks / African Americans age and bitter taste thresholds increase, then they may be more likely to tolerate cigarettes with the addition of menthol, which facilitates the ease of smoking. A second pathway is that African Americans who begin smoking at later ages than whites may experience dramatic increases in cigarette smoking because of menthol. The initiation of menthol cigarette smoking in blacks/African Americans increases the odds of transitioning to regular smoking. Menthol cigarette smoking is lower among whites compared with blacks/African Americans. Because smoking initiation occurs later in life in African Americans compared with whites, the increases in smoking prevalence observed in blacks/African Americans would not be observed among whites during young adulthood.

A third pathway is that menthol increases nicotine dependence and quitting difficulty. Thus, continued smoking among African Americans increases the risk for chronic diseases. A fourth pathway is that menthol increases the availability of nicotine and nicotine has its own effects on biological mechanism that increase disease risk. Menthol cigarette smoking itself may also increase disease risk by inhibiting pain signaling and blunting illness symptoms, resulting in delayed health care and possible late diagnoses of diseases. In summary, empirical studies are needed to confirm or disconfirm the pathways we highlight in this article so that we can better explain paradoxical findings.

There are a myriad of other factors that could help to explain the African American smoking paradox that were beyond the scope of a single article. We acknowledge that poverty, discrimination, neighborhood deprivation and segregation, educational attainment, and social influences should be investigated as independent predictors of smoking and disease. Discrimination, as one measure of social disadvantage, has been associated with cigarette smoking among blacks/African Americans, but not the initiation of smoking among adolescents.[130–132] Future studies are needed to explore the role of social disadvantage in the African American smoking paradox and particularly among adults.

The role of marketing of menthol cigarettes to blacks/African Americans and marketing's role in the African American smoking paradox cannot be understated. TPSAC concluded that marketing messages for menthol have differed from messages used for nonmenthol cigarettes and increases the prevalence of smoking beyond the anticipated prevalence for the whole population, youth, and African Americans. FDA concluded that the marketing of menthol is associated with brand preference.[36] We believe that the evidence related to marketing is quite strong. Heavy marketing campaigns began in the 1960s.[133] African Americans are disproportionately exposed to tobacco advertising,[134] and marketing and promotion can influence purchasing behaviors[135] and smoking initiation and maintenance.[136] The marketing and disproportionate marketing of menthol cigarettes may have helped to establish social norms and normalize menthol smoking and brand preference in African American communities.

As we move forward to address the African American smoking paradox, it is important to consider the role of policies, including those that would reduce menthol marketing to blacks/African Americans. Existing policies have not been shown to have the desired effects on menthol smoking since menthol smoking is increasing among young adults, while nonmenthol smoking is

decreasing.[46] Public health policy related to menthol could arguably have a substantial influence on reducing overall smoking among African Americans. The US Congress had the unique opportunity to implement such a policy and the language in the Family Smoking Prevention and Tobacco Control Act was heavily debated in the media.[137] After much debate and opposition from individuals and organizations, menthol was excluded from the ban on characterizing flavors. Following the passing of the Family Smoking Prevention and Tobacco Control Act in 2009 by Congress, the federal government through the FDA had an opportunity to act upon recommendations of the TPSAC, who in 2011 recommended that menthol cigarettes be removed from the public health market.[35] However, US District Court Judge Richard Leon barred the FDA from using the TPSAC menthol report to inform future regulation. The FDA and TPSAC reports were independent of each other, but made similar conclusions regarding the harms of menthol.

In September 2015, 4 years after the TPSAC report made the recommendation to remove menthol cigarettes from the public health market, the FDA issued orders to R. J. Reynolds Tobacco Company to stop the sales, distribution and marketing of Camel Crush Bold, Pall Mall Deep Set Recessed Filter Menthol, Pall Mall Deep Set Recessed, and Vantage Tech 13.[138] Under FDA, new products that are determined to not be "substantially equivalent" (NSE) to respective predicated products commercially marketed prior to February 15, 2007 can be removed from the public health market. The FDA provides the opportunity for the manufacturer to provide evidence that the product does not raise different questions related to public health or have different features like changes in burn properties, characterizing flavor, flavor delivery, free nicotine or other features.[139] For example, consumers can "self-deliver" the menthol in Camel Crush Bold via a "menthol capsule" and its influences on smoking initiation, dependence and cessation are unknown.

The FDA decision does not impact Newport (formerly manufactured by Lorillard, Inc now owned by R. J. Reynolds Tobacco Company), which is the most common cigarette brand used by African Americans and is a menthol cigarette.[35] Some reports suggest that adding Newport to the Reynolds' portfolio will boost the number of retailers that sign up for the company's discount program, known as Reynolds' Every Day Low Price retailer agreement program.[140] Nearly 65% of retailers believe that Newport sales will grow faster if added to the program.[141] Despite the potential future market gains by Newport cigarettes, FDA's use of the NSE order provides precedence for FDA's future investigation of tobacco industry applications related to menthol cigarettes, smokeless tobacco, and if deemed, menthol flavored cigars and electronic cigarette juices and refill cartomizers. Given menthol's interactions with nicotine, it is critically important that policies consider how these new products impact the public's health, and specifically groups like African Americans who disproportionately use menthol cigarettes.

Policies in all states and localities could potentially influence menthol smoking among African Americans, but targeting geographic areas where African Americans live may be important. In Chicago, where 33% of people are African American and 23% are poor,[142] community organizers succeeded in banning the sales of menthol cigarettes smoking within 500 feet from schools.[143]

Policies could also include reducing natural or synthetic menthol, menthol analogues, and other chemical that mimic the effects of menthol such as it cooling effects produced when TRPM8 receptors[144] or TRPV3[145] are activated. If such actions are taken, the greatest benefit are likely to be observed if done in conjunction with policies related to reducing nicotine levels in tobacco products since menthol and nicotine interact and menthol has desensitizing effects on nicotine.[101] Lowering menthol amounts to levels that are no longer detectable could influence initiation and continued to smoke.

Limitations

Our study does not discuss smoking topography and smoke intake since there are limited data related to African Americans. We do not distinguish between African Americans, Caribbean-born blacks, blacks from different African nations, or Hispanic African Americans since these data are also limited. Other forms of tobacco including cigars, electronic cigarettes, hookah, and smokeless tobacco were not discussed. As we report in the introduction, concurrent use rates of cigarettes and other tobacco are low among African Americans and lower than that of whites. Menthol is a complex compound and our review does not include all the evidence on menthol that could potentially explain the black/African American smoking paradox.

Conclusions

This article summarizes why we should continue to investigate menthol's role in the African American smoking paradox. Prospective studies that include chemosensory measures are needed to better understand how taste sensitivity influences smoking initiation, maintenance, and intensity of smoking in youth and young adulthood. Mechanistic studies in vitro and in vivo are needed to understand how menthol and menthol cigarettes influence the administration of nicotine in youth and in young adults. To understand disease trajectories, studies that examine menthol cigarette effects on cellular mechanism and the association with disease processes, biomarkers of tobacco smoke exposure, and chronic disease risk among racial/ethnic and gender groups are needed. Studies are needed to determine both how menthol cigarettes directly influence smoking and chronic disease risk, and indirectly through its effects on nicotine or other constituents in cigarettes. Future studies may also consider using latent class modeling to better understand different risk profiles among never smokers, experimenters, current smokers and those who are diseased. Although the existing data do not fully explain the smoking paradox among blacks/African Americans, what is known is that if it were not for menthol, blacks/African Americans would not suffer disproportionately from tobacco-caused morbidity and mortality.

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Declaration of Interests

None declared.

Disclaimer

The findings and conclusions are the author's, not necessarily the CDC's.

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