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Review

The Sociopharmacology of Tobacco Addiction: Implications for Understanding Health Disparities

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Abstract

Efforts to reduce the public health burden of tobacco use have not equally benefited all members of society, leading to disparities in tobacco use as a function of ethnicity/race, socioeconomic position, physical/behavioral comorbidity, and other factors. Although multilevel transdisciplinary models are needed to comprehensively understand sources of tobacco-related health disparities (TRHD), the incorporation of psychopharmacology into TRHD research is rare. Similarly, psychopharmacology researchers have often overlooked the societal context in which tobacco is consumed. In an effort to facilitate transdisciplinary research agendas for studying TRHD and the psychopharmacology of tobacco use, this article introduces a novel paradigm, called "sociopharmacology." Sociopharmacology is a platform for investigating how contextual factors amplify psychopharmacological determinants of smoking to disproportionately enhance vulnerability to smoking in populations subject to TRHD. The overall goal of sociopharmacology is to identify proximal person-level psychopharmacological mechanisms that channel distal societal-level influences on TRHD. In this article I describe: (1) sociopharmacology's overarching methodology and theoretical framework; (2) example models that apply sociopharmacology to understand mechanisms underlying TRHD; (3) how sociopharmacological approaches may enhance the public health impact of basic research on the psychopharmacology of tobacco use; and (4) how understanding sociopharmacological mechanisms of TRHD might ultimately translate into interventions that reduce TRHD.

Introduction

Over the past 50 years, tobacco control efforts have dramatically reduced the prevalence of and morbidity and mortality from tobacco use.[1–3] Importantly, the decline in smoking prevalence has been disproportionately accounted for by demographic majority groups and the socioeconomically advantaged.[1,3,4] One unfortunate consequence of this trend is the emergence of disparities in tobacco use uptake, maintenance, and cessation relative to the general population among the following groups: (1) ethnic/sexual minorities (eg, blacks, American Indian/Alaskan Natives, immigrants, and lesbians), (2) individuals of lower socioeconomic position (eg, lower income, education, and employment), (3) individuals with health problems (eg, physical illness or disability, psychiatric disorder, and substance use disorder), and (4) other disadvantaged populations (eg, people with a criminal justice history). In the United States, for example, 42% of the population smoked 50 years ago and smoking was more common among certain advantaged groups relative to the general population (eg, college educated).[1] Presently, the prevalence of smoking in the United States is around 18%. Within the current population of US smokers, 25% have incomes below the poverty line,[1] 12.3% are under criminal justice supervision,[5,6] one-third have a psychiatric

condition,[7] 10.6% are unemployed,[8] 86.8% do not have a college degree,[9] and one-quarter have a non-nicotine substance use disorder.[10,11] Accordingly, understanding the mechanisms that disproportionately promote smoking in these "disparity groups" relative to general population will be key to understanding and eliminating tobacco-related health disparities (TRHD) and ultimately impacting the overall tobacco burden.

Given the complexity of multilayered influences on social disadvantage and tobacco addiction, "multilevel" transdisciplinary approaches that acknowledge the intersection of sociocontextual (eg, culture, class) and individual-level (eg, psychology, biology) factors are necessary to address TRHD.[12] Despite the need for such work, multilevel empirical studies on TRHD are scant, potentially because focused frameworks to guide such research are lacking. To facilitate multilevel transdisciplinary research of TRHD, this article proposes a novel paradigm, which I call "sociopharmacology." As a synthesis of theory and methods of social epidemiology and psychopharmacology, sociopharmacology is a platform for studying how the broader social context amplifies individual-level psychopharmacological determinants of smoking to disproportionately enhance vulnerability to smoking in disparity groups relative to the general population. The overall goal is to identify proximal person-level psychopharmacological mechanisms that channel distal sociocontextual influences on TRHD. In addition to its specific relevance for TRHD, sociopharmacology may enhance the public health significance of basic research on the psychopharmacology of tobacco use, as described in greater detail below.

In this article, I define sociopharmacology and provide a unifying framework for applying sociopharmacology to empirical research on TRHD. Then, in exemplary applications of the paradigm, I describe two sociopharmacologally-informed models. Finally, after noting sociopharmacology's limitations, the article concludes by describing implications for basic research on the psychopharmacology of nicotine and interventions for reducing TRHD.

Theoretical Framework and Methodology of Sociopharmacology

Sociopharmacology is the synthesis of social epidemiology approaches to studying TRHD and psychopharmacology approaches to studying tobacco addiction. Therefore, I briefly outline these two approaches before describing sociopharmacology (Table 1 for a comparison of the three approaches).

Brief Background on Social Epidemiology and Psychopharmacology

Social Epidemiology

Social epidemiology often focuses on cross-population differences and distal societal-level influences on health. Social epidemiological explanations of TRHD purport that members of disparity groups are disproportionately subject to social, psychological, and biological contexts (Figure 1, path "A"), which in turn increase their vulnerability to tobacco use (Figure 1, path "B").[13,14] For instance, relative to the general population, certain disparity groups may experience more discrimination, live in communities with greater cultural acceptance of smoking, receive less tobacco prevention programming, have greater likelihood of genetic variants associated with tobacco use or tobacco-related health consequences, and experience more biological dysregulation due to chronic social stress, each of which may increase tobacco use vulnerability.[13–16] Higher severity and chronicity of tobacco use directly increases tobacco-related morbidity and mortality in disparity groups relative to the general population (Figure 1, "C").[1,17] Furthermore, sociocontextual and system-level factors that are common in disparity populations, such as reduced access to and quality of health care, may increase vulnerability to the health consequences of tobacco use (Figure 1, "D").[18] The tobacco-related health consequences that individuals and families in disparity populations face may further cause social disadvantage (eg, reducing opportunities for upward mobility due to medical and financial consequences of tobacco-related disease; Figure 1, "E").[19] Also, increased tobacco use in disparity groups, relative to the overall population, may feed back into promoting cultural norms for smoking in those communities and further stigmatization and social ostracization (Figure 1, "F").[20,21] The recapitulation of social disadvantage provoked by TRHD (Figure 1, "E" and "F") may further marginalize individuals to become "members" of multiple disparity groups (eg, an individual with a psychiatric disorder who becomes a chronic smoker and has to deal with the sequelae of tobacco-related health consequences may have even more challenges to gaining employment; Figure 1, "G").[19]

Social epidemiology methods typically emphasize generalizability and apply descriptive, naturalistic studies in which correlations among social factors and smoking characteristics are investigated in large community samples, with data collection often occurring in the field.[22] Interventions based on social epidemiology research findings often target policy and systems change or the incorporation of sociological constructs into psychosocial interventions (eg, culturally-adapted interventions; Table 1, left-hand column).

Psychopharmacology

Psychopharmacology focuses on individual-level psychobiological processes that proximally cause or result from acute drug use; these processes are assumed to be applicable to all people within a population irrespective of sociodemographic variation.[23] Psychopharmacology purports that tobacco-related psychopharmacological stimuli that acutely alter the brain and behavior provoke acute behavioral changes (eg, nicotine-induced mood enhancement, abstinence-induced mood dysregulation; Figure 2, path "H"), which in turn modify immediately subsequent motivation to smoke (Figure 2, "I").[24] For example, introduction of nicotine into the brain via smoking stimulates nicotinic-acetylcholine receptors, which promotes the release of other neurotransmitters, including dopamine, which may underlie the smoking's mood-enhancing psychoactive effects, and in turn reinforces smoking behavior and promote motivation to continue smoking.[24] Importantly, the resulting tobacco use leads to additional exposures to psychopharmacological stimuli, which recapitulate these processes and provide positive feedback loops that cycle towards addiction (Figure 2, "J"). For instance, chronic tobacco use leads to conditioning processes whereby cues repeatedly associated with smoking (eg, smoking-related stimuli such as ashtrays, locations such as bars, and internal cues such as anxiety) provoke psychopharmacological effects like urge to smoke, which in turn lead to more tobacco use.[25] Moreover, chronic nicotine exposure can dysregulate a number of biological systems through pharmacodynamic changes and metabolic adaptations, ultimately affecting nicotine metabolism pathways (eg, *CYP2A6*)[26] and brain dopaminergic, serotoninergic, adrenergic, cholinergic, gabergic, glutamatergic, and other systems,[27,28] which can enhance the psychoactive effects of pharmacological stimuli exposure (eg,

Table 1. Theory and Methods of Social Epidemiology, Psychopharmacology, and Sociopharmacology

	Social epidemiology	Psychopharmacology	Sociopharmacology
Level of analysis	Focus at the sociocontextual and system level	Focus at the individual level	Focus on interactions across sociocontextual and individual levels
	Assumes determinants of tobacco use differ across populations	Assumes determinants of tobacco use are common across populations	Assumes a common set of determinants of tobacco use that differ in strength or relevance across populations
			Identifies proximal factors that channel distal influences on tobacco use behavior
	Identifies distal influences on tobacco use behavior	Identifies proximal influences on tobacco use behavior	
Example theoretical constructs	Discrimination	Drug reward	Discrimination serving as a conditioned cue triggering tobacco use
	Cultural acceptance of smoking	Drug-induced reward enhancement	Nicotine-induced distraction away from attending to cues reflecting neighborhood disorder
	Targeted marketing of tobacco products to disparity groups	Negative reinforcement	Nicotine-induced enhancement of the reward value of reinforcers in socioeconomically-deprived environments
			Greater value placed on the arousal-enhancing effects of nicotine for blue-collar workers whose jobs require high levels of arousal
	Physical environment (eg, density of tobacco retailers in communities with high prevalence of people from TRHD groups)	Withdrawal	
	Reduced access to health care	Behavioral economic value	
	Biases in the legal system	Drug-induced changes in cognitive performance	
	Neighborhood deprivation and crime	Conditioning of drug-related and other cues	
	Social class	Alternative reinforcers	
	Clustering of biological vulnerability	Pharmacodynamic and pharmacokinetic processes underlying drug effects	
Methodology	Naturalistic, correlational, or descriptive designs	Experimental designs	Quasi- or fully-experimental designs crossing a sociodemographic TRHD variable or social determinant of TRHD with a psychopharmacological manipulation
	Large community samples	Smaller samples	Correlational designs examining the relation between a social determinant of TRHD and a psychopharmacological cause or consequence of tobacco use
	Data often collected in the field	Data often collected in the laboratory	Value on both internal and external validity
	High value on generalizability and ecological validity	High value on internal validity and isolating narrow mechanisms	
	Evidence for causal effects is modest	Evidence for causal effects is strong	
	Statistical control emphasized	Experimental control emphasized	
	Basic methodology: studying naturalistic associations of sociodemographic variables or social constructs to tobacco use variables	Basic methodology: studying the effects of experimentally-manipulated tobacco administration or deprivation on variables indicative of addiction liability	
Intervention	Target policy and system-level change	Pharmacotherapy	Combination of pharmacotherapy and/or behavioral interventions that offset sociocontextual and psychopharmacological determinants of tobacco use
	Individual-level interventions are adapted for use in specific populations	Interventions are not generally adapted for use for specific populations	Targeting psychopharmacological mechanisms linking sociocontextual factors and tobacco use when social factors are immutable
	Behavioral interventions incorporate sociological constructs (eg, culturally-adapted counseling)	Behavioral interventions that target psychopharmacological processes (eg, contingency management to reinforce abstinence)	Personalized medicine tailored to population based on biological/social factors (eg, polygenetic risk score, sociodemographic risk assessment)
	Risk propensity assessment		

TRHD = tobacco-related health disparities.

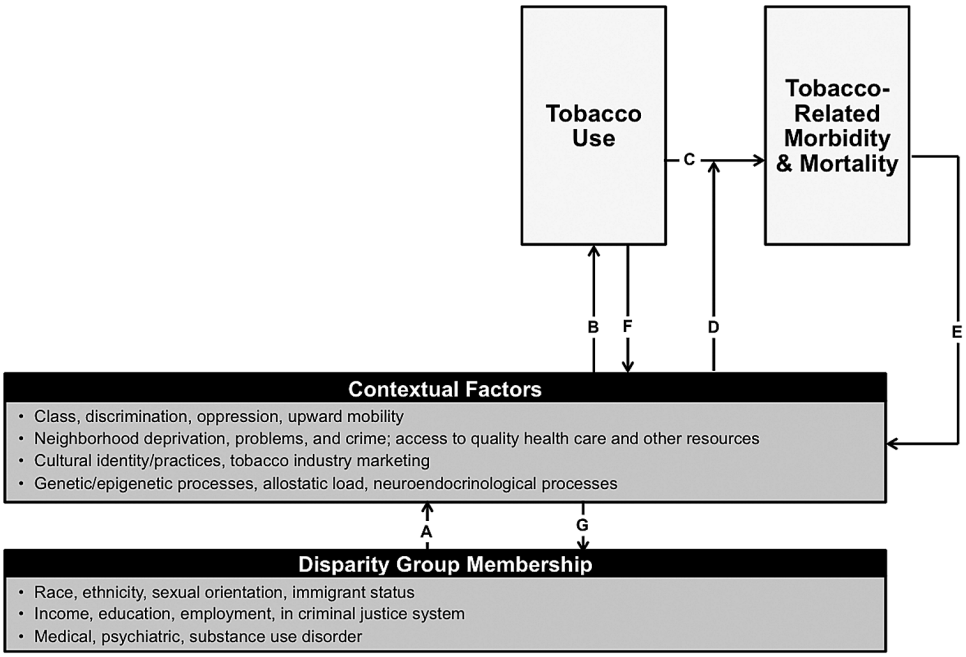

Figure 1. Social epidemiology framework for understanding tobacco-related health disparities.

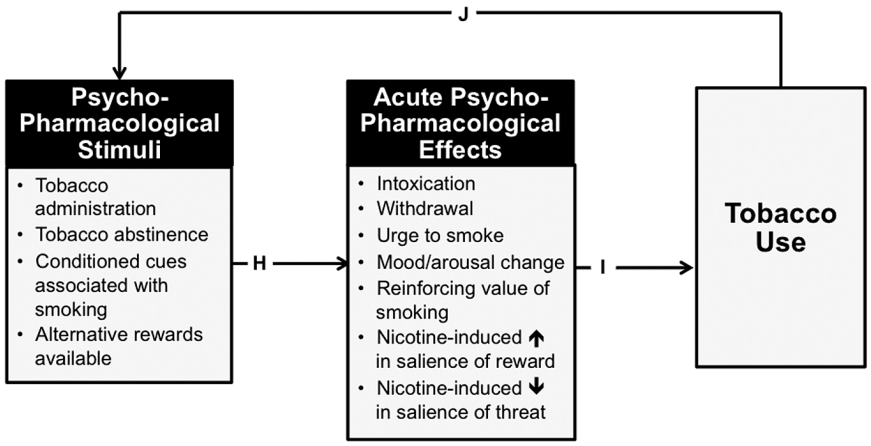

Figure 2. Psychopharmacology framework for understanding tobacco addiction.

abstinence-induced reductions in nicotine levels that provoke withdrawal symptoms in chronic smokers).

Psychopharmacology methods typically emphasize internal validity and apply experimental designs under tightly controlled conditions in the laboratory, with the goal of isolating individual casual mechanisms that underlie the behavioral effects of drugs.[23] The basic design involves investigating the effects of experimentally-manipulated nicotine administration or deprivation on subjective, physiological, and behavioral responses; additional manipulations (eg, crossing a candidate pharmacotherapy) or factors (eg, participant-level moderators such as level of nicotine dependence) can be superimposed on this design. Outcome measures typically correspond to the addiction liability of nicotine (eg, mood changes, cognitive performance enhancement, self-administration of tobacco, behavioral choices to consume tobacco or receive money). Pharmacotherapy is the primary treatment approach informed by psychopharmacology (see Table 1; center column).

Sociopharmacology's Overarching Theoretical Framework

The sociopharmacology framework for understanding TRHD is detailed in Figure 3, with dotted lines representing sociopharmacological mechanisms of TRHD that integrate sociocontextual and psychopharmacological processes. Two key interactive effects that have downstream effects on population-level TRHD are identified in the framework. First, members of disparity groups may be more vulnerable to the acute behavioral effects of tobacco-related psychopharmacological stimuli because of biopsychosocial contexts surrounding disparate populations (Figure 3, "K"). For instance, individuals from certain ethnic/racial minority groups may be more likely to have a genetic variant that increases sensitivity to the psychoactive effects of nicotine. In another example, the experience of discrimination may provoke negative affect states, which may magnify smoking's acute distress-alleviating effects. Related to this mechanism, chronic experience of discrimination and other forms of social stress may perhaps result in dysregulation of neuroendocrinological, inflammatory,

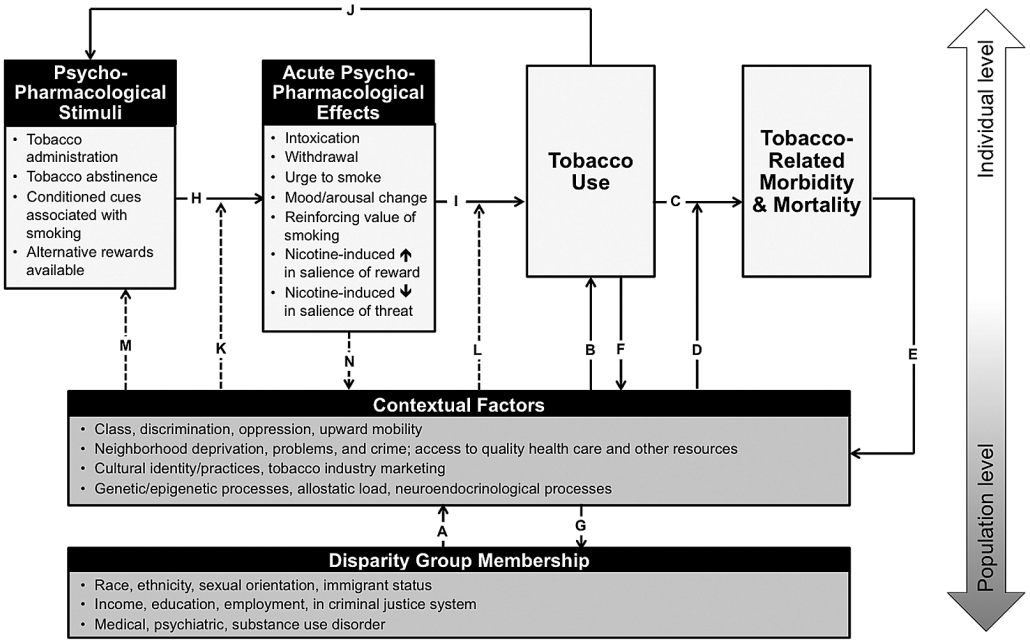

Figure 3. Sociopharmacology framework to understanding tobacco-related health disparities. *Note.* Arrows with broken lines reflect sociopharmacological mechanisms contributing to tobacco-related health disparities.

and epigenetic mechanisms, which may alter one's allostatic load.[16] This is important because some of the biological consequences of these social stressors may intersect with pathways that are affected by nicotine (eg, noradrenergic systems, corticotropin releasing factor), which could perhaps have synergistic effects in modulating the psychoactive effects of tobacco-related psychopharmacological stimuli.[16,29] Second, social factors moderate the extent to which acute psychopharmacological effects translate into motivation to smoke (Figure 3, "L"). For instance, members of disparity populations may also place a larger value on tobacco's mood-modulating effects in order to counteract the stress caused by discrimination. As a result, tobacco's mood-modulating effects may engender stronger motivation to smoke for disparity populations experiencing discrimination. Other specific examples of these pathways are: (1) people from East Asian cultures that discourage the emotional expression of anger[30] may report little irritability during nicotine withdrawal, even though irritability is a robust effect of tobacco abstinence in general samples[31,32] (eg, "K"); (2) nicotine's pharmacological effects on pleasure and feelings of friendliness[33] and social closeness may benefit the incorporation smoking into certain social practices for some cultures ("N"); and (3) blue-collar workers might be more motivated to use tobacco for its stimulating properties, which may enhance physical labor performance, and ultimately the reinforcing value of tobacco for such individuals ("L").

Additionally, sociocontextual factors may disproportionately promote exposure to psychopharmacological stimuli in disparity populations ("M"), which may have downstream effects on TRHD. For example, targeted tobacco industry marketing coupled with cultural norms accepting smoking for disadvantaged communities may bombard members of disparity groups with greater exposure to smoking-related cues ("M") that may provoke urges to smoke. As described in greater detail below, diminished access to resources for individuals in disparity populations can reduce alterative rewards available that may acutely increase the urge and reinforcing value of smoking ("M," "H"). Finally, some of the acute behavioral effects of psychopharmacological stimuli may have reciprocal effects back on sociocultural processes, such as nicotine-induced social enhancement of certain culturally-normative social practices in which smoking is common ("N"). Collectively, each of these novel sociopharmacological mechanisms (Figure 3, pathways "K" to "N") innervate with psychopharmacological ("H" to "J") and sociocontextual ("A" to "G") mechanisms to jointly underlie TRHD.

Sociopharmacology's Methodology

Sociopharmacology synthesizes the strengths of social epidemiology (eg, generalizability, incorporation of sociological constructs key to TRHD, relevance to population-specific interventions) and psychopharmacology (eg, internal validity for making causal inferences, incorporation of psychopharmacological theories key to tobacco addiction etiology, relevance to pharmacotherapy). Sociopharmacology's basic research design is quasi-experimental and involves studying natural variation in a sociocontextual-level variable as a moderator of the effects of experimentally-manipulated tobacco-related psychopharmacological stimuli on behavioral outcomes relevant to tobacco use motivation (eg, mood, smoking urge). An initial sociopharmacological investigation may utilize a standard demographic/clinical variable that explicitly marks "disparity group status" (eg, level of education, psychiatric diagnosis) as the moderator of the psychopharmacological manipulation. Such studies, which are not entirely absent in the literature,[34] may provide critical clues to the biopsychosocial contextual factors that mediate such effects (eg, genetics, neighborhood community influences, and culture). Following such initial inquiries, research incorporating a sociocontextual biomarker (eg, c-reactive protein which may indicate inflammatory process due to altered allostatic load provoked by chronic social stress)[16] or construct (eg, target of discrimination) as a moderator would further elucidate sociopharmacological mechanisms underlying TRHD. There have been some examples of this approach in the literature that are focused on some biological contextual moderators (eg, genetically-determined racial differences in

nicotine effects);[35] however, exploration of sociocultural moderators of psychopharmacological effects is scant.

The basic design proposed above is a prototype for many other design iterations, including: (1) manipulating the sociocontextual variable rather than solely measuring its natural variation (eg, experimentally priming the activation of cultural identities in participants through vignettes); (2) manipulating a psychopharmacological variable other than nicotine/tobacco exposure (eg, nonnicotine drug administration, exposure to smoking-related cues); (3) nonexperimental designs (eg, measuring retrospective reports of subjective drug effects); and (4) naturalistic designs that incorporate a sociocontextual construct and a psychopharmacological process (eg, studying correlations between socioeconomic position and responses to behavioral economic questionnaires assessing the relative reward value of smoking). Many other designs not described here that meaningfully address intersections between sociocontextual and psychopharmacological processes to explain TRHD would also fit into the sociopharmacology framework.

Potential Applications of Sociopharmacology

To illustrate the utility of the approach, I offer two theoretical models that can fall under the sociopharmacology framework described above.

Socially-Determined Stress and Tobacco's Psychopharmacological Effects on Threat Processing

In comparison to the general population, disparity groups are subjected to higher socially-determined stress, including neighborhood crime, area disorder (eg, vandalism, litter), and discrimination.[14] Each of these social determinants of stress has been linked with tobacco use, often over and above other confounding factors; such linkages have often been interpreted as evidence that disparity populations use tobacco to cope with socially-determined stress.[36–38] I propose the following additional sociopharmacological explanation for the link between socially-determined stress and smoking.

Stimuli that signal potential threat tend to automatically capture and hold one's attention.[39] This process is believed to be evolutionarily-hardwired to allow individuals to be prepared to quickly react to threatening stimuli to prevent potential harm.[40] Importantly, nicotine has attentional filtering properties that enhance one's ability to maintain attention on targets and prevent distraction from peripheral cues, an effect believed to be mediated by nicotinic-acetylcholine receptor stimulation.[41,42] Basic psychopharmacology research has shown that nicotine administration reduces attentional distraction by threatening stimuli.[41,43] This psychopharmacological effect of nicotine may be particularly valued by disparity populations that regularly encounter aversive stimuli, such as discriminatory actions by others, dilapidated environments, and criminal acts going on in the neighborhood. Nicotine may help disadvantaged individuals avoid focusing their attention on aversive stimuli saturated in the environment and potentially buffer against the effects of socially-determined stressors on subjective negative affect. As a result, nicotine's effects on threat processing may be more reinforcing and thus have a stronger effect on motivation to smoke in disparity populations facing socially-determined stress.

Individuals who repeatedly smoke in response to socially-determined stress may develop a specific conditioned association between social stress triggers and smoking. As a result, situations in which socially-determined stress arises (eg, experiencing discrimination, witnessing crime) may become triggers for smoking urges, which may in turn provoke smoking. Psychopharmacology research suggests that stressors in general can become powerful conditioned cues that produce reinstatement of drug-taking behavior, even following extended periods of abstinence.[44,45] Hence, cue-induced reinstatement of smoking behavior by socially-determined stress may be a specific, proximal mechanism to account for the disproportionately high relapse rates in some disparity populations; this hypothesis is consistent with some empirical research.[46]

Sociopharmacology studies could address the abovementioned predictions. For example, regular smokers from neighborhoods with high and low rates of crime could be administered nicotine (vs. placebo) following a period of acute smoking abstinence and then perform a modified Stroop task measuring distraction by stimuli associated with crime. The task would instruct participants to name the ink color of crime-related and neutral words presented in various colors (eg, blue, green, and red) as quickly as possible while ignoring the meaning. Attentional interference towards crime related words would be reflected by longer latency to name the color of crime-related (vs. neutral) words due to greater distraction by the meaning of these cues. Based on the model described above, I would predict that: (1) nicotine would diminish attentional interference from crime related words, particularly for the smokers from high-crime neighborhoods (neighborhood crime status × drug interaction); and (2) individual differences in the degree of nicotine-induced suppression of attentional interference by crime-related stimuli in smokers from high crime neighborhoods would correlate with smoking level, chronicity, and dependence. If these predictions were supported, smokers from high-crime neighborhoods may particularly benefit from nicotine replacement formulations administered on an acute as needed basis (eg, nicotine lozenge). Such forms of nicotine replacement could be taken in response to acute episodes of socially-determined stress to prevent a ruminative response that prolongs and intensifies the stress state, and in turn, possibly prevents a stress-induced lapse.

Ecological momentary assessment studies that would fall under the sociopharmacology framework could also address pathways linking socially-determined stress and smoking. Participants can be given mobile devices to be taken with them into their natural environment. In addition to repeated assessment of smoking, urges, and mood (which is often standard in ecological momentary assessment), instances in which crime is witnessed, neighborhood disorganization is observed, or discrimination occurs in one's naturalistic environment could be recorded. I predict that covariation between instances of socially-determined stress, negative affect, smoking would occur within individuals, such that negative affect and smoking is higher during episodes of socially-determined stress exposure.

Dearth of Opportunity for Reward in Disadvantaged Populations and Tobacco's Reward-Enhancing Effects

Because of social inequities, the opportunity to engage in pleasurable, rewarding experiences is lower, on average, for disparity populations (relative to the general population), and diminished resources and opportunity for reward has been linked with greater likelihood of smoking.[37] This finding can be interpreted from a behavioral economic perspective, which purports that vulnerability to tobacco use is higher among individuals with: (1) lower access to experiences that provide pleasure and meaning; and (2) less to lose from social, occupational, and health consequences of tobacco use that may further limit opportunities for alternative nondrug reinforcement.[47] Indeed, many TRHD groups arguably meet both of these criteria

due to social inequities.[21,48] An additional sociopharmacological mechanism may underlie the link between diminished opportunity for reward and TRHD as described below.[49]

The drive to pursue and experience rewards that promote pleasure, meaning, and a sense of wellbeing is evolutionarily hardwired.[50] Basic psychopharmacology research indicates that nicotine is a "reward enhancer" that amplifies the pleasurable and reinforcing effects of other rewards experienced concurrently with nicotine.[51] That is, in addition to nicotine acting as a primary reward that causes direct psychoactive effects irrespective of environmental context, the drug also modulates the mood-enhancing effects of rewarding stimuli that are present in the environmental context in which nicotine is consumed.[51–53] Correspondingly, regular tobacco users who are acutely abstinent appear to experience withdrawal-related deficits in their ability to emotionally respond to reward-related stimuli.[54–56]

Disparity populations who have less opportunity to experience reward may be more motivated to smoke because the pharmacological activity of nicotine may magnify the potency of the limited rewards at hand. Accordingly, tobacco use may be a means for enhancing the well-being one derives from their environment when altering one's environment is difficult or impossible. For instance, if attending a sporting event at the stadium is financially unfeasible, watching the game on television while smoking might magnify the level of pleasure derived from the experience. If one is able to derive greater reward from their environment when smoking, and their environment is otherwise reward deficient, the net gain in reward experience may heighten motivation to continue and escalate tobacco use. Furthermore, given that nicotine withdrawal diminishes reward sensitivity,[56] the loss of reinforcement produced by quitting smoking may be particularly profound for disparate populations who may be left with impotent environmental reward structures that are no longer pharmacologically-enhanced by nicotine. Such deficits may produce a strong motivation to resume smoking and reattain tobacco-induced reward enhancement for disparity populations. Elements of this overarching model have been proposed before by Perkins with regards to socioeconomic position.[49] Below, I flesh out this hypothesis for socioeconomically disadvantaged individuals and extend it to several other populations subject to TRHD.

Applying the Reward-Enhancement Model to Specific Disparity Populations

Socioeconomic Position

Different indicators of socioeconomic position may have unique influences on opportunity for reward. For example, individuals with lower income have fewer resources to obtain material goods and other commodities that may provide a source of reward and pleasure.[57] Those unemployed may lack reward derived from the satisfaction obtained from working,[58] and "blue-collar" workers (eg, crafts and kindred occupations, operatives, transportation operatives, and laborers) may find less stimulation and meaning from their jobs and hence experience a deficiency of reward obtained from employment.[59] Indeed, smoking is more prevalent among workers whose abilities are underused, have monotonous and repetitive jobs, and report less work satisfaction.[60,61] Qualitative research in socioeconomically disadvantaged samples supports the notion that disadvantaged individuals use tobacco as a source of reward and to enhance the limited rewards at their disposal (eg, reporting that smoking while drinking a cup of tea is one of the few "treats" one has).[62,63] We found that smokers with lower (vs. higher) education were more likely to choose smoking over an alternative reward following overnight tobacco deprivation,[64] suggesting enhanced value of smoking relative to alternative rewards in less educated individuals.

Criminal Justice Populations

Imprisoned individuals have substantial restriction of reward opportunities, and evidence suggests that inmates smoke to manage the lack of stimulation experienced in prison.[65] In the reward deficient environment of prison, cigarettes have disproportionate reward value relative to other commodities,[66] which might be explained by sociopharmacological processes. Reward restrictions persist for individuals in the criminal justice system post-incarceration, as these individuals often have fewer opportunities of reward post-release because many people are hesitant to socialize with individuals who have been incarcerated and many employers are unwilling to hire individuals with a criminal history.[67]

Ethnic and Sexual Minorities and Immigrants

Populations in the statistical minority within a community are less likely, on average, than those in the statistical majority to have culturally-relevant rewards available in their immediate environments. That is, community resources for minorities to engage in their own cultural practices, such as religious institutions, will be scarcer for such individuals. In addition, discriminatory practices may prevent access to certain rewards (eg, employment, education, and social status) on the basis of ethnicity or sexual orientation.[68,69] Accordingly, nicotine may have greater value as a reward enhancer for minority populations. We found that African American (vs. white and Hispanic) smokers reported greater reductions in acute positive affect but not other affective states or nicotine withdrawal symptoms following acute tobacco abstinence.[70] Given the specificity of results to diminished positive affect outcomes, one sociopharmacological explanation for this finding is that the loss of affect-enhancing effects of nicotine may have been more salient for African American smokers who otherwise may have had less alternative rewards available in their environment.

Physical Illness or Disability

Individuals with a severe or chronic physical illness or disability often have restrictions in the types of activities they can engage in, leading to constraints in opportunity for reward.[71] Beyond the impact of illness severity and psychosocial variables (age, income, social support, and personality), activity restriction explains significant portions of the variance in well-being among individuals with physical illnesses and disabilities.[72] Furthermore, recent evidence in physically-disabled smokers suggests that restriction of valued life activities (social, professional, pleasurable or otherwise meaningful activities) due to mobility impairment is associated with lower quit motivation and success.[73,74] Hence, restrictions in opportunities for reward imposed by an illness or disability may motivate tobacco use as a means for enhancing the potency of the limited rewards at one's disposal.

Behavioral Health Comorbidities

Individuals with behavioral health comorbidities (ie, psychiatric and/or non-nicotine substance use disorder) have higher levels of smoking, lower cessation likelihood, and greater risk of tobacco-related disease than nearly all other groups subject to TRHD.[75,76] Sociopharmacology is particularly well-suited for addressing TRHD among individuals with behavioral health comorbidities. Like other disadvantaged groups who face stigma, discrimination, and

functional limitations, individuals with behavioral health comorbidities have restricted opportunities and access to rewards that engender happiness and meaning.[77–79] On top of social inequities, many psychiatric and substance use disorders are associated with psychobiological disturbances in the brain's reward system,[80–82] which directly blunt the reinforcing and mood-enhancing effects of nondrug rewards. Consequently, individuals with behavioral health comorbidities are likely to derive less reinforcement, happiness, and meaning in their lives than those without such comorbidities even if available environmental rewards were identical across the two groups (which they are not). The combination of social inequities that diminish access to reward with inherent limitations in reward responsivity may produce profound increases in the motivation to smoke to obtain reinforcement for individuals with behavioral health comorbidities.

Individuals with depression, schizophrenia, and other psychiatric conditions are more likely to prefer smoking over nondrug rewards,[83,84] experience greater mood enhancement in response to nondrug rewards when concurrently smoking,[85] show greater declines in positive mood when abstinent,[31] and escalate their smoking behavior when they experience reductions in pleasure obtained from nondrug rewards.[86] Our laboratory has addressed this phenomenon by focusing on anhedonia—a cross-cutting psychopathological trait common to several behavioral health conditions that reflects the key process described above (ie, diminished happiness, enjoyment, and ability to experience pleasure in response to rewards).[87] We have shown that anhedonia is associated with greater preference for smoking versus alternative rewards[88,89] and larger abstinence-induced declines in positive mood,[31] reductions in cognitive processing of rewards,[90] and increases in urge to smoke for pleasure.[89] Similarly, Cook, Spring, and McChargue[91] found that anhedonic smokers were able to overcome inherently deficient hedonic responses to a rewarding stimulus (ie, happy music) when administered nicotine. An important next step in research on TRHD among individuals with behavioral health comorbidities will be to study joint influences of diminished reward responsiveness in combination with social inequities in access to healthy and meaningful rewards.

Proposed Studies to Test the Reward-Enhancement Model

A common method of assessing reinforcement and pleasure derived from activities involves questionnaires measuring the frequency of engagement in and pleasure obtained from various rewarding activities.[92] This tool has been further leveraged for substance use by instructing participants to indicate whether each activity is experienced in concert with substance use, yielding two primary outcomes: (1) drug-complementary reinforcement, which is the sum of the product of engagement × frequency ratings for each activity identified as being performed while using the substance; (2) alternative reinforcement, which is the corresponding cross-product for activities identified not be associated with substance use.[86] In addition to self-report methods, geocoding of rewards available in the immediate environment (eg, theaters, parks) might also be used to measure reward access and experience. To test if the hypothesized sociopharmacological mechanism may be a source of disparities in tobacco use, smoking-complementary and alternative reinforcement could be explored as statistical mediators of relations between disparity group membership and tobacco use. Consistent with some work in this area,[86] I hypothesize that members of disparity groups relative to the general population: (1) derive less alternative reinforcement, which in turn may motivate smoking uptake and maintenance; and (2) derive greater smoking-complementary reinforcement (ie, pleasure from nondrug activities while smoking), which in turn may motivate more pervasive and severe levels of tobacco use.

Researchers might utilize some of the assessments described above to determine the "typical" reward available and then expose participants to their typical reward under varying levels of nicotine administration in a laboratory experiment. I hypothesize that administration of one's typical reward in the laboratory may generate markedly lower levels of pleasure and greater motivation to smoke in nicotine-deprived versus nicotine-exposed smokers in disparity populations. By contrast, the pleasure and motivation to smoke caused by typical reward exposure would be less robustly modulated by nicotine administration in populations not subject to TRHD (eg, high socioeconomic position).

Limitations

The sociopharmacological approach to addressing TRHD proposed should be considered with several caveats. First and foremost, extant empirical data that applies this approach is virtually absent. Hence, it is possible that some of the key research questions posed by sociopharmacology may not yield definitive insights. That being said, given the novelty of sociopharmacological applications to tobacco research, data that helps to rule out a wide range of potential sociopharmacologically-mediated sources of TRHD may help to sharpen focus on other approaches. Further, some interventions to eliminate sociopharmacological sources of TRHD will be subject to the same challenges facing social epidemiology. For instance, if the abovementioned reward-enhancement model of tobacco disparities ultimately garners empirical support, enhancing access to healthy, nondrug rewards in disparity populations would presumably close the gap in tobacco use between these groups and the overall population. Yet, altering the environmental reward structure of disparity groups at the population level would require a great effort that runs counter to powerful, chronically-entrenched social inequities; though, altering the reward structure for individual persons facing TRHD may be more feasible.

Implications for Efforts to Reduce and Eliminate TRHD

If sociopharmacological mechanisms that disproportionately promote tobacco use in disparity populations can be identified, interventions and policy that counteracts these mechanisms would presumably help to reduce TRHD. Extension of ongoing work on the genomics and pharmacogenomics of smoking cessation treatment and outcome could be straightforwardly adapted to TRHD.[93] One example is evidence that there is racial stratification of genes involved in the metabolism of nicotine (eg, *CYP2A6*); variation in these genes and their biological phenotypes also predict cessation outcome and clinical response to nicotine replacement therapy.[35,93] Hence, prediction models using race (or biomarkers that stratify by race and underlie variation in clinical response to smoking cessation medication, such as the nicotine metabolite ratio)[93,94] may lead to "personalized" interventions that can be tailored to disparity population membership. Such efforts can ultimately enhance chances for quit success across populations and help to increase equity in cessation outcome.

Combination treatments that disrupt the sociocontextual process via behavioral intervention and disrupt the psychopharmacological process via pharmacotherapy would presumably have synergistic

effects in reducing tobacco use among individuals in disparity populations. If the reward-enhancement explanation of TRHD described above was validated, pharmacotherapies that increase responsiveness to reward (eg, nicotine replacement therapy, varenicline)[54,95] and behavioral interventions that increase access to meaningful and pleasurable nondrug rewards (eg, behavioral activation treatment) [96] may synergistically reduce smoking in disparity populations.

Sociopharmacology also offers avenues for reducing TRHD caused by sociocontextual processes that are difficult to modify. Indeed, individual level psychopharmacological pathways that channel the sociocontextual influences on TRHD are modifiable and could be disrupted to offset immutable population level sociocontextual influences. For instance, if the threat processing pathway linking socially-determined stress and smoking identified above was supported, interventions that inhibit automatic attentional interference by threatening cues may help smokers affected by discrimination. Attentional retraining interventions in which computer-based platforms that teach individuals to disengage their attention away threatening cues through cognitive exercises have been used successfully in anxiety disorder treatment.[97] Applying such interventions to modify attentional interference caused by cues associated with socially-determined stress (eg, racial slurs) could perhaps prove useful for reducing TRHD.

In addition to specific interventional strategies, sociopharmacology may inform the development of more precise risk assessment approaches at the population level. Specifically, prediction models that include environmental, sociodemographic, genetic, and other factors to mark accumulative risk indices[98] for likelihood of tobacco use and could be expanded to include psychopharmacological factors (eg, initial psychopharmacological sensitivity to nicotine via retrospective report of early smoking experience).[99] One could envision novel prediction models that incorporate "top down" socioenvironmental factors (eg, number of tobacco retailers in close proximity to one residence), "bottom up" biological factors (eg, genetic susceptibility score), and their interaction (eg, inflammatory biomarkers caused by social stress, reporting that nicotine's stimulating performance-enhancing effects is a reason for smoking for blue-collar workers). The combination of these factors might improve the accuracy of risk models for tobacco use, addiction, and health consequences. Such models could inform policy makers for identifying high risk populations likely to be subject to TRHD as well as the potential biopsychosocical mechanisms that may channel risk to be targeted in intervention.

Implications for Basic Research on the Psychopharmacology of Nicotine and Tobacco

Sociopharmacology may also advance basic science by stimulating psychopharmacology research that considers the social context in which tobacco is consumed. Some evidence suggests that eastern cultures encourage socially-engaging emotional experience (eg, friendliness, guilt), whereas western cultures encourage disengaging emotions (eg, anger, pride).[100] Hence, psychopharmacology research in culturally-heterogeneous samples that fails to separate engaging versus disengaging emotions may be at risk for making faulty conclusions. For instance, an experiment that finds no evidence of moderation of the subjective mood-altering effects of nicotine by a candidate pharmacotherapy may conclude that the pharmacotherapy has limited clinical value. In this circumstance, it is possible the pharmacological agent modulated certain domains of mood for some participants and other domains of mood for others; however, the overall effect in the combined sample was masked because mood assessment focused on higher-order dimensions (eg, positive and negative affect) and failed isolate culturally-relevant discrete lower-order mood dimensions. Furthermore, considering the greater context in which tobacco is consumed can only serve to enhance the public health impact of tobacco psychopharmacology research. Sociopharmacology offers one means of achieving this.

Conclusion

Health disparities are among of the most critical challenges facing tobacco control. The origins of TRHD are highly complex and poorly understood. Perhaps sociopharmacology may benefit efforts to understand and eventually reduce TRHD. Irrespective of possible downstream effects on population-level health disparities, it is hoped that, at the very least, this paradigm may stimulate exciting new tobacco research that brings together fields that are typically unintegrated.

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Declaration of Interests

None declared.

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