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Behavioral Economic Laboratory Research in Tobacco Regulatory Science

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Abstract

Objectives—Research that can provide a scientific foundation for the United States Food and Drug Administration (FDA) tobacco policy decisions is needed to inform tobacco regulatory policy. One factor that affects the impact of a tobacco product on public health is its intensity of use, which is determined, in part, by its abuse liability or reinforcing efficacy. Behavioral economic tasks have considerable utility for assessing the reinforcing efficacy of current and emerging tobacco products.

Methods—This paper provides a narrative review of several behavioral economic laboratory tasks and identifies important applications to tobacco regulatory science.

Results—Behavioral economic laboratory assessments, including operant self-administration, choice tasks and purchase tasks, can be used generate behavioral economic data on the effect of price and other constraints on tobacco product consumption. These tasks could provide an expedited simulation of the effects of various tobacco control policies across populations of interest to the FDA.

Conclusions—Tobacco regulatory research questions that can be addressed with behavioral economic tasks include assessments of the impact of product characteristics on product demand, assessments of the abuse liability of novel and potential modified risk tobacco products (MRTPs), and assessments of the impact of conventional and novel products in vulnerable populations.

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Human Subject Statement

Not applicable.

Conflict of Interest Statement

The authors have no conflicts of interest to report.

Keywords

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With the passage of the Family Smoking Prevention and Tobacco Control Act in 2009, the United States (US) Food and Drug Administration (FDA) was granted the authority to regulate how tobacco products are manufactured, marketed and sold in the US.¹ This includes the authority to mandate changes to the nicotine content of tobacco products (although not to eliminate nicotine), to reduce or eliminate other harmful ingredients, components, and constituents of these products, and to require the evaluation of these products, as appropriate for the protection of the public health. Therefore, research studies that can provide a scientific foundation for the FDA's decisions are needed to inform tobacco regulatory policy.^{2,3} The impact of a tobacco product on public health is a function of 3 factors: its harmfulness per use; the intensity of use per user; and the prevalence of use in the population.⁴ A product's intensity of use is determined by its abuse liability, or reinforcing efficacy, as well as other factors such as consumer perceptions, appeal, price, and availability.⁵ It is with the assessment of the reinforcing efficacy of current and future tobacco products that we believe that behavioral economic laboratory tasks have considerable utility.

The field of behavioral economics applies consumer demand theory and other economic concepts to understanding behavior.⁶ With regard to drug use, behavioral economics researchers examine how varying the cost of the drug (in terms of either money or the effort required to obtain it) affects drug consumption.^{7,8} Plotting drug consumption as a function of cost yields a demand curve and several indices of the relative reinforcing effects of the drug to that individual under those experimental conditions.⁸ Using these indices, it is possible to compare the relative reinforcing effects of different drugs to a particular individual, to compare how different individuals respond to the same drug, and to examine how increasing the price of one drug affects consumption of another. In terms of tobacco regulatory science, behavioral economic laboratory procedures could be used to investigate the influence of manipulating product characteristics on demand for the product, whether certain subpopulations, such as adolescents or people with serious mental illness (SMI), may be more likely to use the product, and whether using the novel product may reduce the consumption of conventional cigarettes.

METHODS

In this paper we summarize several common behavioral economics laboratory procedures, provide a targeted, narrative review of some behavioral economic laboratory studies that have tested the reinforcing efficacies of different tobacco products, and describe how behavioral economic procedures can be applied to studying several potential tobacco regulatory policies. Previous reviews on similar topics include reviews of behavioral economic factors that contribute to drug use disorders and a conceptual review that describes how behavioral economics can be applied to estimate the impact of public policy initiatives related to drug use, transportation choice and charitable giving.^{7,9,10} However, the present

review is the first, to our knowledge, to discuss how human behavioral economic laboratory research can be used to inform tobacco regulatory policy. We focus primarily on operant tasks, choice tasks, and cigarette purchase tasks because of the relevance of these procedures for assessing the reinforcing efficacy of tobacco products. Given space limitations, we do not include discounting tasks such as delay discounting and probability discounting.⁸ However, these procedures have been used to characterize tobacco product use in vulnerable subpopulations of smokers such as adults with SMI, adults with low educational attainment, and adolescents.^{11–13} Other measures that can be used to assess the abuse liability of tobacco products include discriminability, physiologic measures, subjective measures, and use in the natural environment.^{14–16}

Papers that we describe for illustrative purposes were identified through searches of human studies listed in PubMed and ScienceDirect from inception to April 1, 2016, using the search strategy (“behavioral economics” OR “choice task” OR “demand curve” OR “FR schedule” OR “PR schedule” OR “purchase task”) AND (cigarette OR nicotine OR tobacco). Papers also were identified from relevant reviews and the authors’ files.

RESULTS

Operant Studies

Operant drug self-administration studies in humans are closely based on studies conducted in laboratory animals.^{17,18} In these studies, the research participant presses a lever or emits another response to gain access to a dose of a drug, and reinforcement is inferred when the rate of responding for the drug is greater than the rate of responding for placebo.¹⁹ The pattern of responding and number of responses required to obtain drug is referred to as the schedule of reinforcement. Two schedules of reinforcement that are used most frequently in human drug self-administration research are fixed-ratio (FR) and progressive-ratio (PR) schedules (Table 1). In FR schedules, participants make a fixed number of responses to acquire a drug, and the response rate is interpreted as the measure of relative reinforcing efficacy.²⁰ The ratio of response requirement per unit of drug administered is referred to in behavioral economics as the unit price; in this ratio, increasing the response requirement is functionally equivalent to reducing the magnitude of the reinforcer.²¹ In PR schedules, the number of responses required to acquire a drug increases progressively after each drug delivery, and the maximum ratio completed (“breakpoint”) is interpreted as the measure of relative reinforcing efficacy.²⁰ Typically, drug liking and other subjective effects are assessed along with self-administration behavior.¹⁹ However, subjective effects are not always correlated with drug demand, indicating the importance of behavioral measurements in abuse liability assessment.^{22,23}

When the size of the FR schedule varies across sessions, a demand curve can be constructed that relates response cost to consumption.⁸ Several demand indices can be derived from the data that reflect multiple dimensions of the relative reinforcing efficacy of the drug to the individual across changes in response cost: Intensity (Q_0), or the amount of drug consumed at zero price, $O_{\max}$, the maximum amount that participants would spend on drug across all prices, $P_{\max}$, the price at which $O_{\max}$ is reported and α , the rate of decrease in consumption as a function of price,^{7,24} which is derived from the following exponential equation

$$\log Q - \log Q_0 + k(e^{-\alpha Q_0 \cdot C} + 1)$$

where Q represents cigarettes consumed and C is cigarette price, k is set to a constant, and Q_0 is the estimate of cigarette consumption at zero price. These indices, which describe the relationship between behavior and drug consumption in that particular context, can be compared across products, or values for the same product can be compared across subgroups of smokers to provide an indication of how the products or subgroups differ in abuse liability. Furthermore, assessing the effects of increasing response requirements on tobacco intake may model the effects of other environmental restrictions, such as decreasing the density of tobacco outlets.

Choice Tasks

Behavioral choice tasks are well-established laboratory methods for assessing the relative reinforcing effects of different products.²⁵ These tasks have a long history in preclinical behavioral pharmacology research, where they have been used to assess thresholds for abuse liability and toxicity. Later, it became apparent that choice studies in humans were useful for assessing correspondence between subjective effects and drug-seeking behavior and investigating drug effects in special populations considered to be at risk for abuse.²⁵ Choice tasks may involve 2 drugs, a drug versus placebo, or a drug versus a fixed amount of money.²⁶ These tasks typically begin with a sampling phase, in which the participant initially samples and rates the subjective effects of each option (this phase is skipped when the reinforcer is money), followed by a choice phase, consisting of a series of discrete trials in which the participant makes choices between the options. Typically, some level of effort is required to register the choice; for example, participants may have to complete 10 computer mouse clicks (FR 10) to earn 2 puffs of a cigarette. The option that is chosen more frequently is considered to have greater relative reinforcing efficacy (Table 1). Additional measures of reinforcing efficacy include time to first smoking choice in a smoking versus monetary reinforcement choice arrangement, either within a single laboratory session, using a relapse analogue task, or across days, using an abstinence incentive task.^{27,28} Both tasks model latency to smoking lapse or relapse after a period of abstinence. In the context of tobacco regulatory science, these tasks could be used to compare latency to relapse in different subpopulations of smokers, or to evaluate how changes to a tobacco product might affect a smoker's ability to abstain from the product. Behavioral choice tasks can be more sensitive to differences between reinforcers than free-access procedures, in which ad libitum consumption of one or more options is measured.²⁹ Furthermore, choice tasks have ecological validity as they mimic situations in which smokers choose which product to purchase among those concurrently available in the natural environment.

Choice tasks in which the cost of at least one option is manipulated can be used to assess the degree to which one tobacco product is likely to substitute for another product, such as the extent to which a MRTP or e-cigarette substitutes for combustible cigarettes.¹⁰ Substitution is said to occur if the use of one product increases as the cost of the other product increases. The degree of substitution can be characterized by fitting the data to an exponential equation

$$Q = \log Q_{\text{alone}} + Ie^{-\beta C}$$

where Q_{alone} is consumption of the fixed-price product when the price of the primary product is infinity, I is the interaction constant, β is the sensitivity of the fixed-price product to the primary product, and C is the cost of the primary product. A negative interaction constant indicates that the fixed-price product is a substitute of the primary product, and the value of β indicates the degree of substitution.

Cigarette Purchase Tasks

The Cigarette Purchase Task (CPT) evolved from the human operant self-administration procedures described above. Purchase tasks and similar procedures such as the “multiple choice task” assess hypothetical responses that do not require drug self-administration.^{30–32} In the CPT, participants are asked: “How many cigarettes would you smoke in a day if they cost \$X?” From the resultant data, a demand curve can be constructed that relates price to consumption.³³ A sample demand curve using hypothetical data is shown in Figure 1. The same demand indices described above with demand curves that relate response requirement or unit price to consumption can be derived from the data (Table 1).

Cigarette purchase tasks have been shown to generate consistent estimates of demand over time in the absence of a specific manipulation.³⁴ The validity of these tasks has been demonstrated by studies that have found significant associations between demand indices and number of cigarettes smoked per day, severity of nicotine dependence, or smoking behavior in the laboratory.^{11,32,35,36} Demand indices are sensitive to smoking status, and can predict response to smoking treatment, further demonstrating their validity and utility.^{37–39} Importantly for researchers, hypothetical purchase tasks are relatively easy for participants to understand and complete, do not require multiple sessions or specialized equipment to administer, and do not involve actual consumption of the drug. As such, they can be disseminated easily and included in widely varying research protocols, including studies that collect data online.⁴⁰ They also can be administered to populations for whom ethical issues prohibit actual drug administration, such as treatment-seeking smokers.

As with choice tasks, cigarette purchase tasks also can be used to assess the degree to which one tobacco product is likely to substitute for another product. With the CPT, this is assessed by modifying the questions to ask about the use of 2 products as the price of one product is manipulated. As described above in the Choice Procedures section, the data can be fit to an exponential equation that indicates whether the fixed-price product is a substitute of the primary product, and the degree of substitution (Table 1).

Applications of Behavioral Economic Tasks to Tobacco Regulatory Science

Assessing the relative reinforcing efficacies and substitutability of tobacco products—In the context of tobacco regulatory science, dependent measures from behavioral economic studies can be used to compare the relative reinforcing efficacy of a new tobacco product, or an existing product that has been modified in some way, with that of an existing product. Two areas in which behavioral economics measures have been used for

this purpose are assessments of very low nicotine content (VLNC) cigarettes and e-cigarettes. Given the primacy of nicotine in tobacco addiction, the idea of mandating a reduction in the nicotine content of cigarettes to a minimally-addictive level is one potential tobacco regulatory strategy that has received particular attention.^{4,41} The reinforcing efficacies of cigarettes varying in nicotine content have been compared using self-administration, choice, and CPT procedures. Rusted et al⁴² used a progressive ratio schedule to compare the acute reinforcing efficacies of cigarettes varying in nicotine content (0.5 mg vs 0.1 mg yield) in smokers that had been abstinent for at least 8 hours. In participants who smoked either the higher or lower nicotine cigarettes, the cigarettes produced similar breakpoints, suggesting that they had similar reinforcing efficacies. Shahan et al²⁹ compared standard and very low nicotine content (VLNC) cigarettes using a progressive ratio procedure that increased across sessions rather than within the session, and then compared their relative reinforcing efficacies using a choice procedure. Similar to results from Rusted et al,⁴² the cigarettes produced similar breakpoints when each was available in separate sessions. However, when both cigarettes were offered concurrently in the choice task, participants were significantly more likely to choose the higher-nicotine cigarettes. Johnson et al⁴³ used a behavioral economic substitution design to compare the extent to which nicotine gum and very low nicotine cigarettes would substitute for higher-nicotine cigarettes. In the first phase of the experiment, a demand curve for standard-nicotine cigarette puffs was determined by varying the response requirement for puffs across sessions. Then, the demand curve for standard puffs was re-determined with either nicotine gum or VLNC cigarette puffs concurrently available. Although both nicotine gum and VLNC cigarette puffs substituted for standard-nicotine puffs as the price of standard puffs increased, VLNC cigarette puffs were found to be a more effective substitute for standard-nicotine puffs than nicotine gum. These studies demonstrate that choice studies are more sensitive to differences between reinforcers than are self-administration studies in which products are sampled independently, and that VLNC cigarette puffs are highly reinforcing in smokers, presumably because the sensorimotor stimuli associated with smoking have acquired conditioned reinforcing properties through frequent pairing with nicotine delivery.⁴⁴

An abstinence incentive procedure was included in a large clinical trial of VLNC cigarettes, to determine if an extended period of VLNC cigarette use reduced cigarette dependence.⁴⁵ Participants were randomly assigned to receive their usual brand cigarettes or research cigarettes varying in nicotine content (15.8, 5.2, 2.4, 1.3, or 0.4 mg nicotine/g tobacco) for a 6-week period. At the end of this period, participants received a high-value monetary incentive to abstain from smoking for 24 hours, and those who met the biochemical abstinence criterion completed measures of craving and nicotine withdrawal. Study results indicated that participants who had smoked cigarettes with 2.4 mg nicotine/g tobacco or less had lower craving levels during abstinence than those who had smoked normal-nicotine content cigarettes, suggesting that limiting the nicotine content of cigarettes could reduce the difficulty of abstaining from smoking.⁴⁵ Similar studies that are currently underway in smokers sampled from the general population⁴⁶ and smokers with schizophrenia⁴⁷ are using a one-week abstinence incentive task, in which incentives are highest on the first day of abstinence and decrease for each subsequent day of abstinence,²⁸ to determine if VLNC cigarette use facilitates abstinence in these groups.

The CPT also has been used to address research questions related to the reduction of nicotine in cigarettes.⁴⁸ In the large clinical trial of VLNC cigarettes described above, participants were instructed to smoke only their assigned cigarette for 6 weeks before completing a version of the CPT about their study cigarette.⁴⁵ A reduction in nicotine content to the lowest nicotine content (0.4 mg/g) decreased Intensity (Q_0 , estimated cigarette consumption if cigarettes were free), $O_{\max}$ (maximum amount of money spent on cigarettes), and breakpoint (highest price at which participants reported smoking any cigarettes). These results suggest that a reduction in nicotine content is likely to decrease the reinforcing efficacy of cigarettes if VLNC cigarettes are the only cigarettes available. A modified 2-product version of the CPT also would be useful for evaluating the degree to which emerging tobacco products are likely to substitute for combustible cigarettes if cigarettes were made less desirable (eg, by decreasing nicotine content) or available (eg, by decreasing cigarette outlets), effectively increasing their cost.

One additional use of the CPT involves a novel application of behavioral economics to nicotine reduction. According to a behavioral economics framework, changes in consumption are a function of the unit price of the reinforcer (Table 1). If nicotine is the primary reinforcing constituent in cigarettes, then an increase in cigarette cost may be functionally equivalent to a decrease in nicotine content.⁴⁹ If this assumption is true, existing data from the CPT could be used to inform nicotine reduction policy. Rodent data suggest that the increases in cost and decreases in nicotine content may not be equivalent, and nicotine consumption may be more sensitive to changes in nicotine cost than nicotine dose.⁵⁰ However, the relationship between cost and nicotine content has not been evaluated in human smokers.

Electronic nicotine delivery systems (ENDS) are potentially the most important emerging class of tobacco products. ENDS use has risen dramatically in the last 10 years, and now surpasses the use of conventional cigarettes among adolescents.⁵¹ Whether ENDS will have a net beneficial or harmful effect on public health depends on rates of ENDS initiation among non-smokers versus effects of ENDS on smoking cessation in current smokers.⁵² Factors such as nicotine delivery and flavoring affect the reinforcing efficacy of these products.^{53,54} One advantage of using the CPT to evaluate the abuse liability of new products is that it involves minimal exposure to the product in the laboratory; participants could sample the product and then complete the CPT to estimate their use of that product in a single session. Versions of the CPT could be used to compare the abuse liability for ENDS versus conventional cigarettes, for “cigalike” electronic cigarettes versus newer “tank-style” devices, or for preferred-flavor e-liquid versus tobacco-flavored e-liquid. As noted above, the CPT can be modified to assess substitution by asking about the use of 2 products as the price of one product is manipulated. Use of the CPT for this purpose is scarce as of now, but at least one paper has used a modified version of the CPT to characterize substitution of e-cigarettes for combustible cigarettes as the price of cigarettes increases.⁵⁵

However, the CPT first must first be adapted to assess demand for ENDS. The development of an e-cigarette purchase task requires careful thought about the relevant unit of consumption. As the proxy of reinforcing value in purchase tasks is daily drug consumption, the unit of daily use is a critical variable.⁷ Whereas number of cigarettes smoked per day is

an established metric for conventional cigarettes, the relevant daily unit is currently unclear for e-cigarettes. Puffs per day may be the most face valid unit of consumption; however, individual puffs are not easily quantifiable by ENDS users.⁵⁶ Tank style devices are refilled with e-liquid, which is purchased separately in units of milliliters (mLs) per bottle.⁵⁴ For these users, purchase tasks that equate mLs of liquid to money spent may best reflect behavior. In contrast, older style e-cigarettes are sold individually or with refillable cartridges. In short, behavioral economic researchers should strive to ensure their measures to reflect real-world behavior. A validated e-cigarette purchase task that accurately reflects behavior could be used to determine how flavors and other characteristics influence demand for these products, both in absolute terms and in the context of the availability of conventional tobacco products.

Characterizing responses to products in vulnerable populations—Factors such as sex, age, race, ethnicity, nicotine metabolic rate and biological response to nicotine may moderate intensity of tobacco product use.⁵⁷ The FDA's Tobacco Regulatory Science program is particularly concerned with characterizing responses to new or modified tobacco products in subpopulations that have high rates of smoking initiation or low rates of cessation, such as adolescents, women, racial and ethnic minorities, people with low socioeconomic status, pregnant women, the lesbian, gay, bi sexual, transgendered, questioning (LGBTQ) community, and people with mental health or medical co-morbidities.⁵⁸ In behavioral economic laboratory studies, responses of vulnerable subpopulations to tobacco products can be investigated by comparing self-administration rates, product choice, or sensitivity to cost (either financial or in terms of response requirement) among groups. For example, Cassidy et al⁵⁹ examined adolescent smoking behavior using a procedure in which participants were given the opportunity to make choices between receiving cigarette puffs versus a monetary reinforcer that varied in value across sessions. Similar to data from adults, adolescents' choices for cigarette puffs decreased as a function of increasing monetary reinforcement; however, boys were more sensitive to this effect than girls, suggesting that girls may over-value cigarette reinforcement compared to boys.

Given the elevated smoking rates and low cessation rates among smokers with serious mental illness, it is important to understand if these groups may be impacted differentially by tobacco regulatory policy.⁶⁰ Few experimental studies have made a direct assessment of whether smokers with and without serious mental illness differ in their sensitivity to cigarette reinforcement. Tidey et al^{61,62} examined how responses for cigarette puffs among people with schizophrenia were affected by varying the response requirement for puffs and the opportunity to obtain an alternative (monetary) reinforcer, using the same experimental procedure and equipment as a study that had compared these factors in heavy smokers without psychiatric illness. The effect of response requirement on cigarette puff consumption was similar in these groups. Audrain-McGovern et al⁶³ used a similar procedure to compare responses for cigarette puffs versus money in smokers with a history of depression and current depression symptoms versus smokers without current or past depression, and found that the smokers with depression made twice as many responses for puffs than controls across a range of response costs, indicating that they were more sensitive

to nicotine reinforcement but not more sensitive to response cost. MacKillop and Tidey used a CPT to compare changes in cigarette demand as a function of price in smokers with schizophrenia and controls, and found that the smokers with schizophrenia had a higher intensity of cigarette consumption but that the groups were equally sensitive to increases in cigarette price.¹¹ Based on this limited evidence, the relative reinforcing value of smoking appears to be higher in SS and SD, but these groups do not appear to be more or less sensitive to the monetary and behavioral costs of smoking than controls.

As noted above, a current tobacco regulatory science initiative is to characterize the effects of very low nicotine content cigarettes, with the goal of examining whether reducing the nicotine content of cigarettes to a minimally-addictive level would reduce cigarette use and dependence.⁵⁷ However, a nicotine reduction policy may have unintended negative consequences for certain smokers, such as those with increased sensitivity to nicotine reinforcement or withdrawal.^{60,64} Using a laboratory choice paradigm, researchers can simulate and compare, under predetermined constraints, the resultant behavioral profiles of different populations across various reinforcers. For example, choice of normal nicotine content and reduced nicotine content cigarettes could be compared across vulnerable populations by determining the amount of effort participants would expend to earn access to each cigarette. Several studies are currently underway to test the extent to which very low nicotine content cigarettes substitute for standard-nicotine content cigarettes in vulnerable populations. In a preliminary report of a study assessing acute response to VLNC cigarettes in vulnerable populations, VLNC cigarettes were equally effective as standard-nicotine cigarettes in reducing nicotine withdrawal levels among socioeconomically disadvantaged women of reproductive age, opioid dependent adults and adults with comorbid affective disorders; however, in a choice task, participants preferred the standard-nicotine dose over the VLNC doses, demonstrating that choice tasks can be more sensitive for detecting changes in tobacco products than subjective measures.⁶⁵

The CPT is also well-suited for studying the potential impact of regulatory policy on vulnerable populations. The CPT has been used to characterize cigarette demand indices in adolescents and to compare demand indices in individuals with schizophrenia compared to equally-heavy smokers without psychiatric illness.^{11,66,67} However, considerable work remains to be done to characterize and compare other subpopulations with respect to the relative reinforcing efficacy of cigarettes, MRTPs and novel products such as e-cigarettes. The predictive validity of these tasks allows for conclusions to be drawn about real-world behavior. As regulatory pathways are identified, the potential effects of different policies on vulnerable populations will be important areas for researchers to target, and the CPT offers a robust, reliable and data-rich method that can be used to identify initial characteristics of a sample population with regard to motivation to smoke, and to show changes in reinforcing efficacy as a result of an experimental or hypothetical exposure to a product in these populations.

DISCUSSION

Future Directions for Researchers

The field of tobacco regulatory science has an increasing need for behavioral economics assessments of abuse liability. With regard to combustible cigarettes, behavioral economics can be used to assess the impact of various cigarette components on abuse liability including aspects of cigarette design such as ventilation, additives, and individual constituents. When tools are available (ie, cigarettes both with the component of interest and without), choice tasks may be especially useful to the FDA's Center for Tobacco Products in determining the role that these components play in reinforcing smoking behavior. In the case of individual constituents, a version of the cigarette without a given constituent often does not exist for testing, but in some cases animal models of self-administration have filled this gap using behavioral economics.^{68,69} Many of the research priorities outlined by the FDA's Center for Tobacco Products focus on the abuse liability of tobacco products other than combustible cigarettes.⁵⁸ Four of the 10 priorities focus on characterizing products other than combustible cigarettes on several factors including consumer perceptions and dependence (cigars, smokeless tobacco, e-cigarettes, hookah, pipes, and dissolvables are all specifically mentioned). These research questions are rich for a behavioral economic framework because the abuse liability of each product, and the degree to which each product is likely to substitute for other tobacco products, can be assessed. Data from these experiments will be most useful if researchers include a condition with combustible cigarettes for comparison. One barrier in these experiments will be determining the unit of consumption that is the most appropriate dependent variable. Although some headway has been made in this area for ENDS, work is still required for the other products.

Behavioral economics tasks could be used to assess a claim of "less addictive" made by the tobacco industry about one of their tobacco products. One component of the Family Smoking Prevention and Tobacco Control Act required that the FDA's Center for Tobacco Products ensure that any claim from the tobacco industry regarding modified risk be supported by scientific evidence.¹ The FDA has yet to grant any applications for tobacco products to be labeled as modified risk, but to evaluate each application, the FDA's Center for Tobacco Products will need reliable tasks upon which to make such determinations. The tasks outlined in the present paper could be used to assess the abuse liability of a potential modified risk product compared to combustible cigarettes, which are known to carry a high risk of abuse liability.

Two of the FDA's tobacco policy research priorities focus on the impact of communication strategies, including communication of risks by the FDA and marketing by the tobacco industry. Behavioral economics can be useful for these research questions as well because consumer perception is likely to impact how a product is used and may impact abuse liability either directly or indirectly through changes in use leading to changes in dependence.⁵ Researchers can use choice tasks and the CPT to assess (1) how sample messages about a product risk might influence the reinforcing efficacy of that product (which will inform the FDA regarding the creation of effective communication campaigns)

and (2) how potential changes to the marketing and labeling of tobacco products are likely to impact the abuse liability of a product.

Researchers interested in tobacco use among vulnerable populations should consider including behavioral economics tasks in their assessments. One of the research priorities of the FDA's Center for Tobacco Products focuses on the impact of tobacco product characteristics like those discussed above on initiation of tobacco products in adolescents and other vulnerable populations. Whereas these laboratory tasks are unlikely to be useful for assessing abuse liability in those who have not yet used the product (due to ethical issues), they may be useful for individuals who are relatively early in the transition from first use to dependence. The CPT has been well-validated in adolescents and college students who have been presumably been using cigarettes for less time than older adults.^{22,67}

IMPLICATIONS FOR TOBACCO REGULATION

Researchers have begun to use behavioral economics tasks in tobacco regulatory science research areas, especially as they relate to the potential reduction of nicotine in cigarettes, ENDS, and vulnerable populations. Although not the focus of this paper, they also have been used by animal researchers assessing whether tobacco constituents other than nicotine might contribute to reinforcement by tobacco products. However, as we discuss here, behavioral economics tasks may be useful in a variety of other tobacco regulatory science research areas including: (1) assessing impact of various tobacco product characteristics including design, flavorings, additives, and individual constituents; (2) assessing how tobacco products other than combustible cigarettes compare to cigarettes in terms of abuse liability and the degree to which they are likely to substitute for cigarettes if use of cigarettes decreases; (3) assessing claims of modified risk including claims of "less addictive;" (4) assessing the impact of communication campaigns including those that communicate risk by the FDA as well as potential changes to labeling and marketing on abuse liability; and (5) assessing abuse liability among vulnerable populations such as those individuals who are early on in the transition from first use to dependence. These tasks range from highly controlled behavioral choice procedures in which participants' use behavior can shift toward or away from available products, to easily administered hypothetical purchase tasks that do not require actual drug consumption. The behavioral economic framework can encompass data derived from all along this continuum of tasks, and modification of these tasks to fit the needs of tobacco regulatory researchers will result in fruitful new avenues for understanding tobacco product use. Behavioral economics tasks have a long history of being used for assessing reinforcement value, and researchers who are interested in tobacco regulatory science should consider adopting them into their laboratory assessments.

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Figure 1.
Idealized Demand Curve for Cigarettes Depicting the Demand Indices Derived from the
Cigarette Purchase Task

Table 1

Behavioral Economic Laboratory Tasks

Task	Description	Measures	Examples of Studies Relevant to Tobacco Regulatory Science
Fixed Ratio (FR) Task	Participants make a fixed number of responses to acquire a substance.	Response rate is interpreted as the measure of relative reinforcing efficacy. If the number of required responses increases across sessions, demand curve analysis can be conducted to obtain demand parameters: Q_0 (Intensity), O_{max} , P_{max} , Breakpoint, α (see text)	Johnson et al, 2004 Shahan et al, 1999
Progressive Ratio (PR) Task	The number of responses required to acquire a substance increases progressively after each drug delivery.	The maximum ratio completed (breakpoint) is interpreted as the measure of relative reinforcing efficacy.	Rusted et al, 1998
Choice Task	Participants make discrete choices between 2 products, a product vs placebo, or a product vs a fixed amount of money. These tasks typically begin with a sampling phase followed by a choice phase.	The option that is chosen more frequently is considered to have greater relative reinforcing efficacy. Time to first smoking choice is another measure of reinforcing efficacy. If the price of one option is varied, the degree of substitutability of one commodity for another can be obtained (see text).	Audrain-McGovern et al, 2014 Cassidy et al, 2015 Donny et al, 2015 Higgins et al, 2016 Johnson et al, 2004 Shahan et al, 1999 Tidey et al, 1999
Cigarette Purchase Task	Participants estimate the amount of a product they would use in a single day across a variety of prices.	A demand analysis is completed producing demand parameters: Q_0 (Intensity), O_{max} , P_{max} , Breakpoint, α (see text). If the task is adapted to include two commodities, the degree of substitutability of one commodity for another can be obtained.	Donny et al, 2016 Grace et al, 2015 MacKillop and Tidey, 2011