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Examining effects of unit price on preference for reduced nicotine content cigarettes and smoking rate

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ABSTRACT

Cigarette preference increases as a function of greater nicotine content, but manipulating cost can shift preference. The aims of the present study are to model whether (1) the behavioral-economic metric unit price (cost/reinforcer magnitude) accounts for preference shifts and (2) whether preference shifts toward reduced nicotine content are associated with smoking reductions. In a multisite study between 2015 and 2016, 169 daily smokers from vulnerable populations completed two concurrent-choice conditions examining preference for smoking normal (15.8 mg/g) and reduced (0.4 mg/g) nicotine content cigarettes. In Condition 1, both products were available at 10 responses/choice. In Condition 2, availability of the 0.4 mg/g dose remained at 10 responses/choice while the 15.8 mg/g dose was available on a progressive-ratio (PR) schedule wherein response cost increased following each choice. Unit prices were calculated by dividing dose by response requirement. Results were analyzed using ANOVA and binomial tests ($p < .05$). Participants preferred the 15.8 over 0.4 mg/g dose in Condition 1, but shifted preference to the 0.4 mg/g dose in Condition 2 ($p < .001$) immediately before the point in the PR progression where unit price for 15.8 dose exceeded unit price for the 0.4 dose ($p < .001$). This shift was associated with a reduction in smoking ($p < .001$). The unit price of nicotine appears to underpin cigarette product preference and may provide a metric for predicting preference and potentially impacting it through tobacco regulations. These results also demonstrate that reduced compared to normal nicotine content cigarettes sustain lower smoking rates discernible even under acute laboratory conditions and in vulnerable populations.

1. Introduction

Cigarette smoking remains a leading cause of preventable death in the United States, with approximately half a million deaths per year attributable to smoking-related causes (U.S. Department of Health and Human Services (U.S. DHHS), 2014). Nicotine has been well established as the constituent in cigarettes that drives repeated use and dependence (U.S. DHHS, 1988). In a seminal essay, Benowitz and Henningfield (1994) hypothesized that the addiction potential of cigarettes could be reduced by lowering the nicotine content below a threshold that is necessary to promote repeated use and dependence. Reducing the nicotine content of cigarettes could reduce smoking prevalence through two mechanisms: (1) by reducing nicotine dependence severity among current smokers making it easier for them to quit smoking and (2) by reducing likelihood that those experimenting with cigarette use would transition to chronic smoking. The 2009 passage of the Family Smoking Prevention and Tobacco Control Act (FSPTCA) gave the Food and Drug Administration (FDA) regulatory authority over the manufacture and distribution of tobacco products including authority to set a maximal nicotine content level in cigarettes, although complete nicotine elimination is not permitted.

Research on reduced nicotine content (RNC) cigarettes since passage of the FSPTCA has been promising. Studies of acute exposure to RNC cigarettes have demonstrated dose-dependent decreases in both

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reinforcing efficacy and subjective experience of smoking in the general population (Hatsukami et al., 2013) and in populations with comorbidities (Higgins et al., 2017; Tidey et al., 2013). Studies examining extended exposure to RNC cigarettes in the general population of smokers have shown decreases in daily smoking rate and nicotine dependence severity (Donny et al., 2015; Hatsukami et al., 2018). Studies on extended exposure to RNC cigarettes in vulnerable populations are ongoing.

The present investigation is a secondary analysis of the Higgins et al. (2017) study on acute exposure to RNC cigarettes in populations with psychiatric comorbidities and socioeconomic disadvantage. That study demonstrated that while smokers reliably preferred higher over lower nicotine content cigarettes under double blind, concurrent-choice arrangements, cigarette preference was malleable. That is, while a normal nicotine (NNC) content cigarette (15.8 mg/g of tobacco) was robustly preferred over a very low nicotine content (VLNC) cigarette (0.4 mg/g) under conditions of equal response cost, preference shifted to the VLNC cigarette when response cost to obtain the NNC cigarette was systematically increased using a Progressive Ratio (PR) schedule.

In the present study, we examine two unexplored aspects of this effect. First, in an effort to elucidate the process underpinning shifts in product preference we examine whether cigarette preference reversal can be accounted for by the behavioral economic metric of unit price. Unit price is based on economic demand theory wherein demand for a commodity decreases as an orderly function of increases in price (Bickel et al., 1990), which may be conceptualized in terms of response cost or effort required to obtain a commodity (Collier et al., 1986; Hursh, 1980; Watson and Holman, 1977). Within a unit-price framework, the determinant of demand is price per unit of commodity obtained (i.e. commodity price/commodity magnitude). Unit price has been demonstrated to account for differences in consumption across multiple drugs in preclinical and clinical models of drug self-administration (Bickel et al., 1990; Bickel et al., 1991; DeGrandpre et al., 1993). Investigations utilizing unit price to understand demand of cigarette smoking have demonstrated that as unit price increases, cigarette puff purchasing decreases (DeGrandpre et al., 1992) and if available, participants will allocate behavior to another tobacco product (Bickel and Madden, 1999; Johnson et al., 2004; Madden et al., 2000; Shahan et al., 2001). These studies were conducted prior to passage of the FSPTCA and aimed at the basic question of whether drug use can be accounted for by behavioral pharmacology principles. Two of those studies involved VLNC cigarettes (Johnson et al., 2004; Shahan et al., 2001) and provided evidence suggesting unit-price can account for preference of higher over lower nicotine content cigarettes. More recently, potential utility of applying the unit-price model to a nicotine reduction policy has been examined in a conceptual analysis noting numerous strengths but also potential limitations (Smith et al., 2014). Preclinical experiments on nicotine self-administration in rats demonstrated that unit price generally accounted for changes in consumption as a function of changes in response cost and drug dose, but noted that at very low doses there was not an equivalence of manipulating price and magnitude as predicted by the unit-price (Smith et al., 2016). More recently, a laboratory study with 20 participants indicated in a single lab session when given a fixed income, VLNCs priced lower than NNC cigarettes were chosen more when offered concurrently suggesting price may influence preference, although to what degree and the influence of the presence of a lower cost RNC on smoking rate was not examined (Branstetter et al., 2019). The clinical research evidence on RNC and VLNC cigarettes demonstrates reducing nicotine content to very low levels produces the greatest reductions in addiction potential of cigarette smoking (Donny et al., 2015; Hatsukami et al., 2018; Higgins et al., 2017). As such, a need persists for additional empirical evidence on the potential utility of the unit-price model in conceptualizing how a nicotine reduction policy is likely to impact cigarette consumption.

In addition to exploring preference as a function of unit price in the current study, we also examine whether preference is associated with smoking rate reductions. Extended exposure studies using parallel-group, between-subject research designs demonstrated decreases in daily smoking among relatively healthy smokers assigned to RNC compared to NNC cigarettes (Donny et al., 2015; Hatsukami et al., 2018). The present study examines whether that relationship is discernible (a) during acute exposure testing and (b) in populations especially vulnerable to cigarette smoking using a within-subject concurrent choice arrangement in a clinical laboratory setting. A proof of concept study with eight participants, reported no differences in smoking rate during acute exposure to VLNC compared to NNC conditions, but values were in the direction of VLNCs supporting lower smoking rates than NNCs when available at unit prices that overlap with the present study (Shahan et al., 2001). If reductions in smoking rate occur under acute dosing of VLNCs, it has the potential to open opportunities for studying relationships between cigarette nicotine content, smoking rate, and toxin exposure in clinical laboratory studies in addition to clinical trials. Lab studies while certainly not a replacement for clinical trials can provide advantages including greater experimental control over matters such as concurrent use of other tobacco products during exposure to cigarettes while also being less cumbersome and expensive. Additionally, we know of no prior reports examining VLNC impact on smoking rate in vulnerable populations. This would offer additional evidence that reduced nicotine policy has potential to benefit those populations most vulnerable to smoking, addiction, and smoking-related health effects, which is a priority in FDA's tobacco regulatory science research initiative (e.g., Higgins et al., 2019; Perry et al., 2019).

2. Methods

This secondary analysis uses data from a multisite, double-blind, 3-phase laboratory study examining the acute effects of cigarettes with varying levels of nicotine content in populations especially vulnerable to smoking (Higgins et al., 2017). Primary study methods have been reported previously (Higgins et al., 2017) and only methods directly relevant to the current study are described in detail below.

2.1. Participants

Participants were 169 cigarette smokers from one of three populations especially vulnerable to smoking; those with affective disorders as an exemplar of individuals with mental illness ($n = 56$); opioid dependence as an exemplar of individuals with other substance use disorders ($n = 60$); and socioeconomically disadvantaged women of reproductive age (18–44) as an exemplar of individuals with socioeconomic disadvantage ($n = 53$). Across populations, participants had to be at least 18 years old and biochemically verified daily smokers who reported smoking at least five cigarettes-per-day over the past year. Participants had to provide a negative urine specimen for illicit substances with the exception of marijuana. Exclusion criteria included intention to quit smoking within 30 days, significant past month (> 9 days) use of non-cigarette tobacco products, exclusive use of “roll-your-own cigarettes”, current pregnancy, effort to conceive, or breast-feeding, current suicidal ideation or symptoms of psychosis/dementia. Inclusion criteria specific to those with affective disorder were participants had to be between 18 and 70 years of age and meet Mini-International Neuropsychiatric criteria for major depression or anxiety disorders; opioid dependent participants had to be between 18 and 70 years of age, receiving a prescribed opioid maintenance medication for opioid dependence, and confirmed to have submitted > 70% past-month drug-free urine samples; socioeconomically disadvantaged women of reproductive age were between 18 and 44 years of age with their highest academic degree being high school. Participant characteristics are shown in Table 1.

Research Cigarettes.

The study used Spectrum research cigarettes manufactured by 22nd

Table 1
Participant characteristics.

	n = 169
Age, mean (SD)	35.6 (11.4)
Female no, (%)	120 (71.0)
Population	
Affective disorders no., (%)	56 (33.1)
Opioid maintained no., (%)	60 (35.5)
Low SES women no., (%)	53 (31.4)
Race/ethnicity no., (%)	
White	123 (72.8)
Native American/Alaska Native	0
Asian	1 (0.6)
Black/African-American	23 (13.6)
Native Hawaiian/Pacific Islander	1 (0.6)
Other or more than one race	15 (8.9)
Latino	6 (3.6)
Educational attainment no., (%)	
Eighth grade or less	4 (2.4)
Some high school	23 (13.6)
High school graduate or equivalent	58 (34.3)
Some college	64 (37.9)
2-year or associate degree	10 (5.9)
College or 4-year bachelor's degree	6 (3.6)
Graduate/professional degree	4 (2.4)
Marital status no., (%)	
Married	27 (16.0)
Never married	103 (60.9)
Divorced/separated	35 (20.7)
Widowed	4 (2.4)
Cigarette smoked per day, mean (SD)	15.8 (7.5)
Mentholated cigarette smokers no., (%)	59 (34.9)
Breath carbon monoxide, mean (SD)	22.4 (11.9)
Age of first cigarette, mean (SD)	16.3 (4.3)
Heaviness of smoking index, mean (SD)	2.9 ± 1.3

Century Group (Clarence, NY) and obtained from the National Institute of Drug Abuse. Four nicotine dose conditions were examined in the parent study; however, only the highest and lowest doses (15.8 mg/g and 0.4 mg/g of tobacco) are examined in the current study, as these are the two doses examined in Phase 3 of the study. The 15.8 mg/g dose is comparable to doses found in commercial brand cigarettes while the 0.4 mg/g dose falls below the hypothesized dependence threshold. Mentholated or non-mentholated cigarettes were assigned based on participant preference. All cigarettes were tested under double-blind conditions.

2.2. Procedures

Participants completed fourteen 2–4 h experimental sessions in a within-subject research design across three study phases. This analysis uses only data from Phases 2 and 3, described below. All sessions were scheduled no < 48 h apart and occurred following overnight smoking abstinence, defined as 50% intake carbon monoxide (CO) levels. Upon arrival to the laboratory, a brief battery of physiological measures was collected, including breath CO, breath alcohol level, heart rate, blood pressure, weight, urine toxicology screen, and women received a urine pregnancy test. Sessions were rescheduled for participants with > 50% intake breath CO level or breath alcohol ≥ 0.03%. Those with a positive drug screen were administered a field-sobriety test and if failed, the session was rescheduled. A positive pregnancy test resulted in withdrawal. At session start, to equate time since last cigarette across sessions and participants, participants took two ad-lib puffs of their usual brand cigarette, with experimental procedures starting 30 min thereafter (Henningfield and Griffiths, 1981).

Phase 1 of the study consisted of a baseline session and four experimental sessions in which each research cigarette was sampled in separate sessions. Each cigarette was labeled with an arbitrary letter code that remained consistent throughout the study.

Phase 2 of the study consisted of six three-hour sessions in which all possible dose pairs of the available research cigarettes were tested in a concurrent-choice arrangement (Johnson et al., 2004; Lussier et al., 2005). At each Phase 2 session, two different research cigarettes identified by their respective letter codes were made available. Participants were instructed that they were free to choose to smoke either cigarette as frequently as they wanted during the session or could forgo smoking altogether. During Phase 2 sessions, a computer screen displayed the respective letter codes indicating the two available cigarettes. To make a smoking choice, participants were instructed to click ten times on the letter that corresponded to the cigarette they wished to smoke. Once the response requirement was completed, participants were permitted to take two puffs following a standard protocol and using a Clinical Research Support System (CReSS) Desktop smoking topography device. Participants inserted the cigarette into the device, lit the cigarette without inhaling, and then took two puffs with feedback displayed to ensure standardization across puffs. During this period, a 3-min timer was displayed, which indicated time participants were allotted to take the two puffs of their chosen cigarette. No other smoking choices were available during this period. Following completion of this interval, participants were again free to make additional smoking choices.

Phase 3 consisted of three sessions using the experimental arrangement in Phase 2 with the exception that (a) a single dose pair was examined across sessions (0.4 mg/g vs. 15.8 mg/g) and (b) while the 0.4 mg/g dose continued to be available following ten mouse clicks, availability of the 15.8 mg/g dose was now under a PR schedule that incrementally increased each time it was chosen in the following progression: 10,160,320,640,1280,2400,4800,6000,7200,8400 mouse clicks. This PR progression has been previously shown to be effective for examining preference reversals (Sigmon et al., 2003). This procedure was identical across all Phase 3 sessions in order to verify stability of the effect of response cost on choices.

Statistical Method.

Mixed model repeated analyses of variance (ANOVA) were used to test for differences in the preference for the 15.8 mg/g dose vs. the 0.4 mg/g dose by Phase (i.e. Phase 2 compared to Phase 3) and the stability of any preference differences by Phase by examining the effect of session on dose preference (i.e., the Phase 2 session and each of the three Phase 3 sessions).

Analyses examining if unit price accounted for shifts in cigarette preference in Phase 3 sessions were conducted in five steps. First, response requirements for the two cigarettes were converted to unit prices using the following equation:

$$\text{Unit price} = \frac{\text{reinforcer cost}}{\text{reinforcer magnitude}}$$

The 0.4 mg/g dose was always available at a response cost of 10 mouse clicks and thus the unit price was fixed at 25 (e.g., 10 clicks ÷ 0.4 mg/g nicotine dose). The response cost for the 15.8 mg/g dose increased after each time it was selected from a low of 10 to a high of 8400 mouse clicks, and thus unit price increased from 0.63 up to a maximum of 531.65 within each Phase 3 session (Table 2). Second, the maximum PR completed for the 15.8 mg/g dose (i.e., PR breakpoint) and its associated unit price were determined for each Phase 3 session. Third, using the PR breakpoints, a median maximum unit price for the 15.8 mg/g dose was determined, using all data across Phase 3 sessions. Fourth, the total number of Phase 3 sessions where the maximum unit price for the 15.8 mg/g dose occurred at a unit price at or below the fixed unit price of 25 for the 0.4 mg/g nicotine content cigarette was summed and divided by total number of sessions to obtain a proportion. An exact binomial test was conducted to test whether that proportion differed significantly from chance; that is, whether the proportion of sessions in which the maximum unit price for the 15.8 mg/g dose was lower than 25 (i.e., the unit price for the 0.4 mg/g dose) exceeded the proportion expected by chance (0.5).

To determine whether a shift in preference in Phase 3 toward the

Table 2
Unit price conversion of the PR schedule in phase 3 for the 15.8 mg/g nicotine content cigarette.

Progressive ratio schedule	Unit price (to the nearest tenth)
10 mouse clicks	0.63
160 mouse clicks	10.12
320 mouse clicks	20.25
640 mouse clicks	40.50
1280 mouse clicks	81.01
2400 mouse clicks	151.90
3600 mouse clicks	227.85
4800 mouse clicks	303.80
6000 mouse clicks	379.75
7200 mouse clicks	455.70
8400 mouse clicks	531.65

0.4 mg/g dose was associated with decreases in cigarette consumption, we conducted mixed model ANOVAs examining differences in number of choices to smoke per session in Phase 2 compared to Phase 3 and the stability in total choices to smoke across Sessions (i.e., the Phase 2 session compared to each of the three Phase 3 sessions). To confirm that differences in consumption were not due to the PR schedule manipulation in Phase 3 constraining total amount of time available to smoke relative to Phase 2, we examined whether there were significant differences between Phase 2 and 3 in the proportion of time spent earning smoking opportunities and completing the puffing protocol using a mixed model repeated measures ANOVA. There was no significant effect of Phase and thus we did not further examine stability by testing for effect of session. All ANOVAs included study site as a random effect to account for any differences across the three study sites (e.g. University of Vermont, Brown University, Johns Hopkins University). Fixed effects for study populations were included, as inclusion criteria were unique for each population. As the overall sample was highly female (71.0%), a fixed effect for gender was included. A fixed effect for menthol status was included to account for differences in preference and consumption associated with the addition of menthol flavoring. Least square means were reported for all analyses to account for effects of covariates included in the models. Analyses were conducted using SAS 9.4 (SAS Institute, Cary, NC), with significance alpha set a priori at 0.05.

3. Results

3.1. Cigarette preference

There was a significant shift in cigarette preference from a strong preference for the 15.8 mg/g over the 0.4 mg/g dose in Phase 2 (0.71% ± 0.04%) to preference for the 0.4 mg/g dose in Phase 3 (0.61% ± 0.04%) when the access to the high dose was under the PR schedule ($F_{1,167} = 143.57$, $p < .0001$, Fig. 1, Panel A). This effect was stable across the Phase 3 sessions ($F_{3,457} = 74.68$, $p < .0001$; Fig. 1, Panel B). There were no significant differences in the proportion of choices for the 15.8 mg/g cigarette option across Phase 3 sessions (Table 3).

3.2. Unit price

Across Phase 3 sessions (454 sessions), the median maximum unit price or breakpoint for the 15.8 mg/g nicotine content cigarette was 20.25 (i.e. 320 mouse clicks ÷ 15.8 mg/g), which represents the last step in the PR progression in which the 15.8 mg/g nicotine content cigarette was available at a lower unit price than the 0.4 mg/g cigarette unit price of 25. The next step in the PR progression was 40.50 (Table 2). The proportion of Phase 3 sessions in which the breakpoint for the 15.8 mg/g cigarette occurred at a unit price at or below 25 was 0.58 (95% CIs: 0.54, 0.62), exceeding chance levels ($p < .001$).

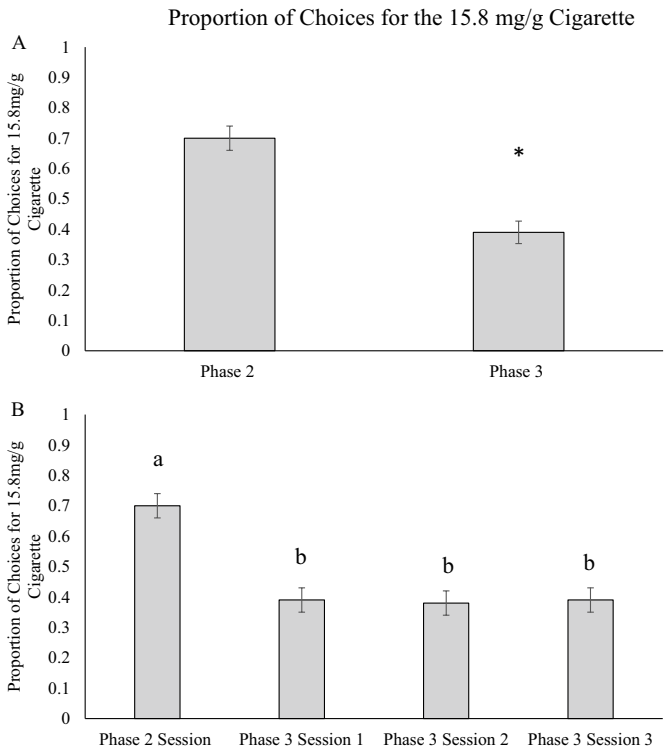

Fig. 1. Panel A: least square mean proportion of choices allocated for the 15.8 mg/g dose in each phase of the study. Asterisk indicates significant difference at $p < .001$. Error bars represent ± 1 SEM. Panel B: least square mean proportion of choices allocated for the 15.8 mg/g dose in each session. Data points not sharing a subscript are significantly different from one another ($p < .05$). Error bars represent ± 1 SEM. Data were collected from March 23, 2015, through April 25, 2016 at University of Vermont, Brown University, and Johns Hopkins University School of Medicine.

Table 3
Between session differences of least square means in cigarette preference and cigarette consumption.

	Difference (SEM)	t value	*p*-value
Proportion of choice for the 15.8 mg/g dose			
Phase 2 session vs. phase 3 session 1	0.31 (0.03)	12.02	< .0001
Phase 2 session vs. phase 3 session 2	0.32 (0.03)	12.29	< .0001
Phase 2 session vs. phase 3 session 3	0.31 (0.03)	11.79	< .0001
Phase 3 session 1 vs. phase 3 session 2	0.01 (0.03)	0.39	.70
Phase 3 session 1 vs. phase 3 session 3	−0.003 (0.03)	−0.11	.89
Phase 3 session 2 vs. phase 3 session 3	−0.01 (0.03)	−0.50	.62
Total cigarette consumption			
Phase 2 session vs. phase 3 session 1	4.25 (0.42)	10.22	< .0001
Phase 2 session vs. phase 3 session 2	4.25 (0.42)	10.09	< .0001
Phase 2 session vs. phase 3 session 3	4.55 (0.42)	10.84	< .0001
Phase 3 session 1 vs. phase 3 session 2	0.001 (0.43)	0.00	.99
Phase 3 session 1 vs. phase 3 session 3	0.30 (0.43)	0.70	.49
Phase 3 session 2 vs. phase 3 session 3	0.30 (0.43)	0.69	.49

3.3. Total cigarette consumption

There was a significant reduction in total smoking choices made in Phase 3 compared to Phase 2 ($F_{1,166} = 97.76$, $p < .0001$) (Fig. 2, Panel A) that was reliable across Phase 3 sessions ($F_{3,459} = 55.44$, $p < .0001$) with total cigarette consumption decreasing from an average rate of 16.48 ± 1.59 choices to smoke in Phase 2 to 12.06 ± 1.54 in Phase 3 ($ps < 0.0001$) (Fig. 2, Panel B). This translated into a reduction of approximately 8–10 puffs per 3-hr session from Phase 2 to Phase 3. Phase 3 sessions did not differ significantly from each other (Table 3). There were no differences in total time spent earning opportunities to

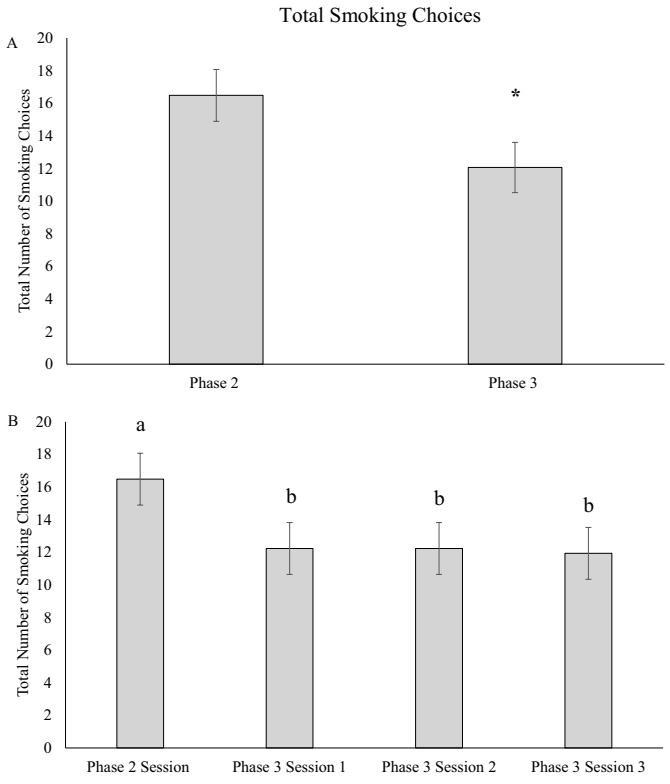

Fig. 2. Panel A: least square mean total cigarette consumption in each phase of the study. Asterisk indicates significant difference at $p < .001$. Error bars represent ± 1 SEM. Panel B: least square mean total cigarette consumption across sessions. Data points not sharing a subscript are significantly different from one another ($p < .05$). Error bars represent ± 1 SEM. Data were collected from March 23, 2015, through April 25, 2016 at University of Vermont, Brown University, and Johns Hopkins University School of Medicine.

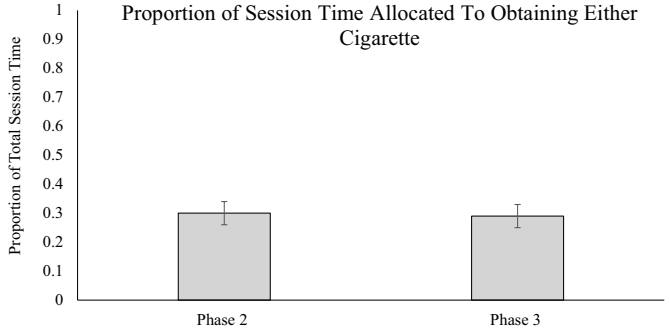

Fig. 3. Least square mean proportion of total session time responding for and consuming reinforcers in each phase of the study. Error bars represent ± 1 SEM. Data were collected from March 23, 2015, through April 25, 2016 at University of Vermont, Brown University, and Johns Hopkins University School of Medicine.

smoke and completing the smoking protocol across Phases 2 and 3 ($F_{1,162} = 1.66$, $p = .20$), with ample time to make more smoking choices in either phase (Fig. 3).

4. Discussion

The results of the present investigation underscore that cigarette product preference is malleable, conditional on cost, and demonstrate that shifts in preference can be accounted for by the behavioral economic metric, unit price. In the present study, when unit price for the preferred product (15.8 mg/g dose) was increased above that of the non-preferred product (0.4 mg/g dose), choice was reliably shifted. That effect is consistent with unit price models of drug self-administration, demonstrating that relative reinforcing value is controlled by the ratio of drug dose to cost (Bickel et al., 1990; Bickel et al., 1991; DeGrandpre et al., 1993). In single schedule arrangements, nicotine consumption decreases as a function of increases in unit price (DeGrandpre et al., 1992; Shahan et al., 2001) and in concurrent schedule arrangements, as in the present study, preference is allocated to the reinforcer with the lower unit price (Bickel and Madden, 1999; Johnson et al., 2004; Madden et al., 2000). The current study adds to this knowledge base by demonstrating that smokers are sensitive to changes in unit price even within a relatively brief session under double-blind conditions and shift behavior in a theoretically predictable manner.

Regarding implications for nicotine reduction policies, our findings suggest that VLNC cigarettes would have to be available at a lower unit price than NNC cigarettes if they were to garner more consumer demand, if both types of cigarettes were concurrently available. If not, one can readily predict that NNC cigarettes would dominate the marketplace similarly to how they dominated preference in Phase 2 of the study (Fig. 1). The current policy direction anticipates that concern and is evaluating merits of policy to set a maximal nicotine content level across all commercial cigarettes (Tobacco Product Standard for Nicotine Level of Combusted Cigarettes, 2018). In a regulatory landscape where higher nicotine content cigarettes are unavailable commercially, smokers would have to engage in a black-market purchase of the product. Such behaviors would be expected to drive up the cost of higher-nicotine cigarettes, in terms of price or effort. The present results suggest that whether a black market will compete effectively with commercially available RNC cigarettes will be determined by relative unit price (i.e., cost of these methods through enforcement of policy against the sale and importing of cigarettes). Another scenario where the unit price model for nicotine reduction is potentially applicable is one where a nicotine reduction policy is limited to cigarettes and not to other combusted products that act as substitutes, such as little cigars. The present results would suggest that to protect against these products substituting for NNC cigarettes in the face of a policy in which they are not similarly regulated, availability of those alternative combusted products would also have to have a higher unit price than RNC cigarettes through methods such as taxation, restrictions on where products are sold, or other constraints that increase relative cost. Lastly, we would anticipate that this same unit price model can be useful in other policy considerations such as how to potentially shift preference from combusted to less toxic non-combusted tobacco products, but, of course, all of these potential extensions of the unit-price model to possible future marketplace scenarios would need to be empirically evaluated. We offer them here to illustrate the potential utility of the unit-price framework for conceptualizing issues that may arise depending on the specific features of a nicotine reduction policy.

To our knowledge, the present study is the first to demonstrate that exposure to VLNC cigarettes is associated with a significant reduction in total smoking rate under acute laboratory conditions and that this effect of reduced smoking rates with RNCs extends to vulnerable populations. The average reduction of 8–10 puffs per session is within the range of the approximately one cigarette per 3-hour session or approximately 5 cigarettes across a day (Zacny and Stitzer, 1996). These decreases appear to be comparable to those observed with the 0.4 compared to the 15.8 mg/g cigarettes in studies of extended exposure (Donny et al., 2015). The findings provide a complement to these studies by demonstrating reductions in an arrangement that is uncompromised by potential confounding associated with non-compliance (i.e., use of non-study tobacco products), a problem that is well documented across studies of extended exposure (Benowitz et al., 2015; Nardone et al., 2016). In both arrangements there appears to a one-quarter to one-third reduction in mean smoking rate when VLNC cigarettes are the predominantly used product. The present observation has considerable

practical implications for the utility of using acute testing in laboratory settings to investigate product differences in potential consumption rate and associated toxin exposure levels, which heretofore was almost exclusively limited to extended exposure arrangements. The evidence from the present study that RNC reductions in smoking rate extend to vulnerable populations adds additional evidence that a nicotine reduction policy has the potential to benefit those segments of the population that are most vulnerable to smoking and its devastating health impacts (e.g., Higgins et al., 2017; Higgins et al., 2019; Tidey et al., 2013; Tidey et al., 2018).

There are limitations of the current study that merit consideration. First, the study was conducted under acute conditions in a laboratory setting with participation limited to smokers from vulnerable populations, which could limit the generality of results. While we cannot rule out this concern, as noted above, the present results appear to align with studies on chronic exposure in naturalistic conditions among participants from the general population. Second, the study was a secondary analysis of an experiment designed for purposes other than explicitly examining how unit price controls preference and as such did not incorporate a research design that may have been best suited for investigating that question, including incorporation of schedule manipulation across a broader range of dose comparisons to more thoroughly test the extent to which unit price predicts shifts in preference. When considered in combination with the broader literature on the generality of unit price in accounting for drug-self administration, we think it is likely that these findings will extend beyond the doses and conditions examined in the present study, but that is an empirical question that can only be resolved through experimental investigation.

5. Conclusion

As cigarette smoking continues to be a leading cause of preventable death in the U.S., a nicotine reduction policy has the ability to markedly improve population health (Apelberg et al., 2018). The findings from the present study contribute to a growing body of empirical evidence supporting such a policy. Our data underscores the potential utility of considering unit price when contemplating nicotine reduction in cigarettes as well as other tobacco regulatory policies aimed toward harm reduction, such as shifting smokers over to exclusive use of less harmful nicotine sources. We also demonstrate that decreases in overall cigarette consumption are discernible even during acute periods of exposure to VLNC cigarettes and among vulnerable populations, which offers the clinical laboratory arrangement as another viable setting for further investigating that effect and further evidence that a nicotine-reduction policy has the potential to reach vulnerable populations. Results from the present study demonstrate the utility of behavioral economic tools and acute laboratory studies in tandem with large-scale extended exposure trials as a means to inform regulatory policy on reducing the nicotine content of cigarettes.

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Declaration of competing interest

None to declare.

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