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Short Communication

The effects of nicotine stimulus and response expectancies on male and female smokers' responses to nicotine-free electronic cigarettes

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HIGHLIGHTS

- Nicotine content beliefs impacted e-cigarrette effects on craving.
- Nicotine expectancies impacted latency to puff but not amount self-administered.
- A-priori response expectancies affected women to a greater extent than men.

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ABSTRACT

Background: Electronic cigarettes (e-cigarettes) have been reported to reduce tobacco craving and withdrawal; however, the mechanisms underlying these effects have not been elucidated.
Methods: This study examined the contributions of nicotine stimulus and response expectancies to responses to nicotine-free e-cigarettes in 21 e-cigarette naïve smokers (12 male). Participants completed two randomized experimental sessions in which they administered a nicotine-free e-cigarette. During one session they were informed that the e-cigarette contained nicotine and during the other session they were informed that the e-cigarette was nicotine-free. Participants completed subjective assessments before and immediately after sampling ten puffs from the e-cigarette and were then invited to earn additional puffs using a computerized progressive ratio task. Prior to their enrolment in the study, participants provided an estimate of the relative importance of the nicotine content of e-cigarettes for craving relief.
Results: Instructions that the e-cigarette contained nicotine were found to reduce both intention to smoke ($p = 0.017$) and withdrawal-related ($p = 0.018$) craving, regardless of a-priori reported beliefs regarding the relative importance of nicotine. Nicotine content instructions were also found to be associated with a shorter latency to self-administration ($p = 0.005$); however, a Sex × Instructions × Response Expectancy interaction ($p = 0.008$) revealed that this effect was specific to women who had strong a-priori nicotine content craving relief expectations. Neither nicotine content instructions nor response expectancies impacted the number of puffs self-administered.
Conclusions: Findings suggest that nicotine content expectations contribute to smokers' responses to e-cigarettes, and that a-priori beliefs about nicotine effects may be especially important in women.

1. Introduction

Electronic cigarettes ("e-cigarettes") have been marketed as a tobacco-free, safer alternative to conventional smoking. E-cigarettes are typically designed to resemble a conventional cigarette as well as to mimic many of the sensory and motor aspects of tobacco smoking. Evidence suggests that e-cigarettes can reduce craving and withdrawal symptoms (Bullen et al., 2010; Dawkins, Turner, Hasna, & Soar, 2012), as well as aid in smoking cessation (e.g. Bullen et al., 2010; Etter & Bullen, 2014; Polosa, Caponnetto, Morjaria, Papale, et al., 2011). Although at least some e-cigarettes have been demonstrated to deliver pharmacologically active doses of nicotine (e.g. Dawkins & Corcoran, 2014), the degree to which nicotine is responsible for various e-cigarette effects remains unclear. For example, in a recent study, nicotine-free e-cigarettes were found to reduce tobacco smoking to a similar degree as nicotine-containing e-cigarettes (Caponnetto, Campagna, Cibella, et al., 2013), and in a second study no relationship was found between the amount of nicotine administered via e-cigarettes and the subsequent reduction in smoking (Polosa et al., 2011). Such findings suggest that non-nicotine factors may be important to e-cigarettes' effects on tobacco craving and withdrawal.

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One non-pharmacological factor that is known to impact responses to various nicotine delivery devices is nicotine content beliefs, or stimulus expectancies. Instructions that one has received nicotine have consistently been found to decrease tobacco craving and/or withdrawal symptoms independent of actual nicotine dose in response to nicotine replacement therapies (NRT) (e.g. Darredeau & Barrett, 2010; Perkins, Grottenthaler, Ciccocioppo, et al., 2009; Schlagintweit, Good, & Barrett, 2014), raising the possibility that nicotine stimulus expectancies may also contribute to e-cigarette effects. Moreover, because the effects of nicotine stimulus expectancies are believed to depend on an individual's "response expectancies" or a-priori beliefs regarding the effects of nicotine (Kirsch, 1999; Perkins, Sayette, Conklin, et al., 2003), one would expect smokers' nicotine response expectancies to mediate any stimulus expectancy effects. There is currently only limited evidence that nicotine response expectancies can directly impact nicotine-related effects. Juliano and Brandon (2002) reported that smokers who expected smoking to relieve anxiety experienced greater anxiety relief from smoking, but this study did not assess nicotine-specific response expectancies. In a second study, smokers reported more positive effects from smoking when they were told that cigarettes would enhance their performance relative to smokers who were told that the cigarettes would impair their performance (Harrell & Juliano;, 2012), but this manipulation failed to impact actual performance. Finally, Fucito and Juliano (2007) found that smokers given information emphasizing the benefits of a placebo nicotine patch reported a greater expectation for the patch to have positive effects than did those given standard patch information, but the two groups did not differ in any smoking-related outcomes following patch use.

The present study examined the impact of nicotine stimulus expectancies and a-priori response expectancies on responses to nicotine free e-cigarettes in a sample of e-cigarette naïve smokers.

2. Methods

2.1. Participants

Twenty-two smokers without quit intentions (12 males) were recruited through local online classified advertisements in the Halifax region (Nova Scotia, Canada). One female participant withdrew prior to completing the study leaving a final sample of 21. All participants were medically healthy and free from psychiatric illness. Participants were naïve regarding e-cigarettes and NRT, had a mean age of 33.7 (sd = 13.2), smoked an average of 15.3 (sd = 6.6) cigarettes per day for a minimum of one year (mean = 15; sd = 13.5) and scored three or higher (mean = 5.3; sd = 1.7) on the Fagerström Test for Cigarette Dependence (FTCD; Fagerström, 2012). Participants were compensated CDN$10 per hour. The study was approved by a local research ethics board.

2.2. Design

Participants completed two randomized sessions, each following a minimum of 3-hour tobacco abstinence. The two sessions were identical except that participants received different nicotine content instructions as well as a different colored e-cigarette during each session. Sessions for a given participant were scheduled to be between two and seven days apart.

2.3. Electronic cigarettes

Electronic cigarettes (Smoke Nv. Inc; Edmonton Canada) were nicotine-free and Canadian tobacco flavored. Participants received a black cigarette during one test session and a white cigarette during the other session. Different colored e-cigarettes were used to enhance the perception that different types of e-cigarettes were being administered; however, they were identical in their contents and differed only in their color. Color order was randomized across participants and post hoc analyses revealed that e-cigarette color did not significantly impact any of the study outcomes.

2.4. Nicotine content instructions

Participants were informed during screening that they would receive a nicotine-containing e-cigarette during one session and a nicotine-free cigarette during the other. Nicotine content information was provided at the beginning of each session (i.e. 'you will be receiving a nicotine-containing/nicotine-free e-cigarette today') by a blinder who was not otherwise involved in the study, and who was blind to the actual nicotine content of the e-cigarettes. The blinder informed participants that it was an ethical requirement to inform them of the e-cigarettes' content and explicitly requested that the information should not be shared with the experimenter. The order of instructions was randomized across participants and e-cigarette color.

2.5. Measures

2.5.1. Cigarette craving

Cigarette craving was measured using the Questionnaire of Smoking Urges-Brief (QSU-B), a psychometrically sound measure of cigarette craving that assesses craving across positive (factor 1: intention to smoke) and negative (factor 2: withdrawal-related craving) reinforcement dimensions (Toll, Katulak, & McKee, 2006).

2.5.2. Self-administration

A computerized progressive ratio task (Barrett, 2010) was used to assess self-administration. Ten key presses were required to earn the first puff, and this number increased by 30% for each subsequent puff. The self-administration measures were the maximum number of key presses completed to earn a puff (i.e., breakpoint), the number of puffs self-administered, and the latency (time in seconds) to initiate self-administration.

2.5.3. Nicotine response expectancies

During screening, potential participants were asked to indicate on a scale from 1 (not at all) to 10 (completely) their beliefs about the importance of the nicotine content of e-cigarettes for craving relief. Inspection of these data revealed a bimodal distribution with the majority of participants providing ratings of either a '5' (28.6%) or a '10' (28.6%). Due to the nature of the distribution, a median split was used to create high (>7; mean = 9.2, sd = 1.0; n = 11) and low (≤ 7; mean = 4.9; sd = 1.5; n = 10) nicotine response expectancy groups to include in the main analyses.

2.5.4. Procedure

At the start of each session, the blinder provided nicotine instructions to the participant, and prepared the e-cigarette for the session using cartridges from containers labeled as nicotine or nicotine-free. The experimenter then entered the laboratory and obtained a carbon monoxide (CO) breath sample (Vitalograph, Lenexa KS). Although there is no reliable CO cut-off to verify 3-hour abstinence, this measurement was included to encourage abstinence compliance (Juliano & Brandon, 2002).

Participants completed a baseline QSU-B before taking ten puffs of their assigned electronic cigarette. Immediately following these puffs they completed a second QSU-B. Participants could then earn additional puffs of their assigned e-cigarette using the progressive ratio task over the next 60 min. As a manipulation check at the end of the second session participants were asked to report what type of e-cigarette they thought they had received during each session.

2.5.5. Statistical analyses

Data were analyzed using linear mixed models. Kolmogorov–Smirnov tests indicated that normality assumptions were best met for