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The impact of anticipated and unanticipated smoking opportunities on cigarette smoking and nicotine lozenge responses

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ABSTRACT

Background: Perceptions regarding the availability of smoking opportunities are known to affect cigarette craving; however, whether they impact actual smoking or how smokers respond to acute nicotine replacement therapy (NRT) administration is not known. This study examined the impact of pharmacological and expectancy components of NRT administration on craving and smoking in smokers anticipating or not anticipating an imminent smoking opportunity.

Methods: In total, 154 smokers (84 male) completed an experimental session in which instructions regarding the nicotine content of a lozenge (4 mg vs. no nicotine) and regarding the availability of a future smoking opportunity were manipulated. Cigarette craving was assessed before and after manipulations and lozenge administration. All participants were then allotted 1 h to self-administer as many cigarette puffs as they wished.

Results: Unanticipated smoking opportunities reduced latency to self-administration ($p < 0.001$), regardless of nicotine expectancy or pharmacology. When analyses included all participants, nicotine reduced intentions to smoke ($p = 0.016$) and withdrawal-related craving ($p = 0.043$) regardless of expectancy. Conversely, analyses using only "believers" of the nicotine content instructions revealed that nicotine expectancy reduced intentions to smoke ($p = 0.034$) and withdrawal-related craving ($p = 0.047$) regardless of actual nicotine administration. "Believers" also reported increased withdrawal-related craving when a smoking opportunity was perceived to be imminent ($p = 0.041$). These effects were not significant when analyses included all participants.

Conclusions: Findings suggest that unexpected smoking opportunities may be more appealing than expected ones regardless of perceived or actual acute NRT use. They also highlight the importance of reporting balanced placebo findings using all participants as well as "believers" only.

1. Introduction

Perceptions regarding the availability of a future smoking opportunity (i.e., believing one will or will not have an imminent opportunity to smoke) have been shown to have a substantial impact on cigarette craving. In a naturalistic study using cigarette-dependent flight attendants, Dar et al. (2010) demonstrated that cigarette craving increases gradually during flights, when smoking is not permitted, and peaks at the conclusion of a flight, when a smoking opportunity becomes imminent. Similar elevations in craving associated with increasing availability of a smoking opportunity have been demonstrated in laboratory based studies (Bailey et al., 2009; Dols et al., 2002; Juliano and Brandon, 1998; Sayette et al., 2003; Wertz and Sayette, 2001). To the best of our knowledge, no study to date has examined the impact of anticipating a smoking opportunity on actual smoking behaviour. However, given that craving has been found to increase with the proximity of a smoking opportunity, one might expect increased smoking behaviour during expected relative to unexpected smoking opportunities. On the other hand, recent findings suggest that laboratory animals display increased responding to obtain reinforcing substances when substances are delivered on a random as opposed to fixed schedule (Lagorio and Winger, 2014). Such findings suggest that unpredictable drug availability is associated with increased drug-related responding and thus it is possible that smokers may be more likely to engage in smoking related behaviours when unexpected opportunities to smoke occur.

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Little is also known about how nicotine replacement therapies (NRTs) impact responses to anticipated and unanticipated smoking opportunities. However, because NRTs appear to be more effective in suppressing tonic or background craving as opposed to phasic or peaks in craving (Ferguson and Shiffman, 2009; Schlagintweit et al., 2014), one might expect that NRTs would be most effective when smoking opportunities are not perceived to be imminently available. NRT effects are generally attributed to the pharmacological properties of nicotine (e.g., Benowitz, 2008; Stead et al., 2012); however, there is growing evidence that suggests that non-pharmacological factors make a substantial contribution (Caggiula et al., 2001; Dar and Barrett, 2014). Balanced placebo research, which crosses instructions regarding nicotine content (told nicotine-containing vs. told nicotine-free) with actual nicotine content (contains nicotine vs. no nicotine) suggests that the belief that nicotine has been consumed reduces cigarette craving and withdrawal regardless of whether or not nicotine was actually consumed (Dar and Barrett, 2014; Darredeau and Barrett, 2010; Gottlieb et al., 1987; Schlagintweit et al., 2014).

This study aimed to (a) examine the impact of varying beliefs about the temporal proximity of a future smoking opportunity on subsequent smoking behaviour, and to (b) assess the impact of the psychological and pharmacological components of NRT administration when smoking opportunities are anticipated versus unanticipated. The study used a balanced placebo design, which manipulated participant expectancies about the nicotine content of nicotine and non-nicotine lozenges. Beliefs regarding the occurrence of a future smoking opportunity were manipulated such that some of the study participants were instructed that they could smoke during the study, while the others were told that they could not smoke until after completing the study. Subjective craving was assessed prior to and following lozenge consumption, and all participants were provided an opportunity to self-administer their preferred brand of cigarette during the final hour of the study.

2. Materials and methods

2.1. Participants

Participants were 154 daily smokers (84 male) recruited through online and community advertisements within Halifax, Nova Scotia, Canada. A telephone interview was used to verify that participants conformed to selection criteria. Specifically, participants reported that they were medication- and NRT-free, medically healthy, had been daily smokers for at least 1 year, had no intention to quit smoking within a month of participation, and had no prior experience using oral NRTs (the gum or lozenge). All participants were dependent smokers (Fagerström Test for Nicotine Dependence (FTND) $\geq$ 3; Heatherton et al., 1991), with mean FTND scores of 5.2 (standard deviation (SD) = 1.6). Participants ranged in age from 19 to 57 (mean = 27.5, SD = 8.74) and smoked an average of 13.3 (SD = 6.0) cigarettes per day. Please refer to Table 1 for additional participant characteristics. All participants provided informed written consent to participate in the study and received compensation of $10 per hour of participation in the study. The study received ethical approval from the Capital District Health Authority Research Ethics Board.

2.2. Materials

2.2.1. Lozenges. Nicotine lozenges (NiQuitin minis 4 mg: GlaxoSmithKline, Marly-le-Roy, France) and non-nicotine lozenges (Ricqles Ricqmint Menthe Sans Sucre, Laboratoire Vie et Santé, France) were similar in size, appearance and mint flavouring; however, nicotine lozenges contained 4 mg of nicotine, while the non-nicotine lozenges were nicotine free. Participants were instructed to keep the lozenges in their mouths until they fully dissolved and not to spit out, chew or swallow them. Nicotine lozenges take approximately 10 min to dissolve, have an average half-life of 2 h (ranging from 1 to 4 h; GlaxoSmithKline Consumer Healthcare, Brentford, UK), and mean blood nicotine levels of ~6.0 ng/ml occur 25–30 min following nicotine lozenge consumption (McEwen et al., 2008; Shiffman et al., 2005). The non-nicotine lozenges were selected because they were not commercially available in Canada, and therefore participants were unlikely to have prior experience consuming them. All lozenges were provided to participants in packaging consistent with instructions regarding nicotine content, such that participants who were informed they received a nicotine lozenge were provided with a lozenge in a NiQuitin minis package, while those who were informed they received a non-nicotine lozenge were given a lozenge in a Ricqles package.

2.2.2. Demographic information and smoking patterns. Demographic (e.g., age, sex) and smoking history (e.g., age of first cigarette use, current smoking frequency) information was assessed using a Demographic and Smoking History Questionnaire.

2.2.3. Subjective cigarette craving. The Questionnaire of Smoking Urges-Brief (QSU-B) consists of 10 items used to assess subjective cigarette craving across two dimensions (factor 1: intention to smoke; factor 2: withdrawal-related craving; Toll et al., 2006). The QSU-B has been demonstrated to be a reliable and sensitive measure of nicotine and tobacco-related craving and other abstinence-related effects (Cox et al., 2001; Toll et al., 2006).

2.2.4. Heart rate. Average heart rate was assessed over the course of 60 s using a Polaris Heart Rate Monitor chest strap and wristwatch (Polar Electro Canada Inc., Lachine, Quebec, Canada).

2.2.5. Cigarette self-administration. Cigarette self-administration was assessed using a computerised progressive ratio (PR) task, where participants were allotted 60 min to earn puffs of their preferred brand of cigarettes by repeatedly pressing a keyboard a predetermined number of times. The first puff required 10 presses, and the number of presses required to earn each subsequent puff increased by a ratio of 1.3. Following the administration of each puff, participants could resume the task at their own pace to earn an additional puff. Participants could earn as many or a few puffs as they wished, but were required to remain seated in front of a cigarette and the PR computer until the session ended. Measures of latency (duration in seconds to initiate the first puff) and total number of self-administered puffs were collected. Similar PR tasks have been demonstrated to be sensitive to changes in subjective cigarette craving (Willner et al., 1995; Willner and Jones, 1996) and to pharmacological manipulations (Barrett, 2010; Barrett and Darredeau, 2012).

2.3. Procedure

Participants attended one experimental session, during which they were randomly assigned to one of the four conditions of the balanced-placebo design. Conditions differed by instructions regarding nicotine content (told nicotine vs. told no nicotine) and nicotine administration (receive nicotine vs. receive no nicotine). Within each condition, participants were also assigned to one of two groups that differed by instructions regarding the temporal proximity of a future smoking opportunity. One group was informed that they could smoke their preferred brand of cigarettes during the study (anticipated smoking opportunity), and the other group was informed that they could not smoke during the study, which lasted for approximately 2 h (unanticipated smoking opportunity). Thus, participants could be assigned to one of eight possible conditions, as outlined in Table 1.

After participants provided written consent to participate, overnight abstinence from smoking ($\geq$12 h) was verified with a breath carbon monoxide sample (Vitalograph, UK) reading of $\leq$15 ppm. Next, participants were informed whether they could (anticipated smoking opportunity) or could not smoke (unanticipated smoking opportunity) during the study session. Participants then completed a craving questionnaire and their heart rate was assessed (Time 1 [*T*1]), and they were provided with a lozenge and allotted 30 min for absorption. Following lozenge absorption, participants completed another craving questionnaire, and their heart rate was reassessed (Time 2 [*T*2]). At this time, participants in the unanticipated smoking opportunity group were informed that the researcher had made an error and that they would have an opportunity to smoke during the study session after all. Next, participants were seated in front of a computer and provided a pack of their preferred brand of cigarettes. Participants were instructed that they