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ORIGINAL INVESTIGATION

Changes in the relative reinforcing effects of cigarette smoking as a function of initial abstinence

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Abstract
Rationale Experimental research is needed in investigating how early smoking abstinence affects relapse risk.
Objective The present study assessed the feasibility of promoting smoking abstinence using once- rather than thrice-daily abstinence monitoring and the relationship between different durations of initial abstinence and changes in smoking preference.
Methods Participants were 34 adult smokers randomized into one of two conditions: 14-day (14C) and 1-day (1C) contingent payment for smoking abstinence. Smoking status and participant ratings were assessed daily; a delay discounting task involving hypothetical money and an inter-temporal choice task involving hypothetical money and cigarettes were administered at baseline and days 7 and 14; a direct test of preference for smoking versus money was assessed on day 14.
Results Once-daily monitoring gained robust experimental control over smoking abstinence. No differences in delay discounting for hypothetical money were observed between the two conditions. Compared to the 1C condition, participants in the 14C condition (1) showed significant increases in the mean percent of delayed hypothetical money over cigarettes choices in the inter-temporal choice task, (2) were significantly less likely to ever choose the smoking option in the direct test of preference for smoking versus money, and (3) reported greater ease of abstaining from smoking and lower nicotine withdrawal and craving.
Conclusions These results offer a more efficient procedure for experimentally promoting smoking abstinence, while providing further evidence that an initial period of sustained abstinence produces a profile of changes consistent with an overall lowering of relapse risk.

Keywords Cigarette smoking · Abstinence · Reinforcing effects · Delayed discounting · Nicotine withdrawal · Craving · Contingency management

Cigarette smoking is the leading cause of preventable mortality and morbidity in the USA [Center for Disease Control and Prevention (CDCP) (2005)]. Cigarette smoking and tobacco exposure in the USA annually contribute to an estimated 438,000 premature deaths, 5.5 million of years of potential life lost, and $92 billion in lost productivity (Centers for Disease Control and Prevention 2005). Millions of individuals attempt to quit smoking each year, yet over half fail within the first few days or weeks of their quit attempt (Hughes et al. 2004). Clearly, greater understanding of the determinants of successful smoking cessation and more effective interventions are needed.

In a seminal study, Kenford et al. (1994) examined potential predictors of success in quitting smoking in two independent randomized clinical trials on active and placebo transdermal nicotine replacement therapy. Smoking status during the first 2 weeks of treatment, particularly in

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week 2, was the only reliable predictor of smoking status at the end of treatment (6–8 weeks) and at a 6-month follow-up in the active patch and placebo conditions. Others have reported similar associations between initial smoking abstinence and relapse risk in smoking-cessation trials (Gourlay et al. 1994; Yudkin et al. 1996) and initial abstinence predicts longer-term abstinence among those treated for other substance use disorders (SUDs) such as cocaine dependence (e.g., Higgins et al. 2000).

The robust nature of such findings raises the question of whether a period of initial abstinence might act to directly lower relapse risk. Unfortunately, causal inferences are not possible from the studies discussed above because participants self-selected into abstainer and user categories. Instead, such questions about abstinence and relapse risk need to be investigated experimentally.

A substantive obstacle to conducting such research has been the challenge of how to gain experimental control over smoking. Our group has been examining the use of contingency management (CM) to surmount that obstacle (Alessi et al. 2004; Chivers et al. 2008; Heil et al. 2004; Lussier et al. 2005). CM promotes abstinence by delivering material incentives contingent on biochemically verified abstinence (Higgins et al. 2008). CM has been effective in promoting differing amounts of early smoking abstinence in these studies (Alessi et al. 2004; Chivers et al. 2008; Heil et al. 2004; Lussier et al. 2005; Roll and Higgins 2000; Roll et al. 1996) and the results have suggested that a period of initial abstinence may be expected to directly lower relapse risk. For example, Lussier et al. (2005) used CM to reinforce smoking abstinence in three groups of smokers using thrice-daily breath carbon monoxide (CO) monitoring for 14 consecutive days. The three groups differed in terms of how long the abstinence criterion was in place: in one condition (14C) payment was contingent on abstinence for all 14 study days, in a second condition (7C) payment was independent of smoking status on study days 1–7 and contingent on abstinence on days 8–14, and in the third condition (1C) payment was independent of smoking status on days 1–13 and contingent on abstinence on day 14. On the evening of day 14, all participants participated in a 3-h smoking-preference test in which they made 20 exclusive choices between two puffs on a cigarette or $0.25. Only 19% of the participants in the 14C condition ever chose to smoke in the preference test compared to 57% and 62% of those in the 7C and 1C conditions, respectively. The decreases in smoking preference observed in the 14C condition suggest a decrease in the reinforcing effects of smoking relative to alternative non-drug reinforcers, which could directly lower relapse risk.

The present study was designed to address two issues. First, we were interested in whether we could systematically replicate the main findings from Lussier et al. while making two procedural changes. We decreased the frequency of daily monitoring from thrice- to once-daily and we implemented a urine-cotinine measure of abstinence during week2 in the 14C condition. In the above studies, breath CO was used to confirm smoking abstinence when using thrice-daily visits to the laboratory, a demanding schedule for staff and study participants alike. Even with thrice-daily monitoring, however, undetected smoking remained a possibility with exclusive reliance on breath CO due to its relatively short half-life (~2–8 h; Benowitz et al. 2002). To improve the rigor of the methods used to biochemically verify abstinence and support less frequent abstinence monitoring, we investigated the use of once-daily CO monitoring and urine-cotinine verification of abstinence during the first and second weeks of the 2-week study period, respectively. The longer half-life of cotinine (~16–20 h; Ahijevych et al. 2002; Benowitz et al. 2002; Skarping et al. 1988) relative to CO provides greater assurance against low-level smoking between visits. Additionally, our group has previously demonstrated that a similar procedure is effective in promoting smoking abstinence among pregnant women (Higgins et al. 2004) and methadone maintained outpatients (Dunn et al. 2008).

Second, we were interested in experimentally examining how performance on two-choice procedures for hypothetical consequences was affected by different durations of initial smoking abstinence. One was a monetary delay-discounting (DD) task in which participants were asked to choose between smaller amounts of money available immediately versus a larger amount available after a fixed delay (Johnson and Bickel 2002). The second was a similar inter-temporal choice (ITC) task asking participants to choose between differing amounts of cigarettes available immediately versus a fixed amount of money available after a delay (Mitchell 2004). An emerging literature has shown that cigarette smokers and others with substance abuse disorders exhibit greater DD than those without SUDs (e.g., Bickel and Marsch 2001; Reynolds et al. 2007). More specifically, robust evidence shows that those with SUDs discount the value of delayed consequences more than those without. While most research on this topic has focused on comparisons between those with versus without SUDs, several studies have investigated the effects of acute drug deprivation on impulsive choice (Giordano et al. 2002; Mitchell 2004). Opioid deprivation was reported to increase DD of heroin and money (Giordano et al. 2002) and acute smoking abstinence was reported to increase preference for immediate cigarettes over delayed money in an ITC task (Mitchell 2004). Additionally, several recent studies have shown that baseline DD can predict smoking relapse in clinical trials (Krishnan-Sarin et al. 2007; Yoon et al. 2007) and human laboratory settings (Dallery and Raiff 2007). Therefore, we examined how performance on two-choice

procedures for hypothetical consequences related to the duration of initial smoking abstinence and whether performance on the choice tasks using hypothetical consequences predicted how participants responded in a smoking-preference session involving choices between real cigarettes and money.

Materials and methods

Participants

Adult cigarette smokers were recruited via newspaper ads and flyers posted in the local community. Thirty-four participants consented to be in the study, with 28 completing the study. All data analyses are based on the 28 completers. Of the six non-completers, one moved out of the country, two did not return after the first orientation session, and three withdrew abruptly during the study (after nine to 12 visits). There were three non-completers from each condition, and there was no evidence that the withdrawals were due to study-related problems. Individuals who answered the ads or flyers were initially administered a brief, 10-min telephone assessment. Cigarette smokers who were potentially eligible for the study were invited to the laboratory for a more detailed interview assessing medical, mental-health, and drug-use histories. Eligibility criteria included being 18–55 years old, in good health, report smoking≥10 cigarettes/day, provide a breath carbon monoxide (CO) sample≥18 ppm, and report no plans to quit smoking in the near future. Smokers not currently trying to quit were specifically chosen in order to increase the likelihood that changes in smoking rates were under experimental control rather than variables extraneous to the study and to eliminate the need to provide formal smoking-cessation clinical services (Alessi et al. 2004; Stitzer et al. 1986). Exclusion criteria consisted of any current use of psychoactive medications, a history of major psychiatric disorders, drug or alcohol dependence other than tobacco, or being pregnant or lactating. Participants were not informed of the inclusion/exclusion criteria except for the age requirements, which were listed on flyers and newspaper ads. All participants provided written informed consent and were randomized to one of two experimental conditions described below. Randomization to the two conditions was stratified on gender and whether the participant was a student. There were no significant differences between experimental conditions in participant characteristics assessed at baseline (Table 1).

Procedure

Orientation session Participants attended a baseline orientation session prior to starting the 14-day study period during which they were informed about the experimental conditions, the respective payment schedules, criteria for earning payment throughout the study, and trained on a standardized-puffing procedure described below. Participants also provided a breath specimen that was assessed for CO using a Micro Smokerlyzer Monitor (Bedfont Scientific, Kent, England) and a urine specimen that was assessed for cotinine and illicit drug use (amphetamines, benzodiazepines, cannabis, cocaine, methadone, and opiates) via an onsite Viva-E analyzer (Siemens Medical Solutions Diagnostics, Deerfield, IL, USA). Participants were required to test negative for illicit drug use prior to starting the study and instructed to abstain throughout the study. During the 14-day study, 95.6% (375/392) of the samples tested were negative for drug use. Regarding the 4.4% (17/392) samples that tested positive, participants showed no signs of acute intoxication and thus completed the study visits and were again encouraged to comply with the study restrictions against drug use.

Abstinence-monitoring program Abstinence monitoring took place over the course of 14 consecutive days.

Table 1 Participant characteristics

	Experimental condition		
	14C (n=13)	1C (n=15)	p-value
Male (%)	61.5	73.3	0.69
Age	29.1±11.5	28.1±12.6	0.84
Caucasian (%)	84.6	100.0	0.21
Years of education	13.6±1.5	13.1±1.6	0.41
Fagerstrom score	6.2±1.3	5.3±1.7	0.10
Number of cigarettes/day	21.7±5.6	18.2±5.5	0.11
Years smoking	4.0(3.0, 24.0)[a]	3.0(2.7, 19.0)[a]	0.99
Nicotine content of usual brand	0.88±0.27	0.85±0.21	0.81
Students (%)	46	53	0.70

Values represent means±SD unless otherwise noted. Statistical significance based on Fisher's exact test for percentages and t-test or Wilcoxon rank sum test for continuous measures

[a] Median (interquartile range)

Participants visited the laboratory once daily where they provided breath and urine samples for verification of smoking status.

When payment was contingent on smoking abstinence, participants received cash immediately after biochemical verification (CO or cotinine). When money was earned independent of smoking status, participants received cash prior to the biochemical assessments. At each visit, participants reported how much they had smoked since their last visit except for day 1 of the study where they described how much they had smoked in the last 24 h. Likewise, participants also reported alcohol consumption, medication or drug use, hours of sleep, and any changes in health or other crises since their last visit with the first visit covering the last 24 h. Additionally, participants were provided a pack of their regular cigarettes to ensure that changes in smoking were under the control of experimental variables and not the result of an inadvertent lack of access to cigarettes.

Experimental conditions and associated payment schedules Participants were randomly assigned to one of two experimental conditions. In one condition (14C), payment was contingent on meeting the abstinence criterion on study days 1–14. The abstinence criterion for week 1 was breath CO at≤ 4 ppm and for week 2 was urine cotinine at≤80 ng/ml (Higgins et al. 2004). Breath CO was used in week 1 because the relatively long half-life of cotinine may produce false-positive test results associated with smoking that occurred prior to the start of the study. Although participants were not explicitly instructed to refrain from nicotine replacement therapy (NRT), they were informed that use of NRT could produce a positive urine-cotinine result and would be registered as positive for smoking. No participants reported using NRT during the experiment. In the other experimental condition (1C), payment was independent of smoking status during days 1–13 and contingent on a breath CO at≤4 ppm on day 14.

In the 14C condition, participants earned $20.50 the first time they met the abstinence criterion. Each subsequent visit in which the abstinence criterion was met increased the amount earned by $4.50 to a maximum of $40. If either the abstinence criterion was not met or the participant missed a visit, no cash was delivered and the amount that could be earned the next time the participant met the abstinence criterion was reset to $20.50 (Higgins et al. 1991). Only 1.3% (5/392) of samples were missing due to participants failing to attend a scheduled session. If the participant met the abstinence criterion for two consecutive visits following a reset, the value of the amount earned on that second visit was restored to the initial value prior to the reset. Maximum potential daily earnings were equal to those used in our prior studies using thrice-daily monitoring (e.g., Chivers et al. 2008; Lussier et al. 2005).

In the 1C condition, participants earned $28 on days 1–13 independent of their smoking status and $40 on day 14 for meeting the abstinence criterion (CO≤4 ppm). The $28 amount was based on average earnings in the 14C contingent condition in a previous study (Chivers et al. 2008). As with the 14C participants prior to their first contingent visit, participants in the 1C condition were advised to quit smoking by 5 pm on day 13 in order to meet the abstinence criterion on day 14.

All payments during the 14-day monitoring period were made in cash. To encourage study completion, participants also received a $50 bonus check for completing the study. On average, participants in the 14C condition ($429.35± $102.03) earned more than those in the 1C condition ($387.73±$25.72) but these differences were not significant.

Choice tasks involving hypothetical consequences At baseline and days 7 and 14, participants completed two-choice tasks for hypothetical consequences conducted on a notebook computer that ran a Microsoft Visual Basic® 6.0 program. A staff member supervised the choice tasks to answer any questions that might arise. Each choice task took approximately 10 min to complete. For both choice tasks, participants were situated in front of the computer screen and asked to choose between two different hypothetical options, a relatively smaller amount available immediately and a relatively larger amount available after a fixed delay. Participants were told that they would not receive either of the options they chose, but to answer as if the options were real.

The ITC task presented hypothetical choices between various numbers of cigarette packs available immediately versus $1,000 in cash available after a fixed delay. The ITC task was based on a procedure reported previously (Mitchell 2004). Prior to beginning the ITC task at baseline, participants were asked how many packs of their usual brand of cigarettes they could obtain for $1,000, which was used to calculate the maximum number of immediately available cigarette packs in the cigarette choice task. A calculator was provided as needed. This value was subsequently used when the ITC task was presented again on days 7 and 14. Participants were also told to assume that when choosing packs of cigarettes that the cigarettes were for the participant's own use (not to be sold or given to others), the cigarettes remained always fresh and were immediately available, and that they were the brand that the participant typically smoked. Participants then made a series of choices between varying numbers of packs of cigarettes available immediately and $1,000 in cash available after a temporal delay (1 day, 1 week, 1 month, 6 months, 1 year, 5 years, or 25 years). At each of the delay intervals, the program systematically changed the immediate number of packs of cigarettes available until an

indifference point was found in which the smaller, more immediate cigarette option was judged by the participant to be equivalent to the larger, more delayed cash option (Johnson and Bickel 2002). Once the indifference point for a given delay was determined, the next delay was introduced until indifference points for each delay were determined. The order of the delays was presented in a fixed ascending or descending order for a given participant but presented randomly across participants.

In the DD task, participants chose between varying hypothetical amounts of money available immediately vs. $1,000 available after fixed delays. As in the ITC task described above, the immediate money amount was changed systematically until an indifference point was determined (Johnson and Bickel 2002). Indifference points were assessed for each of seven delays (1 day, 1 week, 1 month, 6 months, 1 year, 5 years, or 25 years).

Choice task involving real money and cigarettes At the end of the day 14 visit, participants completed a 3-h smoking-preference session involving choices between actual money and cigarettes. During that session, participants were seated alone in a private, ventilated room (4×8×8 ft) facing a notebook computer that ran a Microsoft Visual Basic® 6.0 program. A desktop computer was also in the room and was used for controlling smoke exposure (described below). An open pack of the participant's preferred brand of cigarettes along with a lighter and ashtray were also available in the room. The session duration was 3 h, during which participants could make up to 20 mutually exclusive choices for either $0.25, two puffs on a cigarette, or forgo both options and simply allow the session time to pass. Prior to entering the session, participants were told that they were now free to smoke without any adverse consequences, except for the $0.25 that would be forfeited per smoking choice.

Sessions began with two response options labeled either "SMOKE" or "MONEY" displayed side by side on the notebook monitor. The order of the response options was randomized across participants. Additionally, the session clock was visible and showed how much time was left in the preference session. Participants registered preferences for smoking or money by using the mouse to click on the appropriate response option ten times (fixed ratio 10).

Completion of either response requirement resulted in a brief series of three tones and initiated a 3-min inter-trial interval during which the response options were not available. An interval clock also showed how much time was left during the inter-trial interval. Once the 3-min interval was complete both response options became available again until the 20 choices were exhausted. The number of times either response option was chosen was also displayed under each response option. If the participant chose "MONEY," $0.25 was added to a running tally that was displayed on the notebook monitor. If the participant chose "SMOKE," the monitor flashed "PUFF NOW," and they had 3 min to complete the standardized-puffing procedure described below. If all 20 choices became exhausted, then both response options became unavailable and the monitor displayed the message "No more trials" with the session timer still counting down. The remaining cigarettes and ashtray were also removed from the experimental room at this time. Except for the inter-trial interval, when and how the 20 choices were distributed across the 3-h session was completely under the control of the participant. Participants were not required to complete any choices and could simply let the session time elapse if they chose to do so. When not making choices, participants were allowed to read newspapers and magazines and listen to music. Participants were not permitted to eat, drink, or sleep during session. At the end of session, participants were paid any money that they had earned during the preference session and discharged.

A standard procedure was used to deliver cigarette puffs (Zacny et al. 1987). Once a participant chose the smoking option, he or she lit a cigarette without inhaling and inserted the filter end of the cigarette into a plastic cigarette holder connected by tubing to a puff-volume sensor (CReSS System, Plowshare Technologies, Baltimore, MD, USA). Participants then inhaled until a tone signaled when 60-cc volume of smoke had been inhaled. Participants held the smoke for 5 s at which time another tone signaled that they were to exhale. Following a 25-s inter-puff interval, the sequence was repeated.

Participant ratings At baseline (prior to randomization) and each subsequent visit during the 14-day study period, participants completed the (1) Minnesota Nicotine Withdrawal Questionnaire (NWQ, Hughes and Hatsukami 1986), (2) Tiffany Questionnaire on Smoking Urges (QSU, Tiffany and Drobes 1991), (3) Profile of Mood States (POMS, McNair et al. 1971), (4) a set of visual-analog scales (VAS) developed in our laboratory that included items to assess craving, abstinence self-efficacy, and symptoms of nicotine withdrawal, and (5) the Multiple-Choice Procedure (MCP, Griffiths et al. 1993). All participant ratings were completed on a PC using the CReSS System (Plowshare Technologies).

Statistical methods

Comparisons between the 14C and 1C experimental conditions on subject characteristics were performed using *t*-tests or Wilcoxon rank sum tests for continuous variables and Fisher's exact tests for dichotomous variables. Analyses of data collected during the 14-day study period were conducted separately for days 1–13 and day 14 due to the

change from noncontingent to contingent payments on day 14 in the 1C condition. For days 1–13, mean CO and cotinine levels were examined as a function of condition and session day (1–13) using repeated measures analysis of variance. Scores on the VAS, NWQ, POMS, and QSU were analyzed using repeated measures analysis of covariance with condition and session day (1–13) as factors and participants' baseline scores on each measure as covariates. Analyses corresponding to day 14 comparisons were performed based on one-way analyses of variance and one-way analyses of covariance. Fisher's exact tests or chi-square tests were used to examine group differences on ever choosing to smoke in the smoking-preference session.

For the ITC task, the percentage of total choices for the delayed monetary choice for a given assessment was assessed for each participant. The mean percentage of total of choices was then compared between the 14C and 1C conditions across BL, day 7, and day 14 using an arcsine square root transformation (Box et al. 1978). All statistical analyses were therefore based on the transformed data, but all descriptive means are based on the original values. Statistical significance was determined based on alpha=0.05.

For the DD task, the hyperbolic discounting model, $V = A/(1 + kD)$, was fitted to each subject's delay discounting data using nonlinear regression (SAS, PROC NLIN). In this equation, V represents the subjective value of a reward of some amount A, discounted as a function of delay (D) in days to receiving that reward (Mazur 1987). Each subject's derived discounting parameter (k) for each assessment was used as the outcome measure for subsequent analyses. t-tests were used for comparisons between the two experimental conditions at baseline. Repeated measures analyses of covariance were used to examine group differences in discounting at days 7 and 14, adjusting for baseline. Similar analyses were used to examine differences in discounting at days 7 and 14 between those who chose to smoke during a smoking-preference session and those who did not choose to smoke. Because the distribution of subjects' k values was skewed, analyses were performed based on a logarithmic transformation of k, which resulted in a normal-like distribution within the study sample. Consistent with the logarithmic transformation, means presented for k values represent geometric means. Analyses were performed using SAS V 9.1 (SAS Institute, Cary, NC, USA). Statistical significance was determined based on alpha=0.05.

Results

Smoking abstinence

Smoking abstinence was successfully manipulated, with breath CO (Fig. 1, top; Table 2) and urine-cotinine levels (Fig. 1, middle; Table 2) changing as an orderly function of changes in the reinforcement contingencies. Mean breath CO levels in the 14C condition were significantly lower than those in the 1C condition throughout days 1–13 consistent with payment being contingent on abstinence in the former but not the latter during this period. When payment was made contingent on smoking abstinence in the 1C condition on day 14, mean breath CO decreased to levels comparable to those observed in the 14C condition. Likewise, mean urine-cotinine levels in the 14C condition were consistently below those in the 1C condition during days 1–13 (Fig. 1, middle; Table 2). Cotinine levels remained significantly lower in the 14C condition compared to the 1C condition on day 14 when the abstinence contingency was operating in both conditions (Table 2), but that was expected due to cotinine's relatively long half-life. Collapsing across the 14C and 1C conditions, 87% (171/197) of all specimens submitted during contingent conditions met the reinforcement contingencies compared to 0% (0/195) of the specimens submitted in the noncontingent payment condition.

The practice of waiting until week 2 before using cotinine to verify abstinence was generally supported by the results on cotinine levels over time in the 14C condition (Fig. 1, bottom). The urine-cotinine criterion of ≤80 ng/ml was first met by one participant as early as day 2, but the majority of participants in the 14C condition were unable to meet that criterion until day 6. When the abstinence contingency was placed on urine cotinine in the 14C condition on day 8, 85% (11/13) of participants met the criterion and a peak of 92% (12/13) of participants satisfied the criterion on day 10.

Choice tasks

Choice tasks involving hypothetical consequences As described above, two-choice procedures were used that had participants choose between relatively smaller hypothetical commodities available immediately versus a larger one available after varying temporal delays. In the task assessing choice between varying number of cigarette packs available immediately versus a fixed amount of money ($1,000) available after a fixed delay, no differences in preference for the hypothetical delayed money option was observed between the 14C and 1C condition at baseline (p=0.54; Fig. 2). However, a significant group×day interaction (p=0.01) was observed indicating a shift in preference for the hypothetical delayed money option over immediately available cigarettes as a function of smoking abstinence in the 14C condition relative to the 1C condition (Fig. 2).

Examination of choices among individual participants in the 14C condition revealed that a subset of participants exclusively chose the hypothetical money over the cigarette

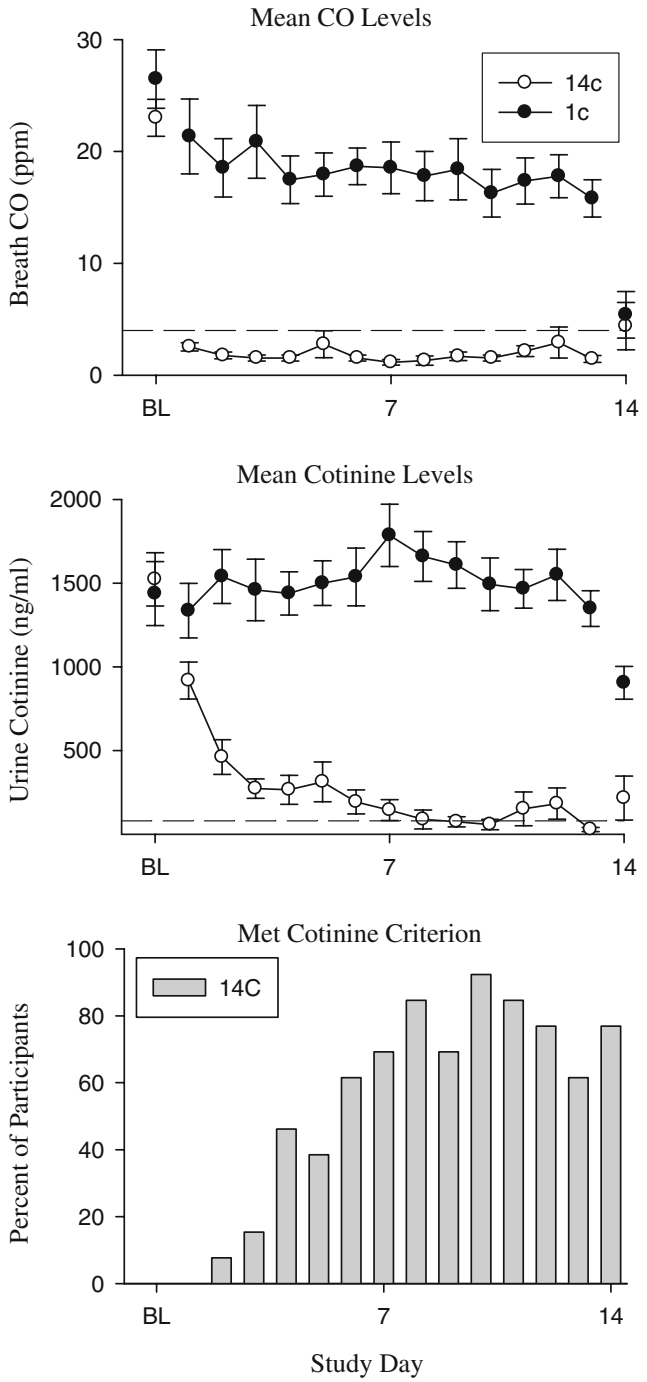

Fig. 1 Mean breath CO (*top*) and mean urine cotinine (*middle*) levels by study day for the 14C (*open circles*) and 1C (*filled circles*). *Horizontal dashed lines* denote the reinforcement criterion for breath CO at 4 ppm (*top*) and urine cotinine at 80 ng/ml (*bottom*). *Vertical bars* represent±SEM. Note that the ordinate on the *middle panel* is on a log scale. The *bottom panel* shows the percentage of participants in the 14C condition satisfying the abstinence criterion by study day

option at the day 7 and day 14 assessments (Fig. 3). The percentage of such "exclusive responders" was comparable in the 14C and 1C conditions at baseline but increased significantly at day 7 (McNemer Test=4.0, p=0.04) and day 14 (McNemer Test=5.0, p=0.03) in the 14C condition, while remaining relatively unchanged in the 1C condition (Fig. 3).

No significant differences in the DD task for hypothetical money were observed between the 14C and 1C conditions at baseline or days 7 and 14 (Table 3). The hyperbolic equation provided a good fit to data from the DD task. Median R^2 values were 0.97, 0.88, and 0.89 across the three assessments for the 14C condition and 0.94, 0.90, and 0.84 for the 1C condition.

Choice task involving real money and cigarettes Participants in the 14C condition were significantly less likely than those in the 1C condition to smoke in the preference session. Only 23% (3/13) of participants in the 14C condition ever chose the smoking option during the smoking-preference session compared to 67% (10/15) in the 1C condition [Fig. 4, left; $\chi^2(1)=5.32$, p=0.02]. Additionally, participants in the 14C condition chose the smoking option an average of only 0.77±0.61 times compared to 3.73±0.94 times in the 1C condition [Fig. 4, right; $t(26)=2.55$, p=0.02].

Relations between the choice tasks involving hypothetical and real consequences We assessed whether performance in the choice tasks involving hypothetical consequences predicted who chose the smoking option when choosing between real money and smoking options. Regarding the ITC task, there were no baseline performance differences between those who did and did not choose to smoke in the session involving real consequences [Fig. 5; $t(26)=1.59$, p=0.12]. Performance on the ITC task, however, was able to differentiate between smokers and abstainers at the day 7 [$t(26)=3.08$, p=0.005] and 14 [$t(26)=3.50$, p=0.002] assessments (Fig. 5). That is, those who were more likely to choose the delayed monetary option when choosing between hypothetical money and cigarette consequences were also more likely to abstain from smoking in the session involving choices between real money and smoking options. This ability of performance in the ITC task to discriminate between smokers and abstainers in the preference session did not interact significantly with experimental conditions.

Performance in the DD task was unable to significantly discriminate between smokers and abstainers in the smoking-preference session at any assessment (data not shown).

Participant ratings

Abstinence ratings Mean VAS ratings of "Ease of Abstaining" increased significantly in the 14C but not the 1C condition during days 1–13 (Fig. 6, top; Table 2). When the abstinence contingency was in place for both conditions on day 14, ratings increased in the 1C condition to levels

Table 2 Biochemical outcomes and participant ratings by experimental condition

Dependent measures	Phase 1 (days 1–13)		Group *p*-value	Group×day *p*-value	Phase 2 (day 14)		Group *p*-value
	14C	1C			14C	1C	
Smoking abstinence							
Breath CO	1.8±0.2	18.3±0.6	**<0.01**	0.42	4.4±2.1	5.4±2.1	0.74
Urine cotinine	242.5±27.5	1,519.8±41.6	**0.01**	**<0.01**	216.4±131.3	904.9±97.7	**<0.01**
VAS ease of abstaining	61.1±2.3	41.9±2.4	**0.03**	0.67	61.7±9.0	52.2±9.7	0.45
VAS confidence in abstaining	75.4±1.6	53.8±2.7	**0.03**	0.51	65.7±8.5	56.4±9.4	0.44
Nicotine withdrawal/related symptoms							
NWQ total	7.4±0.4	4.5±0.3	**0.02**	0.78	6.0±1.0	6.8±1.4	0.63
NWQ desire	1.9±0.1	1.3±0.1	**0.02**	**<0.01**	1.8±0.2	2.6±0.3	**0.02**
POMS vigor	11.6±0.4	14.1±0.6	0.13	0.13	10.6±1.2	15.2±1.8	**0.01**
QSU factor 1	4.1±0.1	4.2±0.1	0.71	0.14	4.3±0.4	5.4±0.4	**0.03**
QSU factor 2	3.0±0.1	2.9±0.1	0.80	**<0.01**	2.6±0.4	3.7±0.4	**0.03**
VAS crave	53.1±2.0	39.4±2.3	0.08	**<0.01**	46.2±7.2	64.3±8.6	0.10
VAS desire	54.0±2.0	40.9±2.4	0.10	**<0.01**	49.1±6.3	64.9±8.1	0.12
VAS need	41.3±2.1	35.2±2.3	0.38	**<0.01**	35.1±6.3	49.8±9.2	0.16
VAS want	51.8±2.1	40.6±2.3	0.12	**<0.01**	49.8±7.1	69.2±7.4	**0.02**
VAS self-confidence	65.6±1.5	72.4±1.6	0.16	**0.04**	62.5±5.9	77.3±5.1	**0.03**
VAS alert	52.7±1.7	62.9±2.0	0.11	**0.03**	53.6±6.0	64.4±6.8	0.22
VAS on edge	28.5±1.9	28.4±2.3	0.99	**0.01**	24.4±6.7	43.1±7.4	**0.05**
VAS tired	42.2±2.2	41.2±2.2	0.87	**0.01**	34.1±6.0	29.3±7.7	0.61

Values represent least square means±SE. Significance levels are based on ANCOVAs for all measures except cotinine and CO, which are based on ANOVAs

slightly below but not significantly different than those in the 14C condition (Fig. 6, top; Table 2).

Mean VAS ratings of "Confidence in Abstaining Tomorrow" were consistently higher in the 14C than the 1C condition until day 13, when ratings increased in the 1C condition as well (Fig. 6, bottom; Table 2). On day 14, ratings in both conditions returned to baseline levels (Fig. 6, bottom; Table 2).

Ratings of nicotine withdrawal and related measures Mean Total scores on the NWQ increased to peak levels on day 1 in the 14C condition and then gradually decreased

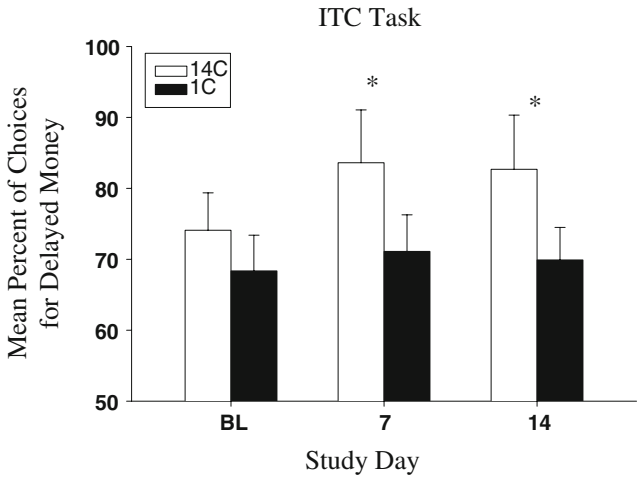

Fig. 2 Mean percentage of total choices for the delayed money option in the ITC task for the 14C (*filled bars*) and 1C (*open bars*) conditions at baseline, day 7, and day 14. *Vertical bars* represent±SEM. Note that the ordinate axis begins at 50%

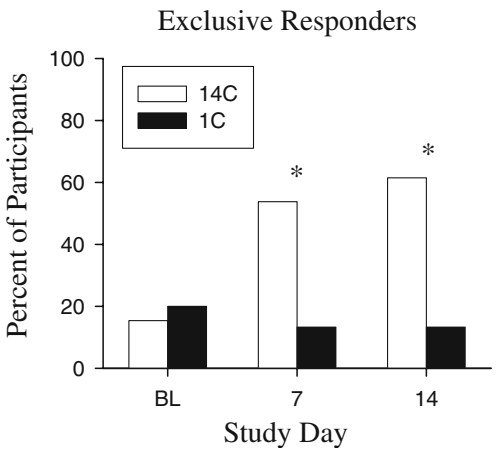

Fig. 3 Percentage of "exclusive responders" during the cigarette versus money DD task for the 14C (*open bars*) and 1C (*filled bars*) conditions obtained at baseline, day 7, and day 14

Table 3 Performance on the money DD task at BL, day 7, and day 14

Condition	BL	k(days^{-1})[a] Day 7	Day 14
14C	2.01±0.84	1.12±0.54	0.49±0.24
1C	2.54±1.37	1.21±0.55	1.30±0.59

Values represent least square means±SE

[a] Values have been multiplied by 10^3 for presentation purposes (e.g., k = 0.49 represents k = 0.00049)

throughout, whereas scores remained relatively unchanged from baseline in the 1C condition across days 1–13 (Fig. 7, top; Table 2). On day 14, withdrawal scores in the 1C condition increased with implementation of the abstinence contingency while remaining relatively unchanged in the 14C condition (Table 2). Total NWQ scores did not differ significantly between the 14C and 1C conditions on day 14.

Mean ratings of "Desire to Smoke" in the 14C condition were at peak levels on days 1–3 and then decreased to baseline levels by day 5 where they generally remained, while ratings in the 1C condition decreased below baseline levels or remained unchanged during days 1–13 (Fig. 7, bottom; Table 2). On day 14, mean ratings were elevated in the 1C condition significantly above those in the 14C condition (Table 2). Other visual-analog ratings of craving to smoke generally showed similar changes.

Mean QSU Factor 1 scores, which measures expectations of positive outcomes from smoking, showed no significant differences between the 14C and 1C conditions during days 1–13 (Fig. 8, top; Table 2). On day 14, however, mean scores for the 1C condition were elevated significantly above those in the 14C condition (Table 2). Mean ratings on the QSU Factor 2 scale, which measures expectation of relief from negative effect with smoking, peaked on day 1 and decreased as a function of time in the 14C condition while remaining relatively unchanged in the 1C condition during days 1–13 (Fig. 8, bottom; Table 2). On day 14, mean scores increased in the 1C condition significantly above those in the 14C condition (Table 2).

Mean VAS ratings of "Alert" decreased and ratings of "On Edge" and "Tired" increased in the 14C condition compared to the 1C condition during days 1–13 (Table 2). On day 14, mean ratings of "On edge" increased significantly in the 1C condition compared to those in the 14C condition, while ratings of "Alert" and "Tired" did not differ between conditions (Table 2).

Other participant ratings None of the POMS subscales showed significant differences between experimental conditions for days 1–13 (not shown). On day 14, only the POMS measure of "Vigor" showed a difference with participants in the 14C condition reporting significantly greater Vigor than those in the 1C condition (Table 2).

The MCP showed no significant differences between the experimental conditions. Crossover points, the monetary values at which participants shifted from preferring cigarettes to money, decreased over time, but there were no significant interactions with experimental conditions (data not shown).

Discussion

The current study replicated the main findings of the Lussier et al. (2005) study while reducing the frequency of abstinence monitoring to once daily and broadening the bio-verification methods to include urine cotinine in addition to breath CO. The robust experimental control achieved over smoking in the present study provides clear support for the feasibility of using once-daily abstinence-monitoring as opposed to the thrice-daily monitoring used in our prior studies. Such a reduction in the frequency of laboratory visits significantly lowers the demands of the model on staff and participants alike. The use of urine-cotinine testing to verify smoking abstinence during week 2

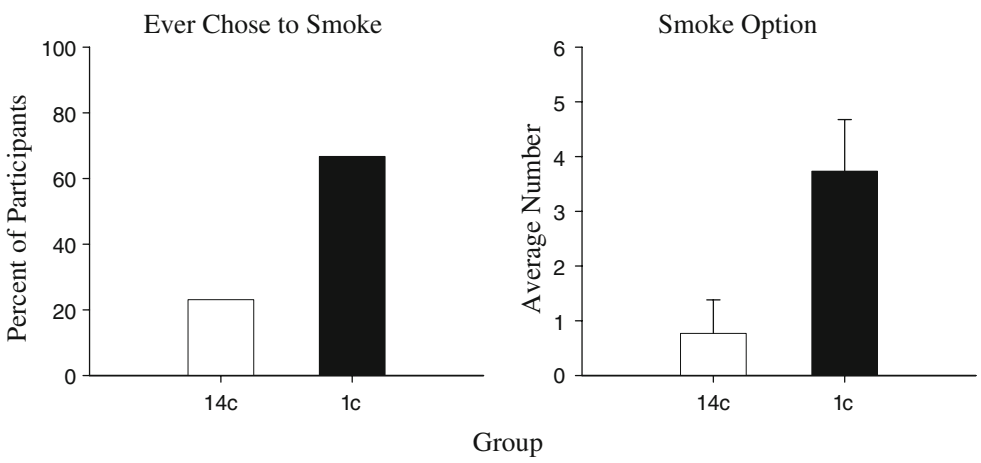

Fig. 4 Smoking patterns during the preference session for the 14C (*open bars*) and 1C (*filled bars*) conditions. The *left panel* shows the percentage of participants who chose the smoking option at least once during the preference session. The *right panel* shows the average number of times the smoke option was chosen during the preference session. *Error bars* represent ±SEM

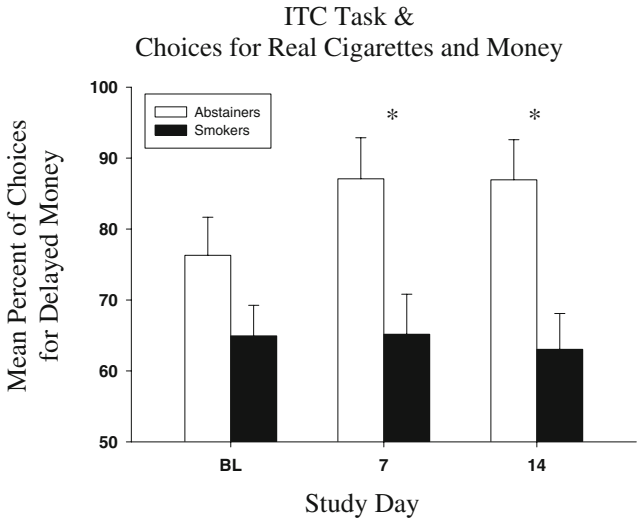

Fig. 5 Mean percentage of total choices for the delayed money option in the ITC task at baseline, day 7, and day 14 for those who were smokers (*filled bars*) and abstainers (*open bars*) during the smoking-preference session. *Vertical bars* represent±SEM. Note that the ordinate axis begins at 50%

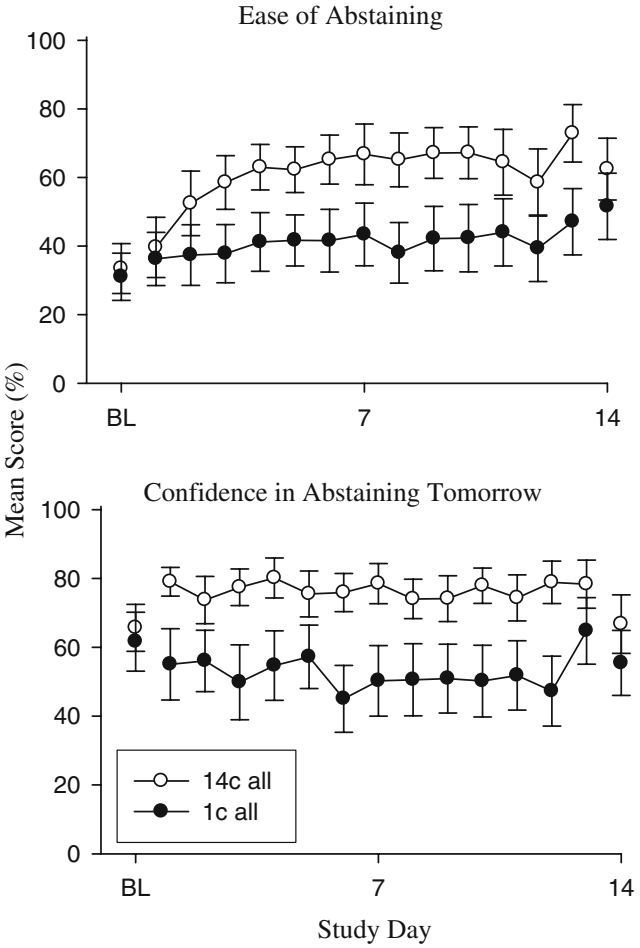

Fig. 6 Mean VAS ratings on "Ease of Abstinence" (*top*) and "Confidence in Abstaining Tomorrow" (*bottom*) as a function of study day. All VAS ratings ranged from 0=Not at all to 4=Extremely. All other details are as in Fig. 1

may permit less than daily monitoring as well although that possibility was not investigated in the present study. This more efficient schedule should make it easier to recruit study participants who have full- or part-time jobs, thereby increasing the size of the pool of potential participants and also the likelihood of obtaining a sample that is more representative of the general population of smokers. For example, in the Lussier et al. (2005) report from our group, the average age of participants was approximately 21 years old; most were college students, whereas the average age in the present study was almost 30 years old and approximately half were non-students. These are all features that should increase the utility of this CM model for experimentally analyzing the effects of initial smoking abstinence.

Inclusion of the two tasks involving choices between hypothetical consequences in the present study resulted in new knowledge that may enhance understanding of the changes that occur during the initial weeks of smoking abstinence. No significant changes in the DD task were observed. Those negative results, however, are congruent with previous observations from our group where discounting of money remained stable across a period of sustained smoking abstinence lasting many months (Yoon et al. 2007). Also worth mentioning is that *k* values observed in the current study are consistent with the extant DD literature showing that smokers are relatively steep discounters on the money versus money task. More specifically, the *k* values observed in the present study were relatively high as has been reported for smokers and relatively lower than *k* values that have been reported for non-smokers (Bickel et al. 1999).

In contrast to the DD task, the choice task examining preference for more immediately available hypothetical cigarettes versus delayed money (ITC task) was sensitive to the effects of smoking abstinence. That is, participants in the 14C condition made significantly more choices for the delayed hypothetical money option relative to those in the 1C condition as a function of smoking abstinence. Considering together the results from the two-choice tasks involving hypothetical consequences, it seems likely that the changes in the ITC task are more attributable to changes in the relative reinforcing effects of smoking than how participants responded to delays to reinforcement per se. By the day-7 assessment, a subset of participants in the 14C condition was already exhibiting an exclusive preference for the hypothetical money over the hypothetical cigarettes option across all delays, an effect that was sustained through the day-14 assessment. Participants in the 1C condition, by contrast, exhibited no such increase in preference for the money option over the cigarettes option

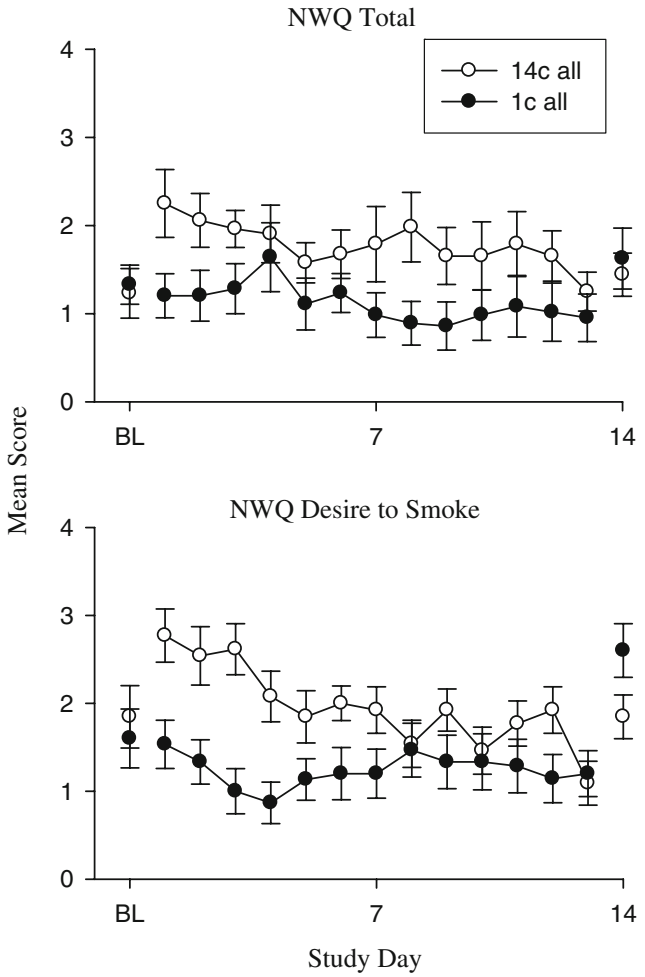

Fig. 7 Mean MNW Total (*top*) and "Desire to Smoke" (*bottom*) scores as a function of study day. Scale ranged from 0=None to 4=Severe. The MNW Total score is the overall average score of all items except "Desire to Smoke". All other details are as in Fig. 1

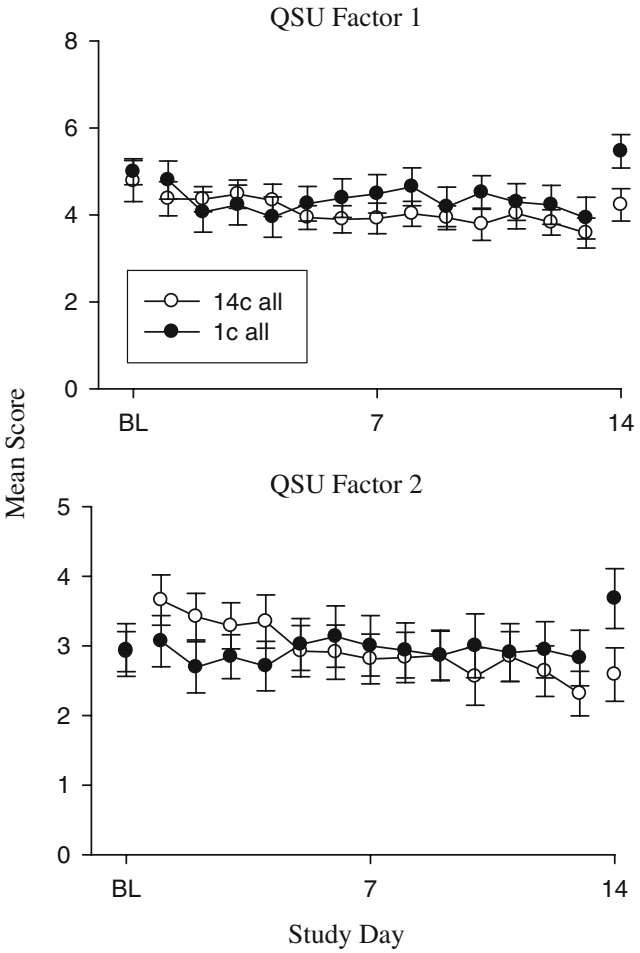

Fig. 8 Mean QSU Factor 1 (*top*) and Factor 2 (*bottom*) scores as a function of study day. Scores for the QSU ranged from 1=Strongly Disagree to 7=Strongly Agree. All other details are as in Fig. 1

across the same period and the single day of exposure to the abstinence-reinforcement contingencies on day 14 in the 1C condition had no discernible effect on ITC of hypothetical cigarettes versus money. Thus, this effect in the ITC task comparing cigarettes versus money appears to be a function of changes in the relative reinforcing effects of smoking rather than delays to reinforcement. The onset of the effect occurs somewhere between 2 and 7 days of continuous exposure to the abstinence-reinforcement contingencies and grows slowly if at all between 7 and 14 days of exposure.

Results from the smoking-preference session involving real money and cigarettes replicate the prior findings of Lussier et al. (2005) that 14 days of exposure to abstinence-reinforcement contingencies significantly decreases the relative reinforcing effects of smoking. In that prior study, 19% versus 62% of participants in the 14C and 1C conditions ever chose the smoking option compared to 23% versus 67% in the present study. Those results also demonstrate congruence between results from a task using real consequences and those obtained in the ITC task using hypothetical consequences. Such reliable effects across studies and consistent results across the smoking-preference and the ITC task suggests that the decrease in the relative reinforcing effects of smoking observed are not likely due to some artifact of the particular smoking arrangement or parameters being investigated in the smoking-preference session. Instead, they appear to reflect a more general and thus potentially more important change in the relative reinforcing effects of smoking during the initial 2 weeks of smoking abstinence.

Participant ratings were generally consistent with a lowering of relapse risk across the study period among participants in the 14C compared to the 1C condition. That is, on day 14 participants in the 14C condition reported significantly less smoking craving and lower expectations of positive and negative reinforcement from smoking as measured by the QSU Factors 1 and 2 scales, respectively, than did participants in the 1C condition who were in their

first day of smoking abstinence. This profile of less craving and lower expectations of reinforcement from smoking is certainly suggestive of a direct lowering of relapse risk following 14 days compared to 1 day of smoking abstinence. Which of the participant-rating measures showed significant differences between the 14C and 1C conditions on day 14 has varied across studies using this model, but what has remained consistent is that the profile is always in a direction suggestive of lower relapse risk in the 14C compared to the 1C conditions (Alessi et al. 2004; Chivers et al. 2008; Lussier et al. 2005).

Important to acknowledge is that not all measures in the present study produced results consistent with a lowering of the relative reinforcing effects of smoking or relapse risk. In particular, no significant changes were noted in the amount of hypothetical money participants would take instead of a pack of cigarettes in the MCP procedure. As was noted above, the MCP task asks participants to choose between either a pack of cigarettes or an amount of money ranging from $0.25 to $20.00 based on how they feel at the moment the test is being administered. The negative results in the current study are consistent with previous results from similar experiments conducted in our laboratory (Alessi et al. 2004; Chivers et al. 2008; Lussier et al. 2005). We previously thought that our exclusive reliance on hypothetical consequences in the MCP may have been responsible for this insensitivity, but the significant effects obtained using hypothetical consequences in ITC task in the present study suggest that is probably not an adequate explanation. Something else regarding, for example, the way that participants are being instructed about the task or the wording used to describe the smoking and monetary options may be leading participants to respond differently in this arrangement. Certainly the MCP has been a sensitive measure of the relative reinforcing effects of drugs in other arrangements (e.g., Griffiths et al. 1993; Mumford et al. 1995). Why it has not been to date in this arrangement will have to be determined in future studies.

Continuing on the topic of potential differences across procedures, a 7C condition included in the Lussier et al. study did not result in any discernible change in smoking preference while in the present study 7 days of exposure to the abstinence-reinforcement contingencies was sufficient to produce a robust change in responding in the ITC task. Likely explanations for that difference are variability in the time-course of a common effect or that the change manifests itself sooner in a task involving hypothetical consequences than it does in a choice arrangement where real cigarettes are present and the opportunity to smoke is relatively immediate. That is another procedural matter that will have to be parsed out in future studies.

We did not conduct follow-ups with any study participants and thus cannot answer whether any of them remained abstinent after the study was completed. Considering that these participants were recruited because they were not currently planning on quitting smoking long-term and the generally high levels of relapse among even those who are seeking to quit, we deem it highly likely that most if not all of our participants resumed smoking shortly following study completion.

The present study has two potential limitations worth noting. First, duration of exposure to the contingent-reinforcement condition and the amount of abstinence achieved were confounded in the current experimental design. Thus, the possibility remains that abstinence achieved through means other than contingent reinforcement might have produced different effects. We think that is unlikely in that type of treatment has not been a significant factor in treatment-outcome studies examining associations between abstinence in the initial weeks of a cessation effort and abstinence at follow-up among cigarette smokers or cocaine-dependent outpatients (Higgins et al. 2000; Kenford et al. 1994). We do think it is likely that interventions that produce abstinence by removing the user from the typical substance-using environment (inpatient/residential treatments) would produce less carryover into the post-treatment period than interventions where abstinence was established in the substance-using environment (outpatient interventions), in that the former provide little opportunity compared to the latter for extinguishing control by drug-associated stimuli and developing alternative sources of non-drug reinforcement. Second, using participants not trying to quit smoking long-term could limit the generalizability of the current findings to those who are trying to quit longer term. We see no obvious reason why the results would not generalize to smokers trying to quit long-term, but this is an empirical question. We recently reported an experiment using different magnitudes of abstinence-contingent voucher-based reinforcement to produce different amounts of cocaine abstinence during the treatment period (Higgins et al. 2007). The experimental condition with significantly greater during-treatment abstinence also achieved significantly greater post-treatment abstinence during an 18-month follow-up period. We know of two published reports with cigarette smokers where abstinence-contingent monetary payment was used to create significantly different levels of abstinence while the contingencies were in place and then assessed abstinence during follow-up (Dunn et al. 2008; Gilbert et al. 1999). In both instances abstinence levels post-treatment were several-fold higher in the condition with greater during-treatment abstinence compared to the condition with less, but in both studies the differences failed to achieve statistical significance. Thus there is prospective, experimental evidence supporting the generalizability of the findings from the present study to individuals trying to quit longer term, although the results

among cigarette smokers are not definitive and will need to be investigated further.

In summary, the present study was designed to investigate methodological changes in a laboratory model of initial smoking abstinence that would make it less demanding and more rigorous while also broadening understanding of changes in behavioral processes that occur during the initial weeks of smoking abstinence. The results offer strong support for the feasibility of using procedures wherein smoking abstinence is monitored only once daily with breath CO in week 1 and urine cotinine in week 2. The results demonstrate for the first time that sustaining smoking abstinence results in significant changes in an ITC task involving choices between more immediate hypothetical cigarettes versus delayed hypothetical money, an effect that is likely attributable to decreases in the relative reinforcing effects of smoking. The results obtained in the session involving real monetary and smoking reinforcement were consistent with the results from the ITC task and offer further evidence that a 2-week period of initial abstinence directly lowers the relative reinforcing effects of smoking reinforcement. Participant ratings across the 2-week study period offer a consistent picture of lower desire to smoke and lower expectations of positive or negative reinforcement from smoking. Taken together these findings support a position that a period of initial smoking abstinence may directly lower relapse risk among cigarette smokers.

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