Approach bias retraining to augment smoking cessation: Study protocol for a randomized controlled trial[☆]

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A B S T R A C T

Heavy users and addicted individuals have shown to develop an approach action tendency – or approach bias – toward stimuli related to the substance of interest. Emerging evidence points to approach bias retraining (ABR) as an effective aid for the treatment of addictive behaviors. The current study seeks to extend this work by testing, in a pilot study, whether standard smoking cessation treatment involving cognitive-behavioral therapy (CBT) and nicotine replacement therapy can be augmented by ABR. To this end, we will randomly assign 100 adult smokers to either ABR-augmented treatment or placebo-augmented treatment and compare the two conditions on short-term and long-term abstinence rates. The hope is that the findings of this study can inform treatment development for adult smokers.

1. Introduction

Cigarette smoking remains the most preventable cause of death in the United States [1]. Combination interventions (e.g., cognitive behavioral therapy [CBT] plus nicotine replacement therapy [NRT]) are effective but associated with high relapse rates [2]. Hence, there is a need for new, innovative smoking cessation strategies that can engage core mechanisms implicated in the maintenance and cessation of smoking [2].

Consistent with incentive-sensitization theory [3], dual process models of addiction posit that repeated drug use sensitizes automated impulsive, implicit processes [4,50]. Specifically, because drug-related cues become a signal of reward over time, heavy users and addicted individuals develop an approach action tendency – or approach bias – toward stimuli related to the substance of interest [4,5].

Among different assessment strategies, the Approach-Avoidance Task (AAT [6]; has emerged as a suitable tool for assessing approach bias [7]. This 15-min computerized task instructs participants to use a joystick to either pull toward themselves or push away from themselves images presented on the screen that vary in content (i.e., substance-related, neutral, positive) and format (e.g., right- or left-tilted). Specifically, using indirect task instructions (i.e., responding to the format instead of content), participants are told that all pictures will be slightly

tilted to the left or right, and that they are to pull right-tilted pictures and push left-tilted pictures. Importantly, pulling the joystick increases the size of the image, while pushing the joystick decreases the size of the image, thus causing visual approach and avoidance effects, respectively. The AAT involves multiple trials and records reaction times (RT) for each trial. The RTs for each trial are then used to compute an index of approach bias – i.e., the relative tendency to pull rather than to push in response to the presentation of substance-related images [8,9]. Using the AAT, researchers have shown that approach bias is evident in problem users of alcohol [4,10,11] and cannabis [8] as well as cigarette smokers [4,12,13], although there are studies that have not observed the relation between substance use problems and approach bias [9].

Manipulating approach bias – or training persons with substance use problems to push away substance-related images – has shown promise for enhancing outcomes of substance use treatments [4,11,14–16]. Approach bias retraining involves repeated administrations (sessions) of a modified AAT, which involves changing the contingencies of the AAT assessment task ensuring that participants learn to engage in avoidance (pushing the joystick) when presented with substance-use related pictures. In the treatment of alcohol use disorder, an initial study involving 214 inpatients receiving CBT showed that, compared to those who received no training or 4 sessions of a control intervention (i.e., repeated AAT assessment tasks involving equal number of

avoidance and approach movements to alcoholic and non-alcoholic drinks), participants assigned to receive 4 sessions of approach bias retraining evidenced significantly lower relapse rates at 1-year follow-up [11]. Importantly, this finding was replicated and extended in a larger sample (N = 509), indicating approximately a 10% reduced relapse rate in training vs. control and evidence of reductions in approach bias mediating the clinical effect [14].

Building upon this research, we recently completed a pilot study [17] involving adult smokers motivated to make a quit attempt (N = 52) and tested (1) whether 4 sessions of approach bias retraining would reduce approach bias (i.e., target engagement) and (2) whether target engagement would be associated with the numbers of days quit in the week following an unaided and self-guided quit attempt (i.e., initial estimate of efficacy; [18]. Data supported both hypotheses and provided evidence for a small, albeit statistically non-significant, effect of training on days quit in the week following the quit attempt [17]. Together, these promising findings support next-stage research aimed at evaluating approach bias retraining to aid standard smoking cessation interventions.

Mechanistic research is critical for optimizing interventions [19]. Hence, although the primary aim of this study is to examine whether approach bias retraining can aid smoking cessation, we will test whether the effect of approach bias retraining on abstinence is in fact accounted for by a reduction in approach bias (i.e., target engagement). Consistent with incentive-sensitization theory [3], initial research in smokers shows that approach bias covaries with self-reported craving [4] and research in alcohol use disorders shows that approach bias retraining reduces craving [11,14,20]. Because reduced craving has been shown to mediate other treatments for smoking cessation [21,22], we will also test whether reduced craving mediates the relation between reduced approach bias and abstinence. Finally, recognizing that the efficacy of interventions and their mechanisms may vary as a result of individual differences [19], we will explore the potential moderator effect of nicotine dependence, which has been related to approach bias [23] and smoking cessation outcomes [24], respectively, as well as sex, consistent with priorities of the NIH.

2. Methods

2.1. Study design

Adult smokers (N = 100) will be randomly assigned to either (1) 7 weeks of standard smoking cessation treatment involving CBT and NRT (standard treatment [ST]) integrated with approach bias retraining (ST + ABR) or (2) ST integrated with sham training (ST + CTRL). Smoking status will be assessed at baseline, during the treatment period, and during the post-treatment period at weeks 8, 9, 13, and 17.

2.2. Specific aims

1. To assess, in a randomized clinical trial, the effects of ST + ABR vs. ST + CTRL on the following smoking cessation outcomes: Short- and long-term point prevalence abstinence (PPA) and prolonged abstinence (PA). We hypothesize that PPA and PA will be higher, both in the short term and long term, for those in the ST + ABR condition than for those in the ST + CTRL condition. We further hypothesize that the rate of decline in abstinence over time will be smaller in the ST + ABR condition than for those in the ST + CTRL condition.
2. To examine potential mechanisms of action. In testing the putative mechanisms of action, we hypothesize that a reduction in approach bias mediates the effects of the intervention on abstinence. Additionally, we will explore the role of reduced cravings as a mechanism underlying the approach bias-abstinence relation. We further hypothesize that reduced craving mediates the relation between reduced approach bias and abstinence. To determine possible

moderators, we will test whether the efficacy and mechanisms vary as a function of nicotine dependence and sex, respectively.

2.3. Participants

Participants will be 100 adult smokers between the ages of 18 and 64, who have been smokers for at least one year, and smoke at least 5 cigarettes per day. Participants must report a motivation to quit smoking of at least a 5 on a 10- point scale and must also be willing and able to commit to a 17-week protocol.

In order to reduce the risk of adverse events, we will employ the following exclusion criteria: (1) a lifetime history of bipolar disorder, schizophrenia, or psychosis; (2) an eating disorder in the last 6 months; (3) an alcohol or substance abuse disorder in the last 6 months; (4) visual or hand-motoric impairments; (5) use of other tobacco products; (6) current use of any other pharmacotherapy or psychotherapy for smoking cessation not provided by the researchers during the quit attempt.

3. Procedures

The study is funded by the National Institute on Drug Abuse (NIDA; R34DA044431) and is registered on clinicaltrials.gov (ID: NCT03325777). The Institutional Review Board of the University of Texas at Austin approved the study and a Data Safety and Monitoring Board provides ongoing oversight. The study is currently in the recruitment phase.

3.1. Screening

We will employ a variety of recruitment strategies to direct interested individuals to an online prescreen using REDCap (Research Electronic Data Capture), an electronic database hosted at the University of Texas at Austin. The prescreen will assess basic study entry criteria, and individuals who pass the initial screen will advance to a clinical phone interview. The DSM-IV edition of the Mini International Neuropsychiatric Interview (MINI) [25] will be used to assess for exclusionary criteria. MINIs will be conducted exclusively by highly trained study staff with at least a bachelor's degree and will be supervised by the principal investigator. MINI phone screenings will be supervised and reviewed on a weekly basis to ensure quality control and rater competency. Eligibility screenings and clinical interview data will be stored in REDCap.

3.2. Enrollment/randomization

If eligible following the MINI, participants will schedule a baseline session at UT Austin. Upon enrollment, eligible participants will be randomized to either ST + ABR or ST + CTRL condition. The project biostatistician will generate the randomization using variable-sized permuted block-randomization, with block sizes varying from 4 to 12. Randomization will be stratified by sex and scores on the Test for Nicotine Dependence (TND) (i.e., 1–4 indicative of low to moderate dependence vs. 5–10 as moderate to high dependence). The participants will be blind to study condition. Prior to any baseline assessment, participants will receive an online consent form outlining the details of the study, potential risks and benefits of participation, and the procedures they will undergo if they choose to participate. Research staff will address concerns and answer any questions the potential participant may have about the study. Once the individual signs the online consent form, he/she will be cleared for the baseline visit.

During this baseline visit, participants will be asked to complete baseline assessment measures. At the beginning of the baseline session, participants will be introduced to the program's cessation goals and reminded of intervention procedures and timeline. Lastly, participants will be oriented to and instructed to complete a baseline assessment of

approach bias for smoking stimuli with the AAT (see below).

3.3. Interventions

Standard Smoking Cessation Treatment + Approach Bias Retraining (ST + ABR). Consistent with the manualized procedures we have employed in past and ongoing NIDA-funded investigations [26–29], the standard intervention (ST) involves a combination of CBT plus NRT. As outlined in the therapist manual, CBT will involve 45-min weekly sessions over a 7-week period. Weeks 1–4 focus on preparing participants for their quit day, which is scheduled for the beginning of week 5. The study therapists will cover topics such as smoking and abstinence history, individualized smoking cessation barriers, maladaptive cognitions around the use of cigarettes, using cigarettes as a way to cope with stress and negative affect, and identifying and planning for triggers and high-risk situations. Therapy sessions will be conducted by trained study staff supervised weekly by the second author. All sessions will be audio recorded and 10% will be rated by independent raters to ensure therapist adherence to the treatment protocol. Participants will be provided with specific instructions on how to use the Nicoderm CQ(R), 24-h transdermal nicotine patches, starting on their quit date. We will provide 8-weeks' worth of nicotine patches consistent with guidelines [2].

Each of the treatment sessions following baseline will begin with a 15-min ABR task. Participants in the ST + ABR condition will be told that the computerized training is designed to complement the behavioral counseling by weakening automatic cigarette-approach and strengthening automatic cigarette-avoidance. Participants will be instructed to pull or push the joystick depending on the tilt of the picture (i.e., right-tilted vs. left-tilted). Each training session will start with a short assessment phase of 48 trials (12x pull smoking, 12x push smoking, 12x pull positive, 12x push positive). We will use this assessment phase to calculate an approach bias score at the start of each ABR training session, allowing us to measure the change in approach bias over time. This will be followed by the training phase of 192 training trials consisting of 96 positive pictures with the to-be-pulled tilt and 96 smoking images with the to-be-pushed tilt. Accordingly, in these trials participants will always avoid smoking-related images and always approach positive images.

Standard Smoking Cessation Treatment + Sham Training (ST + CTRL). Participants assigned to the ST + CTRL condition will be prescribed identical standard care to that of the experimental group. The two groups differ only in the computerized training they will receive. In order to create comparable expectancy effects and enhance experimental control, we will provide participants assigned to this training condition with a highly plausible rationale for augmenting standard smoking cessation. Similar to our pilot study examining ABR for smoking cessation and our other past work examining ABR for preventing relapse in alcohol use disorder, we will tell participants that the computerized training weakens the automatic tendency to approach cigarettes by improving control over this automatic tendency (e.g., learning to ignore urge to approach and respond only to task instructions) and that following the training, they will easily be able to approach or avoid regardless of image content [17]. They also will be instructed to pull or push the joystick depending on the tilt of the picture (i.e., pull right-tilted vs. push left-tilted). However, instead of avoiding all smoking-related pictures, participants in the ST + CTRL condition will pull and push all pictures equally often. This yields an assessment phase of 48 trials (12x pull smoking, 12x push smoking, 12x pull positive, 12x push positive) and 192 training trials consisting of 96 images tilted to the right and 96 images tilted to the left.

3.4. Post-treatment follow-up

Participants will be asked to attend brief 10–15-min follow-up sessions at weeks 8, 9, 13, and 17 (see Table 1). The study staff will check in with participants regarding self-reported smoking status and collect biochemical verification measures. In the event that participants are unable to attend lab follow-visits, study staff will contact participants to collect self-report smoking status assessments.

4. Assessments

4.1. Screening

Demographics. Participants will be asked to provide standard demographic information (i.e. name, contact information, age, sex, race/ethnicity, level of education, etc.).

Smoking History Questionnaire (SHQ). Smoking history and pattern will be assessed with the SHQ, a 30-item measure that includes items pertaining to smoking rate, age of initiation, years of being a habitual smoker [30]. This measure will serve to contextualize the participants' smoking behavior and history at intake.

Test for Nicotine Dependence (FTND). The FTND is a 6-item scale designed to assess gradations in tobacco dependence [31]. This measure will serve to quantify nicotine dependence, which will be used as a covariate in the primary analyses.

Motivation to Quit. Participants will be asked to self-report their motivation to quit smoking cigarettes on a 10-point Likert scale, with 1 being not at all motivated to 10 being extremely motivated.

MINI International Neuropsychiatric Interview (MINI). The MINI is a short structured clinical interview for diagnosis of psychiatric disorders according to DSM-IV [25]. The MINI will be administered by trained research personnel with a B.S. or B.A. in psychology and will be supervised by the doctoral-level staff. Modules B-Suicidality, C-Manic Episode, I-Alcohol Dependence and Abuse, J-Substance Dependence and Abuse, K-Psychotic Disorders, L-Anorexia Nervosa, M-Bulimia Nervosa, and O-Medical, Organic, Drug Cause Ruled Out will be used to assess exclusionary criteria.

4.2. Smoking status

As in past and ongoing work [26–29], self-reported smoking status will be assessed during the intervention (weeks 0–7), at posttreatment (week 8), and at 1-month (week 9), 2-month (week 13) and 3-month (week 17) follow-up (i.e., post-quit). Self-reported abstinence will be verified by expired carbon monoxide (CO). Abstinence at the 2-month (week 13) and 3-month (week 17) follow-up will additionally be verified with saliva cotinine. We will use the timeline follow-back (TLFB) procedure at all assessments to assess daily cigarette consumption; this procedure has demonstrated good reliability and validity [32]. Self-reported abstinence will be overridden by a positive carbon monoxide (> 4 ppm) [33] or saliva cotinine verification (> 10 ng/mL) [34]. If neither CO nor cotinine levels are available to verify abstinence at an assessment, abstinence will be considered missing data [35]. We will employ 7-day point prevalence abstinence (PPA) and prolonged abstinence (PA) as the primary outcomes. PPA will be defined as no smoking, not even a puff, in the 7 days prior to any assessment. Failure to maintain PA at any assessment will be defined by smoking on 7 consecutive days or smoking at least once each week over 2 consecutive weeks [36].

4.3. Approach bias

Assessment. We will administer the AAT [13,17,37] in order to assess approach bias at baseline. The AAT instructs participants to pull a joystick upon seeing an image tilted to the right and to push the joystick upon seeing a left-tilt image, while ignoring the image content (i.e., indirect instructions). By pulling the joystick (approach), the picture grows in size; by pushing the joystick away (avoidance), the picture shrinks. The AAT includes 96 trials in which each of 24 smoking-related pictures (e.g., woman lighting a cigarette) and each of 24 positive

Table 1
Assessment schedule.

	Protocol weeks						
	> -1	0	1–4	5	6	8	9–17
	End points						
	Pre-screen	Baseline	Pre-Quit	Quit Week	1-Week Follow-Up	Post-treatment	1-, 2-, 3- Month Follow-Up
Screening							
Demographics	X						
Smoking history (SHQ)	X						
Motivation to quit	X	X	X	X	X	X	X
Nicotine dependence (FTND)	X						
Psychiatric diagnosis and suicide (MINI)	X						
Aim 1: Efficacy							
Timeline follow-back		X	X	X	X	X	X
Carbon monoxide		X	X	X	X	X	X
Saliva cotinine							X[a]
Aim 2: Mechanisms of Action							
Craving (QSU-B)		X	X	X	X		
Approach Bias (AAT; session data)		X	X	X	X		

[a] Only assessed at 2- and 3- month follow-up.

images (e.g., group of friends exercising) will be pulled and pushed. We selected positive stimuli because there are no intuitive control stimuli to cigarettes (like there is for alcohol; i.e., non-alcoholic beverages) and this set of images has been successfully used in other pilot work by members of our research group [17].

Scoring. An approach bias score for smoking-related pictures will be computed for each participant by subtracting the average time it takes to pull smoking-related images from the average time it takes to push away these images. Thus, a positive value indicates an approach tendency toward smoking stimuli, whereas a negative value is indicative of avoidance of smoking images.

Furthermore, each training session will begin with a short assessment phase of 48 trials (12x pull smoking, 12x push smoking, 12x pull positive, 12x push positive). This assessment phase will be used to calculate an approach bias score at the start of each ABR training session, thus allowing our group to measure any changes in approach bias across protocol weeks. Finally, we will explore scoring algorithms for the AAT and session data that standardize the bias scores by dividing an individual's difference in response times by a personalized standard deviation of these response latencies. A similar scoring approach has been used successfully for a related task, the Implicit Association Test (IAT; [38]).

4.4. Craving

The Questionnaire of Smoking Urges (QSU) is a 10-item measure that assesses urges and cravings for cigarettes [39]. We will administer this measure at baseline, weekly throughout treatment, and at the follow-up assessments.

4.5. Participant adherence and incentives for participation

We will utilize a number of strategies in efforts to promote adherence and retention. Prior to randomization, participants will have completed an extensive screening process. Participants will also be provided a document informing them of the study expectations. Staff will manage retention of the participants. If a participant misses a session, staff will call to check in, encourage attendance, and help problem solve if a barrier to participation is present. Staff will also monitor adherence to the assessment schedule and will place reminder calls/emails to participants three days prior to each scheduled follow-up session.

Finally, we will provide $250 per individual (i.e., $50 for completing each major outcome assessment; weeks 0, 6, 9, 13, and 17) as an incentive for participation in the study. We think this amount is appropriate given the amount of time required for completing the assessments.

5. Data analysis

5.1. Overview

The primary objective of this project is to estimate the effect size for the advantage of ST + ABR over ST + CTRL for smoking cessation. At the same time, we are aware of the dangers of relying on small-scale pilot studies to assess the potential of novel treatment approaches [40] because the effect size estimates have a large standard error. We believe that a sample size of 100 is more than sufficient to provide adequate estimates of the intervention effect size, while staying within the scope of a developmental project. We recognize that small effect sizes will not be detectable as significant with a sample of this size.

We will first assess the equivalence of the treatment groups on key baseline variables (demographics and psychological variables); variables on which the groups differ will be used as covariates in the final analyses. We will then examine missing data patterns, dropout rates (see below), and distributional properties of measures, and use transformations to improve distributions if necessary.

Abstinence data (PPA and PA) will be analyzed using multivariate Generalized Linear Mixed Models (GLMM), employing the program HLM 7.0 with a logistic linking function (see below for details of the model). GLMM includes all subjects, regardless of missing data, and does not require imputation of missing data (e.g., missing data is not automatically coded as smoking, as in last-observation-carried-forward analyses [35]. This is the recommended intent-to-treat approach for longitudinal smoking cessation trials [41].

We will use *multivariate* GLMM (with PA and PPA as the multiple dependent variables [DVs]) because multivariate mixed models have greater power than univariate mixed models [42], and because assessments at each time point are included as long as at least one of the DVs is available at that time point. Thus, multivariate GLMM incorporates all available data from all DVs. In addition, since performing a single multivariate analysis obviates the need for the use of a conservative p-value to correct for the false discovery rate when performing multiple univariate tests of each DV, this multivariate GLMM allows us to maximize power without increasing the false discovery rate. Hereafter, when we use the general term "abstinence" it will refer

to the multivariate outcome of PPA and PA together.

As in previous research [26–28], we will use a 3-phase piecewise growth curve model to track PPA and PA over the 17 week study period. The first phase of the growth model consists of weeks 0–5 (pre-quit treatment phase), the second phase will be weeks 6–8 (post-quit/treatment phase), and the third phase will be from weeks 8–17 (post-treatment phase). Modeling the growth curve starting at week 0 is necessary for intent-to-treat analyses. We will model the change over time as linear within each phase, and model a discontinuity in the growth curve between the first and second phase to reflect the expected effects of the scheduled quit day during week 5. We will use the parameterization of piecewise models described by Singer and Willett (2003). Thus, the models will include a Time variable for each phase of the model (Time1, Time2, and Time3), each of which is coded to reflect weeks since baseline during each phase, and a dichotomous variable (coded 1 for weeks 0–5, and 0 for weeks 6–17) to code the discontinuity between phase1 and phase 2 (see Singer and Willett, 2003). All the Time variables, the discontinuity variable, and the intercept will have random effects. Non-significant random effects will be dropped. The models will also include treatment condition and its interactions with each Time variable and with the discontinuity variable. Demographics, baseline nicotine dependence, and any baseline psychological variables on which treatment conditions differ, will also be included as covariates (and retained if significant). Finally, in order to explore whether dose predicts abstinence, and to reduce variance in abstinence related to treatment dose, we also will include attendance, and the attendance × condition interaction, as terms in the GLMM models and as moderators of the slopes during each phase of the study. Since the primary end-point is the 3-month follow-up, all Time variables will be centered at the 3-month follow-up so that treatment condition differences will reflect differences at the 3-month follow-up. Our secondary endpoint is post-treatment.

In order to minimize Type II error, provide a more parsimonious model that fits the data, and to more clearly elucidate the significant relations between the predictors and abstinence, we will recompute the final model after removing non-significant interaction terms [43,44].

5.2. Aims

Aim 1a (ST + ABR will engender higher abstinence rates (PPA and PA as multivariate DVs) at post-treatment and at the 3-month follow-up, compared to ST + CTRL)

In two multivariate GLMM analyses, we will alternately "center" our Time variables at 1) the 3-month follow-up or at 2) post-treatment, to estimate between-group differences at these respective end points, which will be indicated by the treatment condition main effect in each analysis. If significant in an analysis, the treatment condition effect will demonstrate that abstinence rates are significantly different between the treatment conditions at the respective end point. In addition, we expect slopes of decrease in abstinence after quit week (in phases 2 and 3) to be steeper (worse) in ST + CTRL compared to ST + ABR (the Condition × Time interaction).

Aim 1b (Mean time to first lapse and to relapse to be greater for those in the ST + ABR condition than for those in the ST + CTRL condition)

We will use Cox proportional hazard models to assess the between-group difference in time to lapse and time to relapse.

Aim 2a (Greater abstinence in ST + ABR compared to ST + CTRL will be partially mediated by reductions in approach bias)

We will use multilevel modeling (MLM) instead of GLMM to calculate the "a" path in our mediation model (the effect of treatment on approach bias) because the outcome for the "a" path is continuous. The "b" path in our mediation model will be the regression coefficients for *approach* bias when it is added to the multivariate GLMM analysis predicting abstinence (the model in Aim 1a). In order for the "b" path to more closely estimate the causal relation between *approach* bias and

abstinence, we will use a cross lag mediation analysis, in which the mediator at time "t" predicts the outcome at the next assessment ("t +1"), controlling for the outcome at time "t" (as we have done in previous multimediator longitudinal models [45]). Further, for accurate calculation of the cross lag effects, recent research [46–48] indicates that one must disaggregate the between-person and within-person components of the time-varying predictor (i.e., the mediator), but still estimate both effects in the same model. Thus, we will include both between- and within-person effects of all mediators in our models. The significance of the mediated pathway (and all mediated pathways in this grant) will be calculated using the distribution of products test performed by the program RMediation [49].

Aim 2b (Craving will mediate the effect of approach bias on abstinence)

We will calculate the "a" path in this mediation analysis by calculating the disaggregated cross lag effect of *approach* bias at time "t" on craving at time "t+1", controlling for craving at time "t" (we must calculate the cross lag effect for the "a" path in this analysis because *approach* bias is not randomized). The "b" path will be calculated using disaggregated cross lag mediation analysis, with craving at time "t" and abstinence at time "t" predicting abstinence at time "t+1".

Aim 2c (Sex and nicotine dependence as moderators of treatment effects)

To determine whether sex moderates the effect of condition on abstinence, we will add interactions between sex and all of the growth curve parameters in the multivariate GLMM piecewise growth curve model testing Aim 1a. Any significant interaction will indicate that there are sex differences in that portion of the piecewise growth curve. To investigate if mediation depends on sex, we will add the interaction of sex with the "a" path, the "b" path, and the "c'" path in our mediation model in Aim 2a. If moderation is significant, we will calculate the significance of the mediated pathway for males and for females, separately. We will use a similar approach to investigate nicotine dependence as a moderator.

5.3. Missing data

We will use pattern mixture modeling to assess the effect of missing data. We will rerun our analyses coding for various missing data patterns (no missing data, sporadic missing, dropouts, etc.) to determine (1) if missingness impacts our findings and (2) how the differences between treatment conditions depends on the missing data pattern.

5.4. Statistical power

Aim 1a We performed a Monte Carlo study to calculate the minimum between-group differences in abstinence rates detectable by our analysis. For this study, we conservatively assumed an average of 8 assessments per participant (73% of the assessments) for the 100 participants and a 20% smoking abstinence rate in ST + CTRL at the 3-month follow-up. We examined numerous abstinence rates for ST + ABR to determine the lowest rate detectable by our analysis with 0.80 power, performing 1000 simulations for each tested abstinence rate. The results indicated that we would have greater than 0.80 power to detect a significant condition effect if the abstinence rate in ST + ABR was 42% or greater (effect size $\omega = .238$). This between-group difference is between a small ($\omega = .10$) and a medium ($\omega = .30$) effect size.

Aims 2a and 2b Our Monte Carlo study indicated that we would have greater than 0.84 power to detect mediation for a mediated pathway if the "a" path and the "b" path were of medium effect size or greater.

Aim 2c. For the exploratory aim of sex (or nicotine dependence) moderating the effects of condition on abstinence, again we would have 0.80 power to detect an effect size of $\omega = .238$, since adding the sex interaction terms just decreases the degrees of freedom for the

significance tests very slightly. Similarly, the power to detect medium sized-mediated pathways is just slightly decreased by having additional sex interactions in the model. In this case, we have 0.83 power to detect a mediated pathway if both the "a" and "b" paths are medium effect sizes or greater.

6. Discussion

Smoking remains a significant public health problem and there is a need for more effective interventions. Theory and initial empirical findings justify testing whether a simple computerized intervention targeting the approach action tendency – or approach bias – toward stimuli related to cigarette smoking can augment existent smoking cessation treatments. The goal of the current research is to evaluate the potential efficacy of an intervention that integrates this computerized intervention with standard smoking cessation care. The proposed study represents a crucial and important stage in translating basic research to strategies for treating nicotine dependence. The investigation addresses an important public health issue by testing an integrated intervention - informed by basic research - that may lead to a more effective treatment for at-risk smokers while simultenously isolating explanatory mechanisms. The expected findings should: (1) guide advances in the theoretical conceptualization of the mechanisms involved in smoking; and (2) provide initial effect size data for the integrated smoking cessation intervention, and thus provide the necessary data for a large-scale follow-up trial.

Conflicts of interest and source of funding

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.conctc.2019.100340.

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