Engaging Working Memory and Distress Tolerance to Aid Smoking Cessation

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PROTOCOL

Design Overview

This study is designed to evaluate the success of mechanistic target engagement in two specific contexts: under standard smoking conditions and under nicotine deprivation (stress) conditions. After screening, consent, and baseline assessment, participants selected on the basis of inclusion/exclusion criteria will be randomized to one of three intervention conditions: (1) a health-education control condition (CC), (2) a mindfulness training condition (MT), or (3) a mindfulness training condition combined with training applying mindfulness skills in the context of interoceptive exposure (Mindfulness+IE). Following 6 sessions of these interventions, delivered over 3 weeks, participants will then undergo the standard smoking assessment of mechanistic targets. Two days later (and matching the progression to quit-attempt challenges following treatment), participants will undergo the deprivation window assessment (14 hours of smoking abstinence) of these same mechanistic targets, followed by evaluation of lapse behavior and smoking topography in the McKee paradigm to yield: (1) latency to initiate smoking during a monetarily reinforced delay period, (2) the number of cigarettes smoked during a subsequent 60-minute self-administration period, and (3) exploratory analysis of smoking topography: puff volume, puff duration, and inter-puff interval. Participants will be recruited to Boston University through study advertisements targeted to low SES neighborhoods, with attention to health service centers and religious institutions serving low SES individuals. Investigators will work closely together to ensure the scientific integrity (rigor and reproducibility) of the project and data analyses.

Participant Selection

We anticipate consenting and randomizing up to 107 participants in order to reach an assessed sample (defined as providing post-treatment assessments, including the McKee protocol) of 75, low SES, male and female smokers (ages 18-65). For inclusion in the study, participants must (1) be between 18 and 65 years of age; (2) have reported household income of less than $30,000 per year; (3) be a regular smoker for at least one year; (4) report daily smoking (minimum of 5 cigarettes per day and biochemically confirmed via Carbon Monoxide [CO] analysis; > .10ppm CO); and (5) and not be presently engaged in a quit attempt. Exclusion criteria include history of psychosis as determined by a brief psychotic screen, pregnancy, nursing mothers, medical conditions that would contraindicate smoking (e.g., current diagnoses of chronic medical diseases including heart disease, chronic obstructive pulmonary disease, or seizure disorders - assessed during telephone prescreen and initial assessment via medical checklist), nicotine use other than cigarette smoking, current use of any pharmacotherapy for smoking cessation, or insufficient command of the English language (i.e., cannot carry on a conversation with an interviewer in the English language or read associated text).

Feasibility and Participant Compensation

The study team and consultants have a rich publication history reflecting collaboration on studies of health behaviors, distress intolerance, and, specifically smoking characteristics and treatment outcome.[1,73,76,90-93] Dr. Otto at Boston University has a history of successfully attracting smokers for psychopathology studies, easily completing 100 screens per year. Moreover, Dr. Otto is directing mindfulness interventions to low SES adolescents recruited to his ongoing study, R21DA041531. Recruitment/adherence is aided in the current study by financial compensation for all assessments and intervention sessions, with compensation of up to $180 per participant, depending on McKee Lapse paradigm results.

Procedures and the McKee Protocol

Following telephone screening for basic eligibility, participants will be scheduled for an informed consent interview and subsequent baseline assessment session. Interventions are to be completed over the subsequent 3 weeks, and post-treatment assessments of the mechanistic targets are scheduled for one-week (standard smoking assessment) and one week + 2 days (deprivation-window assessment) from the last intervention session. For the standard smoking window assessments, participants are asked to smoke .5 hour before the scheduled assessment session. The deprivation-window assessment is scheduled two days later, (for example, scheduled for 12:00 noon, with smoking to cease at 10PM the night before). Upon arrival to the lab, nicotine abstinence will be verified by expired CO levels, as determined by a cut-off of half of the participant's screening session CO concentration or <10 PPM (those failing will be rescheduled). After verification of abstinence, participants will complete assessment of the triple-risk mechanistic target variables. These assessments will be followed by the McKee Lapse protocol (Dr. McKee, *Study Consultant*, will train the study team and help monitor quality in these procedures): participants will be instructed that over the next 50 min, they will have the option to initiate a cigarette self-administration (smoking) session at any point or to delay initiation in exchange for monetary reinforcement. If participants choose to delay, they will be awarded funds for each 5-minute increment they are able to resist smoking. Once participants choose to end the delay period in order to smoke (or resist smoking for the entire 50 minute delay period), they will then participate in a 60-minute cigarette self-administration session, in which they will be given the choice to either smoke their

preferred brand of cigarettes or receive monetary reinforcement for cigarettes not smoked. Participants will be given funds at the beginning of the self-administration session and will lose a portion of the funds for each cigarette smoked. When participants smoke in this protocol, we will use the Clinical Research Support System (CReSS; Plowshare Technologies, Borgwaldt KC, Inc) to measure smoking topography. The reliability and acceptability of use of the portable CReSS device is well documented,[88,94] and is recommended over direct observation. Topography data will include puff CO volume, puff duration, and inter-puff interval. Puff level data will be averaged to compute mean topography variables for each participant.

Baseline Assessments

- **Demographics**. Participants will be asked to provide standard demographic information (age, gender, race/ethnicity) as well as history of medical problems and current treatments.
- **Smoking History Questionnaire**. Smoking history and pattern will be assessed with a semi-structured interview with items targeting smoking frequency, age of smoking initiation, years of being a regular smoker, etc. The Timeline follow-back method will be used to establish degree of cigarette use in the last 30 days (a baseline predictor).
- **Fagerström Test for Cigarette Dependence (FTCD)**. The FTCD is a six-item scale designed to assess gradations in cigarette dependence.[95] The FTCD will be used as a baseline covariate in the analyses.
- **Questionnaire of Smoking Urges-Brief (QSU-Brief)**. The QSU-Brief measures urge to smoke and craving.[96,97] The baseline and deprivation window Total Craving Scores will be used as predictors.
- **Executive Function – Behavioral Regulation**. Baseline levels of behavioral regulation will be assessed with the Behavioral Regulation Index from the from the SOBC assay, Behavioral Rating Inventory of Executive Function – Adults (BRIEF-A, http://scienceofbehaviorchange.org/measures/).
- **Psychological Distress.** Baseline levels of psychological distress will be assessed with the SOBC assay, Kessler Psychological Distress Scale (K6+, http://scienceofbehaviorchange.org/measures/).

Mechanistic Targets: The Triple-Risk Variables

Each of the mechanistic targets will be assessed at the post-intervention standard-smoking and deprivation-window assessments.

- **Negative Affectivity/Stress:** Negative affect will be assessed with the SOBC assay, PANAS (PANAS-state negative (http://scienceofbehaviorchange.org/measures/), and withdrawal symptoms will be assessed with the Wisconsin Smoking Withdrawal Scale (WSWS).[98] Each of these mechanistic targets will be assessed at the standard smoking and deprivation-window assessments.
- **WM.** We focus on WM capacity as a mechanistic target due to its centrality to executive functions; its predictive validity across a wide range of health behavior applications, specifically including smoking; relevance as a modifiable treatment target; and interaction with negative affectivity/stress.[1] To provide multi-domain assessment of WM,[99,100] we will adopt 3 specific SOBC assays **:** Adaptive N-Back, Digit Span, and Spatial Span (http://scienceofbehaviorchange.org/measures/). Dr. Bickel, *Study Consultant*, will aid the study team in quality control for these assessments.
- **Distress Tolerance.** We likewise focus on DT as a mechanistic target due to its predictive validity across a wide range of health behaviors (specifically including smoking); relevance as a modifiable treatment target; and amplification of negative affectivity/stress.[1] Because self-report and behavioral measures of DT are only partially correlated,[35] we will utilize both assessment strategies. For self-report we will use the ASI-3, an 18-item measure of AS.[101] The ASI-3 has sound psychometric properties, including excellent internal consistency, predictive validity, and reliability among treatment-seeking smokers.[102] Behavioral Distress Tolerance will be assessed with the computerized Mirror-Tracing Persistence Task (MTPT-C),[103] with evidence this measure captures the inability to tolerate distress and not just the experience of distress itself.[104] Dr. Zvolensky and Smits will aid the study team in quality control for these assessments.

Interventions

All interventions are delivered in six, 90-minute individual sessions over 3 weeks. Sessions will be recorded for supervision/quality assurance review by Dr. Otto.

- **CC:** The wellness education control condition (CC) will be modeled after that used in our studies of exercise for smoking cessation,[73] but delivered in an individual format. Content focuses on discussions of a variety of healthy lifestyle topics, such as healthy eating, time management, recommended health screenings, and cancer and cardiovascular prevention. Content is delivered using a combination of lectures, videos, handouts, and discussions while allowing participants to set their own realistic wellness goals, which they can gradually incorporate into their lives. Dr. Smits, *Study Consultant*, will aid the study team in quality control of this intervention.

- **MT:** Mindfulness training will be adapted for 6 individual sessions from previous MT manuals for substance dependence.[105-107] The length of treatment in the current protocol corresponds well to the mean number of sessions [5.2] attended by smokers in treatment, even when eight sessions are offered.[105] Formal intervention elements include: (1) a body scan designed to teach participants to pay attention to specific parts of their bodies as a strategy to increase attentional capacities/reduce habitual mind-wandering; (2) non-judgmental awareness, and (3) 'awareness of breath' meditation, with an additional focus on helping participants become more aware of the present moment and refrain from habitually engaging in self-related pre-occupations concerning the future or the past. Informal daily practices include (1) performing daily activities mindfully, (2) setting daily aspirations, and (3) techniques designed for cravings (recognize/ accept/investigate mind-states, emotions, and body sensations from moment-to-moment). Participants will be asked to record both the number of minutes and number of episodes of mindfulness practice each day using structured diaries. Dr. Witkiewitz, *Study Consultant*, will aid the study team in adapting mindfulness skill training to the current protocol, and consult with Dr. Otto on treatment fidelity issues.
- **MT+IE.** This condition will mirror the MT condition for the first 4 individual sessions, then for the final 2 individual sessions, MT will be rehearsed under conditions of sensations of anxiety/tension induced by interoceptive exposure procedures (IE). Dr. Otto and the study team are adept in delivering IE training to those about to undergo benzodiazepine withdrawal sensations,[69-71] and to smokers as part of quit attempts.[74,75] In the two in-session rehearsals (sessions 5 & 6 of mindfulness training), the focus will be on maintaining mindful, non-judgmental awareness despite the presence of induced bodily sensations of anxiety/tension.