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Targeting cognitive and emotional regulatory skills for smoking prevention in low-SES youth: A randomized trial of mindfulness and working memory interventions

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HIGHLIGHTS

- Adolescents from low socioeconomic households are vulnerable to smoking initiation.
- Lower distress tolerance and working memory are vulnerability factors for smoking.
- These vulnerability factors were inadequately engaged in the current study.

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ABSTRACT

Research to date provides striking evidence that youth from low socio-economic status (SES) households are at an increased risk for smoking. Converging evidence from developmental studies, psychopathology studies, intervention studies, and basic research on self-control abilities have identified working memory and distress tolerance as potential crucial modifiable risk factors to prevent smoking onset in this cohort. To confirm the value of these mechanistic targets, this randomized trial was designed to evaluate the influence of working memory and distress tolerance interventions on risk of smoking initiation. Recruiting primarily from low-income community afternoon programs, we randomized 93 adolescents to one of three intervention conditions, all of which were a prelude to a smoking-prevention informational intervention: (1) a working memory intervention, (2) a mindfulness training intervention to target distress tolerance, and (3) a wellness-focused control condition. Despite a number of adherence efforts, engagement in treatment was limited, and under these conditions no significant evidence was found either for differential efficacy for smoking prevention or for intervention effects on mechanistic targets. However, working memory capacity and distress tolerance were found to be negatively related to smoking propensity. As such, our mechanistic targets—working memory and distress tolerance–may well be processes undergirding smoking, despite the fact that our interventions did not adequately engage these targets.

1. Introduction

Adolescents are particularly vulnerable to smoking initiation, in part due to higher impulsivity and greater sensitivity to life stressors and negative affect associated with this developmental period (Bickel, Moody, Quisenberry, Ramey, & Sheffer, 2014; Jessor, 1993; Khuder, Dayal, & Mutgi, 1999). This vulnerability is further heightened for adolescents from low socio-economic status (SES) families, with evidence for greater rates of smoking initiation, poorer response to informational smoking prevention interventions, greater increases in smoking over time, and greater smoking duration (Droomers, Schrijvers, Casswell, & Mackenbach, 2005; Mathur, Erickson, Stigler, Forster, & Finnegan, 2013; Mercken et al., 2012; Patnode et al., 2013; Soteriades & DiFranza, 2003; Steinberg, 2008). The consequence over

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time is that smoking initiation and maintenance are twice as likely for individuals from low income households relative to those living well above the poverty level (Siahpush, Singh, Jones, & Timsina, 2009; Wang et al., 2018).

One contributing factor to the elevated smoking appears to be the increased exposure to multiple stressors associated with low SES environments, which in turn may lead to disruptions in cognitive and emotional processes (Doan & Evans, 2011; Evans & Fuller-Rowell, 2013; Khurana et al., 2013; Kim-Spoon et al., 2017; Kim-Spoon et al., 2017; McEwen & Gianaros, 2010). Specifically, low SES and the chronic stress of poverty in children is associated with working memory (WM) capacity (Adamkovič & Martončik, 2017; Noble et al., 2005, 2007). Further, WM capacity is associated with a wide variety of negative health behaviors, including smoking and other drug use (Day et al., 2015; Loughead et al., 2015; Otto et al., 2016; Patterson et al., 2010). WM is also linked to delay discounting, itself a predictor of substance use (Bickel, Christensen, & Marsch, 2011; Bickel, Yi, Landes, Hill, & Baxter, 2011; Snider et al., 2018; Wesley & Bickel, 2014). Finally, the potential of WM capacity as a treatment target in children is supported by *meta*-analytic findings of reliable improvements in working memory capacity from both verbal and non-verbal training tasks, but with poor transfer to other cognitive abilities (Sala & Gobet, 2017).

Additionally, living in poverty has been associated with low distress tolerance (DT), a perceived or behavioral tendency to not tolerate affective and physical distress (Doan, Fuller-Rowell, & Evans, 2012). More generally, the degree of DT is an effective predictor of maladaptive coping across a wide range of disorders and health-related behaviors (Otto et al., 2016). Concerning smoking specifically, DT has been linked to the duration of abstinence from smoking in a variety of studies (Brandon et al., 2003; Brown et al., 2002, 2009; Hajek, Belcher, & Stapleton, 1987; Hajek, 1991), and treatment that includes efforts to facilitate DT produces better smoking cessation outcomes (Brown et al., 2013; Zvolensky, Bogiaizian, Salazar, Farris, & Bakhshaie, 2014).

Given these findings, we hypothesized that interventions targeting the enhancement of WM and DT would be useful preventive strategies for adolescents from low SES households, to enhance response to antismoking interventions (Otto et al., 2018). We designed this prevention pilot study to allow testing of risk models outside a full longitudinal prevention study. Smoking risk proximal outcomes were assessed by smoking susceptibility self-report, delay discounting, and positive implicit associations toward smoking evaluated at baseline and one week post-intervention. Actual smoking was also assessed both objectively and via self-report at baseline and one-month follow-up. Susceptibility to smoking (defined as not being able to rule out the idea of smoking) is an established self-report measure for studies of smoking onset in adolescents (Forrester, Biglan, Severso, & Smolkowski, 2007; Leatherdale, Brown, Cameron, & McDonald, 2005; Pierce, Choi, Gilpin, Farkas, & Merritt, 1996). The Implicit Association Test (IAT) has been successfully used to assess implicit associations toward smoking in children (Andrews, Hampson, Greenwald, Gordon, & Widdop, 2010). Delay discounting functions as a behavioral marker of addiction potential by identifying those at risk of developing drug dependence as well as serving as a gauge of addiction severity (Bickel, Koffarnus, Moody, & Wilson, 2014), including the prediction of new onset smoking and increased rates of smoking in a large longitudinal study of adolescents (Audrain-McGovern et al., 2009), and poorer response to smoking cessation treatment in low-SES (Sheffer et al., 2012) and adolescent samples (Stanger et al., 2012).

Following an experimental medicine approach (Bickel, Snider, & Mellis, 2019; Nielsen, Riddle, King, & Science, 2018; Riddle & Science of Behavior Change Working Group, 2015), mechanistic target engagement was assessed via measures of WM capacity (using an averaged z score representing performance across three tasks) and DT (using an averaged z score representing a self-report and a behavioral index of DT). We hypothesized that the WM training and DT training interventions, relative to the control intervention, would lead to higher WM and DT, respectively. We further hypothesized that WM would be higher in the WM condition than the DT condition, and likewise that DT outcomes would be higher in the DT than the WM condition. We also hypothesized that the treatment conditions, and their hypothesized effects on the mechanistic variables (WM and DT post-intervention), would predict both proximal smoking risk outcomes—susceptibility to smoking, implicit attitudes toward smoking, and delay discounting—as well as actual smoking behavior. Finally, we hypothesized that we would achieve an adequate level of treatment acceptability/feasibility in the WM and DT intervention conditions as represented by treatment engagement, which we defined *a priori* as attendance of 80% of intervention sessions by 70% of the randomized sample.

2. Methods

2.1. Recruitment and participant characteristics

Full methods for this study are detailed elsewhere (Otto et al., 2018). In brief, recruitment consisted of advertisements and presentations at youth mentorship programs, charter schools, and community centers serving youth from low-income families (all five community center neighborhoods were in the lowest income bracket for median household income for Boston: $10,446 to $30,000), as well as community postings at local businesses frequented by youth in these locales. Potential participants were given parental consent forms and, upon return of the signed form, were scheduled for an initial baseline screening visit where written participant assent was obtained after additional review of study procedures. To promote initial interest in this study, individuals returning signed consent forms from their parents were entered in a drawing for iPad devices, regardless of whether parents had consented or whether participants chose to provide assent and participate in the study. Additionally, to increase the acceptability of intervention procedures, whenever possible we conducted sessions at locations where the adolescent participants already congregated (e.g., one of five community centers from which the adolescents were enrolled) rather than in our lab, and snacks and snack breaks were provided for all interventions. Monetary compensation was also provided for each attended intervention ($11 per intervention) or assessment session ($20 to $30 depending on the assessment), totaling up to $296 if all sessions were attended.

A total of 122 adolescents (60 male and 62 female), ages 12 to 16 years (mean = 13.97, *SD* = 1.24), were enrolled in this study and completed baseline assessment; 32.6% of the sample reported their race and ethnicity as Black/non-Hispanic, 7.2% as Black/Hispanic, 2.5% as Asian/non-Hispanic, 2.5% as White/Hispanic, less than 0.8% as native Hawaiian/Pacific Islander, 38.2% as multiple races/ Hispanic, 13.1% as multiple races/non-Hispanic, and 3.2% as unknown/other. Of consented individuals, 108 (89.2%) returned for randomization and attended at least one session of the assigned intervention condition. Fig. 1 provides a CONSORT diagram of attendance across the study phases.

2.2. Assessments

The study utilized three primary assessment visits: the baseline visit, a one-week post-intervention assessment, and a one-month follow-up assessment. Evaluations completed at these assessment visits are detailed in Table 1. Baseline covariates used in our analytic models included the degree of parental smoking (ranging from no smoking to current smoking in both parents) (Jackson & Henriksen, 1997), degree of peer smoking (Choi, Pierce, Gilpin, Farkas, & Berry, 1997; Hoffman, Sussman, Unger, & Valente, 2006), and sensation seeking (Black & Ricardo, 1994; Zuckerman, 1979), all variables linked to rates of smoking initiation. Each of these measures is described in detail elsewhere (Otto et al., 2018).

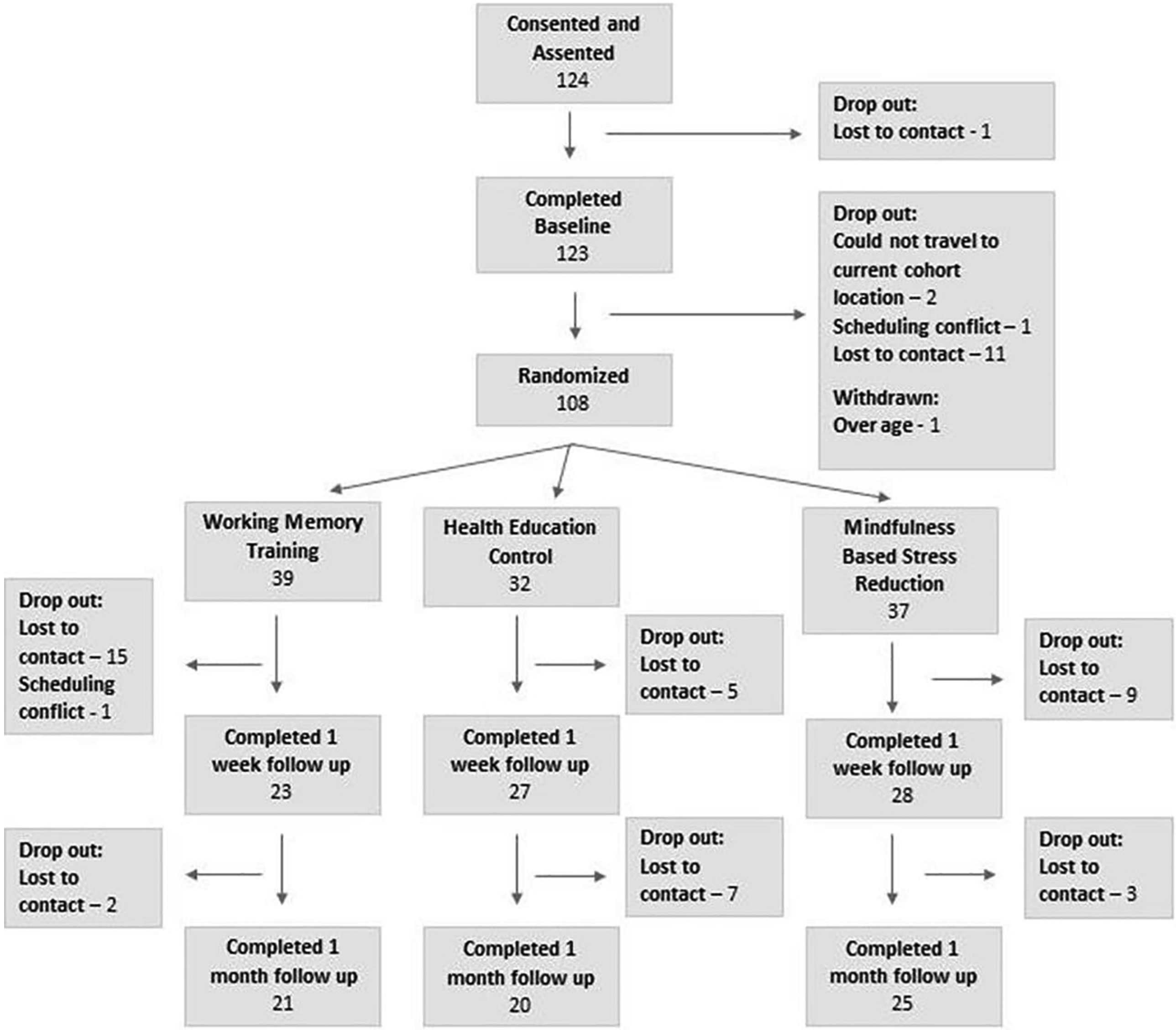

Fig. 1. CONSORT diagram showing progress of participants through the study phases.

2.3. Mechanistic outcome measures

2.3.1. Distress tolerance (DT)

Self-report and behavioral measures of DT are only modestly correlated (McHugh et al., 2011). Accordingly, we used both assessment strategies and used the sum of the z-scores on these two measures as our core assessment of DT, but also evaluated each measure individually. Self-reported DT was assessed with the Distress Intolerance

Table 1
Time Line and Schedule of Assessments for Study Implementation.

Measures	Baseline	Intervention	1-Week Post- Intervention	1-Month Post Intervention
Initial Assessment				
Demographics	X			
Additional Covariates				
Parental Smoking	X			
Peer Smoking	X			
Sensation Seeking	*X*			
Mechanistic Outcome Variables				
Working Memory (WM)	X		X	
Distress Tolerance (DT)	X		X	
Proximal Smoking Risk Outcomes				
Smoking Susceptibility	X		X	X
Smoking IAT	X		X	X
Delay Discounting	X		X	X
Actual Smoking Outcomes				
Timeline Follow-Back	X			X
Carbon Monoxide	X			X

Index (DII), a 10-item instrument constructed from a confirmatory factor analysis of items from four commonly used distress intolerance (DI) measures, with higher scores indicating greater distress intolerance (McHugh & Otto, 2012). Behavioral DT was assessed with the computerized Mirror-Tracing Persistence Task (MTPT-C) (Strong, Lejuez, Daughters, Marinello, Kahler, & Brown, 2003). This task assesses participants' willingness to persist with a frustrating and difficult task: tracing three shapes on the computer screen using a cursor that moves in reverse to their mouse commands (analogous to a mirror image). On the third and most difficult shape, participants are given the option to end the task at any time by pressing a computer key; the duration of time spent on this third shape is used to index distress tolerance. Longer times indicate greater distress tolerance.

2.3.2. Working memory (WM) capacity

WM assessment consisted of three well-validated computerized WM measures: the N-back (Pelegrina et al., 2015), the Auditory Digit Span (backward) (Conway et al., 2005), and the Corsi Block Tapping task (Kessels, van Zandvoort, Postma, Kappelle, & deHaan, 2000), all administered via *Inquisit* (https://www.millisecond.com). Our core WM capacity measure was the sum of the z-scores on these three tasks, but we examined individual task scores in follow-up analyses. For the N-back task, participants were presented with a continuous series of letters and were asked to signal (with a button press) anytime the current letter matched the one presented N letters back. We administered the one-back, two-back, and three-back versions in the current trial and used the two-back data for analysis, in line with past research involving adolescents (Conway et al., 2005; Pelegrina et al., 2015). For the Auditory Digit Span task, participants were presented with a verbal series of numbers, which got progressively longer throughout the task, and were asked to enter the series of numbers heard using the computer mouse (backward recall was used for analysis). For the Corsi Block Tapping task, nine boxes were presented on the screen. A series of these boxes lit up in a certain order, and participants were then asked to click the boxes in the corresponding order. As in the Auditory Digit Span task, the series got progressively longer throughout the task.

2.4. Proximal smoking risk outcomes

2.4.1. Smoking susceptibility self-report (SSA)

Consistent with previous work (Racicot, McGrath, & O'Loughlin, 2011), we assessed smoking susceptibility with a five-item scale that asked about attitudes and likelihood of smoking (e.g., "If one of your best friends were to offer you a cigarette, would you smoke it?"). Total scores ranged from 0 (no susceptibility) to 11 (highest susceptibility).

2.4.2. Smoking IAT

We used an adapted version of the Brief Implicit Association Test (B-IAT) (Andrews, Hampson, Greenwald, Gordon, & Widdop, 2007; Greenwald, McGhee, & Schwartz, 1998) to assess participants' implicit tendency to appraise smoking-related stimuli as either "positive" or "negative." Based on the design of Kahler, Daughters, Leventhal, Gwaltney, and Palfai (2007) participants sorted pictorial and verbal stimuli based on whether or not they belonged to either of two categories displayed on the screen. In two of the four task blocks, the displayed categories were "Smoking" and "I feel positive"; in the other two blocks, the displayed categories were "Smoking" and "I feel negative" (blocks were administered in random order). Stimuli presented in each block included smoking-related images (e.g., cigarette, ashtray), non-smoking-related images (furniture items), and words of either positive or negative valence (e.g., "Appreciated", "Insulted"). Shorter response latencies when sorting stimuli in the "Smoking—Positive" versus "Smoking—Negative" blocks indicate an implicit tendency to associate "smoking" with "positive." Standardized difference scores (D-scores) were computed using the improved scoring algorithm recommended in past IAT research (Greenwald, Nosek, & Banaji, 2003), with higher D-scores indicating *less* positive implicit attitudes toward smoking.

2.4.3. Delay discounting task

For the Delay Discounting Task, participants completed a series of computerized decision trials in which they selected between a smaller immediate cash reward and a larger delayed cash reward at levels appropriate to our low SES adolescent sample (e.g., "$10 in 30 days" versus "$5 today"). The computerized task systematically titrated the immediately available amount to determine indifference points to a delayed $10 at each of the 3 delays (Du, Green, & Myerson, 2002). The discount rates (i.e., k), which were then natural-log transformed, were calculated by fitting the difference points Mazur's hyperbolic equation (Mazur, 1987).

2.5. Smoking behavior

We collected secondary self-report and objective indices of smoking behavior. Self-reports of smoking status were collected using timeline follow-back methodology (previously validated for use in adolescent samples) (Lewis-Esquerre et al., 2005) to determine the number of cigarettes smoked. We also utilized a piCO Smokerlyzer manufactured by Bedfont Scientific Ltd. to measure carbon monoxide (CO) in exhalations. We considered a participant positive for smoking for either a self-report of cigarette use or a CO reading greater than 4 ppm (Perkins, Karelitz, & Jao, 2013).

2.6. Interventions

Participants were randomized to one of three study conditions using a random number table utilizing separate block sizes of 6 for males and females. Condition assignments were stratified by parental smoking status and gender due to associations between these variables and smoking (Bauman, Foshee, Linzer, & Koch, 1990; Gilman et al., 2009; Syamlal, Mazurek, & Dube, 2014; Wilkinson, Shete, & Prokhorov, 2008). Each intervention was delivered twice a week in 1-hour sessions over eight consecutive weeks by trained interventionists supervised by doctoral and masters level clinicians. Group sizes were variable depending on attendance and ranged from one to nine participants.

2.6.1. Working memory training

We used the Cogmed RM program (https://www.cogmed.com/) for working memory training using both verbal and visuospatial tasks. While supervised in a group setting, participants used the computer-driven game-like program for an hour, twice weekly. Participants were also encouraged to use the program outside the study sessions for approximately one hour each week. The program resembles a video game, and comprises several different "games" that require visuospatial working memory (remembering the position of objects) and a combination of verbal and visual working memory (remembering phonemes, letters, and digits). The program adapts to the performance of the user, increasing task difficulty (list length) when performance is good and reducing task difficulty when performance is poor.

2.6.2. Mindfulness-based distress tolerance (DT) training

To enhance DT, we used a Mindfulness-Based Stress Reduction program that has been specifically adapted for use with adolescents (Biegel, Brown, Shapiro, & Schubert, 2009) and has shown promising results in a low-income minority sample (Edwards, Adam, Waldo, Hadfield, & Biegel, 2014). Moreover, mindfulness and DT are positively associated (Hsu, Collins, & Marlatt, 2013: Vujanovic, Bonn-Miller, Bernstein, McKee, & Zvolensky, 2010) and mindfulness training improves persistence and other measures of DT to a variety of stimuli (Feldman, Dunn, Stemke, Bell, & Greeson, 2014; Lillis, Hayes, Bunting, & Masuda, 2009; Liu, Wang, Chang, Chen, & Si, 2013). The interventions stresses formal and informal mindfulness practices, which encourage participants to foster intention, attention, and attitude. Session content included a variety of mindfulness activities ranging from formal and guided meditations (e.g., body scan, breathing meditations, sitting meditations, mindful eating) to more informal mindfulness-based discussions surrounding topics such as identification of personal values and methods for coping with stress. In addition to in-group instruction and practice, participants were encouraged to practice their mindfulness skills for approximately one hour each week outside of the twice weekly, sessions.

2.6.3. Control intervention

The wellness-focused control intervention was adapted from an intervention used in previous studies by our group (Smits et al., 2012). Clinician-led group discussions covered a variety of healthy lifestyle topics of relevance to our adolescent sample, such as healthy eating, stress/time management, exercise, and sleep (smoking was explicitly excluded). Participants were provided with wellness-related worksheets to complete in-between sessions.

2.6.4. Smoking prevention informational intervention

This informational intervention was common to all randomized conditions in the study, and was delivered during the final 2 sessions of intervention. We selected the intervention from brief primary-care-based interventions which followed guidelines from the National Institute of Health and the U.S. Public Health Service Tobacco Use and Dependence Clinical Practice Guideline. Youth were provided with age-appropriate education on the norms and health consequences of smoking, guided to reflect on the pros and cons of smoking and affirm their personal commitment to not smoking, and helped in developing a personalized strategy to maintain abstinence. We also included Colby and associates' guided imagery about future smoking/non-smoking life status (Colby et al., 2005), and incorporated open-ended discussion about perceived likes and dislikes related to smoking. Additionally, participants viewed videotaped vignettes to stimulate discussion on four content areas: health effects, social consequences, addiction, and financial cost.

3. Data analysis

Data for the continuous outcomes were analyzed using multilevel modeling (MLM). Data for the dichotomous outcome (smoking or not) were analyzed using GLMM (MLM with a logistic linking function). MLM and GLMM include all participants who provide at least one data point for the analysis. Since participants received their intervention in groups, the models were 3-level models with repeated measures nested within participants who were nested within groups. However, the full 3-level models for the GLMM analyses for actual smoking behavior would not converge when including the time predictor, so these analyses were conducted dropping that predictor. Two-level analyses including the time predictor yielded identical results in terms of significance.

We used an ANOVA-type model (performed using MLM or GLMM) for the repeated measures over time because the change in the dependent variables over time might not be linear. The 3 treatment conditions were coded using 2 dummy variables contrasting each active treatment with the control intervention. Time was alternately centered at post-treatment or follow-up so that the dummy variable contrasts would reflect group differences at those time points. All models included baseline covariates (parental smoking, peer smoking, sensation seeking, gender, race, and age). Due to administration error, only a partial index of the sensation seeking scale (representing the first 34 items of the 40-item full scale) was available for analysis.

To evaluate the impact of cognitive/affective target activation on proximal smoking risk and behavior (i.e., the relations of WM and DT with smoking risk and behavior), WM and DT were added as time-varying predictors (TVPs) of outcome in the models for each of the three measures of smoking risk (SSA, implicit attitudes toward smoking, and delay discounting) and for actual smoking behavior. Because TVPs conflate the between-subjects and within-subjects components of the TVP (e.g., a high score on WM at an assessment could reflect that a participant was generally high on WM, or that the participant had a substantial increase in WM from their lower average level of WM), we disaggregated each TVP into the participant's average level of the TVP across assessments, and their deviations from their own average level at each assessment. Following Wang and Maxwell (Wang & Maxwell, 2015), each participant's average level of a TVP (their between-subjects level of the TVP) was calculated by simply averaging their scores on that TVP over time. Each participant's deviations from their average level at each assessment point (their within-subjects change on the TVP) was calculated by subtracting the participant's average level on the TVP from their raw score at each assessment. In models examining the relation between a TVP (e.g., WM) and an outcome (e.g. smoking), both disaggregated components of WM (the between-subjects average level of WM and the within-subjects changes in their level of WM) are included in the model as predictors of the outcome. The regression coefficients for WM and DT predicting outcome in these models indicate the degree to which each is related to smoking risk. The "deviations" component of the TVP indicates the relation of deviations in WM (or DT) with proximal measures of smoking risk within-subjects over time. The "average" level component of WM (or DT) indicates whether participants with higher average levels of WM have higher (or lower) levels of smoking risk (this latter relation is not generally considered to be causal since it may be affected by 3rd variable confounds).

Because of skewed distributions, the natural logs of smoking susceptibility, delay discounting, and the mirror tracing task were used for analyses. The Corsi Block Tapping task was less skewed so a square root transformation was used.

4. Results

4.1. Intervention attendance

Among the 108 randomized participants, the mean number of sessions attended was 10.6 of the 16 sessions (*SD* = 4.1; the median attendance was 11 sessions); no significant differences in attendance were observed between intervention groups ($F_{2,105} = 0.57$; $p = 0.568$). As such, intervention conditions do not appear to be differentially acceptable to participants. Unfortunately, we did not seem to sufficiently engage the adolescent sample overall in our smoking prevention program. Only 44% of the sample attended over 80% of the sessions, well below our *a priori* target of 70% of the sample.

4.2. Intervention effects on mechanistic targets (WM and DT)

We found no significant Intervention main effects nor Intervention × Time interactions for WM or DT z-score outcomes. Significant Time main effects reflected a general trend toward lower DT (greater distress intolerance) and improving WM scores over time regardless of intervention group (DT: $F_{1,110} = 5.28$, $p = 0.024$; WM: $F_{1,109} = 4.47$, $p = 0.037$). Figs. 2 and 3 show raw means for these variables.

To provide the broadest perspective on the mechanistic outcomes, in exploratory analyses we examined whether the intervention groups differed on any of our individual measures of DT or WM. Indeed, correlations among component measures of DT and of WM were either non-existent ($r = 0.058$ for the two DT measures, with reverse scoring for mirror tracing) or modest ($r = 0.239$ to 0.353 for the three WM measures), suggesting that our individual measures are relatively independent of one another. When each mechanistic variable was examined independently in univariate tests, no intervention group effects were evident for the DT measures. For the individual WM measures, the change from baseline to post-intervention for the Corsi Block Tapping measure was marginally greater in the WM group compared to the

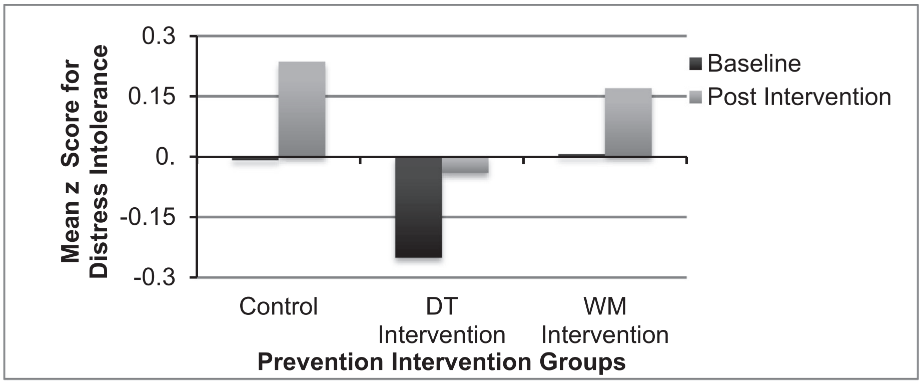

Fig. 2. Mean z-values for distress intolerance (higher scores reflect worse tolerance) for each intervention group at baseline and one week post-intervention.

control group, effect size of $b = 0.66$, $p = 0.052$. Hence, the WM intervention used in the current study may be more effective for visuospatial (Corsi Block Tapping) than for verbal or auditory WM tasks.

We next investigated whether treatment effects were related to the dose (number of sessions attended) of the intervention. To do so, we added "dose" as a moderator of all the effects in our basic model (treatment, Time, and treatment × Time), both for WM and for DT. However, we found that dose was not a moderator of any effects for either DT or WM outcomes, nor was it a predictor of these outcomes across treatment conditions. Results were similar when dose was evaluated categorically as adherent (defined as attendance at least 80% [13 of 16] of sessions) or not.

4.3. The relation between cognitive/affective targets and smoking-related outcomes (smoking susceptibility self-report, IAT, delay discounting, smoking behavior)

We found that participants with higher average levels of WM exhibited significantly less delay discounting ($b = -1.01$, $p = 0.001$), consistent with the often observed relations between these variables. We further found that within-subject deviations in WM scores were related to the smoking IAT ($b = -0.30$, $p = 0.036$); at assessments at which a participant's WM was higher their average WM score, they exhibited lower automatic attraction to cigarette cues. For example, if a participant had a lower than their average WM score at baseline and higher than their average WM score at post, their automatic attraction to cigarette cues tended to be higher at baseline and lower at post. For those who had higher WM at baseline and lower at post, their automatic attraction to cigarette clues tended to be lower at baseline and higher at post. WM was not significantly associated with self-reported smoking susceptibility ($p > 0.78$). In terms of actual smoking behavior, GLMM analyses showed that deviations from a person's mean level of WM were related to actual smoking behavior ($b = -1.91$, $p = 0.021$). At the assessments at which participants had higher than their mean level of WM, they were more likely to be abstinent. For example, if a participant had lower than their average WM score at baseline and higher than their average WM score at post, their odds of smoking tended to be higher at baseline and lower at follow-up. However, we should note that variations in smoking outcomes were very limited, with 12.3% smoking at baseline and 6.1% smoking at the final evaluation.

Of the individual components of the composite DT measure, higher average levels of the DII were associated with higher smoking susceptibility scores, $b = 0.02$, $t(106) = 2.64$, $p = 0.010$, indicating that greater distress intolerance was linked to greater smoking susceptibility. There were not significant associations between DT components and IAT or delay discounting scores. In terms of actual smoking behavior, we found that within-subject increases in DII were related to lower smoking, $b = -0.20$, $p = 0.003$, but again variability in smoking behavior was low at baseline and final assessment.

Finally, consistent with the failure to find reliable target activation, no intervention-level analysis reached significance ($p > 0.233$), with the single exception of an increase in smoking susceptibility from baseline to the 1MFU that was greater in the WM condition than in the Control, $b = 0.33$, $p = 0.013$.

5. Discussion

The purpose of this project was to investigate the extent to which interventions designed to improve cognitive and emotional regulatory processes would enhance the efficacy of standard no-smoking informational interventions among adolescents from low socioeconomic status (SES) neighborhoods. Following an experimental medicine approach (Bickel et al., 2019; Riddle, 2015), we evaluated both mechanistic outcomes and the link between these outcomes and smoking prevention outcomes.

Conducting a prevention trial in adolescents from low SES families in a pilot-study format resulted in several challenges. First, a pilot study makes large-scale assessments over longer-term follow-up periods

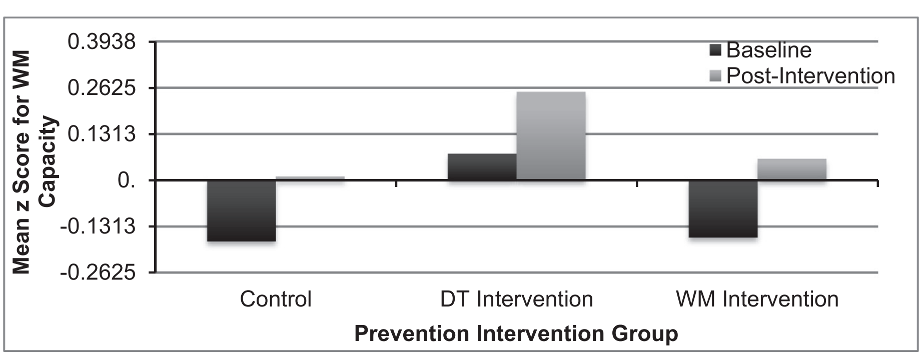

Fig. 3. Mean z-values for working memory capacity (higher scores reflect greater capacity) for each intervention group at baseline and one week post-intervention.

prohibitive. To address this limitation, our study was designed around smoking propensity measures and was complemented by evaluation of actual smoking rates observed at a one month follow-up evaluation. Second, our study targeted cigarette smoking just at the time that e-cigarette use was dramatically increasing in Massachusetts among adolescents, so that by 2017, its use was twice that of conventional cigarettes (Department of Public Health, 2019). This alternative form of nicotine use may have decreased the frequency of cigarette use and/or propensities toward combustible cigarettes more generally. Third, motivation is a challenge for health behaviors that have markedly delayed consequences, and this challenge may make engagement in behavioral change programs more daunting among low SES/minority samples (Biglan et al., 1987; Chacko et al., 2016; Moroshko, Brennan, & O'Brien, 2011). As such, the ability to engage our sample is an important consideration for evaluating both the potential efficacy of our intervention and the ultimate effectiveness of this approach for smoking prevention among adolescents.

Unfortunately, our study apparently failed to strongly engage participants in the interventions. Under these low engagement conditions, the effects of the intervention conditions on the mechanistic variables were weak and limited to specific components of the larger WM and DT constructs. Also, we did not obtain a significant dose/response relationship based on session attendance, raising questions about how engaged individuals were in the trainings provided, as well as the efficacy of those trainings in this age group. Yet, other evidence indicates significant effects of WM training, for example, under the right conditions (Brandon et al., 2003; Brown, Lejuez, Kahler, & Strong, 2002; Doan et al., 2012). The degree to which engagement was hampered by our prevention model is unclear: by way of example, other prevention programs (e.g., depression prevention) have failed when delivered in a primary prevention format, but succeeded when applied instead to those under a different motivational frame – those with prodromal symptoms (Dray et al., 2017; Hetrick, Cox, & Merry, 2015; Merry et al., 2011). Hence, our interventions may have had more relevance if applied as an early intervention rather than a prevention strategy. Also, many participants failed to attend the final two intervention sessions when the smoking informational interventions were delivered; yet, this issue only affects the analyses of smoking propensities, not the analyses of mechanistic target engagement or direct effects of WM and DT on smoking that are not aided by antismoking informational interventions. Finally, we cannot judge the degree to which e-cigarette use influenced smoking propensities in our sample.

Although our interventions failed to influence mechanistic variables, our study did provide evidence that our target constructs were meaningfully related to select smoking-relevant variables. Consistent with previous findings (Bickel et al., 2011; Wesley & Bickel, 2014), we found a significant negative association between WM and delay discounting; those with higher WM discounted the future less. Further, WM values were linked to the small rates of actual smoking we observed: at assessments at which participants had higher than their mean level of WM, they were more likely to be abstinent, consistent with a previous studies showing an association between low WM and smoking behaviors (Day et al., 2015; Loughead et al., 2015; Otto et al., 2016; Patterson et al., 2010). Select associations with mechanistic and clinical variables were also found for our measures of DT. The self-report component of DT (the DII, McHugh and Otto, 2012) in particular was related to smoking propensity self-report scores, consistent with a variety of findings linking DT to smoking behavior (Leventhal & Zvolensky, 2015; Leyro, Zvolensky, & Bernstein, 2010; Otto et al., 2016) but occurring at an earlier point in smoking propensity than observed previously. Yet, DT failed to show the expected direction of association with actual smoking behaviors, raising questions about the reliability of DT predictive findings at the earliest stage of smoking initiation.

In summary, the current study extended support for the value of WM and DT as risk factors for negative health behaviors (Otto et al., 2016) to a sample of adolescents from low SES neighborhoods. Variations of WM and DT within this sample offer specific prediction of smoking risk, including rates of actual smoking associated with low WM. These findings encourage further consideration of ways to harness this knowledge of risk for prevention interventions, given that we did not find support for the specific WM training and DT (targeted via mindfulness) interventions under study in this prevention trial.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Contributors.

Author Otto co-designed and co-led this clinical prevention trial and wrote the initial draft of this manuscript and edited drafts thereafter. Author Rosenfield performed the data analysis and edited the manuscript. Authors Gorlin, Hoyt, and Patten helped conduct this trial, manage data, and edit the final manuscript. Authors Bickel and Zvolensky provided consultation on the study design and the conduct of the trial and edited the final manuscript. Author Doan co-designed and co-led the trial and edited this final manuscript.

Clinical Trial Registration.

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Conflict of Interest.

Although the following activities/relationships do not create a conflict of interest pertaining to this manuscript, in the interest of full disclosure, the authors would like to report the following. Dr. Otto receives support as a speaker and Chair of the Scientific Advisory Board for Big Health. Dr. Bickel is a principal of HealthSim, LLC; Notifius, LLC; BEAM Diagnostics, Inc.; and Red 5 Group, LLC. In addition, he serves on the scientific advisory board for Sober Grid, Inc.; Ria Health; US WorldMeds, LLC; and is a consultant for Alkermes, Inc. Sandoz, and Nektar Therapeutics. No other authors have conflicts to report.

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