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Acute Effects of Cannabis on Breath-Holding Duration

Samantha G. Farris
University of Houston and Alpert Medical School of Brown University

Jane Metrik
Providence Veterans Affairs Medical Center, Providence, Rhode Island, and Brown University

Distress intolerance (an individual's perceived or actual inability to tolerate distressing psychological or physiological states) is associated with cannabis use. It is unknown whether a biobehavioral index of distress intolerance, breath-holding duration, is acutely influenced (increased or decreased) by cannabis. Such information may further inform understanding of the expression of psychological or physiological distress postcannabis use. This within-subjects study examined whether smoked marijuana with 2.7%–3.0% delta-9-tetrahydrocannabinol (THC), relative to placebo, acutely changed duration of breath holding. Participants (n = 88; 65.9% male) were nontreatment-seeking frequent cannabis users who smoked placebo or active THC cigarette on two separate study days and completed a breath-holding task postsmoking. Controlling for baseline breath-holding duration and participant sex, THC produced significantly shorter breath-holding durations relative to placebo. There was a significant interaction of drug administration × frequency of cannabis use, such that THC decreased breath-holding time among less frequent but not among more frequent users. Findings indicate that cannabis may exacerbate distress intolerance (via shorter breath-holding durations). As compared to less frequent cannabis users, frequent users display tolerance to cannabis' acute effects including increased ability to tolerate respiratory distress when holding breath. Objective measures of distress intolerance are sensitive to contextual factors such as acute drug intoxication, and may inform the link between cannabis use and the expression of psychological distress.

Public Health Significance
This study indicates that cannabis, relative to placebo, decreases ability to tolerate physical distress, which is a risk factor associated with psychological symptoms and disorders. Infrequent cannabis users, relative to frequent users, evidenced lower ability to tolerate physical distress after acute cannabis use. Findings contribute to the broader knowledge base on the acute impact of cannabis use on emotion regulation and stress tolerance.

Keywords: marijuana, psychopathology, distress tolerance, task persistence

Distress intolerance, defined as one's perceived or objective inability to withstand aversive psychological or physiological states (Leyro, Zvolensky, & Bernstein, 2010), is a key vulnerability factor associated with the acquisition and maintenance of various forms of psychopathology, including substance use disorders (Brandon et al., 2003; Vujanovic, Bernstein, & Litz, 2011). Distress intolerance is implicated in problematic cannabis use. For example, individuals who perceive that they are less able to tolerate psychological distress report more frequent cannabis use (Buckner, Keough, & Schmidt, 2007) and more severe problems related to use (Buckner et al., 2007; Bujarski, Norberg, & Copeland, 2012; Dvorak & Day, 2014). Cannabis users with high perceived intolerance for distress also endorse stronger coping-oriented cannabis use motives (Bujarski et al., 2012; Potter, Vujanovic, Marshall-Berenz, Bernstein, & Bonn-Miller, 2011; Zvolensky et al., 2009), which may in part account for more problematic use (Bujarski et al., 2012). Consistent with affective motivational theories of drug addiction (Baker, Piper, McCarthy,

Samantha G. Farris, Department of Psychology, University of Houston, and Department of Psychiatry and Human Behavior, Alpert Medical School of Brown University; Jane Metrik, Providence Veterans Affairs Medical Center, Providence, Rhode Island, Center for Alcohol and Addiction Studies, Brown University School of Public Health, and Department of Psychiatry and Human Behavior, Alpert Medical School of Brown University.

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Correspondence concerning this article should be addressed to Jane Metrik, Center for Alcohol and Addiction Studies, Brown University, Box G-S121-4, Providence, RI 02912. E-mail: Jane_Metrik@brown.edu

Majeskie, & Fiore, 2004; McCarthy, Curtin, Piper, & Baker, 2010), it is possible that high distress intolerant individuals may be particularly likely to rely on cannabis use to acutely reduce situational negative affect (Haney, Ward, Comer, Foltin, & Fischman, 1999; McDonald, Schleifer, Richards, & de Wit, 2003; Phan et al., 2008; Metrik et al., 2011) or to attenuate uncomfortable withdrawal symptoms (Budney, Moore, Vandrey, & Hughes, 2003). As these behavioral patterns are strongly negatively reinforcing, cannabis users are at greater risk not only for the development of cannabis use disorder but may actually experience increased psychological distress states (Zvolensky, Bernstein, Marshall, & Feldner, 2006).

Importantly, while distress intolerance is posited as a stable, trait-like construct (e.g., Kiselica et al., 2014), it is plausible that cannabis-specific contexts (acute intoxication, deprivation) may result in within-person changes in one's ability to tolerate distress states. Data suggest that distress intolerance may be context dependent/sensitive (e.g., Bernstein, Trafton, Ilgen, & Zvolensky, 2008; Szuhany & Otto, 2015). In particular, behavioral measures of distress intolerance that are designed to induce mental or physical distress states may tap a more state-dependent (contextually sensitive) construct. However, there is currently a dearth of controlled studies that examine the acute effects of cannabis administration on distress intolerance.

There are two possible ways cannabis could affect distress intolerance. One, it may decrease intolerance of distress states, which would be observed via longer persistence during a stressful behavioral task. Ecological momentary data and human laboratory studies document reductions in negative affect, withdrawal severity and craving following cannabis use (e.g., Buckner et al., 2015; Haney et al., 2004, 2008; Metrik et al., 2015; Metrik, Kahler, McGeary, Monti, & Rohsenow, 2011). Moreover, delta-9-tetrahydrocannabinol (THC) attenuates subjective pain ratings (Abrams et al., 2007; Ellis et al., 2009; Wilsey et al., 2008, 2013) and increases persistence during pain tolerance tasks (cold-presser test; Cooper, Comer, & Haney, 2013), although the pain modulation effects may only be seen at low versus high doses of THC (4% vs. 8%; Wallace et al., 2007). Alternatively, it is possible that THC increases distress intolerance, as indicated by shorter persistence during a stressful behavioral task, due to the effects of THC on motivational processes. That is, following cannabis use, individuals may be more likely to give up on tasks that involve self-regulatory abilities (i.e., tasks that require greater cognitive effort), consistent with "amotivational syndrome" (McGlothlin & West, 1968). Indeed, relative to placebo, THC produces increased passive leisure behavior relative to work behavior (Kagel, Battalio, & Miles, 1980), and decreased reinforced responding (less time spent and money earned) during a monetary progressive-ratio schedule task (Cherek, Lane, & Dougherty, 2002). Cannabis also acutely impairs executive functioning involved in self-regulation (Crean, Crane, & Mason, 2011; Hart, van Gorp, Haney, Foltin, & Fischman, 2001), which could influence persistence in the distressing tasks following THC use.

Given these considerations, the current study aimed to examine the effect of THC versus placebo on distress intolerance via a breath-holding challenge. In this task the duration (in seconds) that one is able to hold one's breath (i.e., tolerate the build-up of carbon dioxide in their lungs) is used as a behavioral indicator of distress intolerance, with shorter durations reflecting greater intolerance of physical distress. Importantly, recent research has suggested breath-holding duration maintains unique explanatory value relative to physical health problems in the prediction of other distress intolerance processes, such as discomfort intolerance and mirror-tracing task persistence (Hogan, Farris, Brandt, Schmidt, & Zvolensky, 2015). Breath-holding duration is differentially associated with participant sex with females typically demonstrating shorter persistence during this task (Berenz, Vujanovic, Coffey, & Zvolensky, 2012; Hogan et al., 2015; Kahler, McHugh, Metrik, Spillane, & Rohsenow, 2013). Thus, we expected that female cannabis users, relative to male, would have shorter breath-holding durations, and the acute effects of THC on breath-holding duration would be conditional on participant sex. Additionally, because more frequent cannabis users show greater tolerance to the acute effects of THC (e.g., Chait & Perry, 1992; D'Souza et al., 2008; Kirk & de Wit, 1999; Lichtman & Martin, 2006; Metrik et al., 2011), we expected the effects of THC on breath-holding duration would be conditional upon frequency of cannabis use and more pronounced among infrequent users.

Method

Participants

Data were obtained from participants who completed a larger experimental study investigating variability in cannabis' acute and cue-elicited effects (Metrik et al., 2015). Cannabis smokers recruited from the community met the following inclusion criteria: native English speaker, 18–44 years of age, non-Hispanic Caucasian (due to aims of the parent study), cannabis use at least 2 days per week in the past month and at least weekly in the past 6 months, and self-reported ability to abstain from cannabis for 24 hr without withdrawal. Exclusion criteria were intent to quit or receive treatment for cannabis abuse; pregnancy; nursing; positive urine toxicology screen for drugs other than cannabis; current *DSM–IV* Axis I affective disorder or panic disorder, psychotic symptoms or suicidal state assessed by the Structured Clinical Interview for *DSM–IV* (Non-Patient Ed.; SCID-I/NP; First, Spitzer, Gibbon, & Williams, 2002); contraindicated medical issues by physical exam or body mass index >30; and ≥ 20 tobacco cigarettes a day (Metrik et al., 2015). Of the 89 participants who completed the study (Metrik et al., 2015), one participant did not complete the breath-holding task following one experimental session thus was excluded from the current analyses.

Participants ($n = 88$; $M_{age} = 21.5$, $SD = 4.5$; 65.9% male) reported cannabis use on an average of 72.3% ($SD = 21.9\%$) of days in the 60 days prior to baseline, with a mean of 2.1 ($SD = 1.24$) times a day. Additionally, 13.6% and 29.5% met criteria for past year *DSM–IV* cannabis dependence and abuse, respectively. Of note, the presence of cannabis withdrawal was additionally assessed as a cannabis dependence symptom, consistent with *DSM–5* (American Psychiatric Association, 2013). About half of participants ($n = 47$; 46.6%) reported tobacco cigarette use in the past 60 days. Tobacco cigarette smokers reported cigarette use an average of 58.3% ($SD = 41.7$) of days in the past 60 days, and averaged 4.2 ($SD = 3.8$) cigarettes per day on smoking days. Alcohol use was reported on an average of 29.5% ($SD = 19.7$) days in the 60 days prior to baseline, with an average of 4.2 ($SD = 2.4$) drinks per drinking day. There were no significant differences in any descriptive characteristics (e.g., cannabis use, tobacco cigarette smoking, or alcohol use) by participant sex. Additional demographic data can be found in Metrik et al. (2015).

Procedure

Full details of procedures used in the current study have been previously outlined (Metrik et al., 2015), and all procedures were approved by the institutional review board. Participants completed a baseline session followed by two experimental double-blind smoking sessions during which they smoked either one cannabis cigarette (2.8–3.0% THC) or one placebo cigarette (0% THC). Experimental session order was counterbalanced. The two experimental sessions occurred an average of 11.8 (SD = 10.8) days apart. Participants were told to abstain from cannabis and tobacco smoking for 15 hr, alcohol for 24 hr, and caffeine for 1 hr before both sessions. A conservative alveolar carbon monoxide (CO) reading of ≤6 ppm was used to confirm no recent smoking (Cooper & Haney, 2009; Metrik et al., 2015) with a Bedfont Scientific Smokelyzer®. Tobacco smokers were permitted to smoke a tobacco cigarette following the CO test to prevent nicotine withdrawal, approximately 1 hr prior to drug administration. Zero breath alcohol concentration was verified with an Alco-Sensor IV (Intoximeters, Inc., St. Louis, MO).

At baseline, participants completed interview and self-report assessments including demographics, diagnostic interview, assessment of distress intolerance, and cannabis use questions. At the experimental sessions, participants completed a breath-holding task within a 45- 60-min window after the start of drug administration. Cannabis cigarettes (active THC: 2.7%–3.0% and placebo made of cannabis from which THC had been removed) were provided by the National Institute on Drug Abuse, rolled at both ends, humidified, and smoked according to the standardized paced puffing procedure until the ash reached a mark 10 mm from the end (Foltin, Fischman, Pedroso, & Pearlson, 1987; Metrik et al., 2015). An objective count of the number of puffs to complete a cigarette was recorded (observed puff range = 6–13). Participants remained in the laboratory for 4 hr after smoking, passed a field sobriety test, and were transported home by taxi. All participants were compensated upon completion of the study.

Measures

The Time-Line Follow-Back Interview (TLFB; Dennis et al., 2004) assessed past 60-day number of marijuana, alcohol, and tobacco cigarette use days using a calendar-assisted structured interview.

Heart rate (HR; beats per minute) was recorded via a blood pressure cuff attached to the nondominant arm (Datascope Accutorr Plus). Subjective drug effects were assessed with the Addiction Research Center Inventory—Marijuana scale (ARCI-M; Chait, Fischman, & Schuster, 1985; Martin, Sloan, Sapira, & Jasinski, 1971). Data on heart rate (45 and 60 mins from the start of smoking) and ARCI-M (presmoking and at 45 min) were used as manipulation checks of THC's acute effect relative to placebo.

Biobehaviorally indexed distress intolerance was assessed with the Breath-Holding Duration Task (Asmundson & Stein, 1994). During the task, participants are asked to hold their breath for as long as they can while being timed with a stopwatch. Breath-holding duration is time to exhalation. This task has been frequently used as measure of physical distress intolerance (Hajek, Belcher, & Stapleton, 1987; Brown et al., 2009), with shorter durations of breath-holding indicating greater intolerance of physical distress.

Self-reported distress intolerance was also assessed at baseline per the Distress Tolerance Scale (DTS; Simons & Gaher, 2005). The DTS includes 15 items rated on a 5-point Likert-type scale ranging from 1 (*strongly agree*) to 5 (*strongly disagree*) that assess individuals' perceived ability to tolerate negative emotional states. Items are summed and a mean score is computed; possible range is 1–5, with higher scores reflecting greater tolerance (lower intolerance) for distress. This scale has good psychometric properties, including high internal consistency and convergent validity (Simons & Gaher, 2005).

Data Analytic Strategy

Prior analyses found THC, relative to placebo, significantly increased heart rate and subjective intoxication on the ARCI-M and demonstrated significant effect of time reflecting the fact that effects were more pronounced toward the beginning of the postsmoking period (Metrik et al., 2015). Paired-samples t tests were used in the current study to confirm that differences in HR and subjective drug effect between drug conditions remained significant when the breath-holding duration task was administered. To test the main aims, we performed regression analyses with SAS version 9.4 (SAS Institute Inc., Cary, NC). Specifically, PROC REG was used to test the effects of experimental condition (0 = placebo; 1 = THC) on changes in breath-holding duration postsmoking. Mean-centered baseline breath-holding duration was entered as a covariate in the model. Participant sex and tobacco cigarette smoking status were examined for differences in terms of baseline breath-holding duration (Hogan et al., 2015; Kahler, McHugh, Metrik, Spillane, & Rohsenow, 2013). In a separate analysis, frequency of cannabis use (percentage of days used cannabis per the TLFB; mean centered) was tested as a moderator of THC's acute effect on breath-holding duration by adding the interaction term of experimental condition × frequency of cannabis use to the model.

Table 1
Distress Tolerance Scale and Breath-Holding Duration Scores

Assessment time point	Total sample (n = 88) M (SD)	Males (n = 58) M (SD)	Females (n = 30) M (SD)
	Distress Tolerance Scale		
Baseline	4.0 (.69)	4.1 (.64)[a]	3.7 (.72)[a]
	Breath-holding duration		
Baseline	51.0 (22.57)[a]	59.6 (20.93)[b]	34.5 (15.43)[b]
Placebo	49.4 (21.85)	59.3 (19.09)[c]	30.3 (12.00)[c]
THC	43.4 (21.86)[a]	52.9 (20.31)[d]	25.0 (9.66)[d]

Note. Superscript letters denote statistically significant mean differences (ps < .05). Raw breath-holding durations are reported. THC = delta-9-tetrahydrocannabinol.

Results

As a manipulation check, THC, relative to placebo, produced significantly higher heart rate at 45 min (M = 79.9, SD = 14.2, vs. M = 64.2, SD = 10.7), $t(174) = -8.38$, $p < .0001$, and at 60 min (M = 76.7, SD = 13.8, vs. M = 65.7, SD = 11.1), $t(174) = -5.81$, $p < .0001$. Heart rate was not differentially affected by tobacco cigarette smoking status. Number of puffs did not significantly differ when participants smoked THC relative to placebo cigarettes (M = 9.2, SD = 1.4, vs. M = 8.8, SD = 1.4), $t(174) = -1.60$, p = .112. There was also no significant difference in number of puffs for THC or placebo when stratified by participant sex or tobacco cigarette smoking status. Frequency of cannabis use was not significantly associated with puff count during THC or placebo administration. After adjusting for presmoking subjective intoxication on the ARCI-M, THC relative to placebo increased subjective intoxication at 45 min postsmoking (b = 3.4, SE = .35, t = 8.68, $p < .0001$).

Descriptive means and standard deviations for baseline DTS scores and breath-holding duration at three time points are presented separately by sex in Table 1. The DTS was not significantly correlated with breath-holding duration at baseline (r = .18, p = .09). Female participants, relative to males, had significantly lower DTS scores which are indicative of higher perceived distress intolerance. An analysis of variance (ANOVA) with a Tukey post hoc test indicated that women had significantly shorter average breath-holding durations than men at baseline, $t(86) = 5.79$, $p < .0001$, and postsmoking THC, $t[85.6] = 7.10$, $p < .0001$, and postsmoking placebo, $t(82.7) = 8.72$, $p < .0001$; shorter durations are indicative of higher behavioral distress intolerance. There was a nonsignificant effect of tobacco smoking status in terms of breath-holding duration at baseline or postsmoking THC or placebo (all ps > .05); thus this variable was omitted from subsequent analyses.

In the main regression analyses, after adjusting for participant sex and baseline breath-holding duration, there was a significant effect of THC on postsmoking breath-holding duration (see Table 2). As illustrated in Figure 1, THC significantly reduced breath-holding duration relative to placebo (full-model adjusted R^2 = .72). Based on sex differences in mean levels of breath-holding duration at each assessment point, the Sex × THC condition effect was tested; this was a nonsignificant effect (p = .77).

Next, retaining participant sex as a covariate, frequency of cannabis use was added to the regression model as a moderator of THC's effect on breath-holding duration. Results of the full model were significant (full-model adjusted R^2 = .73). There was a nonsignificant main effect of cannabis use frequency ($b = -0.06$, $SE = 0.06$, $t = -0.99$, p = .325; sr^2 = 0.01); however, the interaction of cannabis use frequency × THC condition was significant (b = 0.21, SE = 0.08, t = 2.68, p = .008; sr^2 = 0.01). Tests of the simple slopes were conducted using values of ±1 SD on cannabis use frequency. Probe of the interaction revealed that the effect of THC on breath-holding duration was not differentially affected by more frequent cannabis use (+1 SD: $b = -1.30$, $t = -0.35$, p = .724). However, the effect of THC on breath-holding duration appeared to be conditional upon less frequent cannabis use (−1 SD: $b = -10.65$, $t = -2.95$, p = .004). Specifically, plot of the interaction (see Figure 2) revealed that among less frequent cannabis users, THC, relative to placebo, significantly reduced breath-holding duration.

Table 2
Regression Predicting Breath-Holding Duration

Predictor	b	SE	t	p	sr^2
Intercept	53.5	1.46	36.63	<.0001	—
BL breath-holding	.7	.05	14.09	<.0001	.32
Sex	−12.0	2.20	−5.45	<.0001	.05
Condition	−6.1	1.78	−3.42	.0008	.02

Note. Sex (coded 0 = male; 1 = female); BL = baseline; condition (coded 0 = placebo; 1 = THC); THC = delta-9-tetrahydrocannabinol.

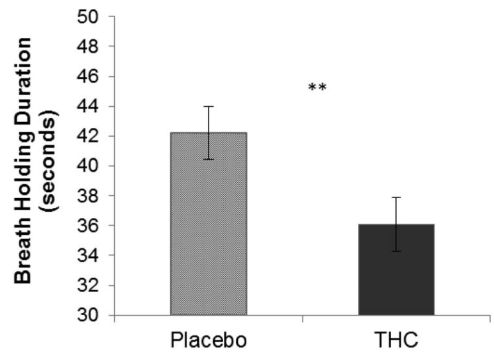

Figure 1. Breath-holding duration after THC versus placebo. Covariate-adjusted mean breath-holding duration following administration of THC and placebo. Error bars represent standard error of the mean. ** $p < .001$. THC = delta-9-tetrahydrocannabinol.

Discussion

Findings offer novel evidence that THC decreased persistence during a breath-holding duration task (a behavioral index of distress intolerance), relative to placebo. This effect was evident after adjusting for the significant effects of baseline breath-holding duration and participant sex. There may be several possible explanations for the observed main effect of THC on breath-holding

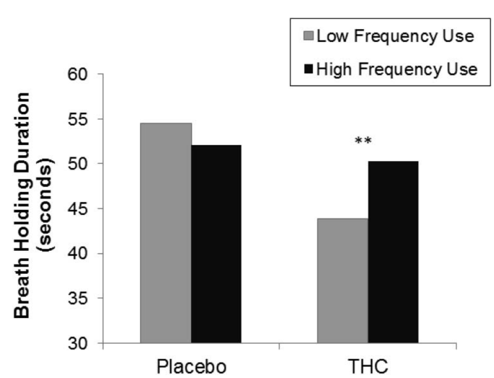

Figure 2. Drug Condition × Frequency of Cannabis Use on breath-holding duration. Effect of THC relative to placebo by high and low frequency of cannabis use on breath-holding duration. ** p = .004. THC = delta-9-tetrahydrocannabinol.

duration. First, this patterning of findings is consistent with "amotivational syndrome" (McGlothlin & West, 1968). Laboratory data indicate that THC acutely affects behavioral disengagement (e.g., Cherek et al., 2002), which may be particularly likely in a distressing task if the task is lacking in personal relevance. Personal salience on task performance was evident when financial incentive attenuated amotivational effects (e.g., Cherek et al., 2002). Similarly, persistence in a physically distressing task (e.g., cold-pressor task) is longer when individuals are asked to utilize values-based imagery to increase personal salience for enduring acute pain, relative to a control group without personalized component (Branstetter-Rost, Cushing, & Douleh, 2009). Thus in the current study, participants' shorter persistence in the breath-holding task may be indeed related to "amotivation" following acute THC use.

Alternatively, results may be explained by THC's acute impairment of cognitive/self-regulatory efforts. Cannabis acutely impairs key aspects of cognitive functioning that may be relevant to our findings. In particular, THC is found to consistently impair disinhibition (Metrik et al., 2012; McDonald et al., 2003; Ramaekers et al., 2006, 2009), divided attention, and psychomotor control (Desrosiers et al., 2015). Relatedly, THC impairs time perception (Sewell et al., 2013), specifically, increases the internal clock which results in overestimation of time perception, which may explain shorter breath-holding durations following THC administration. In the context of our study, these cognitive impairments may contribute to one's inability to self-regulate (i.e., cannot maintain persistence in breath-holding duration task). The current data on self-reported subjective intoxication at the time of the breath-holding duration task reflects self-awareness of perceived impairment from the drug, which may signal inability to regulate task performance or may lead to less effort on the task. It is also possible that observed THC-induced increases in physiological arousal (heat rate) may have led to (a) faster oxygen depletion or (b) heightened attention to interoceptive cues, both which might have translated to behavioral increases in distress intolerance on the breath-holding task.

Additionally, as expected, frequency of cannabis use moderated the effect of THC administration on breath-holding duration. Specifically, relative to placebo, THC decreased breath-holding time among less frequent but not among more frequent users. Findings support the role of drug tolerance among frequent cannabis users extending prior investigations on tolerance to cannabis' subjective (Chait & Perry, 1992; D'Souza et al., 2008; Kirk & de Wit, 1999; Metrik et al., 2011) and cognitive effects (Ramaekers et al., 2009) to that of behavioral intolerance of respiratory distress. Importantly, frequent cannabis users in the current sample were using on 94.4% of days (approximately 6.6 days per week), whereas the infrequent users were using on 50.0% of days. Thus, daily users may develop tolerance to the acute physiological effects of THC (e.g., increased heart rate) and, in turn, may be less reactive to bodily sensations more generally (e.g., respiratory distress due to breath-holding task). The current findings align with existing studies that demonstrate that heavy cannabis users develop tolerance to the impairing effects of THC on neurocognitive functions (Desrosiers et al., 2015; Hart et al., 2001; Ramaekers et al., 2009). In contrast, among occasional cannabis users, THC impairs performance on measures of divided attention, perceptual motor control, and executive functioning related to decision-making/planning (Ramaekers et al., 2009). Among frequent users, longer breath-holding duration (i.e., tolerance of distress) following THC may, in part, perpetuate maladaptive cannabis use if individuals learn that cannabis aids in their ability to tolerate uncomfortable distress states. Such learned associations may be especially likely among individuals who expect cannabis to promote relaxation/tension reduction (Metrik et al., 2011).

Two additional findings warrant comment. First, female cannabis users, relative to male, reported lower perceived ability to tolerate psychological distress, per the self-report DTS. This is consistent with the finding that female users, relative to male, had shorter average breath-holding durations at baseline and following both drug conditions. These findings contribute to the growing literature that document sex differences in perceived distress intolerance (e.g., Johnson, Berenz, & Zvolensky, 2012; Simons & Gaher, 2005) and breath-holding duration in community-recruited samples with and without psychopathology (Johnson et al., 2012), trauma-exposed individuals (Berenz et al., 2012) and substance-using populations, including cigarette smokers (Hogan et al., 2015; Farris, Zvolensky, Otto, & Leyro, 2015; Perkins, Giedgowd, Karelitz, Conklin, & Lerman, 2012) and smokers who are also heavy drinkers (Kahler et al., 2015). This sex difference has also been found in other behavioral distress intolerance tasks among cigarette smokers (e.g., persistence during a carbon dioxide challenge; Brown et al., 2002). Second, while nearly half of the cannabis users in the current sample were also cigarette smokers, cigarette-smoking status was not associated with breath-holding duration. This is important given data that indicate smoking tobacco cigarettes and cannabis, relative to only smoking tobacco cigarettes, is associated with increased odds of respiratory symptoms (Moore, Augustson, Moser, & Budney, 2005) and lower spirometric performance (Taylor, Poulton, Moffitt, Ramankutty, & Sears, 2000). Thus, despite known respiratory differences in these subgroups, the index of distress intolerance (breath-holding duration) was not differentially influenced by cigarette smoking status.

There are a few important interpretive caveats that warrant mention. First, due to the genetic aims of the parent study, the current sample included participants who were exclusively Caucasian, thereby potentially limiting the generalizability of the current findings. Second, cannabis users were excluded on the basis of having a past-month affective or panic disorder, which may have potentially resulted in overall longer breath-holding duration scores relative to if the sample included cannabis users with affective psychopathology. However, baseline means of breath-holding duration in the current sample are well within 1 SD of means reported in a study of drug-dependent individuals with affective psychopathology (McHugh & Otto, 2011). Third, differential effects of smoking cannabis with THC versus placebo cigarette on bronchial dynamics (e.g., acute THC-induced bronchodilation; Tashkin, 2013) could have accounted for some variability in breath-holding duration persistence. However, data consistently indicate that breath-holding duration scores are not significantly associated with lung functioning (Hajek et al., 1987) or presence of tobacco-related medical conditions (Hogan et al., 2015). Lastly, while number of puffs were examined and did not differ between THC and placebo drug conditions, the present study did not measure puff volume, which may be related to changes in plasma concentrations of THC (Azorlosa et al., 1992; Azorlosa, Greenwald, & Stitzer, 1995).

The current study exclusively examined the acute effect of cannabis on breath-holding duration. Interestingly, at certain doses, THC appears to increase persistence during physical distress intolerance tasks that do not require pulmonary functioning (e.g., cold-pressor test; Cooper, Comer, & Haney, 2013). It would be important to extend this line of work to examine alternative behavioral measures of distress intolerance—including those that tap intolerance of mental distress (e.g., Paced Auditory Serial Addiction Test, Lejuez et al., 2003; Mirror Tracing Persistence Task, Strong et al., 2003; Anagram persistence task, Eisenberger & Leonard, 1980). Future work should also examine THC's acute effects on distress intolerance (behavioral disengagement) in the context of personally salient conditions. Another important future direction would be to examine the nature of distress intolerance in the context of alternative drug states (e.g., acute cannabis deprivation). For example, data nonspecific to cannabis use indicate that among daily tobacco smokers, breath-holding duration was shorter following acute (12 hr) nicotine deprivation, relative to when smoking as usual (Bernstein, Trafton, Ilgen, & Zvolensky, 2008). Moreover, laboratory data indicate that shorter breath-holding duration is predictive of early tobacco cigarette-smoking lapse during controlled relapse analogue tasks (Kahler et al., 2013).

Together, these data indicate that distress intolerance (via breath-holding duration) may be exacerbated by varying drug-specific contexts, and may promote shorter latency to initiating drug use (i.e., lapse/relapse; Haney et al., 2010). In concert, given the consistent evidence that distress intolerance is linked to various forms of psychopathology, including the maintenance of problematic substance use (Leyro et al., 2010), these data have the potential to uniquely inform the nature of affective symptoms following acute cannabis use. Specifically, given distress intolerance is linked to heightened physiological/subjective distress and emotional reactivity (Farris et al., 2015; Marshall et al., 2008), following cannabis use, increases in distress intolerance may promote emotion-focused coping (e.g., Bujarski et al., 2012), which may in turn result in reinitiation of cannabis use (Hasan, Babson, Banducci, & Bonn-Miller, 2015).

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