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Emotion Regulation and Coping Motives Serially Affect Cannabis Cessation Problems Among Dually Diagnosed Outpatients

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Abstract

Little empirical work has evaluated why anxious cannabis users are especially vulnerable to poorer cannabis cessation outcomes. Presumably, these individuals rely on cannabis because they have difficulties with emotion regulation and they therefore use cannabis to manage their negative emotions. The current study examined the direct and indirect effects of anxiety severity on a range of cannabis cessation variables among 79 (63.3% non-Hispanic White; 43.0% female) adults with anxiety disorders seeking outpatient treatment for cannabis use disorder. The independent and serial indirect effects of difficulties with emotion regulation and coping motives were examined in relation to the anxiety-cannabis variables. Anxiety severity was directly and robustly related to greater cannabis withdrawal symptom severity, less self-efficacy to refrain from using cannabis in emotionally distressing situations, and more reasons for quitting. Anxiety was indirectly related to cannabis outcomes via the serial effects of emotion regulation and coping motives. These findings document the important role of emotion regulation and coping motives in the relations of anxiety with cannabis cessation variables among dually diagnosed outpatients.

Keywords

cannabis; marijuana; difficulties with emotion regulation; coping motives; dual diagnosis

Anxiety and its disorders are highly related to cannabis use disorder (CUD). To illustrate, up to 50% of people with CUD have an anxiety disorder and those with CUD are nearly six

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times more likely to experience a co-occurring anxiety disorder compared with those without CUD (Stinson, Ruan, Pickering, & Grant, 2006). In fact, anxiety disorders may be a risk factor for CUD -- anxiety disorders tend to onset before cannabis dependence in the vast majority of dually diagnosed individuals (Agosti, Nunes, & Levin, 2002) and prospective work indicates that anxiety and anxiety disorders tend to onset prior to cannabis problems, including CUD (Buckner et al., 2008; Marmorstein, White, Loeber, & Stouthamer-Loeber, 2010). This co-occurrence has important clinical implications. For example, greater anxiety symptoms at treatment termination predicts greater post-treatment cannabis use and use-related problems (Bonn-Miller & Moos, 2009; Buckner & Carroll, 2010). Thus, identification of factors that play a role in cannabis-related problems among anxious patients could inform treatment and prevention efforts.

One such vulnerability factor that may be especially relevant is difficulties with emotion regulation. Accumulating evidence supports that severity of anxiety symptoms is related to difficulties with emotion regulation (e.g., Amstadter, 2008; Cisler, Olatunji, Feldner, & Forsyth, 2010; Gonzalez, Zvolensky, Vujanovic, Leyro, & Marshall, 2008; Hofmann, Sawyer, Fang, & Asnaani, 2012; Mennin, Heimberg, Turk, & Fresco, 2005). In line with negative reinforcement models of drug use (e.g., Baker, Piper, McCarthy, Majeskie, & Fiore, 2004), anxiety may be related to cessation problems because anxious persons have greater difficulty regulating emotion and thus rely on cannabis to cope; that is, the indirect effects of difficulties with emotion regulation and coping motives serially impact cannabis processes. Difficulties with emotion regulation are related to but distinct from cannabis coping motives (e.g., Bonn-Miller, Vujanovic, Boden, & Gross, 2011; Bonn-Miller, Vujanovic, & Zvolensky, 2008). Extant data suggest that anxiety severity may be related to cannabis use variables indirectly via the serial effects of difficulties with emotion regulation and coping motives: (1) severity of symptomatology of various anxiety conditions is related to coping motivated cannabis use (e.g., Buckner, Bonn-Miller, Zvolensky, & Schmidt, 2007; Johnson, Bonn-Miller, Leyro, & Zvolensky, 2009; Zvolensky et al., 2009); (2) some types of anxiety are indirectly related to coping motives via difficulties with emotion regulation (Bonn-Miller et al., 2011); and (3) severity of anxiety symptoms is indirectly related to cannabis use and related problems via coping motives (e.g., Buckner et al., 2007; Johnson et al., 2009; Zvolensky et al., 2009).

In a sample of adults with both CUD and anxiety disorders seeking outpatient psychotherapy for CUD and anxiety, the current study tested the hypothesis that anxiety symptom severity would be related to a variety of cannabis cessation variables (withdrawal symptoms during most recent quit attempt, self-efficacy to abstain from cannabis, reasons for quitting) indirectly via the serial effects of difficulties with emotion regulation and then coping motivated cannabis use. Specifically, it was hypothesized that anxiety severity would be positively related to withdrawal and reasons to quit and negatively related to self-efficacy to quit. These cannabis cessation variables were chosen given that withdrawal symptoms and self-efficacy to abstain are related to cannabis cessation outcomes (Buckner et al., 2015; Chung, Martin, Cornelius, & Clark, 2008; Stephens, Wertz, & Roffman, 1995) and that more reasons for quitting are negatively related to substance use (Foster, Schmidt, & Zvolensky, 2015).

Methods

Participants and Procedures

Participants ($n=79$) were adults seeking treatment to reduce or cease cannabis use ($M_{age}=24.0$, $SD=7.9$, range=18–56; 43.0% female) who were recruited from the community (via flyers, newspaper ads, online advertisements) to participate in a randomized controlled trial examining the efficacy of two psychosocial interventions for CUD (clinicaltrials.gov #NCT01875796). Inclusion criteria included being 18–65 years of age, meeting DSM-5 criteria for CUD and an anxiety disorder, having used marijuana in the past week to manage anxiety, marijuana being the drug of choice to manage anxiety, endorsing motivation to quit smoking marijuana, being interested in treatment to manage anxiety, and being willing to complete 12 weekly treatment sessions and follow-up assessments for up to 6 months following treatment. Exclusion criteria included currently receiving psychological or substance use treatment, being mandated to receive treatment, and currently being pregnant or interested in becoming pregnant during the study timeframe. The current study is based on secondary analyses of pre-treatment data.

The racial/ethnic composition of the current sample was non-Hispanic White (63.3%), Hispanic White (6.3%), non-Hispanic African American (21.5%), Asian/Asian American (1.3%), multiracial (3.8%), and other (3.8%). Regarding highest educational level attained, 1.3% reported less than high school, 13.9% had a high school diploma, 64.6% completed some college, 5.1% had a technical degree, and 15.2% had a 4 years bachelor's degree. In terms of relationship status, 79.7% were single, 7.6% were cohabitating, 5.1% were divorced, 3.8% stated "other", 2.5% were married, and 1.3% were separated. Age of first cannabis use was on average 16.1 years old ($SD=3.1$). In the month prior to their appointment, participants used cannabis a mean of 22.0 ($SD=8.7$) days, an average of 3.0 ($SD=2.3$) joints per cannabis use day. The most common primary methods of use were bowls (34.6%), joints (46.2%), bongs (3.8%), and "other" (usually preferring more than one method; 15.4%). The majority reported at least one previous cannabis quit attempt (78.5%), with an average of 3.6 ($SD=13.5$) previous attempts. However, only 9.4% endorsed a history of treatment for drug use whereas 42.2% endorsed a history of treatment for anxiety. Primary DSM-5 diagnoses were as follows: CUD (44.3%), social anxiety disorder (32.9%), generalized anxiety disorder (13.9%), panic disorder (3.8%), other specified anxiety disorder (2.5%), and other (2.6%; e.g., agoraphobia).

Participants provided informed consent prior to participation and the study protocol was approved by the university's Institutional Review Board. Participants underwent a clinical interview and completed a computerized battery of self-report questionnaires.

Measures

The *Structured Interview Guide for the Hamilton Anxiety Scale* (SIGH-A) (Hamilton, 1959) was used to assess anxiety symptom severity. This measure was developed to assess anxiety in clinical populations and it demonstrates high inter-rater and test-retest reliability (Shear et al., 2001). The SIGH-A was administered at screening and again at baseline by two independent doctoral students in clinical psychology (the baseline rater was blind to prior

ratings). Baseline ratings were conducted on average 12.6 (SD = 11.13) days after screening. Intraclass Correlation Coefficient (ICC = .81, 95% CI: .69–.88) was excellent. The scale also demonstrated good internal consistency at baseline ($\alpha=.87$).

The *Difficulties in Emotional Regulation Scale* (DERS; Gratz & Roemer, 2004) is a 36-item assessment of emotion dysregulation. Items are rated from 1 (*almost never*) to 5 (*almost always*). In the current investigation, the DERS total sum score was used as a global index of emotion dysregulation (Gratz & Roemer, 2004). Consistent with past work (Gratz & Roemer, 2004), the scale demonstrated excellent internal consistency in the current sample ($\alpha=.93$).

Coping motives for cannabis use were assessed with the coping scale of the *Marijuana Motives Measure* (Simons, Correia, Carey, & Borsari, 1998), a 5-item measure of the degree to which participants have smoked cannabis for coping (e.g., to forget my worries) reasons from 1 (*almost never/never*) to 5 (*almost always/always*). The coping scale has demonstrated good construct validity (Zvolensky et al., 2007) and internal consistency in prior work (Chabrol, Ducongé, Casas, Roura, & Carey, 2005) and in the present sample ($\alpha = .85$).

Marijuana Withdrawal Checklist (MWC; Budney, Novy, & Hughes, 1999) assessed 15 withdrawal symptoms during participants' most recent period of abstinence from 0 (*not at all*) to 3 (*severe*) for participants who endorsed a prior cannabis quit attempt. This measure is sensitive to the effects of abstinence (Budney, Hughes, Moore, & Novy, 2001; Budney et al., 1999) and has demonstrated good internal consistency in prior work (Budney, Moore, Vandrey, & Hughes, 2003; Vandrey, Budney, Kamon, & Stanger, 2005) and in the current sample ($\alpha=.91$).

Situational Self-Efficacy Scale (Stephens et al., 1995) measures of the degree to which one feels confident in their ability to not use cannabis across several high-risk cannabis use situations on a scale from 1 (*not at all confident*) to 7 (*extremely confident*). The scale is comprised of two subscales (DeMarce, Stephens, & Roffman, 2005): self-efficacy for psychologically-distressing situations (PDSE) that includes seven items (e.g., feeling depressed or worried, feeling frustrated; current $\alpha=.90$) and self-efficacy in non-distressing situations (NDSE) that includes eight items (e.g., feeling like celebrating, at a party where people were using; current $\alpha=.90$). Means for each subscale were used.

The *Reasons for Quitting Questionnaire* (Steinberg et al., 2002) consisted of a list of 25 reasons to change their cannabis use (e.g., "To show myself that I can quit if I really want to") and asked to select all the reasons that applied to them. Endorsed items were summed to create an index of total number of reasons. This measure evidenced good internal consistency in the current sample ($\alpha=.86$).

The clinician-administered *Timeline Follow Back* (TLFB; Sobell & Sobell, 1992) was used to assess frequency and quantity of cannabis use during the 30 days prior to the baseline appointment. The TLFB is a reliable and valid self-report measure of cannabis use (O'Farrell, Fals-Stewart, & Murphy, 2003; Robinson, Sobell, Sobell, & Leo, 2014).

Data Analytic Strategy

Analyses were conducted in SPSS 23 (IBM SPSS Inc., Chicago, IL, USA). First, zero-order correlations among predictor (anxiety symptom severity), proposed mediators (DERS and MMQ-Coping, and criterion variables (MWC, situational self-efficacy scales, Reasons for quitting) were examined. Although anxiety severity tends to be unrelated to cannabis use frequency (Twomey, 2017), we tested whether anxiety symptom severity was correlated with cannabis use in the current sample to determine whether cannabis use should be included as a covariate in our model testing. Next, serial multiple mediator models were conducted to examine the impact of DERS and MMQ-Coping as mediators of the relation between anxiety severity and criterion outcomes. Separate models were conducted for each criterion. These conceptual path models are presented in Figure 1. Hayes (2013) describes this type of model as a serial multiple mediator model, in which the independent variable can affect the dependent variable through four pathways: directly and/or indirectly via difficulties with emotion regulation only, via coping motives only, and/or via both sequentially, with difficulties in emotion regulation affecting coping motives. Although mediational models are ideally tested using prospective data, cross-sectional tests of putative indirect effects is thought to be an important first step (Hayes, 2013). These analyses were conducted using PROCESS, a conditional process modeling program that utilizes an ordinary least squares-based path analytical framework to test for both direct and indirect effects (Hayes, 2013). All specific and conditional indirect effects were subjected to follow-up bootstrap analyses with 10,000 resamples from which a 95% confidence interval (CI) was estimated (Hayes, 2009; Preacher & Hayes, 2004, 2008).

Results

Descriptive information and correlational results are presented in Table 1. Anxiety symptom severity was significantly correlated with greater withdrawal, less PDSE (but was unrelated to NDSE), and more reasons to quit. It was unrelated to cannabis use frequency. DERS and MMQ-Coping were significantly inter-correlated and were significantly related to criterion variables. Importantly, DERS and MMQ-coping remained significantly correlated after controlling for anxiety symptom severity ($pr = .37$, $p = .001$), suggesting that one affects the other, supporting the use of serial multiple mediator analyses (Hayes, 2013).

Results for paths a , b , c , and c' are presented in Table 2, which correspond to each of the three models. The estimates of the specific and conditional indirect effects are presented in Table 3. Each model is described below.

Withdrawal Symptoms

Among the 62 participants who had made a prior quit attempt, the total effects model accounted for significant variance in withdrawal symptoms ($R^2 = .235$, $df = 1, 60$, $F = 18.452$, $p = .0001$). The full model with DERS and MMQ-Coping predicted significant variance in withdrawal severity ($R^2 = .278$, $df = 3, 58$, $F = 7.460$, $p = .0003$), and there was a significant direct effect of anxiety symptom severity on withdrawal severity after controlling for DERS and MMQ-Coping (see Table 2, Problems, path c'). The indirect effects were estimated (see Table 3, Model 1); greater anxiety symptom severity was indirectly related to

more severe withdrawal symptoms through MMQ-Coping (but not DERS) and through the serial effect of DERS and MMQ-Coping.¹

Psychologically Distressing Situations Self-Efficacy

The total effects model accounted for significant variance in PDSE ($R^2 = .155$, $df = 1, 76$, $F = 13.95$, $p = .0004$). The full model with DERS and MMQ-Coping predicted significant variance in PDSE ($R^2 = .274$, $df = 3, 74$, $F = 9.30$, $p < .0001$), and there was a significant direct effect of anxiety symptom severity on PDSE after controlling for DERS and MMQ-Coping (see Table 2, Problems, path c'). The indirect effects were estimated (see Table 3, Model 2); greater anxiety symptom severity was indirectly related to less PDSE only through the serial effect of both DERS and MMQ-Coping.

Reasons for Quitting

The total effects model accounted for significant variance in reasons for quitting ($R^2 = .335$, $df = 1, 73$, $F = 9.210$, $p = .0033$). The full model with DERS and MMQ-Coping predicted significant variance in reasons for quitting ($R^2 = .217$, $df = 3, 71$, $F = 6.573$, $p = .0006$), and there was a significant direct effect of anxiety symptom severity on reasons to quit after controlling for DERS and MMQ-Coping (see Table 2, Problems, path c'). The indirect effects were estimated (see Table 3, Model 3); greater anxiety symptom severity was indirectly related to more reasons to quit only through the serial effect of both DERS and MMQ-Coping.

Alternate Model Testing

Given the limitations of testing mediation using cross-sectional data, we tested whether anxiety symptom severity was related to cannabis outcomes via the serial effects of MMQ-Coping then DERS. This indirect effects were not significant for cannabis withdrawal, $B = .002$, $SE = .025$, 95% CI: $-.047, .055$, PDSE, $B = .002$, $SE = .002$, 95% CI: $-.001, .110$, or reasons for quitting, $B = .004$, $SE = .019$, 95% CI: $-.030, .051$.

Alternatively, it may be that difficulties with emotion regulation lead to more severe anxiety symptoms which could result in more coping-motivated cannabis use, etc. However, anxiety symptom severity was no longer significantly correlated with MMQ-Coping after controlling for DERS ($pr = .13$, $p = .277$), thereby violating a key assumption of serial multiple mediator analyses (Hayes, 2013).

Discussion

The current study is the first known test of the serial effects of difficulties with emotion regulation and coping motives on anxiety symptom severity's relation to an array of

¹Given that anxiety is a symptom of cannabis withdrawal, analyses were rerun with the anxiety item removed from the MWC. The total effects model accounted for significant variance in the remaining withdrawal symptoms ($R^2 = .230$, $df = 1, 60$, $F = 17.945$, $p = .0001$). The full model with DERS and MMQ-Coping predicted significant variance ($R^2 = .284$, $df = 3, 58$, $F = 7.650$, $p = .0002$), and there was a significant direct effect of anxiety severity on withdrawal severity after controlling for DERS and MMQ-Coping, $B = .388$, $SE = .135$, $p = .006$. Anxiety severity was indirectly related to withdrawal severity through MMQ-Coping, $B = .067$, $SE = .050$, 95% CI: $.004, .210$ (but not DERS, $B = .004$, $SE = .068$, 95% CI: $-.127, .150$), and the serial effect of DERS and MMQ-Coping, $B = .042$, $SE = .027$, 95% CI: $.007, .130$.

clinically relevant cannabis use constructs among dually diagnosed cannabis users seeking outpatient treatment. Anxiety symptom severity was associated with more severe withdrawal and more reasons for quitting. It was associated with less self-efficacy to refrain from cannabis use in psychologically distressing situations (but not other situations). In fact, anxiety symptom severity was robustly related to these clinically relevant variables even after controlling for difficulties with emotion regulation and coping motives. Importantly, anxiety was related to the cannabis cessation variables indirectly via the serial effects of difficulties with emotion regulation and coping motives, suggesting a possible explanatory pathway.

The current findings extend the extant literature in several key ways. First, the findings from the current study expand upon prior work by determining key variables (difficulties with emotion regulation, coping motivated cannabis use) that help explain the relationship between anxiety and cannabis cessation problems. Difficulties with emotion regulation have been implicated in anxiety disorders (Amstadter, 2008; Cisler et al., 2010; Hofmann et al., 2012) and coping-motivated cannabis use (Bonn-Miller et al., 2011; Hyman & Sinha, 2009). Although it has been posited that difficulties with emotion regulation lead to coping motivated use as a maladaptive attempt at emotion regulation (Bonn-Miller et al., 2011), the current study extended the literature by determining that difficulties with emotion regulation and coping motives work serially in the relations between anxiety symptom severity and cannabis cessation-related factors. Notably, although difficulties with emotion regulation were correlated with coping motives (Table 1), they share only 19.4% of the variance with one another, suggesting they are distinct constructs.

Findings have important clinical implications. Given that the data suggest that patients with more severe anxiety suffer from more problems with emotion regulation which may increase their reliance on cannabis to cope with negative affectivity (leading to greater cessation problems and withdrawal symptoms), clinicians may consider explicitly teaching these patients more adaptive ways to manage negative affect to reduce their reliance on cannabis. Both adaptive and maladaptive emotion regulation strategies have been found to change during cognitive behavioral therapy (CBT), dialectical behavioral therapy (DBT) and acceptance and commitment therapy (ACT) (Aldao, Jazaieri, Goldin, & Gross, 2014; Blackledge & Hayes, 2001; Forkmann et al., 2014; Gratz & Roemer, 2004; Moscovitch et al., 2012). Importantly, targeting emotional regulation skills during psychotherapy leads to enhancement in emotion regulation skills (Berking, Meier, & Wupperman, 2010) and better treatment outcomes (Berking et al., 2008).

The present study has several limitations that can inform future work in this area. First, the study was limited to a cross-sectional design and temporal association of variables was not evaluated. Although attempts were made to evaluate alternative models, future work will need to evaluate whether anxiety severity increases difficulties with emotion regulation which increases coping-motivated use, increasing cessation problems -- or whether difficulties with emotion regulation increase anxiety severity which increases coping motivated use, etc. Further, given that anxiety is a symptom of cannabis withdrawal (Budney, Hughes, Moore, & Vandrey, 2004), future work is necessary to test whether withdrawal increases anxiety symptom severity, resulting in a positive feedback loop

between anxiety and cannabis use. Second, participants were recruited for a CUD treatment trial. Given that most individuals with CUD do not seek treatment (Stinson et al., 2006), future work should test these models among cannabis users with anxiety disorders not seeking treatment to generalize to the results to a large group of persons. It also may be advisable to explore whether a similar explanatory model is applicable to cannabis users without anxiety disorders. Third, although the study benefited from a sample with good gender (43% female) and racial (63% non-Hispanic White) diversity, participants were younger than other CUD treatment samples and although they reported smoking approximately the same number of joints per day as prior samples, they used cannabis somewhat less frequently (e.g., Marijuana Treatment Project Research Group, 2004). This may reflect that the sample was required to also suffer from co-occurring anxiety and to note that they use cannabis to manage their anxiety. It may be that the co-occurrence of pathological anxiety prompts those with CUD to seek psychological services at a younger age. Additional research is necessary to determine whether results generalize to older patients and those that use cannabis more frequently.

In sum, findings indicate that patients with more severe anxiety symptoms suffer from difficulties with emotion regulation, which may be related to their reliance on cannabis to cope with negative mood disturbances. Such emotion-driven cannabis use may be further related to in an array of cannabis use processes.

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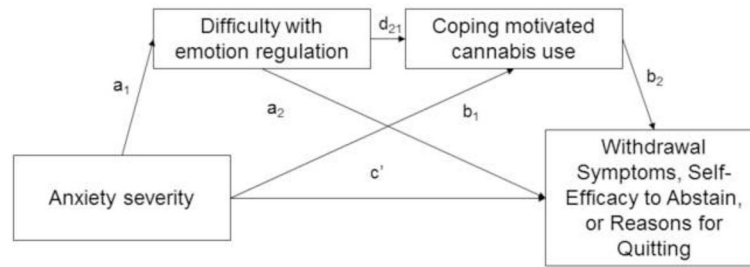


Figure 1.

Three separate models were conducted for each criterion variable to test the direct and indirect (via the serial effects of difficulties with emotion regulation and then coping motivated cannabis use) effects of anxiety symptom severity on cannabis outcome (withdrawal symptoms, self-efficacy to abstain in psychologically distressing situations, or reasons for quitting).

Table 1

Descriptive data and intercorrelations among study variables

	1	2	3	4	5	6	7	8
1. Anxiety	-							
2. Difficulties with emotion regulation	.41**	-						
3. Coping motives	.28**	.44**	-					
4. Cannabis withdrawal severity	.49**	.29*	.39**	-				
5. Self-efficacy to abstain in psychologically distressing situations	-.39**	-.20	-.43**	-.37**	-			
6. Self-efficacy to abstain in non-psychologically distressing situations	-.15	-.14	-.14	-.07	.65**	-		
7. Reasons for quitting	.25*	.22*	.31**	.37**	-.11	-.09	-	
8. Cannabis use	.15	.03	.12	.28*	-.31**	-.29**	-.07	-
<i>M</i>	19.42	96.19	17.19	16.76	3.90	3.54	11.54	68.36
<i>(SD)</i>	(8.56)	(22.42)	(5.18)	(9.66)	(1.48)	(1.47)	(5.07)	(72.34)

Table 2

Regression results for three mediation models

Criterion	Path	b	SE	t	p
Cannabis withdrawal severity	a ₁	1.165	.295	3.95	<.001
	a ₂	.148	.072	2.06	.044
	d ₂₁	.079	.028	2.81	.007
	b ₁	.006	.059	.103	.918
	b ₂	.435	.254	1.71	.092
	c'	.434	.146	2.98	.004
	c	.546	.127	4.30	<.0001
Self-efficacy to abstain in psychologically distressing situations	a ₁	.1077	.279	3.85	<.001
	a ₂	.075	.069	1.10	.277
	d ₂₁	.090	.026	3.48	.009
	b ₁	.007	.008	.875	.385
	b ₂	-.110	.032	-3.00	<.001
	c'	-.069	.019	-3.73	<.001
	c	-.057	.019	-3.00	.003
Reasons for quitting	a ₁	1.021	.287	3.56	<.001
	a ₂	.085	.069	1.24	.220
	d ₂₁	.100	.026	3.85	<.001
	b ₁	.011	.060	.18	.856
	b ₂	.684	.250	2.73	.007
	c'	.290	.147	1.97	.053
	c	.429	.142	3.03	.003

Table 3

Bootstrap estimates of the standard errors and 95% confidence intervals (CI) for the indirect effects

Indirect Effects	b	SE	CI (lower)	CI (upper)
Model 1: Marijuana Withdrawal Symptoms				
Anxiety → Difficulty with emotion regulation → Withdrawal	.007	.074	-.132	.167
Anxiety → Coping Motives → Withdrawal	.065	.051	.0003	.214
Anxiety → Difficulty with emotion regulation → Coping Motives → Withdrawal	.040	.028	.005	.130
Model 2: PDSE				
Anxiety → Difficulty with emotion regulation → PDSE	.007	.008	-.007	.024
Anxiety → Coping Motives → PDSE	-.008	.009	-.031	.006
Anxiety → Difficulty with emotion regulation → Coping Motives → PDSE	-.012	.005	-.025	-.004
Model 3: Reasons for quitting				
Anxiety → Difficulty with emotion regulation → Reasons	.011	.060	-.090	.134
Anxiety → Coping Motives → Reasons	.058	.060	-.028	.218
Anxiety → Difficulty with emotion regulation → Coping Motives → Reasons	.070	.042	.018	.199

Note. PDSE = self-efficacy to abstain in psychologically-distressing situations. The 95% CI's for indirect effects were obtained by bootstrapping with 10,000 resamples. → = affects.