THE MEDIATING ROLE OF EMOTION REGULATION IN THE RELATION BETWEEN

PANIC DISORDER AND SMOKING COGNITIONS

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ABSTRACT OF THE THESIS

The Mediating Role of Emotion Regulation in the Relation between Panic Disorder and Smoking

Cognitions

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Smoking and panic disorder (PD) are highly comorbid and their combination is associated with greater panic symptoms and worse smoking outcomes. It has been posited that smoking may be an overlearned automatized response to panic relevant distress among smokers with PD. Here smoking is negatively reinforced, via relief of nicotine withdrawal symptoms that may be associated with panic. Over time, these processes may contribute to the development of a set of beliefs and expectancies about smoking that may place smokers with PD at greater risk for greater dependence and difficulty quitting. In order to break down this cycle, research may benefit from identifying underlying and malleable vulnerabilities that may in part contribute to over-learned beliefs about smoking. Emotion regulation (ER), the extent to which one is aware and clear of their emotions as well as their ability to modulate emotional responding, is one relevant vulnerability within this framework that is positively associated with smoking beliefs and panic psychopathology. It is possible that smokers with PD who are not able to regulate emotional states may more readily rely upon smoking to manage affective distress, thereby developing corresponding smoking motives and outcome expectancies. However, to date, no research has investigated the role of ER in the relation between PD and smoking cognitions among daily cigarette smokers. In the current study, the mediating role of difficulty in ER in the relation between PD status and smoking cognitions was examined among 74 daily smokers (39.2%, $n=29$, diagnosed with PD). Findings indicate that PD status is positively associated with

habitual, addictive, and negative affect reduction smoking motives as well as negative reinforcement and negative personal consequence smoking expectancies through difficulties in ER. These results contribute to the understanding of underlying psychological mechanism of persistent smoking behaviors in this population. Interventions that develop and shape ER skills in smokers with PD may help break down negative reinforcement oriented smoking behavior in smokers with PD helping to reduce use and promote cessation.

Dedication

To my husband, Youngrok, my parents and my brothers.

It is with your unwavering love and support that I have been able to accomplish this feat.

Thank you – I love you.

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Introduction

Cigarette smoking remains the leading preventable cause of disability, disease, and death in the United States (US Department of Health and Human Services, 2014). Despite a decrease in smoking over the past several decades, prevalence among individuals with mental illness is disproportionately high as compared to the general US adult population (McClave, McKnight-Eily, Davis, & Dube, 2010). Past month estimates of daily smoking for individuals with mental illness range from 21% to 30.5% as compared to 13.5% for of those in the general population (Glasheen, Hedden, Forman-Hoffman, & Colpe, 2014).

Smoking prevalence among individuals with panic disorder (PD), characterized by recurrent unexpected panic attacks, persistent worry about future panic attacks, and avoidance (American Psychiatric Association, 2013) ranges from 35% to 60% (Kalman, Morissette, & George, 2005; Lasser et al., 2000). Research on PD/smoking (PDSM) comorbidity has found that having a history of panic attacks and a diagnosis of PD is linked to aversive smoking outcomes such as increased likelihood of current daily smoking (Lasser et al., 2000; Mathew, Norton, Zvolensky, Buckner, & Smits, 2011) and transition to nicotine dependence (Breslau, Novak, & Kessler, 2004), as well as decreased likelihood of quitting (Lasser et al., 2000). Also, regular daily smoking is associated with panic psychopathology including higher lifetime prevalence of panic attacks and PD (Isensee, Wittchen, Stein, Höfler, & Lieb, 2003) and increased likelihood of panic attack onset or PD (Breslau & Klein, 1999). Notably, prospective research examining these relations has found that daily smokers are more likely to later experience a panic attack and be diagnosed with PD, as compared to nonsmokers (Breslau & Klein, 1999; Cougle, Hakes, Macatee, Chavarria, & Zvolensky, 2015; Isensee et al., 2003), whereas the inverse relation has not been demonstrated (e.g., Isensee et al., 2003), suggesting smoking precipitates the onset of panic psychopathology and PD (Cosci, Knuts, Abrams, Griez, & Schruers, 2010; Zvolensky & Bernstein, 2005).

The combination of PD and smoking appears to bidirectionally influence associated symptomatology. Specifically, daily smokers with a panic attack history report significantly greater nicotine dependence, pre-quit nicotine withdrawal, post-quit cessation fatigue (Piper, Cook, Schlam, Jorenby, & Baker, 2011), shorter quit attempts, and higher intensity of anxiety-related withdrawal symptoms, compared to those without a panic attack history (Zvolensky, Lejuez, Kahler, & Brown, 2004). Moreover, frequency of panic attacks is associated with greater cigarette consumption and longer duration of smoking (Mathew et al., 2011). With regard to panic outcomes, those with PDSM show greater severity of panic symptoms than nonsmokers with PD (Zvolensky, Schmidt, & McCreary, 2003). Also, in studies utilizing a biological challenge paradigm (e.g., hyperventilation or 10% CO_2-enriched air), meant to illicit panic responsivity, those with PDSM report higher levels of anxiety, bodily distress (Zvolensky, Leen-Feldner, et al., 2004), and panic attack symptoms (Leyro & Zvolensky, 2013) than those without PD in response to the challenge. Taken together, research indicates that the combination of smoking and panic symptoms is associated with worse smoking outcomes as well as greater panic symptoms compared to either smoking or panic alone.

Zvolensky and colleagues (Zvolensky & Bernstein, 2005; Zvolensky & Schmidt, 2003) have posited that the high comorbidity between PD and smoking and associated symptomatology may be the result of unique learning processes. For example, smokers vulnerable to panic, who are more vigilant to interoceptive cues, as compared to those without panic vulnerability, may experience nicotine withdrawal symptoms (e.g., anxiety, restlessness, gastrointestinal distress) as indicative of a panic attack, and thus, more distressing. Over time, over-attendance to, and fear of withdrawal symptoms, may increase the likelihood of experiencing a panic attack (e.g., in response to biological challenge; Abrams et al., 2011; Vujanovic & Zvolensky, 2009), whereas, continued smoking becomes an overlearned behavior to manage these distressing symptoms by relieving associated aversive affect. Following repeated pairings of smoking and subsequent relief of distress, panic vulnerable smokers may generalize this learning such that smoking is

reflexively relied upon in all situations associated with anxious distress (Zvolensky & Schmidt, 2003). As a result, a specific set of smoking motives and expectancies may be developed, which may place them at greater risk for continued smoking and difficulty quitting.

Limited research investigating smoking cognitions among those with PDSM has found that they are motivated to smoke in order to relieve negative affect (Zvolensky et al., 2005). Moreover, laboratory studies have found that among PDSM individuals, PD status interacted with nicotine withdrawal symptoms to predict greater subjective and physiological reactivity and slower recovery from a biological challenge than their non-PD counterparts (Leyro & Zvoelnsky, 2013; Leyro & Zvolensky, In press; Zvolensky, Leen-Feldner, et al., 2004). Together, the behavioral model of PDSM and these findings suggest that smokers with PD are more susceptible to adopting a stronger set of smoking cognitions than their counterparts who perhaps are less sensitive to nicotine withdrawal and exposed to fewer learning trials. However, individual factors that specifically link PD and smoking cognitions remain poorly understood. (Piper et al., 2011; Zvolensky, Leen-Feldner, et al., 2004)

Work in this area as well as subsequent treatment refinement may be extended by identifying malleable vulnerabilities that further explain the relation between panic vulnerability and smoking cognitions, such as a deficit in emotion regulation (ER). ER has been defined by Gratz and Roemer (Gratz & Roemer, 2004) as a multidimensional construct that includes awareness and acceptance of one's emotions, the ability to modulate emotional *responding* in accord with one's personal goals. As such, it is posited that individuals high in ER are able to adaptively respond to external and internal threats in a flexible manner that is aligned with their goals. In contrast, difficulty in ER has been positively associated with a wide range of psychopathology including self-harming behaviors (Gratz & Tull, 2010), depression (Bardeen, Fergus, & Orcutt, 2012), generalized anxiety disorder (Roemer et al., 2009) and substance use (Fox, Axelrod, Paliwal, Sleeper, & Sinha, 2007). Thus, individuals with difficulty in ER may

respond to external and internal threats in an inflexible manner that is maligned with their long-term goals.

Currently, no research has linked difficulties in ER to PD, specifically. However, studies have suggested that greater utilization of ER skills may reduce panic symptoms. For example, following experimentally induced panic sensations, individuals who are instructed to use skills consistent with adaptive ER (e.g., acceptance of distress) versus maladaptive ER (e.g., suppression of distress), report less distress and recover more quickly (Eifert & Heffner, 2003; Feldner, Zvolensky, Stickle, Bonn-Miller, & Leen-Feldner, 2006; Levitt, Brown, Orsillo, & Barlow, 2004). Moreover, among individuals with a diagnosis of panic attacks, panic symptoms are associated with a tendency to engage in maladaptive ER skills in response to distressing experimental stimuli (Tull & Roemer, 2007). Taken together, studies suggest that difficulties in ER are associated with panic symptomatology whereas utilization of adaptive ER skills may help individuals adaptively respond to panic relevant distress.

With regard to smoking, specifically, cross-sectional work has found that difficulty in ER is positively associated with stimulation, habitual, sensorimotor (Gonzalez, Zvolensky, Vujanovic, Leyro, & Marshall, 2008; Short, Oglesby, Raines, Zvolensky, & Schmidt, 2015), addictive, and negative affect reduction smoking motives (Short et al., 2015), as well as perceived cessation barriers among daily smokers (Gonzalez et al., 2008). Also, studies have found that difficulty in ER may underpin the relation between psychopathology and smoking. For example, among daily smokers with posttraumatic symptoms, difficulty in ER fully mediates the relation between severity of posttraumatic symptoms and negative affect reduction smoking motives and cessation barriers (Short et al., 2015). In depressed smokers, suppression of emotions following a negative mood induction is related to greater attentional bias to smoking cues, whereas reappraisal is associated with lower expectancies that smoking will relieve negative affect (Fucito, Juliano, & Toll, 2010). Together, ER difficulties are linked to smoking behavior, and

may play an important role in smoking motives and expectancies among smokers with psychopathology.

Based on independent lines of research suggesting ER, in the context of stress, may be one of key mechanism that explains the relation between panic symptoms and both smoking cognitions and behavior, it is possible that the inability to adaptively respond to and cope with distress, may explain why those with PDSM, who are more likely to perceive nicotine withdrawal as more intense, are motivated to immediately relieve withdrawal related distress. And this may be why they return to smoking more quickly in an automatized way, leading to heavier use and greater addiction. A related investigation in this domain found that ER and anxiety sensitivity (AS; the fear of anxiety and related bodily sensations; Reiss & McNally, 1985) are associated with greater negative affect smoking motives and outcome expectances and perceived cessation barriers, through its relation to difficulty in ER, among treatment-seeking daily smokers (Johnson, Farris, Schmidt, & Zvolensky, 2012). Taken together, evidence suggests that ER may play an important role in understanding the relation between panic vulnerabilities and smoking.

However, to date, no work has directly examined the explanatory role of ER in the relation between PD and smoking cognitions. This is a highly relevant research area given previous models of PDSM have posited that smokers with panic symptoms may smoke for emotion regulation purposes (Zvolensky & Bernstein, 2005) and anticipate the effect of smoking to be anxiolytic and distress reducing (Leventhal & Zvolensky, 2015). In particular, this model suggests that over repeated pairings, the negative reinforcement properties of smoking may lead smokers with PD to invariably and reflexively rely on smoking to manage distress and withdrawal, while not engaging in alternative adaptive coping strategies, therefore, developing a specific set of smoking related cognitions in a manner that further reinforces smoking behavior. Given observed relations between ER, PD and smoking, we speculate an ER deficit will explain observed relations between PD status and smoking motives and outcome expectancies among daily cigarette smokers.

The overarching aim of the current study is to examine the explanatory role of difficulty in ER in the relation between PD status and smoking motives and outcome expectancies (see Figure 1). Specifically, among a sample of daily smokers with and without PD, PD status will be evaluated in relation to smoking motives (i.e., habitual, addictive, and negative affect reduction) and outcome expectancies (i.e., negative consequences and negative reinforcement) implicated in Zvolensky et al.'s model (2005). It is hypothesized that (i) diagnosis of PD (i.e., PD status) will show significant positive association with each criterion variable, (i.e., the total effect; path c in mediation model), (ii) and difficulty in ER will be significantly positively correlated with both PD status (path a) and criterion variables (path b) and (iii) the relation between PD status and criterion variables will be explained via difficulty in ER (i.e., indirect effect; a*b) regardless of presence of significance in total effect (path c); that is, PD status is theorized to indirectly influence the criterion variables through its effect on difficulty in ER. In particular, these predictions are expected to be above and beyond the variance accounted for by age, sex, and cigarette dependence.

Methods

Participants

The current study is a secondary data analysis of previously collected data investigating the interaction of nicotine withdrawal and PD among daily smokers with and without PD, in the prediction of fearful responding to bodily sensations under carbon dioxide (CO_2)-enriched air biological challenge (Leyro & Zvolensky, 2013). The parent study was composed of two lab sessions. The data utilized in the current study was collected during the first lab session, when the verification of smoking status via carbon monoxide analysis of breath sample, completion of questionnaires, and structured clinical interview were conducted. Participants included 74 daily smokers. Inclusion criteria for the parent study included (a) being a daily smoker for at least the past year (cigarettes per day $\geq 7^{1}$); (b) having not decreased the number of cigarettes smoked per day by more than half in the past 6 months; (c) being 18 to 65 years old; and (d) reporting a willingness to abstain from smoking for a 12-hr period. The exclusion criteria of the parent study were: (a) a current medical condition that contraindicated CO_2 administration (cardiovascular, endocrine, pulmonary, respiratory [including severe asthma], or gastrointestinal illness); (b) a life-time diagnosis of PD except current diagnosis, (c) limited mental competency (not oriented to person, place, or time) and the inability to give informed, voluntary, written consent to participate; (d) pregnancy or the possibility of being pregnant (by self-report); (e) current use of nicotine replacement therapy; (f) current or past history of psychotic-spectrum symptoms or disorders; (g) current substance dependence; (h) prior experience with CO_2 challenge; (i) suicidality; and (j) any current use of psychotropic medication which could impact the effectiveness of the laboratory challenge.

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[1] The inclusion criteria in the parent study for cigarettes per day was equal to or more than 10 cig/day. However, in order to increase recruitment, the number was decreased to 7 cig/day. In this sample, 2.7% of the sample (n=2) reported less than 10 cig/day.

Measures

Structured Clinical Interview-Non-Patient Version for DSM-IV, non-patient edition (SCID-IV-N/P; First, Spitzer, Gibbon, & Williams, 1994). The SCID-IV-N/P was administered to determine diagnostic inclusion and exclusion. Reliability has been proved to be adequate (First et al., 1994). The principal investigator of the parent study or trained senior graduate students administered the SCID-N/P. Interviews were audio-recorded and 20% were cross-checked by different interviewers, indicating 98% agreement. Regarding PD diagnosis, there was no disagreement.

Smoking History Questionnaire (SHQ; Brown, Lejuez, Kahler, & Strong, 2002). The SHQ is a well-established questionnaire that assesses smoking history and pattern of use. The items pertain to smoking rate, age of onset of initiation, and years of regular smoking. In the current study, the SHQ was used as a descriptive measure of smoking history.

Fagerström Test for Cigarette Dependence (FTCD; Fagerström, 2012; Heatherton, Kozlowski, Frecker, & Fagerstrom, 1991). The FTCD is a 6-item self-report scale assessing continuous levels of tobacco dependence. The FTCD is a revised tool from the Fagerström Tolerance Questionnaire (FTQ; (Fagerström, 1978), which original name was Fagerström Test for Cigarette Dependence (Heatherton et al., 1991). Despite low internal consistency (α = .61; Heatherton et al., 1991), its test-retest reliability is high (Pomerleau, Carton, Lutzke, Flessland, & Pomerleau, 1994) and it is positively correlated with key smoking variables such as saliva cotinine (Heatherton et al., 1991; Payne, Smith, McCracken, McSherry, & Antony, 1994). In the current investigation, the FTCD was employed to index nicotine dependence (Cronbach's α = .44 among the present sample).

Difficulties in Emotion Regulation Scale (DERS; Gratz & Roemer, 2004). The DERS is a 36-item self-report scale assessing difficulty in ER on a five-point Likert-style scale (1 = *almost never* to 5 = *almost always*). There are six subscales: non-acceptance (e.g., "when I'm upset, I feel guilty for feeling that way."), goals (e.g. ''when I'm upset, I have difficulty getting work

done."), impulse (e.g. ''when I'm upset I have difficulty controlling my behaviors."), awareness (e.g. ''I pay attention to how I feel."), strategies (e.g. ''when I'm upset any emotions feel overwhelming."), and lack of clarity (e.g. ''I have no idea how I am feeling."). The total score of DERS was used as an index of general difficulties in ER such that higher scores suggest greater difficulty in ER (Cronbach's α = .95 among the present sample).

Reason for Smoking (RFS; Ikard, Green, & Horn, 1969). The RFS is a validated 23-item self-report scale used to assess smoking motives on a five-point Likert-style scale (1 = *never* to 5 = *always*) (Shiffman, 1993). In the current study, the Habitual (RFS-HA; e.g., "I've found a cigarette in my mouth and didn't remember putting it there"), Addictive (RFS-AD; e.g., "Between cigarettes, I get a craving only a cigarette can satisfy"), and Negative Affect Reduction (RFS-NA; e.g., When I feel uncomfortable or upset about something, I light up a cigarette") subscales were utilized to measure theoretically relevant smoking motives (Cronbach's α for each subscale of interest was as follows; RFS-HA = .66, RFS-AD = .80, and RFS-NA = .87 among the present sample).

Smoking Consequences Questionnaire (SCQ; Brandon & Baker, 1991). The SCQ is a validated 50-item self-report scale assessing smoking expectancies on a 10-point Likert-style scale (0 = *completely unlikely* to 9 = *completely likely*) (Brandon & Baker, 1991; Buckley et al., 2005; Downey & Kilbey, 1995). In the current study, the Negative Consequences (SCQ-NC; e.g., "the more I smoke, the more I risk my health") and Negative Reinforcement (SCQ-NR; e.g., "smoking helps me calm down when I feel nervous") subscales of the SCQ were utilized to measure theoretically relevant outcome expectancies for smoking (Cronbach's α for each subscale of interest was as follows; SCQ-NC = .88, and SCQ-NR = .94 among the present sample).

Analysis

Analyses were conducted in PASW Statistics 22.0 (IBM SPSS Statistics). First, zero order correlations among predictor (current panic disorder status), proposed mediator (DERS total), criterion variables (RFS-HA, RFS-AD, RFS-NA, SCQ-NC, and SCQ-NR), and covariates (age, sex, and FTCD) were conducted. Participants with a current diagnosis of PD were coded 1, and those without a history of PD were coded 0.

Next, a series of mediator models were used to examine the mediating role of ER in the relation between PD status and the outcome variables. Five mediation models were tested with each of five criterion variables. In each model, age, sex, and cigarette dependence were included in the models as covariates in order to control potential confounding effects for predictive variance accounted for by these variables in relation to criterion variables. The mediation analyses were carried out utilizing 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). Conditional process modeling was utilized because it allows for quantification of the indirect effect, a notable limitation of former common mediation approach (Baron & Kenny, 1986). Baron and Kenny's (1986) causal steps approach has been criticized because it relies on each path (i.e., path a, b, c, and c') being significant in order to examine the mediation effect, while not considering the presence of an indirect effect, which may occur in the absence of the path c relation (for review, Hayes, 2009). Alternatively, the conditional process analysis makes the inferential indirect effect detectable in the absence of total effects (path c; Hayes, 2009). Moreover, Kenny and Judd (2013) have shown that, in a given sample size, the power to test the indirect effect (a*b) is greater than the tests of either the total effect (path c [with mediator in the model]) or direct effect (path c'). Regarding the determination of statistical significance of indirect and direct effects, we utilized 95-percentile bias-corrected confidence intervals (CI), estimated with bootstrap analyses of 10,000 samples (as recommended by Hayes, 2009; Hayes & Scharkow, 2013; Preacher & Hayes, 2004, 2008). The bias-corrected bootstrap CI is purported to be a relatively better index of statistical significance for indirect effect (i.e.,

highest power and the best Type I error control; Hayes, 2009) as compared to other methods such

as test of joint significance or Monte Carlo CI (Hayes & Scharkow, 2013).

Results

Participants

Participants included 74 daily smokers (52.7% male, M_{age}=29.9, SD=12.6) who reported smoking on average 19.9 cigarettes/day (SD=7.8), for an average of 12.7 years (SD=11.8). Sample characteristics are shown in Table 1. The sample met for low to moderate levels of cigarette dependence (M=3.9, SD=1.7; Fagerström, 2012). Approximately 39.2% (n=29) met DSM-IV criteria for current PD with and without agoraphobia where 20 participants among them met criteria for additional current mood or anxiety disorder. Also, an additional 20.3% (n=15) without PD met criteria for another current mood or anxiety disorder, and 40.5% (n=30) did not meet criteria for any current Axis I disorder. Of the participants, 93.2% were identified as Caucasian, 2.7% African American, 1.4% Asian, and 2.7% "other."

Zero-Order Correlations

PD status was significantly correlated to difficulty in ER (DERS total) and negative personal consequence smoking outcome expectancies (SCQ-NC) (all p's<.01), but not other smoking cognitions as shown in Table 2. The mediator, DERS total, showed significant positive associations with each criterion variable (all p's<.01); correlations were moderate in strength. Examination of theoretically relevant covariates revealed female gender was significantly correlated with addictive reasons for smoking (p<.01). Cigarette dependence was positively associated with difficulty in ER (p<.05), habitual, addictive, and negative affect reduction reasons for smoking (all p's <.01), and negative reinforcement smoking outcome expectancies (p<.05). However, age did not show any significant association with difficulty in ER or smoking cognitions.

Mediation Analyses

Five path models were planned for the examination of the impact of PD status on each criterion variable, through difficulty in emotion regulation. The regression coefficients for paths a, b, c, and c' are shown in Table 3. The paths are for each of the five models. Table 3 also presents the estimates of the indirect effects, which were the paths tested for mediation.

In the first path model examining habitual motives (Y1=RFS-HA), both the total effect model ($R^2_{y1,x}$ = .227, df = 4, 68, F = 5.218, p < .01: path c) and the full model with the mediator ($R^2_{y1,x}$ = .316, df = 5, 67, F = 5.690, p < .0001) were significant. In the full model, cigarette dependence was significantly predictive of higher scores on the RFS-HA (b = .153, t = 3.045, p < .01). Both the total effect (path c) of PD status and the direct effect (path c') of PD status on RFS-HA, after controlling for the mediator, were nonsignificant. Regarding the test of the indirect (mediational) effect, PD status was predictive of greater habitual smoking reason indirectly through greater levels of difficulty in emotion regulation (effect a*b).

In the second path model examining additive motives (Y2=RFS-AD), both the total effect model ($R^2_{y1,x}$ = .307, df = 4, 68, F = 10.980, p < .0001) and the full model with the mediator ($R^2_{y1,x}$ = .405, df = 5, 67, F = 14.066, p < .0001) were significant. In the full model, gender (b = .516, t = 3.159, p < .01) and cigarette dependence (b = .156, t = 2.700, p < .01) were significantly predictive of higher scores on the RFS-AD. Both the total effect of PD status and the direct effect of PD status on RFS-AD, after controlling for the mediator, were nonsignificant. Regarding the test of the indirect effect, PD status was predictive of greater addictive smoking reason indirectly through greater levels of difficulty in emotion regulation (effect a*b).

With regard to negative affect reduction motives, (Y3=RFS-NA), both the total effects model ($R^2_{y1,x}$ = .213, df = 4, 68, F = 6.221, p < .0001) and the full model with the mediator ($R^2_{y1,x}$ = .290, df = 5, 67, F = 6.028, p < .0001) were significant. In the full model, gender (b = .374, t = 2.067, p < .05) and cigarette dependence (b = .146, t = 2.727, p < .01) were significantly predictive of higher scores on the RFS-NA. The direct effect of PD status on RFS-NA, after

controlling for the mediator, was nonsignificant. Regarding the test of the indirect effect, PD status was predictive of greater negative affect reduction smoking reason indirectly through greater levels of difficulty in emotion regulation (effect a*b).

With regard to expecting smoking to result in negative personal consequences, (Y4=SCQ-NC), both the total effects model ($R^2_{y1,x}$ = .177, df = 4, 68, F = 2.996, $p < .01$) and the full model with the mediator ($R^2_{y1,x}$ = .250, df = 5, 67, F = 3.028, $p < .05$) were significant. In the full model, no covariates were significant. After controlling the mediator, the direct effect of PD status on SCQ-NC was nonsignificant. Regarding the test of the indirect effect, PD status was predictive of greater negative consequence smoking expectancy indirectly through greater levels of difficulty in emotion regulation (effect a*b).

Lastly, with regarding to negative reinforcement outcome expectancies (Y5=SCQ-NR), both the total effects model ($R^2_{y1,x}$ = .176, df = 4, 68, F = 6.040, $p < .0001$) and the full model with the mediator ($R^2_{y1,x}$ = .278, df = 5, 67, F = 5.510, $p < .0001$) were significant. In the full model, cigarette dependence (b = .270, t = 2.118, $p < .05$) was significantly predictive of higher scores on the SCQ-NR. After controlling the mediator, the direct effect of PD status on SCQ-NR was nonsignificant. Regarding the test of the indirect effect, PD status was predictive of greater negative reinforcement smoking expectancy indirectly through greater levels of difficulty in emotion regulation (effect a*b).

Post-Hoc Analyses

Based on the significant main effects of gender, a series of five post-hoc moderated meditational models were conducted in order to examine the extent to which gender moderated the indirect of PD status on criterion variables through DERS and the direct effect of PD status on criterion variables. Tests of the conditional and overall indirect effects were estimated based on 10,000 bootstrapped resamples. A non-significant indirect effect of gender*DERS in terms of PD status on RFS-HA (b=-.284, $CI_{95\%}$=-.746, .070), SCQ-NC (b=-.276, $CI_{95\%}$=-1.145, .449), or SCQ-

NR (b=-.293, $CI_{95\%}$=-1.361, .686) was found whereas a significant indirect effect of gender*DERS was found for RFS-AD (b=-.453, $CI_{95\%}$=-.882, -.128) and RFS-NA (b=-.517, $CI_{95\%}$=-1.118, -.119). That is, gender did not moderate the effect of DERS on habitual smoking motives, negative consequence or negative reinforcement outcome expectancies. However, only among male gender, but not female gender, higher levels of DERS were significantly associated with greater addictive and negative affect reduction smoking motives. A non-significant conditional direct effect of gender and PD status on all of the criterion variables was observed (RFS-HA: b=-.253, $CI_{95\%}$=-.960, .454; RFS-AD: b=-.039, $CI_{95\%}$=-.726, .647; RFS-NA: b=-.012, $CI_{95\%}$=-.795, .772; SCQ-NC: b=-.158, $CI_{95\%}$=-1.567, 1.251; SCQ-NR: b=.212, $CI_{95\%}$=-1.700, 2.125).

Discussion

Smokers with panic psychopathology are vulnerable to a set of smoking motives and expectancies about smoking that may place them at greater risk for continued use (Johnson, Farris, Schmidt, Smits, & Zvolensky, 2013). In order to identify targetable mechanisms that may explain these relations, the current study sought to examine whether ER difficulties mediate the relation between panic symptomatology and smoking cognitions in a group of smokers with and without a current diagnosis of PD. Consistent with study hypotheses, smokers with a diagnosis of PD reported greater habitual, addictive, and negative affect reduction smoking motives as well as negative consequences and negative reinforcement smoking outcome expectancies, through a deficit in ER, as compared to smokers without such a diagnosis.

Our models found no differences between smokers with and without a diagnosis of PD in terms of habitual and addictive smoking motives, a finding that is inconsistent with previously observed relations in smokers high in anxiety sensitivity (AS), a risk factor for PD (Gonzalez et al., 2008; Leyro, Zvolensky, Vujanovic, & Bernstein, 2008) but somewhat consistent with results from smokers with PD diagnosis (Zvolensky et al., 2005). It is conceivable that given the high rates of current (33.3% in non-PD group) and past (89.7% in PD group and 80% in non-PD group) diagnoses of psychopathology based on the DSM-IV, smokers both with and without PD may be elevated in AS, a transdiagnostic vulnerability (Olatunji & Wolitzky-Taylor, 2009), which may explain our inability to detect a difference in addictive and habitual motives. However, having a diagnosis of PD was related to both habitual and addictive smoking motives, through its relation to ER difficulties. Our results indicate that difficulties in ER among those with PDSM may result in greater reports of smoking because it is habitual and addictive, a novel finding suggesting ER may be a key explanatory mechanism for smoking maintenance in this group.

Consistent with our hypotheses, PD status was associated with negative affect reduction smoking motives and negative reinforcement outcome expectancies, a relation that was mediated by ER difficulties. Whereas the above findings suggest that PD status, specifically, was not directly related to differences in habitual and addictive smoking motives, PD status does differentiate reports of negative affect reduction motives and negative reinforcement outcome expectancies. These results are aligned with the previously observed specific nicotine dependence motives (e.g., mood control) over automatized smoking dependence motives (e.g., craving) among smokers with a history of anxiety disorders (Piper et al., 2011). Moreover, it is in line with PDSM model such that smokers with PD learn that smoking is an effective strategy to manage withdrawal relevant and affective distress, regardless of perceived difficulties in ER. Yet, inclusion of difficulty in ER in the model reveals an underlying mechanism that explains the relation between PD status and these motives and expectancies. This finding extends previously observed relations between AS and ER (Kashdan et al., 2008; Tull, 2006) and findings that ER difficulties are related to negative reinforcement smoking motives and outcome expectancies (Johnson et al., 2013; Johnson et al., 2012; Johnson et al., 2008). In addition, given that AS is a well-known risk factor of PD, these findings are consistent with research suggesting a deficit in ER explains the relation between high AS and negative affect reduction smoking motives as well as negative reinforcement outcome expectancies, among daily smokers (Johnson et al., 2012), Therefore, improving ER skills in smokers with PD, may reduce smoking behavior driven by the desire to, and expectation, that it will relieve affective distress.

Our finding that individuals with PDSM report greater awareness that smoking is harmful to their health, an association that was mediated by difficulties in ER, as compared to those without PD, is, in part, consistent with elevations in the expectancies that smoking is harmful to health previously observed in smokers high in AS (Johnson et al., 2008; Leyro et al., 2008; Zvolensky, Feldner, et al., 2004), as compared to those low in AS. This finding is also aligned with research suggesting individuals with PD report hypervigilance to bodily sensations, greater

fear of anxious arousal (Schmidt, Joiner Jr, Staab, & Williams, 2003; Yartz, Zvolensky, Gregor, Feldner, & Leen-Feldner, 2005), and worries about health (Starcevic et al., 2009). Moreover, considering the distressing and salient nature of nicotine withdrawal symptoms (Jarvik et al., 2000; Shadel, Niaura, Brown, Hutchison, & Abrams, 2001), those with PDSM may be more conscious of negative smoking related health outcomes in the context of nicotine withdrawal. Given research indicating smokers who expect smoking to be harmful to their health are more motivated to plan a quit attempt (Copeland, Brandon, & Quinn, 1995; Rose, Chassin, Presson, & Sherman, 1996), we might expect high levels of motivation to quit among PDSM. However, our novel finding that ER difficulties mediates the relation between PD status and health concerns due to smoking may offer another interpretation that this unique constellation of cognitions in smoking and ER difficulties may paradoxically confound the ability to successfully abstain. For example, reliance on smoking to relieve distress may overpower or obstruct motivation to quit due to elevated health concerns. Further, continued smoking despite awareness of negative health consequences may lead to additional affective distress, resulting in a forward feeding cycle (Zvolensky & Schmidt, 2003).

Our observation of a main effect of gender led us to explore its moderating role in post-hoc analyses. We found that gender moderated the relation between greater ER difficulties and addictive, and negative affect reduction, smoking motives. Specifically, the relation between PD status and these motives through difficulty in ER was significant for males, but not females. These results are somewhat surprising given previous studies have shown female smokers high in AS report greater addictive (Johnson et al., 2013), negative affect reduction smoking motives (Johnson et al., 2013; Johnson et al., 2012; Leyro et al., 2008) and negative reinforcement outcome expectancies (Johnson et al., 2013; Johnson et al., 2012; Pang et al., 2014). However, limited work to date has examined the conditional effect of gender in similar models, which may be an important line of inquiry given observed gender differences in treatment response and

cessation success (Pang & Leventhal, 2013; Weinberger, Maciejewski, McKee, Reutenauer, & Mazure, 2009), suggesting the possibility that treatment adjuncts may be differentially beneficial for males versus females.

Several limitations to the current investigation should be noted. First, due to the cross-sectional nature of this study based on the theoretical framework, causal inferences regarding observed relations cannot be inferred. Future work may benefit from longitudinal studies investigating ER difficulties among smokers with panic psychopathology that lead to more problematic smoking motives and expectancies, over time. Second, the results of this study solely rely on the self-reports of daily smokers. Future work may benefit from laboratory studies investigating whether manipulation of ER strategies (e.g., suppression, acceptance, and reappraisal) in the context of challenge or withdrawal affect smoking motivation (e.g., craving, attentional bias to smoking cues; Szasz, Szentagotai, & Hofmann, 2012), expectancies (Fucito et al., 2010), and smoking behavior (Beadman et al., 2015; Fucito et al., 2010) among smokers with panic psychopathology. Third, due to limited sample size and degree of diversity in race and ethnicity in the current study, our findings may not be generalizable to all individuals with PDSM across various race and ethnic groups. Therefore, replication in a larger sample is required. Finally, because the current study utilized a general index of ER (i.e., DERS total score), it is not clear whether a specific set of ER difficulties (e.g., clarity of emotion; Kun & Demetrovics, 2010) or reappraisal (Gross, 1998; John & Gross, 2004) has a greater impact on smoking cognitions than others. Moreover, the validity of DERS total score as a general index of ER has been questioned. For example, Bardeen and colleagues (2012) have evidenced greater construct and concurrent validity of the revised DERS (i.e., DERS without awareness subscale), compared to the original 36-item index among female undergraduate students. However, Fowler et al. (2014) found equivalence validity between the revised and original version among in-patients with various psychiatric diagnoses (Fowler et al., 2014). These findings suggest a need for additional research in this area, but may indicate that the validity of the DERS and its subscales vary across

factors such as age, gender and severity of mental illnesses (Fowler et al., 2014). Future work on smokers may benefit from a comprehensive examination of DERS total and subscale scores to better inform targeted intervention.

The current study is the first study to examine the mediating role of ER difficulties in the relation between PD status and smoking cognitions. Collectively, our findings suggest that the inability to regulate one's emotional experience in order to engage in behaviors consistent with long-term goals may explain the association between panic psychopathology and cognitive-based smoking processes, adding to previous work (Johnson et al., 2013; Leyro et al., 2008; Zvolensky, Farris, Schmidt, & Smits, 2014) suggesting smokers sensitive to anxiety may automatically rely on smoking in the absence of adaptive coping strategy under distressed emotional state. Further, among individuals with PDSM, reports of greater motives to smoke and expectancies about smoking may be due to difficulties in ER, which may impede their quit proclivity, confidence, and success. In this context, gender difference in smoking cognitions also may play an important role. Therefore, interventions that develop and shape ER skills in smokers with PD (e.g., reappraisal; Szasz et al., 2012) by considering gender as one of moderators, may help ameliorate the link between symptoms that may characterize smokers with PD and place them at risk for greater smoking motives.

Tables

Table 1. Descriptive Statistics of Sample Characteristics

Descriptive summary	Total N=74	PD n=29	Non-PD n=45	Test for Group Difference
Age M (SD)	29.9 (12.6)	30.6 (12.7)	29.5 (12.7)	t(72) = -.36
Sex				X^2 = .67
Male	39 (52.7%)	17 (58.6%)	22 (48.9%)	
Female	35 (47.3%)	12 (41.4%)	23 (51.1%)	
Race[2] n (%)				X^2 = 3.46
White	69 (93.2%)	29 (100.0%)	40 (88.9%)	
Black	2 (2.7%)	0 (0.0%)	2 (4.4%)	
Asian	1 (1.4%)	0 (0.0%)	1 (2.2%)	
Other	2 (2.7%)	0 (0.0%)	2 (4.4%)	
Marital status n (%)				X^2 = 7.99
Never married	51 (68.9%)	16 (55.2%)	35 (77.8%)	
Married/cohabitating	9 (12.2%)	6 (20.7%)	3 (6.7%)	
Divorced/anulled	8 (10.8%)	4 (13.8%)	4 (8.9%)	
Separated	4 (5.4%)	3 (10.3%)	1 (2.2%)	
Widowed	2 (2.7%)	0 (0.0%)	2 (4.4%)	
Education n (%)[3]				X^2 = 6.18*
At least high school	31 (41.9%)	7 (24.1%)	24 (53.3%)	
At least part college	42 (56.7%)	22 (75.9%)	21 (46.7%)	
Smoking history M (SD)				
Cigarettes per day	19.9 (7.8)	18.2 (6.3)	21.0 (8.5)	t(72) = 1.50
Age of first use	14.2 (3.7)	13.6 (2.1)	14.6 (4.4)	t(71) = 1.10
Years of use	12.7 (11.8)	13.7 (12.2)	12.1 (11.6)	t(71) = -.57
Psychiatric disorders, current n (%)				
Number of total current disorder M (SD)	1.3 (.2)	2.6 (1.5)	.5 (.8)	t(38[a]) = -6.80**
Major depressive disorder	8 (10.8%)	5 (17.2%)	3 (6.7%)	
Dysthymic disorder	6 (8.1%)	6 (20.7%)	0 (0.0%)	
Panic disorder with and without agoraphobia	29 (39.2%)	29 (100.0%)	0 (0.0%)	
Social phobia	15 (20.3%)	10 (34.5%)	5 (11.1%)	
Specific phobia	3 (4.1%)	1 (3.4%)	2 (4.4%)	
OCD	6 (8.1%)	6 (20.7%)	0 (0.0%)	
GAD	8 (10.8%)	8 (27.6%)	0 (0.0%)	
PTSD	4 (5.4%)	3 (10.3%)	1 (2.2%)	
Alcohol use disorder	6 (8.1%)	2 (6.9%)	4 (8.9%)	
Other SUDs	3 (4.1%)	2 (6.9%)	1 (2.2%)	

[2] All of participants were non-hispanic/latino.
[3] Missing one data point

FTCD *M (SD)*	3.9 (1.7)	3.8 (1.7)	4.0 (1.8)	$t(71) = .31$
Key Study Variables *M (SD)*				
DERS total	81.7 (23.3)	94.8 (20.0)	73.3 (21.6)	$t(72) = -4.29$**
RFS-HA	2.4 (.8)	2.4 (.7)	2.3 (.8)	$t(72) = -.34$
RFS-Addictive subscale	3.3 (.8)	3.4 (.7)	3.2 (.9)	$t(70) = .26$
RFS-NA	3.6 (.8)	3.7 (.8)	3.5 (.8)	$t(72) = -.1.41$
SCQ-NC	6.0 (1.4)	6.5 (1.3)	5.6 (1.3)	$t(72) = -2.84$**
SCQ-NR	5.8 (1.9)	6.2 (2.0)	5.5 (1.8)	$t(72) = -1.57$

Note. * *p*<.05, ** *p*<.01, two-tailed; M=Mean; SD=Standard deviation; aEqual variances not assumed; SUD=Substance use disorder; PD=Panic disorder; OCD=Obsessive-compulsive disorder; PTSD=Posttraumatic stress disorder; GAD=Generalized anxiety disorder; FTCD=Fagerström test for cigarette dependence; DERS=Difficulties in emotion regulation scale; RFS=Reasons for Smoking; HA=Habitual subscale; AD=Addictive subscale; NA=Negative affect reduction subscale; SCQ=Smoking consequences questionnaire; NC=Negative consequences subscale; NR=Negative reinforcement subscale

Table 2. Zero-Order Correlations for Study Variables

	1	2	3	4	5	6	7	8	9	10
1. Age	1	.021	.435**	.042	.110	.212	.155	.076	.204	-.055
2. Sex[a]		1	-.022	-.095	.081	.196	.323**	.201	.141	.170
3. FTCD			1	-.037	.238*	.433**	.383**	.316**	.092	.234*
4. PD Status[a]				1	.463**	.062	.119	.188	.310**	.220
5. DERS total					1	.414**	.479**	.437**	.420**	.449**
6. RFS-HA						1	.572**	.583**	.277*	.356**
7. RFS-AD							1	.673**	.315**	.495**
8. RFS-NA								1	.412**	.738**
9. SCQ-NC									1	.373**
10. SCQ-NR										1

Note. * $p<.05$, ** $p<.01$, two-tailed; [a]Spearman correlation coefficients; Sex was coded 1 for males and 2 for females; FTCD=Fagerström test for cigarette dependence; PD=Panic disorder (1=yes, 0=no); DERS=Difficulties in emotion regulation scale; RFS=Reasons for Smoking; HA=Habitual subscale; AD=Addictive subscale; NA=Negative affect reduction subscale; SCQ=Smoking consequences questionnaire; NC=Negative consequences subscale; NR=Negative reinforcement subscale

Table 3. Regression Results for the Mediation Models

Y	Model	B	SE	t	p	CI (lower)	CI (upper)
1	PD → DERS (a)	23.336	4.883	4.779	0.000	13.593	33.08
	DERS → RFS-HA (b)	0.012	0.004	2.965	0.004	0.004	0.019
	PD → RFS-HA (c')	-0.136	0.184	-0.737	0.464	-0.504	0.232
	PD → RFS-HA (c)	0.133	0.166	0.798	0.427	-0.199	0.464
	PD → DERS → RFS-HA (a*b)	0.268	0.097			0.114	0.512
2	PD → DERS (a)	23.336	4.883	4.779	0.000	13.593	33.08
	DERS → RFS-AD (b)	0.013	0.005	2.574	0.012	0.003	0.023
	PD → RFS-AD (c')	0.016	0.181	0.089	0.929	-0.345	0.377
	PD → RFS-AD (c)	0.317	0.164	1.930	0.058	-0.011	0.645
	PD → DERS → RFS-AD (a*b)	0.301	0.125			0.098	0.597
3	PD → DERS (a)	23.336	4.883	4.779	0.000	13.593	33.08
	DERS → RFS-NA (b)	0.012	0.005	2.182	0.033	0.001	0.023
	PD → RFS-NA (c')	0.101	0.224	0.448	0.655	-0.347	0.549
	PD → RFS-NA (c)	0.379	0.188	2.017	0.048	0.004	0.755
	PD → DERS → RFS-NA (a*b)	0.279	0.143			0.044	0.608
4	PD → DERS (a)	23.336	4.883	4.779	0.000	13.593	33.08
	DERS → SCQ-NC (b)	0.019	0.007	2.791	0.007	0.005	0.033
	PD → SCQ-NC (c')	0.496	0.311	1.593	0.116	-0.126	1.118
	PD → SCQ-NC (c)	0.941	0.331	2.846	0.006	0.281	1.601
	PD → DERS → SCQ-NC (a*b)	0.445	0.206			0.123	0.938
5	PD → DERS (a)	23.336	4.883	4.779	0.000	13.593	33.08
	DERS → SCQ-NR (b)	0.031	0.01	3.023	0.004	0.011	0.052
	PD → SCQ-NR (c')	0.169	0.469	0.360	0.720	-0.767	1.104
	PD → SCQ-NR (c)	0.896	0.446	2.008	0.049	0.005	1.787
	PD → DERS → SCQ-NR (a*b)	0.728	0.304			0.264	1.476

Note. PD=Panic disorder; DERS=Difficulties in emotion regulation scale; RFS=Reasons for Smoking; HA=Habitual subscale; AD=Addictive subscale; NA=Negative affect reduction subscale; SCQ=Smoking consequences questionnaire; NC=Negative consequences subscale; NR=Negative reinforcement subscale

Figures

Figure 1. Hypothetical Study Model on the Relation between PD status and Smoking Cognitions through ER Difficulties.
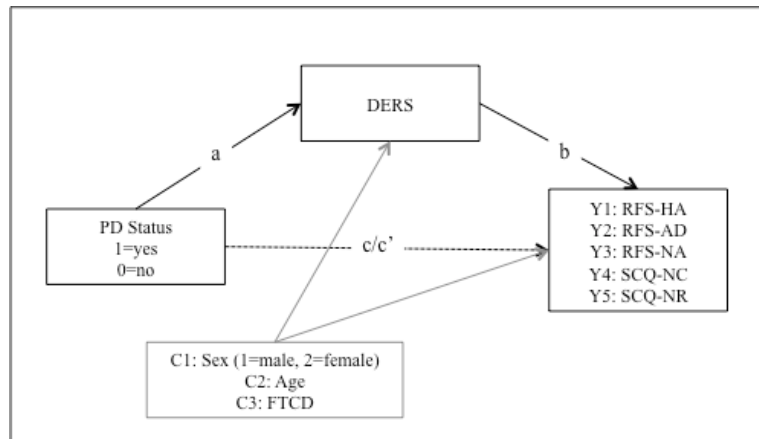
Note. Y=Outcome variables; C=Covariates; FTCD=Fagerström test for cigarette dependence; PD=Panic disorder; DERS=Difficulties in emotion regulation scale; RFS=Reasons for Smoking; HA=Habitual subscale; AD=Addictive subscale; NA=Negative affect reduction subscale; SCQ=Smoking consequences questionnaire; NC=Negative consequences subscale; NR=Negative reinforcement/negative affect reduction subscale.

Acknowledgement of Previous Publications

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