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## Co-use of Electronic Nicotine Delivery Systems and Combustible Cigarettes, and Their Association with Internalizing Pathology and Vulnerabilities

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### Abstract

Nicotine use and psychological distress exert negative bidirectional effects on one another, and are impacted by shared vulnerabilities. Little work has examined the extent to which these relations differ between adult electronic nicotine delivery system (ENDs) users with varied combustible cigarette use histories. The current study examined differences in internalizing symptoms and vulnerabilities between adult dual and single ENDs users with and without a history of combustible cigarette use. Single ENDs users without combustible use histories reported significantly greater stress and anxiety symptoms than single ENDs users with combustible use histories. Single ENDs users without combustible use histories reported greater anxiety and difficulty regulating their emotions than dual-users. Dual-and single users with prior combustible use histories did not differ in internalizing pathology or vulnerability presentations. This suggests that pathology and vulnerability presentation among nicotine users are influenced by both current and past nicotine use history.

### Keywords

Nicotine; Electronic cigarettes; Anxiety; Distress tolerance; Anxiety sensitivity; Emotion regulation

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A 57% decline in cigarette smoking has been observed in the United States since 1965 (Jamal et al. 2015). Yet the advent of electronic nicotine delivery systems (ENDs) has created an alternative nicotine use modality that is growing in prevalence (Schoenborn and Gindi 2015). Initial evidence suggests that ENDs use places users at less risk of poor

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**Ethical Approval** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

**Informed Consent** Informed consent was obtained from all individual participants included in the study.

**Animal Rights** No animal studies were carried out by the authors for this article.

physical health outcomes as compared to combustible cigarette smoking (US Department of Health and Human Services 2013). However, nicotine use is also associated with poorer psychological health (Lasser et al. 2000), including comorbid anxiety and depression (e.g., Caponnetto and Polosa 2008; Leventhal and Zvolensky 2015). Motivational models of substance use (Baker et al. 2004) suggest that psychological distress and cigarette smoking exert negative bidirectional effects (Lawrence et al. 2011; Lawrence and Williams 2015; Taylor et al. 2014). For example, smoking has been posited to precede and even increase risk for anxiety (Morrell and Cohen 2006; Johnson et al. 2000; Moylan et al. 2013), while smoking cessation is associated with depression remission (Blalock et al. 2008; Cavazos-Rehg et al. 2014). Greater internalizing pathology has a marked effect on successful cessation, as smokers with comorbid psychological disorders evidence worse cessation outcomes (Abrantes et al. 2008; Brown et al. 2001; Weinberger et al. 2010). Considering this, the promotion of ENDS as a safer alternative to combustible cigarettes, either as a means of promoting cessation or as a harm-reduction intervention, needs to also consider their relative effects on mental health.

In order to better inform the promotion of ENDS for harm reduction and tobacco cessation, it is important to begin to characterize how use may be related to vulnerabilities that promote psychopathology, as well as psychiatric distress. Deficits in emotion regulation—responding to a distressing event in a maladaptive manner—may manifest as a sensitivity to and inability to tolerate negative emotional states (Gratz and Tull 2010), and is associated with greater reported craving and attentional bias to smoking relevant cues (Szasz et al. 2012), and earlier lapses after cessation (Farris et al. 2016), among combustible cigarette users. Moreover, trait level characteristics such as distress intolerance and anxiety sensitivity that affect the manner in which individuals respond to internal and external cues appear to confer risk for increased frequency and intensity of negative affect experienced during nicotine withdrawal (Abrantes et al. 2008; Zvolensky et al. 2004). These particular cognitive-affective vulnerabilities create more opportunities to learn that smoking (an escape/avoidance behavior) can reduce aversive affective experiences, thereby promoting the use of nicotine as a primary means of affect regulation and enhancement. Moreover, this process may be bidirectional; for example, elevated emotional distress in smokers may undermine processes central to emotion regulation (Baker et al. 2004). Due in part to this bidirectional relationship, both elevations in internalizing psychopathology symptoms and vulnerabilities are consistently associated with combustible nicotine dependence (Piper et al. 2011; Gonzalez et al. 2008) and difficulty cessating (Piper et al. 2010, 2011; Covey et al. 2006; Morissette et al. 2007; Abrantes et al. 2008; Brown et al. 2001, 2009; Farris et al. 2016).

Despite the role psychological distress and associated vulnerabilities play in nicotine use maintenance and difficulty abstaining from conventional cigarettes, less is known about the role of psychological distress and vulnerabilities among ENDS users. Relevant work has found that greater perceived stress (Leventhal et al. 2017), impulsivity (Spindle et al. 2017), and depressive symptomatology (Lechner et al. 2017; Bandiera et al. 2017) are each independently associated with greater likelihood of later ENDS use. Also, work examining differences in internalizing pathology between ENDS users and non-nicotine users has found that ENDS users were more likely to endorse lifetime mood (e.g., major depressive disorder, dysthymia) and anxiety (e.g., social phobia, generalized anxiety disorder) pathology (Chou

et al. 2017), as well as broad psychological distress (Park et al. 2017). In adolescents specifically, ENDS and dual ENDS and combustible cigarette users displayed greater internalizing pathology (depression, anhedonia, panic symptoms) than single ENDS users, whereas these groups did not display differences in distress tolerance and anxiety sensitivity (Leventhal et al. 2016).

Together, extant research suggests that ENDS use is related to elevations in internalizing symptoms, and several unique associations based on single-or dual-use. These differences are of particular importance in understanding the potential utility of ENDS for harm reduction and warrant extension to an adult sample. Motivation for use differs greatly across age, as the majority of adult ENDS users report initiating ENDS use as a substitute for combustible cigarette smoking (Chapman and Wu 2014), whereas adolescent users report experimentation as the primary reason for ENDS use (Kong et al. 2015). Age is also positively associated with ENDS use frequency, a meaningful marker of nicotine dependence (Delnevo et al. 2015), suggesting that adult ENDS users have been exposed to greater amounts of nicotine over the course of their lifetime, potentially increasing the likelihood of experiencing internalizing psychopathology (John et al. 2004; Leyro et al. 2011).

Considering the aforementioned potential differences in ENDS using adults, this study sought to examine the differential presence of internalizing psychopathology and individual differences in cognitive-affective vulnerabilities between adult dual nicotine users and single ENDS users. Importantly, capturing pathology and vulnerability presentations in an adult population can provide insight into whether ENDS can be appropriately utilized for cessation or harm-reduction purposes. Specifically, understanding the potential role that ENDS use, and dual-use of nicotine inhalation modalities have on mental health sequelae informs whether transitioning to ENDS use improves users' quality of life and whether likelihood of complete nicotine cessation improves. As these factors may serve to maintain nicotine use, understanding differences between ENDS use-groups may also inform whether or not the use of targeted interventions to address co-occurring psychological distress is warranted, especially among dual-users. Furthermore, prior combustible use history amongst single ENDS users may be differentially associated with pathology or vulnerability presentations, as these users' successful transition may suggest that they are characterized by a greater ability to tolerate the aversive consequences of nicotine reduction (e.g., withdrawal symptoms), and perhaps, lesser overall impairment. We hypothesize that dual nicotine users will exhibit greater impairment in pathology and vulnerability indices relative to single ENDS users without a prior use history, who in turn will evidence greater impairment than single ENDS users with a prior history of combustible cigarette use.

## Method

### Participants

Subjects ( $N = 264$ ; 139 dual nicotine users, 88 single ENDS users with a prior combustible cigarette use history, 37 single ENDS users without a prior combustible cigarette use history;  $M_{age} = 24.61$ ,  $SD = 5.34$ ) were adults between the ages of 18–44 recruited from an online platform (Amazon Mechanical Turk). The sample was predominantly male (58.3%), Caucasian (80.3%), and non-Hispanic (85.2%) (see Table 1 for group demographics).

Participants were excluded if they could not speak or read English fluently, possessed insufficient computer literacy to complete online surveys, and if they did not report using ENDS within the past month and had not used ENDS at least ten times in their lifetime, consistent with previous work (e.g., Sutfin et al. 2013).

## Measures

**Psychopathology Assessment**—Anxiety and depression symptoms were measured via the *Depression, Anxiety, and Stress Scale* (DASS-21; Henry and Crawford 2005; Lovibond and Lovibond 1995), a 21-item self-report measure. The DASS-21 captures core symptoms of depression, anxiety, and stress, indexed via separate subscales. Internal consistency across subscales was excellent (depression  $\alpha = 0.91$ , anxiety  $\alpha = 0.93$ , stress  $\alpha = 0.90$ ).

### Vulnerability Measures

**Anxiety Sensitivity Index—3 (ASI-3):** Anxiety sensitivity was measured using the ASI-3 (Taylor et al. 2007), an 18-item self-report measure. The ASI-3 captures fear of anxiety across three domains (physical, cognitive, and social concerns) and yields a total score assessing general fear of anxiety. Only the total score was utilized in the current study, yielding excellent ( $\alpha = 0.91$ ) internal consistency.

**Distress Intolerance Index (DII):** Distress intolerance was measured using the DII, a 10-item self-report measure (McHugh and Otto 2012). The DII yields a total score of perceived ability to withstand and tolerate general somatic and psychological distress, with very good internal consistency in the current sample ( $\alpha = 0.88$ ).

**Difficulties in Emotion Regulation Scale (DERS):** The DERS is a 36-item multidimensional assessment of emotion dysregulation (Gratz and Roemer 2004). The measure includes subscales capturing emotion regulation deficits in specific domains, as well as a total score assessing general emotion regulation difficulties; the overall score was examined to understand whether use-groups exhibited global emotion regulation differences. Internal consistency was very good ( $\alpha = 0.87$ ).

**Procedure and Analyses**—All study procedures were approved by the University Institutional Review Board. The survey was made available on the Amazon Mechanical Turk online web platform, wherein the survey was described as “An examination of E-Cigarette (E-Cig) use in Adults in the United States.” The survey was visible to all members of the Amazon Mechanical Turk website. Interested participants were directed to an online survey where they provided electronic consent after reviewing a detailed description of the study. Next, participants completed online questionnaire batteries using the Qualtrics online survey system. During the survey, nicotine (conventional and ENDS) use was assessed via self-reported daily timeline followback assessments of past 30-day use. All study procedures were conducted in accordance with the Declaration of Helsinki, as approved and monitored by the Rutgers University Institutional Review Board.

To ascertain the effect of ENDS use group on depression/anxiety symptoms and vulnerabilities, multivariate analyses of variance (MANOVAs) were conducted, separating

the sample into three use-groups (dual-users, single ENDS users without a history of combustible cigarette use, single ENDS users with a history of combustible cigarette use). If an omnibus effect was observed, Tukey's HSD post-hoc test was utilized to examine potential between-group differences.

## Results

### ENDS Use Groups and Anxiety/Depression Symptoms

Statistically significant variability in depression, anxiety, and stress symptoms were observed across the three ENDS use groups,  $F(6, 466) = 2.247, p = .028$ . With regards to anxiety symptom severity, users exhibited significant omnibus differences,  $F(2, 235) = 4.053, p = .019$ , partial  $\eta^2 = 0.033$ , small effect. Post-hoc comparisons using Tukey's HSD indicated that single users with no history of combustible cigarette use ( $M = 11.8, SD = 9.7$ ) exhibited more severe anxiety symptoms than single users with history of combustible cigarette use ( $M = 7.5, SD = 8.9, p = .049$ ) and current dualusers ( $M = 7.0, SD = 8.7, p = .011$ ). Single users with combustible use history did not differ from current dual-users ( $p = .913$ ). With regards to stress severity, users exhibited significant omnibus differences,  $F(2, 235) = 4.096, p = .018$ , partial  $\eta^2 = 0.034$ , small effect. Post-hoc comparisons using Tukey's HSD indicated that single users with no history of combustible cigarette use ( $M = 15.2, SD = 10.9$ ) exhibited more severe stress symptoms than current dual-users ( $M = 9.8, SD = 9.9, p = .013$ ). Single users with combustible use history ( $M = 10.9, SD = 8.7$ ) did not differ from single users without combustible use history ( $p = .076$ ) or current dual-users ( $p = .750$ ). With regards to depression severity, users did not exhibit significant omnibus differences,  $F(2, 235) = 1.244, p = .290$ , partial  $\eta^2 = 0.010$ .

### ENDS Use Group and Vulnerabilities

Statistically significant variability in DI, AS, and emotion regulation was also observed across the three ENDS use groups  $F(6, 430) = 2.241, p = .030$ . With regards to emotion regulation severity, users exhibited significant omnibus differences,  $F(2, 217) = 6.313, p = .002$ , partial  $\eta^2 = 0.055$ , medium effect. Post-hoc comparisons using Tukey's HSD indicated that single users with no history of combustible cigarette use ( $M = 88.2, SD = 26.7$ ) exhibited greater difficulty regulating their emotions than current dual-users ( $M = 72.4, SD = 23.4, p = .002$ ). Single users with combustible use history ( $M = 78.32, SD = 22.87$ ) did not differ from single users without combustible use history ( $p = .104$ ) or current dual-users ( $p = .234$ ). With regards to DI severity, users did not exhibit significant omnibus differences,  $F(2, 235) = 2.856, p = .060$ , partial  $\eta^2 = 0.026$ . Likewise, users did not exhibit significant omnibus differences in AS severity,  $F(2, 235) = 2.566, p = .079$ , partial  $\eta^2 = 0.023$ .

## Discussion

The current study examined differences in psychopathology and vulnerabilities between adult single ENDS users—with and without a history of combustible cigarette use—and dual-users of ENDS and combustible cigarettes. This study is the first to examine these differences by use status and history of combustible use in a sample of adult ENDS-users in

an attempt to better characterize the psychiatric profile of this sample and identify risk factors that may promote beliefs about the anticipated affect-enhancing effects of ENDS use. These findings may also inform the use of ENDS as a harm-reduction method.

Single-users without a history of combustible use reported greater anxiety than dual users and single-users with a history of combustible cigarette use; single-users without a history of combustible use reported greater stress and poorer emotion regulation capabilities than dual-users. These findings are suggestive of important differences in groups and may inform the use of ENDS as a harm reduction strategy. Single-users with a history of combustible cigarette use may represent a minority group that has successfully transitioned to ENDS-only use. These differences may indicate a greater ability to tolerate the aversive consequences of nicotine reduction (e.g., withdrawal symptoms). The current findings serve to extend prior work showing that ENDS are associated with greater internalizing pathology (Chou et al. 2017) and psychological distress (Park et al. 2017), suggesting that the degree of pathology and vulnerability impairment is not simply dependent upon the presence of nicotine use, but also varies by nicotine use history. Further, dual-users may differ from single-users without a history of combustible use in their self-reported stress and emotion regulation strategies given the unique pharmacological effects of combustible cigarettes.

Although the study did not examine causal relations between use status and psychopathology/vulnerabilities, our findings suggest that ENDS-only use is associated with a greater likelihood of anxiety symptoms, stress, and difficulties with emotion regulation. Considering prior work suggesting that elevated vulnerabilities (Leventhal et al. 2017; Spindle et al. 2017) and internalizing symptomatology (Lechner et al. 2017; Bandiera et al. 2017) precede ENDS initiation, these findings suggest that this elevation may be driven by ENDS users with non-combustible use histories. Individual differences in cognitive-affective vulnerabilities (i.e., global emotion regulation) may also impede the ability to successfully transition from dual-use to single use given the observed differences between groups. For example, empirical research indicates that higher levels of AS prior to cessation are predictive of sustained elevated withdrawal symptoms over time (Johnson et al. 2012). Individuals with elevations in these vulnerabilities may experience more intense withdrawal symptoms during cessation that may subvert cessation, discourage future attempts, and predict poorer future quality of life.

Additionally, these novel findings may be associated with the unique pharmacological profile of ENDS. Specifically, the pharmacokinetics of nicotine administered through combustible cigarettes may differ from ENDS, leading to variations in nicotine's anxiolytic effects. Combustible cigarette use results in rapid and efficient delivery of nicotine to the bloodstream (Benowitz et al. 2009) with anxiolytic effects occurring in a dose-dependent nature (Brioni et al. 1993; Picciotto et al. 2002). Conventional cigarette users may, therefore, more rapidly experience withdrawal symptoms and a rebound in symptoms of anxiety (Hendricks et al. 2006; Hughes et al. 1994), motivating re-administration. Conversely, delivery of nicotine to the bloodstream in ENDS users is less efficient (Farsalinos et al. 2014), which may promote continuous use of ENDS that mitigates the intensity and or frequency of withdrawal symptoms and anxiety. As such, dual nicotine users, relative to single users, may be engaging in an 'adaptive' pattern of nicotine administration, wherein

they receive acute, high doses of nicotine while being able to mitigate the onset of withdrawal symptoms or anxiety by titrating ENDS use between combustible cigarette administrations. As with the presence of psychopathology, it is conceivable that the perceived anxiolytic effects of both ENDS and combustible cigarette use contribute to one's perceived ability to regulate distress and negative affect. Regulating these aversive mood and physiological states may also result in a perceived increase in access to strategies, and may be indicative of an increased awareness of psychological and physiological distress (i.e., emotional clarity) for dual-users of ENDS and combustible cigarettes. This is an empirical question, which warrants further investigation, yet consideration of these potential profiles of nicotine administration may be central to understanding our findings that dual nicotine users are less likely to be characterized by elevations in anxiety, stress, and difficulties with emotion regulation than single-users.

The current study was the first to examine differences in psychopathology and vulnerabilities between adult ENDS dual and single users. The results differ from literature on ENDS use in adolescents, as single-users exhibited elevations in vulnerabilities and anxiety symptoms relative to dual-users (Leventhal et al. 2016). History of use and access to ENDS may differ between adolescent and adult populations. The current findings may indicate a bidirectional relation between psychopathology and nicotine use that occurs over a longer period of nicotine use (Boden et al. 2010; Chaiton et al. 2009) that will need to be examined through longitudinal research. Future research should also examine the extent to which dual use, specifically, affects beliefs about distress and ability to cope, and additional work should compare differences in psychopathology and vulnerabilities to non-nicotine users.

When considering the findings, several limitations should be noted. First, comparison groups consisting of combustible cigarette users or non-users were not included, making it difficult to examine whether the associations between ENDS use and psychopathology differs from adults using only combustible cigarettes or not using nicotine at all. Second, patterns of use including quantity and frequency may have meaningfully contributed to our findings, yet accurately quantifying ENDS nicotine administration and comparing it with combustible use remains a challenge among researchers. However, momentary assessment strategies and in vivo tracking of use in the lab may offer a possible alternative for conducting this comparison. Finally, the study did not include an assessment of externalizing symptoms as examined by Leventhal et al. (2016).

Despite these limitations, this study provides an important initial step in characterizing psychopathology and vulnerabilities in adults who use ENDS given the shifting landscape of nicotine use and use of alternative modes of nicotine delivery. This work has important implications for transdiagnostic interventions intending to limit ENDS use or utilize ENDS as a cessation method in itself, and provides foundational research for longitudinal work examining the course of psychopathology and vulnerabilities in ENDS users. The psychological and pharmacological function of ENDS use may be important to consider when developing theoretical models of ENDS use in relation to both anxiety and depression. Results also suggest that transitioning to ENDS use for individuals reporting difficulties with emotion regulations may be more difficult or require additional methods than for those who

do not report these vulnerabilities. Further exploration may identify how best to tailor interventions for ENDS users through a better understanding of motives and reasons for use.

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**Table 1**

Demographic and vulnerability characteristics for use groups

	Dual-users (1)	Single users w/prior combustible use (2)	Single users w/o combustible use (3)	Group differences*
Age (years)	24.18 (4.9)	25.11 (5.9)	24.7 (5.3)	–
Ethnicity (% Hispanic)	12.0%	19.0%	6.0%	–
Race (% Caucasian)	76.3%	84.4%	81.1%	–
Sex (% female)	63.0%	52.0%	54.0%	–
DASS-21 <sup>a</sup> anxiety	7.2 (8.6)	7.7 (8.7)	11.6 (9.8)	3 > 1,2
DASS-21 <sup>a</sup> depression	8.9 (11.1)	9.4 (11.5)	11.4 (11.7)	–
DASS-21 <sup>a</sup> stress	9.8 (9.9)	10.9 (8.7)	15.3 (11.0)	3 > 1
DII <sup>b</sup>	24.9 (8.8)	25.5 (8.8)	28.8 (8.1)	–
ASI-3 <sup>c</sup>	18.0 (12.6)	19.9 (13.3)	22.9 (12.0)	–
DERS <sup>d</sup>	73.0 (24.3)	78.8 (22.7)	88.2 (26.7)	3 > 1

Values displayed refer to Mean (SD)

\* Significance set at  $p < .05$

<sup>a</sup>DASS-21-depression, anxiety, and stress scale

<sup>b</sup>DII-distress intolerance index

<sup>c</sup>ASI-3-anxiety sensitivity index-3

<sup>d</sup>DERS-difficulties in emotion regulation scale