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Effects of time-varying changes in tobacco and alcohol use on depressive symptoms following pharmaco-behavioral treatment for smoking and heavy drinking.

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Abstract

Background: Complete abstinence from alcohol as well as smoking cessation have been shown to predict reductions in depressive symptoms over time. However, whether *reducing* alcohol use or smoking positively affect depressive symptoms has yet to be examined. The current study examined depressive symptoms as a function of time-varying changes in alcohol use and smoking status following a pharmaco-behavioral treatment addressing smoking cessation and alcohol reduction.

Methods: Participants were heavy-drinking smokers (n=150) followed for 26 weeks after their quit smoking date, with assessments of smoking, alcohol use, and depressive symptoms at baseline and 2, 8, 16, and 26 weeks.

Results: Abstinence from smoking was associated with significantly lower depressive symptoms, as compared to little to no reduction in smoking (B=−6.1) as well as significant reductions in smoking (B=4.01). Exploratory analyses, which excluded observations in which a participant was abstinent, revealed a significant effect of percent change in cigarettes smoked, modeled continuously, on depressive symptoms, (B=4.39). By contrast, no differences were observed in depressive symptoms in relation to changes in alcohol use.

Conclusion: It appears that smoking abstinence is associated with improvements in depression as compared to any level of sustained or reduced use and that the magnitude of smoking reduction

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Contributors

WVL conducted primary data analyses with advisement from CWK. WVL conceptualized and wrote the majority of the manuscript text. CWK, NS and PAC aided in conceptualization and contributed significantly to revision. All authors read and approved the final manuscript.

Authors Disclosures

Conflict of Interest

No conflict declared.

may be associated with lower depressive symptoms among those who did not quit successfully. If replicated, these findings may inform treatment for individuals for whom depression is a major barrier to cessation and who have been unable or are unwilling to be completely abstinent from smoking.

Keywords

Smoking; Nicotine; Smoking Cessation; Depression; Alcohol; Abstinence

1. Introduction

The extant literature provides evidence that both smoking cessation and abstinence from alcohol (independently) predict reduced depressive symptoms over time. However, many smokers are unsuccessful in achieving sustained abstinence or are unwilling to commit to complete abstinence in the foreseeable future, e.g. (Begh et al., 2015). Similarly, many heavy drinkers report willingness and motivation to reduce their alcohol consumption but do not intend to be abstinent from alcohol (Marlatt and Witkiewitz, 2002). Whereas the effects of abstinence on depressive symptoms have been studied extensively, the question as to whether or not *reducing* smoking or alcohol use positively affects depressive symptoms has yet to be examined.

Previous studies examining the link between smoking cessation and depressive symptoms generally show positive effects for those who quit successfully. Smokers who successfully quit and maintain abstinence for one year following treatment have demonstrated significant reductions in depressive symptoms over the assessment period, whereas those who relapsed showed no associated change (Kahler et al., 2002). A second study found similar effects: participants who had stopped smoking successfully reported a significant improvement in depression; those with moderate to severe depression reported the largest improvement (Stepankova et al., 2017). Some research has indicated that smoking cessation may lead to a worsening or re-emergence of depressive symptoms (Aubin, 2009), no change in symptoms (Rodriguez-Cano et al., 2016), or that depression changes post-cessation may depend on medication effects (Cinciripini et al., 2013). Despite some mixed findings, a recent meta-analysis found that smoking cessation (compared to continued smoking) was associated with a significant decrease in depression over time (Taylor, G. et al., 2014). Part of the difficulty of examining the relationship between cessation and depressive symptoms is that baseline depressive symptoms at the time of quit attempt are strongly tied to the outcome; thus, assessing the effect of cessation on subsequent depressive symptoms between individuals carries significant limitations. One study accounted for this limitation by modeling individual-level *changes* in smoking status over time in relation to depressive symptoms, allowing for transitions between smoking statuses within a participant. Results indicated that being abstinent at a particular time point was associated with lower levels of concurrent depressive symptoms (Kahler et al., 2011).

Several studies have found similar reductions in depression in individuals following treatment and successful abstinence from alcohol. Brown and Schuckit (1988) found that among the 46% of individuals with alcohol dependence who were admitted with clinically

significant levels of depression, only 6% had clinically elevated levels of depression following four weeks of abstinence achieved through inpatient treatment (Brown and Schuckit, 1988). A second study found that, regardless of the presence of baseline diagnosis of a depressive disorder, individuals with an alcohol use disorder demonstrated a significant decrease in depressive symptoms as the result of a four to five-week inpatient detoxification program (Liappas et al., 2002). These findings are also in line with studies examining the effects of alcohol abstinence on a broader range of psychological symptoms (Brown et al., 1995; Brown et al., 1991); each showing reductions in symptoms following abstinence.

General and substance-specific theories have been proposed to explain the relationship between abstinence and reduced negative affect. In general, success in attaining a goal of reduced use or abstinence may result in greater positive mood and reduced negative mood regardless of the substance, and increases in perceptions of physical well-being that occur following a successful also may contribute to reduced depression (Carbone, J. et al., 2005; Peters and Hughes, 2009; Stead and Lancaster, 2007). Frequent tobacco use leading to physiologic dependence can result in recurring mood oscillations where negative affect occurs during smoking abstinence and is attenuated by smoking (Parrott, A., 1994; Parrott, A.C., 1994; Parrott, 2006, 2015). Removing or dampening these daily oscillations in mood through sustained abstinence or reduction in use and dependence may result in less negative affect overall. In regards to alcohol, mood also may improve following abstinence as a result of decreases in negative consequences associated with heavy drinking (problems with relationships, legal issues, financial issues) (Markman Geisner et al., 2004).

Although the literature supports that both smoking cessation and abstinence from alcohol reduce depressive symptoms over time, no studies to our knowledge, have examined the relationship as a function of *reduction* in use from baseline. Given that successful cessation is likely dependent on a variety of psychological factors, including depression, how any reduction in smoking impacts depression has significant implications for treatment planning. If a reduction in use significantly decreases depressive symptoms, then smoking reduction as a step-down process towards cessation may be indicated in smokers for whom depressive symptoms are a key barrier to cessation. Similar implications may exist for individuals seeking abstinence from alcohol use; or, could serve as a critical motivator for those who seek to moderate their alcohol use.

The current study examined changes in depressive symptoms following a smoking cessation treatment, which also addressed reducing alcohol use, as a function of 1) no significant change in use relative to baseline 2) a 50% or greater reduction in use, and 3) abstinence from use of the substance for each substance independently. Additionally, we examined if continuous measures of smoking and alcohol use, among the group of participants who did not abstain, were associated with depressive symptoms. The theories detailed above regarding the link between change in substance use and depressive symptoms suggest that there may be a linear relationship between the degree of reduction in use and reduction in depressive symptoms due to attainment of a behavior change goal, increase in physical well-being, reduction in dependence, and a reduction in negative consequences associated with use. Therefore, we hypothesize a linear relationship between reductions in use and associated depressive symptoms.

2. Method

2.1 Participants

Participants were 150 heavy drinking smokers recruited in Providence RI, and surrounding communities, through posted advertisement, radio, internet, newspaper and flyers in physicians' offices and primary care clinics to participate in a randomized controlled trial of naltrexone for reducing alcohol use and improving smoking outcomes in heavy drinkers seeking smoking cessation treatment. Primary inclusion criteria included that participants (i) be ≥ 18 years old; (ii) have smoked cigarettes regularly for at least 1 year; (iii) currently smoke ≥ 5 cigarettes a day; (iv) currently use no other tobacco products or nicotine replacement therapy; and (v) currently report drinking heavily at least once per month on average (≥ 4 drinks per occasion for women; ≥ 5 drinks for men). Primary exclusion criteria included (i) meeting DSMIV criteria for substance dependence (excluding nicotine and alcohol) in the past 12 months; (ii) reported opioid use in the past month, had a drug screen positive for opioids, or required opioid medication for pain management; (iii) met criteria for a current major depressive or manic episode; (iv) had current psychotic symptoms; (v) had an unstable or serious medical condition that would preclude use of nicotine patch or naltrexone; or (vi) were currently pregnant or lactating. See (Kahler et al., 2017) for a list of all inclusion / exclusion criteria.

The sample was 58.7% male, 75.3% non-Hispanic white. Mean age was 42.11 (*SD* = 12.72) years, 46% of the sample had never married, and 64.6% of the sample had taken some college courses or achieved higher degrees. Participants smoked an average of 17.85 (*SD* = 9.5) cigarettes per day prior to their quit attempt and the mean Fagerström Test for Cigarette Dependence (FTCD; (Fagerström, 2012) score was 5.3 (SD = 2.27). Participants consumed an average of 25.2 (SD = 23.6) drinks per week in the 8-weeks prior to smoking quit date. Past Major Depressive Disorder, assessed by the Structured Clinical Interview for DSM-IV, was reported by 66 (44%) participants. Mean CESD score at baseline was 11.82 (SD = 8.65).

2.2 Procedure

The current analysis is secondary to the primary aims of a parent study in which heavy-drinking smokers were recruited from the community and randomized to receive 10 weeks of either (i) 50 mg naltrexone (n = 75) or (ii) placebo (n = 75) daily (Kahler et al., 2017). In addition, participants received 6-weeks of both transdermal nicotine patch and 6-sessions of counseling that addressed heavy drinking and smoking. The Counseling and Medication Management (CMM) intervention provided (i) smoking cessation treatment consistent with clinical practice guidelines (Brown et al., 2014; Fiore et al., 2008; Kahler et al., 2008), (ii) counseling on alcohol and its impact on smoking cessation (Kahler et al., 2008), and (iii) monitoring of oral study medication use and safety following guidelines in medical management (Pettinati et al., 2004). In addition to standard smoking cessation modules, session 1 included normative feedback on drinking and discussion of goals related to short and long-term changes in drinking. Subsequent sessions focused on study medication use, side effects, progress in quitting smoking, provision of support, review of current drinking, efforts to modify drinking, and problem-solving for high-risk situations for smoking relapse.

Full detail on counseling and pharmacotherapy has been published previously (Kahler et al., 2017). Quit date was set in the second week of the 10-week treatment. Participants were followed for 26 weeks after their target quit smoking date, with assessments of smoking, alcohol use, and depressive symptoms at 2, 8, 16, and 26 weeks after quit date.

2.3 Measures

2.3.1 Smoking.—Seven-day point-prevalence smoking abstinence was assessed at 2, 8, 16, and 26 weeks after quit date. Self-reported smoking abstinence was verified by carbon monoxide analysis of breath samples with a ≤4 ppm cutoff. Data on cigarettes smoked per day in the past week was collected at baseline and each follow-up assessment. Individuals self-reporting abstinence (no cigarettes in the past week) who were not biologically confirmed as abstinent, were removed from the analyses (2 week post quit = .9%, 8-week post quit = 16.9%, 16 week post quit = 11.7%, 26 week post quit =33.1%) (see Table 1 for n's).

2.3.2 Alcohol Use.—The Timeline Follow-Back Interview (TLFB; (Sobell et al., 1996), a well-validated calendar assisted interview, was administered at baseline to document alcohol use in the previous 8-weeks. Additionally, TLFB was conducted at 2, 8, 16, and 26 weeks after quit date to assess alcohol use since the last study visit. From the TLFB, we calculated average drinks per week directly preceding each point-prevalence smoking assessment.

2.3.3 Depressive Symptoms.—Depressive symptoms during the past week were assessed using the Center for Epidemiologic Studies Depression Scale (CESD; Radloff, 1977), a 20-item self-report scale with scores ranging from 0 to 60. CESD was administered at baseline and at 2, 8, 16, and 26 weeks after quit date, in line with the smoking and alcohol use measurements. Diagnostic exclusion (for current), and lifetime prevalence of Major Depressive Disorder (single episode and recurrent) were assessed at baseline using the Structured Clinical Interview for DSM-IV (SCID), non-patient version (First et al., 1995).

2.4 Analytic Strategy

Multi-level modeling MLM (Singer and Willett, 2003) was used to examine the association of changes in smoking and alcohol use with depressive symptoms at concurrent assessments. Analyses were conducted with full maximum likelihood estimation and a variance components covariance structure (as indicated by examining model fit with – 2 Log Likelihood; other covariance structures tested included compound symmetry, unstructured, and first-order autoregressive) using the linear mixed-effects models (MIXED) procedure in IBM SPSS Statistics 24. In level 1, we modeled within-participant change in depressive symptoms using mean level (intercept), rate of change (the linear effect of weeks since quit date, coded 0, 1, 2, and 3), and time-varying abstinence (abstinent = 2; >50% reduction in drinks or cigarettes per week = 1; <50% reduction in drinks or cigarettes per week = 0). Additionally, we conducted exploratory analyses in which the percent reduction of each substance was modeled as a continuous variable in the level-1 model. The level-2 model tested whether parameters were significantly different from zero across participants. In level-2 we covaried the effect of treatment condition, MDD history, gender, baseline CESD

score, baseline drinks per week, and baseline cigarettes per week on mean levels of depressive symptoms, given that these variables could be related both to depressive symptoms and to smoking outcomes. All models included changes in both smoking and alcohol use given that both have demonstrated relationships with depressive symptoms.

3. Results

Means and standard deviations for CES-D scores by smoking and alcohol use category, as well as sample percentages, are listed in Table 1. Mean baseline CES-D score was 11.8 (SD = 9.9); mean CES-D did not change significantly over time; Week 2 CES-D = 10.43 (SD = 9.28), Week 8 CES-D = 10.94 (SD = 9.2), Week 16 CES-D = 11.97 (SD =10.8), Week 26 CESD = 11.49 (SD = 9.78). Smoking and drinking reductions (analyzed as ordinal variables [0, 1, or 2] as described above) were not significantly correlated at any time point; week 2 r_s = −.017, p = .865; week 8 r_s = −.012, p = .905; week 16 r_s = .136, p = .165; week 26 r_s = −.044, p = .695.

Results of the MLM analyses including participants randomized to treatment and submitting any data on CES-D during follow-up (N = 132) are presented in Table 2. In terms of changes in smoking, abstinence at a given assessment was associated with a 4.01-point reduction in depressive symptoms (95% C.I. = 1.71–6.30) when compared to those who reduced by 50% or more, and a reduction of 6.1 points (95% C.I. = 3.19–8.93)) when compared to those who reduced smoking less than 50%. Reducing cigarette use by 50% or more was not associated with significant decreases in depressive symptoms as compared to a 50% or less reduction, mean difference = −2.04 points (95% C.I. = −4.41 – 0.34). Exploratory analyses, which excluded observations in which a participant was abstinent (126 observations across the 4 time-points), revealed a significant effect of percent change in cigarettes smoked, modeled continuously, on depressive symptoms, 4.39 (95% C.I. 0.14 – 8.64)), with larger reductions in percentage of cigarettes smoked predicting lower depressive symptoms.

In terms of alcohol use, abstinence was not associated with a significant reduction in depressive symptoms compared to a 50% or greater reduction in consumption, or less than 50% reduction. No significant differences were observed when comparing the >50% reduction group with the <50% reduction group. Exploratory analyses, which excluded participants who were abstinent from alcohol, revealed no significant effect of percent change in alcohol consumed, modeled continuously, on depressive symptoms.

4. Discussion

The current study is the first, to our knowledge, to model depressive symptoms in heavy-drinking smokers making a quit attempt as a function of 1) abstinence from smoking or alcohol use, independently 2) a significant reduction (>50%) in use of either substance and 3) little or no change in use following a smoking cessation and alcohol reduction intervention. In accordance with previous findings, i.e. (Kahler et al., 2011; Mathew et al., 2013; Stepankova et al., 2017), abstinence from smoking was associated with significantly lower depressive symptoms as compared to continued smoking at any level. This study extended the literature by demonstrating that abstinence was also associated with lower

depressive symptoms as compared to a 50% or greater reduction in smoking, suggesting that abstinence has a meaningful psychiatric benefit as compared to any level of continued smoking. Comparison of the two reduced use groups demonstrated no significant difference. However, an exploratory analysis modeling the continuum of smoking reduction following quit date (observations in which abstinence was achieved were removed from analysis), revealed a significant effect of smoking reduction on depressive symptoms. Specifically, participants who reported a larger reduction in smoking experienced significantly less depressive symptoms. The significant relationship between smoking abstinence or reduction, and depressive symptoms may be explained by the psychological benefits of goal attainment (e.g. Peters and Hughes, 2009; Stead and Lancaster, 2007), the psychological benefits of perceptions of improved health associated with quitting or reducing smoking (Carbone, J.C. et al., 2005), or reduction in tobacco dependence that causes repetitive mood oscillations due to withdrawal and subsequent reversal of withdrawal effects via smoking (Parrott, A., 1994; Parrott, A.C., 1994; Parrott, 2006, 2015). This result is partially discordant with results reported previously demonstrating that individuals who smoked moderately in the immediate two weeks following a quit attempt reported significantly higher negative mood symptoms as compared to those who reported minimal smoking or relapsed completely (abstainers reported the lowest level of negative mood and depressive symptoms)(Kahler et al., 2002). However, the result currently reported is in concordance with the finding that minimal smokers reported less depressive symptoms than those who smoked moderately or relapsed completely following a quit attempt (Kahler et al., 2002). Differences observed between these studies may be due to differences in analytic strategy and length of follow up. Specifically, the current analysis focused on *reductions* in smoking at a particular time point as compared to baseline and followed participants for a period of 26 weeks, whereas Kahler et al. classified post-quit smoking groups by cigarettes per day and followed participants in the short term following cessation (2 weeks).

As would be hypothesized by prior research (Brown et al., 1996; Brown et al., 1995; Brown and Schuckit, 1988; Liappas et al., 2002), we expected to observe significant associations between alcohol abstinence and depressive symptoms. However, no significant differences in depressive symptoms were found between abstinence and any level of alcohol intake reduction, including an exploratory analysis of the effects of reduction in alcohol use on depressive symptoms modeled as a continuous variable. It may be that a longer period of sustained abstinence (e.g. (Brown et al., 1995) than what was modeled in the current analyses, is required to observe corresponding changes in depressive symptoms or that the current sample was less severe in terms of their baseline alcohol use. An intermediate variable such as negative consequences of alcohol use or motivation to reduce alcohol use may mediate the effect of changes in the volume of consumption on depressive symptoms, thus limiting the ability of the current study to detect such effects. Lastly, it is important to note that the current sample of heavy drinkers was not specifically seeking treatment for alcohol use; thus, a different relationship between changes in alcohol use and changes in depressive symptoms may be observed in a treatment-seeking sample.

The results of this study must be interpreted in light of several important limitations. The study was limited to heavy drinkers seeking smoking cessation treatment; therefore results may differ in non-smoking heavy-drinkers, smokers who use alcohol moderately, or

individuals seeking stand-alone treatment for alcohol use disorder. The current study also excluded individuals with Major Depressive Disorder which may have attenuated effects that may have been observed in a sample that included more severe depressive symptoms. Additionally, the majority of the sample was non-Hispanic White; thus results may not generalize to other ethnic or racial groups . Furthermore, analyses explored parallel associations between abstinence and depressive symptoms, allowing for the possibility that changes in depression may have precipitated shifts between smoking and abstinence, rather than the other way around.

Taken together, it appears that abstinence from smoking offers significant psychiatric benefits as compared to any level of sustained use and that the magnitude of smoking reduction may be associated with lower depressive symptoms among those who did not quit successfully. In terms of abstinence from smoking, several studies have now demonstrated improved mental health following a successful quit attempt including increased happiness (Shahab and West, 2009, 2012), reductions in anxious arousal (Farris et al., 2015), and meta-analysis examining general mental health (Taylor, Gemma et al., 2014). Replication is needed to confirm the current finding that reductions in smoking as compared to baseline may be associated with significantly lower depressive symptoms. Similar benefits were not observed for those abstaining from or reducing alcohol use. Future research that includes a measure of negative consequences associated with drinking, and a variable quantifying sustained alcohol abstinence or reduction will help clarify the current results. Additionally, an examination of potential mediators (goal attainment, perception of improved health, neurobiological mechanisms) of the relationship between smoking abstinence / reduced smoking and depressive symptoms will help to elucidate causal mechanisms. Lastly, if the significant association between reduced smoking and lower levels of depressive symptoms can be replicated, it warrants investigation as a potentially beneficial step-down process for smokers who endorse depressive symptoms as a major barrier to cessation and who are unwilling or have been unable to achieve complete abstinence. In this case, emerging approaches such as nicotine patch pre-loading could be used to reduce daily smoking (Lindson-Hawley et al., 2014), and repeated assessments of depressive symptoms could indicate when an individual may be ready to attempt complete abstinence (once depressive symptoms have reduced in line with reduced smoking). These methods may be particularly useful in those who are initially unwilling to make a complete quit attempt (Klemperer et al., 2018; Wu et al., 2015).

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Highlights

- Quitting was associated with lower dep sx compared to any level of sustained use.
- Larger reductions in smoking are associated with lower depressive symptoms.
- Reductions in alcohol use were not associated with changes in depressive symptoms.

Table 1.

Percent of sample and CESD for Smoking and Alcohol Use Categories by Assessment point

Status	Week 2		Week 8		Week 16		Week 26	
Smoking	% (n)	CESD	% (n)	CESD M	% (n)	CESD M	% (n)	CESD M
<50%	9.1	17.94	17.7	17.33	32.5	18.0	16.9	12.95
>50%	40.9	11.86	40.3	13.24	35.0	9.72	37.1	14.95
Abstinent	42.9	7.09	25.0	6.35	20.8	8.1	12.9	7.34
Alcohol	% (n)	CESD	% (n)	CESD M	% (n)	CESD M	% (n)	CESD M
<50%	43.6	10.42	42.3	12.9	53.2	13.9	42.4	13.25
>50%	33.3	9.77	33.3	8.9	24.2	9.9	35.6	11.25
Abstinent	23.1	10.38	24.4	10.1	22.6	9.46	22.0	8.81

* Observations in which self-reported smoking abstinence was not biologically confirmed were removed from analyses: 0.9% at time 1, 16.9% at time 2, 11.7% at time 3, and 33.1% at time 4.

Table 2.

MLM predicting Depressive Symptoms as a function of change in smoking and alcohol use.

Parameter	*B*	95% C.I.	S.E.	*p*
Mean Level (intercept)				
Intercept	0.36	(−3.67 – 4.40)	2.04	.861
Baseline CES-D	0.43	(0.28 – 0.58)	.07	<.001
Past MDD (vs. none)	2.72	(0.90 – 4.55)	.925	.004
Male (vs. Female)	0.73	(−1.81 – 3.27)	1.28	.573
Baseline Cigarettes Per Week	0.07	(−.06 – 0.21)	.068	.267
Baseline Drinks Per Week	−0.03	(−0.09 – 0.03)	.029	.335
Naltrexone (vs. Placebo)	0.25	(−2.17 – 2.67)	1.22	.837
Time-varying Smoking Status				
50% or greater reduction (vs.	4.02	(1.70 – 6.33)	1.17	.001
< 50% reduction (vs. Abstinence)	6.10	(3.22 – 8.98)	1.45	<.001
Time-varying Alcohol Use				
50% or greater reduction vs.	.41	(−1.81 – 2.63)	1.13	.717
< 50% reduction or no change vs.	.25	(−1.86 – 2.40)	1.07	.818
Variance Components				
Level 1				
Within-person residuals	32.53	(25.87 – 40.90)	3.79	<.001
Level 2				
In mean level (intercept)	22.57	(11.75 – 43.34)	7.51	.003
In rate of change (time)	2.90	(1.22 – 7.06)	1.31	.026
In time-varying smoking abstinence	8.53	(2.11 – 34.41)	6.006	.160
In time-varying alcohol abstinence	0.33	(0.00 – 2.25)	4.55	.937

Note. CES-D = Center for Epidemiologic Studies Depression Scale; MDD = major depressive disorder