Full length article

Gender differences in self-reported withdrawal symptoms and reducing or quitting smoking three years later: A prospective, longitudinal examination of U.S. adults

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A R T I C L E   I N F O

Article history:
Received 2 January 2016
Received in revised form 16 June 2016
Accepted 17 June 2016
Available online 20 June 2016

Keywords:
Smoking
Withdrawal
Gender
Epidemiology

A B S T R A C T

Background: Little is known about gender differences in withdrawal symptoms among smokers in the community. This study used longitudinal epidemiologic data to examine gender differences in current smokers’ report of withdrawal symptoms during past quit attempts and the relationship between withdrawal symptoms and the odds of reducing or quitting smoking three years later.

Methods: Data were drawn from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC; Wave 1, 2001–2001, n = 43,093; Wave 2, 2004–2005, n = 34,653). Analyses were conducted on respondents who reported current daily cigarette smoking at Wave 1 (n = 6911). Withdrawal symptoms during past quit attempts were assessed at Wave 1. Current smoking status was assessed at Wave 2.

Results: Wave 1 current smoking women, compared to men, were more likely to endorse any withdrawal symptoms, withdrawal-related discomfort, and withdrawal-related relapse (ps < 0.0001). Women endorsed a greater number of withdrawal symptoms than men (M = 2.37, SE = 0.05 versus M = 1.78, SE = 0.04; p < 0.0001). The odds of reducing and quitting smoking were significantly lower for respondents who reported any Wave 1 withdrawal symptoms, withdrawal-related discomfort, and withdrawal-related relapse. These relationships did not differ for women versus men. Among men, the odds of reducing smoking at Wave 2 decreased significantly with each cumulative withdrawal symptom compared to women (β interaction = 0.87; p = 0.01).

Conclusions: Women were more likely to report withdrawal while the relationship between withdrawal symptoms and decreased likelihood of reducing smoking was stronger in men. Identifying gender differences in withdrawal can help develop strategies to help reduce withdrawal for both men and women.

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1. Introduction

Most smoking quit attempts end in relapse to cigarette use within the first week (Pisaecki, 2006) when withdrawal symptoms are the strongest (Pisaecki et al., 2002). A number of laboratory and clinical studies have reported that women experience both a greater number and a wider variety of withdrawal symptoms than men following either a quit attempt in clinical studies or a period of smoking abstinence in laboratory studies (Jorenby et al., 1995; Leventhal et al., 2007; Pang and Leventhal, 2013; Pisaecki et al., 1998, 2003; Wetter et al., 1999a, 1999b). For example, in a laboratory study of 203 smokers (Leventhal et al., 2007), women reported greater increases in negative affect, withdrawal-related distress, and the urge to smoke to relieve withdrawal-related distress after 12 h of smoking abstinence. In another laboratory study, female smokers reported higher levels of overall negative affect and anxiety during abstinence than male smokers after 16 h of smoking abstinence (Pang and Leventhal, 2013). In a placebo-controlled clinical trial of transdermal nicotine patch and/or bupropion for smoking cessation, women displayed more day-to-day variability in withdrawal symptoms (Pisaecki et al., 2003). Together, clini-

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http://dx.doi.org/10.1016/j.drugalcdep.2016.06.013
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eral and laboratory data suggest that men and women differ in their report of withdrawal symptoms. As the severity of withdrawal symptoms are strongly linked with smoking lapse after quit attempts (Piasecki, 2006), a better understanding of the experience of withdrawal for men and women, and the implications of gender differences in withdrawal for smoking abstinence, is warranted.

While past studies have examined gender differences in withdrawal within specific geographic communities and groups of smokers (e.g., treatment seeking smokers), little is known about gender differences in self-reported withdrawal symptoms using epidemiologic data that is more generalizable to the general population and that assesses smoking behavior over a lengthy period of time. Breslau et al. (1992) surveyed 1007 young adults (ages 21–30) who were members of a health maintenance organization in the metro Detroit area of the U.S. state of Michigan. Among the 241 participants who reported they had unsuccessfully attempted to quit or cut down on their smoking, there were no differences in the average number of withdrawal symptoms (range 0–12) by gender (men M = 3.93, SD = 2.12, women M = 4.39, SD = 2.23, p = n.s.). It is not yet known if there are gender differences in the report of withdrawal symptoms or withdrawal-related experiences (e.g., returning to smoking during a quit attempt to relieve withdrawal symptoms) in more recent samples that are nationally representative of the full U.S. adult population. In addition, it has not yet been examined whether gender differences exist in the association between self-reported withdrawal symptoms and continued smoking versus reducing or quitting smoking over a number of years.

The current study uses longitudinal epidemiologic data from the U.S. adult population to examine gender differences in withdrawal symptoms and the relationship between withdrawal symptoms reported by current daily smokers and the likelihood of reducing or quitting smoking three years later. The first aim of the study was to examine withdrawal symptoms for current daily smoking women versus men. Based on the laboratory and clinical research cited above (e.g., Leventhal et al., 2007), it was expected that current daily smoking women would be more likely to report withdrawal symptoms, withdrawal-related distress, and withdrawal-related relapse to smoking during past quit attempts than current daily smoking men. The second aim was to examine the relationship between self-report withdrawal symptoms during past quit attempts and reducing or quitting smoking three years later. Based on the relationship between withdrawal and smoking relapse (e.g., Piasecki, 2006), it was expected that the endorsement of withdrawal symptoms, withdrawal-related distress, and withdrawal-related relapse would be associated with a decreased likelihood of reducing and quitting smoking. The third aim was to explore whether gender differences existed in the relationship between self-reported withdrawal symptoms during past quit attempts and reducing or quitting smoking three years later.

2. Methods

2.1. Data source and study population

This study analyzed data from the National Institute on Alcohol Abuse and Alcoholism’s National Epidemiologic Survey on Alcohol and Related Conditions (NESARC; Wave 1, 2001–2002, n = 43,093; Wave 2, 2004–2005, n = 34,653). Participants were non-institutionalized U.S. civilian adults (ages 18 and older) in all 50 states and the District of Columbia. African-Americans, Hispanics, and young adults (ages 18–24) were oversampled. The response rate for the Wave 1 assessment was 81% and 86% of the eligible Wave 1 participants completed the Wave 2 assessment. Details of the NESARC, including the procedures related to data collection and weighting, have been described in past publications (Grant and Kaplan, 2005; Grant et al., 2003b). The sample for the current analyses included participants who reported current daily cigarette smoking at the Wave 1 interview (n = 6911).

2.2. Material and methods

2.2.1. Smoking status. Smoking behavior was assessed at Wave 1 and Wave 2 using the Alcohol Use Disorders and Associated Disabilities Interview Schedule—DSM-IV (AUDADIS-IV; Grant et al., 2001, 2003a). Individuals were classified as Wave 1 current daily smokers, and included in the analytic sample if they reported smoking cigarettes every day (i.e., seven days per week) during the past year at the Wave 1 assessment. Smoking status at Wave 2 was categorized into three mutually exclusive groups: current daily smokers (reported smoking every day in the past year at the Wave 2 assessment), current non-daily smokers (reported smoking some days in the past year at the Wave 2 assessment; range: 6 days/week – once a month or less), and current non-smokers (reported no smoking in the past year at the Wave 2 assessment).

2.2.2. Withdrawal symptoms. During the Wave 1 interview, participants were asked if they had experienced each of eight symptoms when attempting to quit smoking during the past 12 months: depression, sleep problems, difficulty in concentrating, increased appetite, irritability or frustration, anxiety or nervousness, heart beating more slowly, and restlessness. A response of Yes to each item was coded as a “1” while a response of No to each item was coded as a “0.” The cumulative number of symptoms ranged from 0 to 8. Participants were considered to have endorsed “any withdrawal symptoms” if they reported at least 1 withdrawal symptom. Participants were also asked to report whether withdrawal symptoms experienced over the past 12 months caused discomfort, distress, or impairment (“withdrawal-related discomfort”, Yes/No) and whether they used cigarettes to avoid withdrawal symptoms (“withdrawal-related relapse”, Yes/No).

2.2.3. Demographics. Wave 1 demographic information was categorized based on previous work (Grant et al., 2004) and included gender (male, female), age (18–29, 30–44, 45 and older), race/ethnicity (Non-Hispanic White, Non-Hispanic Black, Non-Hispanic Other, Hispanic), education (Less than High School, High School Graduate, Attended/Completed College), and marital status (Married or Living As Married, Not Married).

2.2.4. Psychiatric and substance use disorders. At Wave 1, the AUDADIS-IV assessed mood disorders (major depressive disorder, dysthymia, manic disorder, hypomanic disorder), anxiety disorders (panic disorder with or without agoraphobia, agoraphobia, social phobia, specific phobia, generalized anxiety disorder), alcohol use disorders (abuse and dependence), and substance use disorders (nicotine dependence; abuse and dependence of 10 classes of drugs: cannabis, sedatives, tranquilizers, opiates, heroin, stimulants, cocaine, hallucinogens, inhalants, solvents). Participants were classified into one of two mutually exclusive responses for each disorder category: (1) Lifetime Diagnosis (met criteria for a diagnosis at any point during the lifetime) or (2) Never Diagnosis (no lifetime diagnosis of the disorder).

2.3. Statistical analyses

All tests were completed in STATA using weighted analyses (StataCorp, 2011) to account for residual differences between the sample and the population profile according to the 2000 United States Population Census, as well as to account for nonresponse
and sample attrition. The weighted Wave 2 data represent the same baseline population as represented in Wave 1.

Sample frequencies of demographic, psychiatric, and substance use covariates were calculated to compare sample differences between males and females. Also, the proportion of withdrawal symptoms, the mean number of symptoms, and smoking status at Wave 2 follow-up were compared between males and females. Standard errors were computed using Taylor series linearization and bivariate frequencies were tested using Rao Scott chi-squared tests to account for complex survey design. Statistical tests were two-tailed and differences were considered significant when \( p < 0.05 \).

A series of multinomial logistic regression models were run to estimate the odds of reducing smoking or quitting smoking (versus continued smoking) at Wave 2 for four withdrawal variables assessed at Wave 1: (1) the report of any withdrawal symptom, (2) the cumulative number of withdrawal symptoms, (3) the report of withdrawal-related discomfort, and (4) the report of withdrawal-related relapse. Participants were considered to have reduced their smoking if they reported daily smoking at Wave 1 and non-daily smoking at Wave 2 while participants were considered to have quit smoking if they reported daily smoking at Wave 1 and no smoking at Wave 2. First, unadjusted odds ratios (ORs) were calculated for each withdrawal variable. Then a series of models were run to examine these associations with adjustment for potential confounders. The first model adjusted for demographics and smoking quantity at Wave 1 while a second model adjusted for demographics, smoking quantity, substance use disorders, and psychiatric disorders. A third set of models were run for the withdrawal-related discomfort and withdrawal-related relapse that added an adjustment for the mean-centered reported number of withdrawal symptoms as a measure of withdrawal severity. For each of the four withdrawal variables, a final model tested for statistical interaction between the withdrawal variable and gender. If the interaction parameter estimate was significant, two sets of models were run, one without any adjustments and the second adjusting for all covariates from the third model, and stratified by gender. Only the adjusted model results were reported for the stratified models. An odds ratio (OR) and 95% confidence interval (CI) was calculated for each model and were considered to be statistically significant if the 95% CI did not include 1.0.

3. Results

3.1. Sample characteristics (Table 1)

See Table 1 for demographics and prevalences of psychiatric and substance use disorders for the full analytic sample and by gender. Just over half of the sample (55.4%) was male and the majority of the sample identified as Caucasian. Though statistically significant due to the large sample, demographic frequencies were generally similar between men and women with the largest gender difference seen for income. Women were significantly more likely to endorse mood and anxiety disorders while men were more likely to report alcohol and substance use disorders.

3.2. Self-reported withdrawal symptoms at wave 1 (Aim 1; Table 2)

At Wave 1, 69.4% of current daily smoking women and 61.6% of current daily smoking men endorsed at least one withdrawal symptom. Women reported a higher average number of symptoms than men (Women M = 2.6, SE = 0.06; Men M = 2.0, SE = 0.05; \( p < 0.0001 \)). Current daily smoking women were significantly more likely to endorse seven out of the eight withdrawal symptoms (with the exception of slower heartbeat; see Table 2). Current daily smoking women were also significantly more likely than current daily smoking men to report experiencing withdrawal-related discomfort and withdrawal-related relapse (see Table 2).

3.3. Association between self-reported withdrawal symptoms and the odds of reducing or quitting smoking three years later (Aim 2; Table 3)

At Wave 2, 16.0% of Wave 1 daily smokers reported that they were not currently smoking (men = 17.1%, women = 14.7%) while 5.3% of Wave 1 daily smokers reported reducing their smoking frequency to non-daily use (men = 5.4%; women = 5.1%). The unadjusted odds of reducing and quitting smoking at Wave 2 were significantly lower among respondents who at Wave 1 reported (1) any withdrawal symptoms, (2) a greater number of withdrawal symptoms, and (3) withdrawal-related relapse (see Table 3). The unadjusted odds of quitting smoking were also significantly lower among respondents who reported withdrawal-related discomfort. After adjustment for demographics and smoking quantity, the associations were significant in the models for all withdrawal variables including the odds of reducing smoking and withdrawal-related discomfort. After additional adjustment for substance use and psychiatric disorders, the associations between both cumulative withdrawal symptoms and withdrawal-related relapse and smoking cessation outcome remained significant although the relationship of withdrawal-related relapse and smoking cessation outcome relationship was then no longer statistically significant after an additional adjustment for number of withdrawal symptoms. In the fully-adjusted model, the odds of quitting smoking at Wave 2 decreased by 3% for each additional withdrawal symptom reported by respondents at Wave 1 (95% CI = 0.95-0.99).

3.4. Gender differences in the association between self-reported withdrawal symptoms and the odds of reducing or quitting smoking three years later (Aim 3; Table 3)

The only withdrawal variable for which the statistical interaction of gender was significant was for cumulative Wave 1 withdrawal symptoms. There was a stronger relationship between the odds of reducing smoking at Wave 2 and greater cumulative withdrawal symptoms at Wave 1 for men compared to women (\( \beta \) interaction = 0.87; \( p = 0.01 \)). With each additional reported withdrawal symptom, men who were current smokers at Wave 1 were 6% less likely to have reduced smoking at Wave 2 (95% CI = 0.90-0.98). The relationship was not significant for women. The unadjusted stratified models were slightly further from the null association and became attenuated after adjusting for model confounders. Further, there was no interaction between gender and any withdrawal symptom (\( \beta = 0.05, p = 0.75; \beta = 0.007, p = 0.93 \)), withdrawal-related discomfort (\( \beta = 0.72, p = 0.17; \beta = 0.15, p = 0.44 \)) or withdrawal-related relapse (\( \beta = 0.34, p = 0.22; \beta = 0.17, p = 0.22 \)) in reducing or quitting smoking, respectively.

4. Discussion

The current study is the first to use longitudinal data from a representative sample of U.S. adults to examine gender differences in self-reported withdrawal symptoms during past quit attempts and in the association of self-reported withdrawal and quitting or reducing smoking. As expected, women were more likely than men to report experiencing withdrawal symptoms, a greater number of withdrawal symptoms, withdrawal-related discomfort, and withdrawal-related relapse. Also as expected, the endorsement of any withdrawal symptoms, cumulative number of withdrawal
symptoms, withdrawal-related distress, and withdrawal-related relapse were associated with a decreased odds of both reducing smoking and quitting smoking three years later among both men and women. With regard to gender differences in the relationship between withdrawal and reducing or quitting smoking, men and women did not differ in the relationship between withdrawal and reducing or quitting smoking for most withdrawal symptoms. Men reported a stronger relationship between number of withdrawal symptoms and reduced likelihood of reducing smoking with compared to women.
The finding that women were more likely than men to report withdrawal symptoms in a nationally representative sample of U.S. adults is consistent with previous clinical and laboratory studies that were more selected and geographically constrained (e.g., Leventhal et al., 2007; Pang and Leventhal, 2013). While it is possible that women experience greater absolute withdrawal symptoms than men, it is also possible that women are more likely to report or expect (vs. experience) withdrawal symptoms than men. For example, there is evidence that men underreport withdrawal symptoms when assessed retrospectively in contrast to prospective assessment while women report the same number of symptoms retrospectively and prospectively (Pomerleau et al., 1994).

Both the experience and the expectation of more withdrawal symptoms may have an impact on quit behavior. Adults smokers who reported expecting greater risks of quitting smoking (e.g., cravings, depression) then reported greater levels of cravings, withdrawal symptoms, and depressive symptoms during a week of smoking abstinence compared to adults who expected fewer risks of quitting (Weinberger et al., 2008). Greater perceived risks of quitting have also been found to be associated with decreased motivation to quit and less success at quitting (McKee et al., 2005; Toll et al., 2008). With regard to withdrawal symptoms, a greater expectation that withdrawal symptoms will occur during smoking abstinence is associated with the report of greater withdrawal symptoms (Hendricks and Leventhal, 2013). Further, women are more likely than men to expect to have withdrawal symptoms during quit attempts and report lower motivation to quit smoking with withdrawal expectancies mediating the relationship between gender and motivation to quit (Hendricks et al., 2014). Based on the association between expected withdrawal and experienced withdrawal, it may be useful for those who work with smokers, especially female smokers, to identify expectancies about withdrawal prior to quit attempts and include these beliefs as part of pre-quit counseling (e.g., identifying, examining, and modifying these beliefs).

Withdrawal symptoms, withdrawal-related distress, and withdrawal-related relapse were all significantly associated with decreased odds of reducing or quitting smoking three years later for both women and men. While many behavioral and pharmacological treatments (Fiore et al., 2008) focus on reducing withdrawal symptoms, there may be benefits to working with both male and female treatment-seeking smokers on reducing distress related to withdrawal symptoms. Distress tolerance has been associated with smoking lapse (Brown et al., 2005, 2009; Rohsenow et al., 2015) and decreasing distress tolerance, especially tolerance specifically related to withdrawal symptoms, may be a useful aim to incorporate into treatment in order to improve quit attempt outcomes (Brown et al., 2013). Prophylactic emphasis on avoiding the use of cigarettes to cope with withdrawal symptoms may also help to improve quit outcomes.

In the current study, a significant interaction between gender and cumulative withdrawal symptoms emerged related to smoking reduction. Even though women reported a greater number of withdrawal symptoms than men, the relationship between number of withdrawal symptoms and reducing smoking was stronger for men compared to women. As men may underreport withdrawal symptoms when asked to recall them retrospectively (Pomerleau et al., 1994), the relationship between cumulative withdrawal symptoms and reducing smoking may even be an underestimate of the impact of withdrawal symptoms for men. Future research should examine whether male smokers benefit from education about withdrawal symptoms in order to increase their ability to identify withdrawal symptoms that have impacted them in the past and whether this information can be used in treatment to improve quit outcomes.

While the decreased likelihood of reducing or quitting smoking was significant for all withdrawal variables after adjusting for demographics, several aspects of withdrawal were no longer significant after adjusting for comorbid psychiatric and substance use disorders. Psychiatric and substance use disorders have been associated with greater withdrawal symptoms (e.g., Pomerleau et al., 2005; Smith et al., 2014a; Weinberger et al., 2010, 2009) and lower likelihoods of quitting smoking (e.g., Smith et al., 2014b). The relationship between higher numbers of withdrawal symptoms and reporting relapse to smoking to relieve withdrawal symptoms remained significant after accounting for these disorders suggesting that alcohol and substance use disorders do not fully account for the relationship between withdrawal and quitting.

While there are strengths associated with the use of epidemiologic data (e.g., large sample size, longitudinal data), there are also limitations. First, research would be needed to confirm that these results generalize to persons not included in the NESARC study (e.g., adolescents, adults in countries other than the U.S.). A second potential limitation related to the NESARC data is that of loss to follow-up between Wave 1 and Wave 2. In a sensitivity analysis of our analytic sample (data not shown), non-Hispanic white respon-
udents were significantly more likely to have completed the Wave 2 follow-up interview than other race/ethnicity groups (p = 0.003). There were no differences in follow-up rates by gender, age, marital status, education, or income. Though this difference was statistically significant, Wave 2 data were weighted to represent the same baseline population as represented in Wave 1. Therefore, it does not appear that the Wave 2 sample represents a meaningfully different population. Nevertheless, these differences could affect the external validity of our findings by impacting the representative of the U.S. population among the sample of NESARC participants who completed both waves of data collection.

Third, the retrospective recall of withdrawal symptoms may be subject to recall bias (Hughes, 2007). For example, smokers are more likely to remember and report quit attempts that occurred more recently compared to attempts that occurred further in the past (Borland et al., 2012). Longitudinal data may reduce recall bias compared to cross-sectional data due to a shorter recall period required (Elliot et al., 2008; Morris et al., 2006); however, it must be noted that, even with the longitudinal data used in this study, participants were asked to report on withdrawal symptoms that may have occurred up to 12 months before the interview. Fourth, data were limited to the information collected at the two assessments. There is a lack of information about number of quit attempts, the timing of changes in smoking, reasons for quitting (including gender-specific reasons for quitting such as pregnancy and quitting due to environments where smoking is not allowed such as hospitalization or incarceration), and the context of quitting or relapse at time points between the two assessments. While cravings are an important part of withdrawal (Piper, 2015), they were not assessed by the AUDADIS-IV and therefore could not be examined as part of the analyses. Future research should examine gender differences in the relationship between withdrawal and abstinence in more detail including cravings, the impact of pharmacological and behavioral treatments on outcomes by gender, and the association of withdrawal and quitting over shorter periods of time. Further, while the analyses were adjusted for mood disorders, premenstrual dysphoric disorder (PMDD) was not assessed by the AUDADIS-IV. Withdrawal symptoms overlap with premenstrual symptoms (Allen et al., 2000) and changes in ovarian hormones are associated with differences in a range of smoking behaviors including withdrawal (see Weinerberger et al., 2015 for a review). Additional research is needed to understand the role of PMDD in the relationship between withdrawal symptoms and smoking cessation for women.

Further, it is not known whether the respondents who reduced their smoking were doing so with the intention of quitting smoking completely at a later time, as a consequence of a quit attempt that did not achieve full abstinence, or for other reasons. Reviews and meta-analyses have shown that interventions to reduce smoking improve abstinence outcomes (Asfar et al., 2011; Begh et al., 2015; Wu et al., 2015) and have similar outcome to interventions that ask smokers to quit abruptly (Lindson-Hawley et al., 2012). While there is mixed evidence regarding whether smoking reduction decreases the harmful health consequences of smoking such as cancer and respiratory disease (Begh et al., 2015; Gerber et al., 2012; USDHHS, 2014), quitting smoking has clear benefits for reducing mortality and morbidity (Carter et al., 2015; Thun et al., 2013; USDHHS, 2014).

Withdrawal symptoms are a critical factor in the maintenance of smoking behavior (Piper, 2015). The current results suggest that withdrawal symptoms, withdrawal-related distress, and withdrawal-related discomfort are all associated with decreased odds of reducing and quitting smoking for men and women. Men and women in this study displayed similarities regarding the relationship between withdrawal and smoking abstinence after three years; however, there were also a number of areas in which men and women differed. These differences include the report-

ing of more withdrawal symptoms by women and the stronger relationship between withdrawal symptom number and smoking reduction among men. While it is important to address withdrawal in both men and women who want to quit smoking, there may be additional benefits to understanding which aspects of withdrawal differ for men and women so that strategies can be developed that provide the best quit outcomes for men and women.

Role of funding source

Funding for this study was provided by the National Institutes of Health (National Institute on Drug Abuse) grant R01-DA20892 (to Dr. Goodwin). The NIH / NIDA had no further role in study design; in the collection, analysis and interpretation of data; in the writing of the report; or in the decision to submit the paper for publication.

Contributors

Dr. Weinerberger conceived the study and wrote the first draft of the manuscript. Mr. Platt undertook the statistical analyses. Dr. Shuter and Goodwin contributed to the writing of the manuscript. All authors contributed to and approved the final manuscript.

Conflicts of interest

Dr. Weinerberger, Mr. Platt, Dr. Shuter, and Dr. Goodwin have no conflicts of interest to report.

Acknowledgments

None.

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