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Gender differences in cannabis use disorder treatment: Change readiness and taking steps predict worse cannabis outcomes for women



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HIGHLIGHTS

- We examined gender differences in cannabis outcomes from a clinical trial.
- Women high in taking steps were less likely to achieve abstinence during treatment.
- · Greater readiness to change predicted higher cannabinoid levels in women.
- What motivates change behavior may vary by gender.
- Attention to gender differences in cannabis use treatment is needed.

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ABSTRACT

Introduction: Gender differences in cannabis use and cannabis use disorder have been established. Regarding treatment, some evidence suggests that women are less responsive, though the mechanisms are not well understood. Motivation to change and self-efficacy are associated with better outcomes overall, and may help explain gender differences in cannabis use outcomes.

Methods: A secondary data analysis of a double-blind placebo controlled trial of buspirone treatment for cannabis dependence (N = 175) was conducted. Self-report assessments of motivation to change, self-efficacy, and other clinical correlates were completed at baseline, and cannabis use was measured throughout the study.

Results: There was a significant interaction between gender and taking steps on abstinence. Counter to hypothesis, higher taking steps reduced likelihood of achieving abstinence among women; there was no association among men. Subsequently, taking steps was associated with self-efficacy and quantity of use among men, and cannabis related problems among women. There was a significant interaction between gender and readiness to change on creatinine adjusted cannabinoid levels. Change readiness was positively associated with cannabinoid levels among women, but not men.

Conclusions: Motivation to change and initiation of change behavior predict worse cannabis outcomes in women. Men and women differ in what motivates change behavior. Social desirability, neurobiology, and treatment type may impact these effects. Gender differences in cannabis use and treatment responsiveness must be considered in future studies.

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1. Introduction

Gender differences in cannabis use and cannabis use disorder (CUD) have been found in both preclinical and clinical studies. Men initiate cannabis use earlier and are more likely to develop CUD than women (Khan et al., 2013; Wagner & Anthony, 2007). However, women demonstrate a "telescoping effect" progressing from first use to

disorder and treatment entry faster than men (Hernandez-Avila, Rounsaville, & Kranzler, 2004; Khan et al., 2013). Likewise, research suggests greater abuse-related effects among women (Cooper & Haney, 2014) and greater physiological withdrawal symptoms (Copersino et al., 2010) compared to men. In preclinical studies, female rodents show greater sensitivity to anxiogenic, reinforcing, and sedative effects of cannabinoids than males (Fattore, Fadda, & Fratta, 2009; Fattore et al., 2007; Harte-Hargrove & Dow-Edwards, 2012). Neuroimaging studies show activation of amygdalar/hippocampal regions in women, but not men, in response to subliminal marijuana cues, as well as an association between craving and activation in executive control related brain regions (Wetherill, Jagannathan, Hager, Childress, & Franklin, 2015).

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Despite evidence of gender differences in behavioral and neural correlates of cannabis use, few studies have examined gender differences in CUD treatment.

Motivation has been defined as "personal considerations, commitments, reasons, and intentions that move individuals to perform certain behaviors" (DiClemente, Schlundt, & Gemmell, 2004). Interventions that enhance motivation are considered essential to effective substance abuse treatment outcomes (Miller & Rollnick, 2013). Motivation to change has been associated with treatment-seeking behaviors, treatment attendance, and positive clinical outcomes across settings (Amaro et al., 2010; Capone & Wood, 2009; DiClemente et al., 2004; Simpson, Joe, Rowan-Szal, & Greener, 1995). However, few studies examine gender differences in motivation to change and clinical outcomes. One study interviewed 511 adults in treatment for drug and alcohol dependence and found that among women, but not men, treatment readiness was associated with abstinence at 1-year follow-up (Hser, Huang, Teruya, & Anglin, 2003). Motivation to change is a potentially critical factor to understanding gender differences in CUD treatment.

Self-efficacy refers to the strength of an individual's belief that they will successfully engage in a specific planned behavior (i.e. meet their stated goals). In the context of addiction, self-efficacy is one of the best predictors of using behavior. Higher self-efficacy is associated with significantly better treatment outcomes (Greenfield et al., 2000; Litt, Kadden, & Petry, 2013), and has recently been identified as an essential mechanism of therapeutic change (Forcehimes & Tonigan, 2008; Kadden & Litt, 2011). Yet, there is a dearth of evidence examining how gender impacts self-efficacy and substance abuse, and existing evidence is inconsistent. Among 100 inpatient alcohol-dependent individuals, self-efficacy was associated with fewer days abstinent during a 12month follow-up period for men, but not women (Greenfield et al., 2000). However, a recent study combining data from three clinical trials, examined mediators of self-efficacy and found that coping skills partially mediated the association between self-efficacy and cannabis outcomes, but gender did not moderate this mediation relationship as expected (Litt & Kadden, 2015). While self-efficacy seems to play a key role in substance use treatment outcomes, it remains unclear how gender impacts this effect.

In a randomized placebo-controlled trial, McRae-Clark et al. (2015), investigated buspirone treatment for CUD in treatment seeking adults in conjunction with brief motivational enhancement therapy (MET). While there was no main effect of buspirone, there was a gender by treatment interaction; women randomized to buspirone had significantly worse outcomes than men randomized to buspirone. Motivational models of behavior change may provide a framework for understanding this finding. Specifically, the transtheoretical model (TTM; Prochaska & DiClemente, 1984, 1992), which consists of five stages of behavior change: precontemplation, contemplation, preparation, action, and maintenance. Progression through the five stages reflects increasing motivation to change, which has been shown to predict better treatment outcomes (Norcross, Krebs, & Prochaska, 2011). A critical factor in actualizing a person's motivation to change is the belief that they can perform a specific behavior in a specific situation, or *self-efficacy*. Self-efficacy is consistently associated with positive substance use outcomes (Kadden & Litt, 2011) and likewise is important to consider alongside motivation to change.

Given the potential for motivation to change and self-efficacy to impact substance use outcomes, the purpose of this study is to examine the role these factors may play in explaining the gender differences found in McRae-Clark et al. (2015). We hypothesized that gender would moderate the effect of treatment motivation and self-efficacy on cannabis outcomes, such that women who report higher treatment motivation and self-efficacy at baseline would be more likely to achieve abstinence and have lower cannabinoid levels during treatment than women low in motivation and self-efficacy.

2. Materials and methods

2.1. Participants

The current study is a secondary analysis of a double-blind, placebocontrolled trial of buspirone in cannabis-dependent individuals conducted between November 2009 to March 2014. Eligible participants met DSM-IV criteria for current cannabis dependence and were between 18 and 65 years of age. Exclusion criteria included current dependence on another substance (except caffeine or nicotine), current major depression, current suicidal risk, current treatment with psychotropic medication (except stimulants and non-benzodiazepine sedative/ hypnotics), history of psychotic, bipolar, or eating disorder, major medical illness or disease, significant cognitive impairment, hypersensitivity to buspirone or other product component, current consumption of any substance that inhibits or induces CYP3A4, and pregnancy, lactation, or inadequate birth control.

2.2. Procedures

Stratified randomization by gender and amount of daily cannabis use (one joint and above or less than one joint) determined treatment assignment. Both groups received three adjunctive Motivational Enhancement Therapy sessions during the first four weeks of the trial. Personalized Feedback Reports (PFRs) gleaned from the initial worksheets (Steinberg, Roffman, Carroll, et al., 2005) were used to guide MET sessions and focused on participants' frequency of use, reasons for quitting, marijuana-related problems, behavioral contingencies of use, and short- and long-term goals. Escalating scale contingency management (CM) was used for session attendance, starting at \$5 and increasing by \$5 each week beginning at week 1; compensation was reset to \$5 in the event of a missed session. For full original study procedures please see McRae-Clark et al. (2015).

2.3. Assessments

The Stages of Change Readiness and Treatment Eagerness Scale (SOCRATES; Miller & Tonigan, 1996) was used to assess motivation to change. The SOCRATES assesses an individual's level of motivation or readiness to change, and is comprised of three subscales: Recognition, Ambivalence, and Taking Steps. Recognition reflects the level of awareness that a problematic use pattern exists, ambivalence reflects the simultaneous desire to stop versus continue using, and *taking steps* reflects initiation of behavior change. Higher scores reflect greater recognition, less ambivalence, and taking more steps towards change. The SOCRATES is widely used in substance abuse research, including with cannabis using populations (Serafini, Shipley, & Stewart, 2016; Simons, Clarke, Simons, & Spelman, 2016), and has demonstrated reliability and validity across settings (Campbell, 1997; Long & Hollin, 2009). Self-efficacy to resist marijuana was assessed using the Selfefficacy Questionnaire (SEQ; Stephens, Wertz, & Roffman, 1993), which consists of a total self-efficacy score and has also been validated with marijuana abusing populations (Stephens, Wertz, & Roffman, 1995). Additional assessments used to examine clinical characteristics included the Marijuana Ladder (Slavet et al., 2006), a single item analog measure of readiness to change marijuana use; the Inventory of Drug Taking Situations (IDTS; Turner, Annis, & Sklar, 1997), a self-report measure that provides a profile of situations in which a person has used a drug in the past year; the Marijuana Effect Expectancy Questionnaire (MEEQ; Schafer & Brown, 1991), a measure assessing the expected effect of marijuana use; and the Marijuana Problems Scale (MJPS; Stephens, Roffman, & Simpson, 1994), which assesses the negative consequences of marijuana use. Pre-treatment cannabis use was assessed with the Time-line Follow-back (TLFB; Sobell & Sobell, 1992), a widely used measure capturing frequency and quantity of substance use for the preceding 30 days.

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