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Interaction between Pre-treatment Drug Use and Heterogeneity of Psychiatric Diagnosis Predicts Outcomes in Outpatients with Co-Occurring Disorders

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Abstract

We examined whether the interaction of baseline stimulant use, assessed by urine drug tests, and type of serious mental illness (SMI) diagnosis predicted stimulant use in a trial of contingency management (CM). The interaction between baseline stimulant use and SMI diagnoses was significant in the overall sample (p=0.002) when controlling for the main effects of treatment condition, baseline stimulant use, and SMI diagnosis. Similar results were also found within the CM sample. Individuals with bipolar disorder were more or less likely, depending on their baseline stimulant-drug test results, to use stimulants during treatment compared to those with other SMI diagnoses.

Keywords

stimulant use; contingency management; serious mental illness

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1. Introduction

Approximately 1.5 million Americans report stimulant drug use, including cocaine, amphetamine, and methamphetamine yearly (Substance Abuse and Mental Health Services Administration, 2015). Twenty-five percent of cocaine users have a co-occurring serious mental illness (SMI) such as major depression, bipolar, or schizophrenia-spectrum disorders (Falck, Wang, Siegal, Carlson, 2004). These individuals are at an increased risk for emergency room visits (Nicosia, Pacula, Kilmer, Lundberg, Chiesa, 2009) and unstable housing (US Department of Housing and Urban Development, 2010).

Contingency management (CM) is an intervention that provides tangible reinforcers when individuals demonstrate drug abstinence, and is an effective treatment for stimulant drug use (Dutra et al., 2008). CM is associated with reduced substance use in adults with SMI (McDonell et al., 2013; Weiss et al., 2007). We found that outpatients with co-occurring stimulant use disorders and SMI receiving CM were two and a half times more likely to submit stimulant-negative results during treatment relative to controls (McDonell et al., 2013). Several other studies have found that CM is an effective treatment for stimulant use in those with psychiatric problems (Gonzalez, Feingold, Oliveto, Gonsai, Kosten, 2003; Lester et al., 2007; McNamara, Schumacher, Milby, Wallace, Usdan, 2001; Milby et al., 2000; Shaner et al., 1997).

Less is known about the predictors of treatment outcomes in those with co-occurring disorders receiving CM. We previously found that a baseline stimulant-positive urine sample and higher psychological symptoms, not SMI diagnosis, were associated with a shorter duration of abstinence during CM (Angelo et al., 2013). In non-SMI populations, stimulant-positive pre-treatment drug test is a robust predictor of CM outcomes (Petry, Barry, Alessi, Rounsaville, Carroll, 2012; McDonell et al., 2017). The relationship between psychiatric symptoms or diagnosis and CM treatment response has been less consistent. For instance, one study found that in CM, psychiatric symptoms were not associated with longest duration of abstinence (Weinstock, Alessi, Petry, 2007). Although not a CM study, Compton and colleagues (2003) found that diagnosis of major depression predicted poor treatment outcomes for alcohol use compared to other psychiatric disorders. Because no previous study had investigated the interaction of pre-treatment drug use and SMI diagnosis, we analyzed data from a CM trial (N=176) targeting stimulant use to determine if the interaction between baseline stimulant use and type of SMI predicted stimulant drug abstinence.

2. Methods

2.1. Participants

Participants were 176 adults with SMI and stimulant dependence in a randomized trial of CM for stimulant abstinence. Participants received treatment-as-usual (TAU) and were randomized to 12-weeks of CM for stimulant abstinence (n=91) or reinforcers for providing urine samples (non-contingent control [NC], n=85) (McDonell et al., 2013). SMI diagnoses were major depression (CM n=26, 29%; NC n=21, 25%), bipolar (CM n=30, 33%; NC n=30, 35%), and schizophrenia-spectrum disorders (CM n=35, 39%; NC n=34, 40%).

Written informed consent was obtained and the study was approved by the university Institutional Review Board.

2.2. Measures

Researchers administered the *Mini International Neuropsychiatric Interview (MINI)* major depressive episode, (hypo) manic episode, psychotic disorders, and drug and alcohol dependence and abuse diagnostic sections (Sheehan et al., 1998). Urine samples were tested for stimulant drugs using Integrated E-Z Split Key® cups (amphetamines=1,000 ng/mL, methamphetamines=1,000 ng/mL, and benzoylecgonine [cocaine]=300 ng/mL (Innovacon, Inc, San Diego, CA.), at baseline and three times per week during treatment.

2.3. Treatment Conditions

TAU included mental health (e.g., medication and case management), addiction (e.g., counseling), and vocational services. CM participants drew for tokens that represented different prizes (50% read "good job" valued at $0, 41.8% read "small" valued at $1, 0.8% read "large" valued at $20, 0.2% read "jumbo" valued at $80) for each stimulant-negative sample submitted. Participants earned prize draws for stimulant-negative urine samples. An additional draw was added for each week of continued stimulant abstinence, and a bonus draw was provided for abstinence from other substances. No prizes were given for stimulant-positive or missing samples. The NC group received TAU and draws for each urine sample submitted even if results indicated stimulant use. The number of prize draws given to NC participants was equal to the average number of prize draws received by the CM participants in the previous week.

2.4. Statistical Analysis

Investigators descriptively analyzed the interaction of SMI diagnosis (major depression, bipolar, schizophrenia-spectrum disorders) and baseline stimulant use in both treatment conditions (CM, NC). Based on these findings and consistent with the parent study and other CM trials, we used generalized estimating equations ([GEE]; McPherson, Barbosa-Leiker, McDonell, Howell, Roll, 2013; Twisk, 2004) to determine whether baseline stimulant use; SMI diagnosis; treatment condition; and the interaction of baseline stimulant use and SMI diagnosis were associated with the stimulant-positive results (1=yes, 0=no) during treatment (up to 36 tests). Participants were excluded from the analyses if they had less than two measurements. Missing data was 1997/3276 in the CM group and 1525/3060 in the NC condition. Two separate GEE analyses were conducted: the overall sample controlling for treatment conditions and another was within the CM condition only (*n*=91). All possible pairwise comparison tests were conducted on the interaction term using the Bonferroni correction to avoid an inflated alpha rate. Results were reported as odds ratios (OR). Significance was $p<.05$ with 95% confidence intervals (CI). Analyses were conducted in SPSS 24.0 and post-hoc analyses performed in Stata 12.0 (StataCorp, College Station, TX).

3. Results

Figure 1 displays results of descriptive analyses of the interaction of SMI diagnosis and baseline stimulant use across the treatment period. After controlling for treatment conditions

(χ^2 (1) =11.83, p=0.001), baseline stimulant use (χ^2 (1) =58.84, p=0.001), and SMI diagnosis (χ^2 (2) =0.86, p=0.65) in the randomized sample (N=176), the interaction of baseline stimulant use and SMI diagnosis (χ^2 (2) =12.52, p=0.002) was associated with stimulant use during treatment.

Post-hoc analyses revealed that among participants with stimulant-negative results at baseline, those with schizophrenia-spectrum disorders were 3.40 times (95% CI=1.33–8.70) more likely than those with bipolar disorder to submit stimulant-positive samples during treatment. Among those with stimulant-positive results at baseline, participants diagnosed with bipolar disorder were 2.24 times (95% CI=1.06–4.75) more likely than those with major depression to submit stimulant-positive samples. Compared to participants who were stimulant-negative at baseline, participants who were stimulant-positive at baseline were more likely to submit stimulant-positive treatment samples for each SMI diagnoses; major depression (OR=5.12, 95% CI: 2.23–11.79), bipolar (OR=26.54, 95% CI: 10.38–81.45), schizophrenia-spectrum (OR=4.01, 95% CI: 1.96–8.18) disorders.

Within the CM condition, after controlling for baseline stimulant use (χ^2 (1) =21.99, p=0.001), and SMI diagnosis (χ^2 (2) =0.25, p=0.88), the interaction of baseline stimulant use and SMI diagnosis (χ^2 (2) =12.09, p=0.002) was a significant predictor of treatment outcomes. In post-hoc analyses, individuals with schizophrenia-spectrum disorders with stimulant-negative results at baseline were 11.18 times (95% CI=1.53–81.26) more likely to submit stimulant-positive samples during treatment compared to participants with bipolar disorder. Among those with stimulant-positive results at baseline, individuals with schizophrenia-spectrum disorders were less likely (OR=0.20, 95% CI=0.06–0.63) than participants with bipolar disorder to submit stimulant-positive samples. Participants who were stimulant-positive at baseline were more likely than those who were not to submit stimulant-positive samples within SMI diagnoses of major depression (OR=4.13, 95% CI: 0.98–17.36) and bipolar disorder (OR=77.62, 95% CI: 10.30–584.93).

4. Discussion

Individuals with bipolar disorder who used stimulants at baseline had the poorest treatment outcomes, relative to those with other SMI diagnoses, while those with bipolar disorder who had not used stimulants at baseline responded most favorably to treatment (Figure 1). These results identify subgroups that may not respond to standard co-occurring disorder treatment and more specifically, CM for stimulant abstinence.

In a separate trial of CM targeting alcohol use in adults with SMI, we found that among those with major depression the likelihood of submitting alcohol-negative urine samples was dependent on pre-treatment drinking levels (Oluwoye et al., 2017). Differences in the results of these two studies are possibly an artifact of the different types of substance use; however, both suggest that the assessment of drug use severity and SMI diagnosis are important when predicting CM efficacy.

Limitations include participant recruitment from one agency, possible diagnostic errors, and missing data due to attrition. The recruitment site was similar to other community mental

health centers, assurances (i.e., trained research personnel validating diagnoses) preventing diagnostic errors were made, and our statistical methodology (i.e., GEE) accounted for missing data by using all available pairs in analyses. We did not examine psychological distress, contrary to findings in our previous study (Angelo et al., 2013) which may explain some variance in outcomes. However, we chose to use SMI diagnosis instead of psychological distress due to diagnosis being a more clinically meaningful measure that has been found to be a significant predictor in previous studies (Compton, Cottler, Jacobs, Ben-Abdallah, Spitznagel, 2003; Weinstock, Alessi, Petry, 2007).

Findings provide initial evidence that outpatients with SMI differ in terms of their response to co-occurring stimulant disorders treatment, based on the interaction of pre-treatment stimulant use and type of SMI diagnosis. Importantly, these factors can be easily assessed upon entering treatment using urine drug tests and diagnostic interviews, providing a feasible way to predict treatment response and a potential opportunity to tailor treatment to specific subgroups of individuals with co-occurring disorders.

Acknowledgments

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Highlights

- The interaction of baseline stimulant use and type of SMI predicted stimulant use.

- Results in overall sample were replicated in the contingency management only group.

- Responses differed for those with bipolar disorder depending on baseline use.

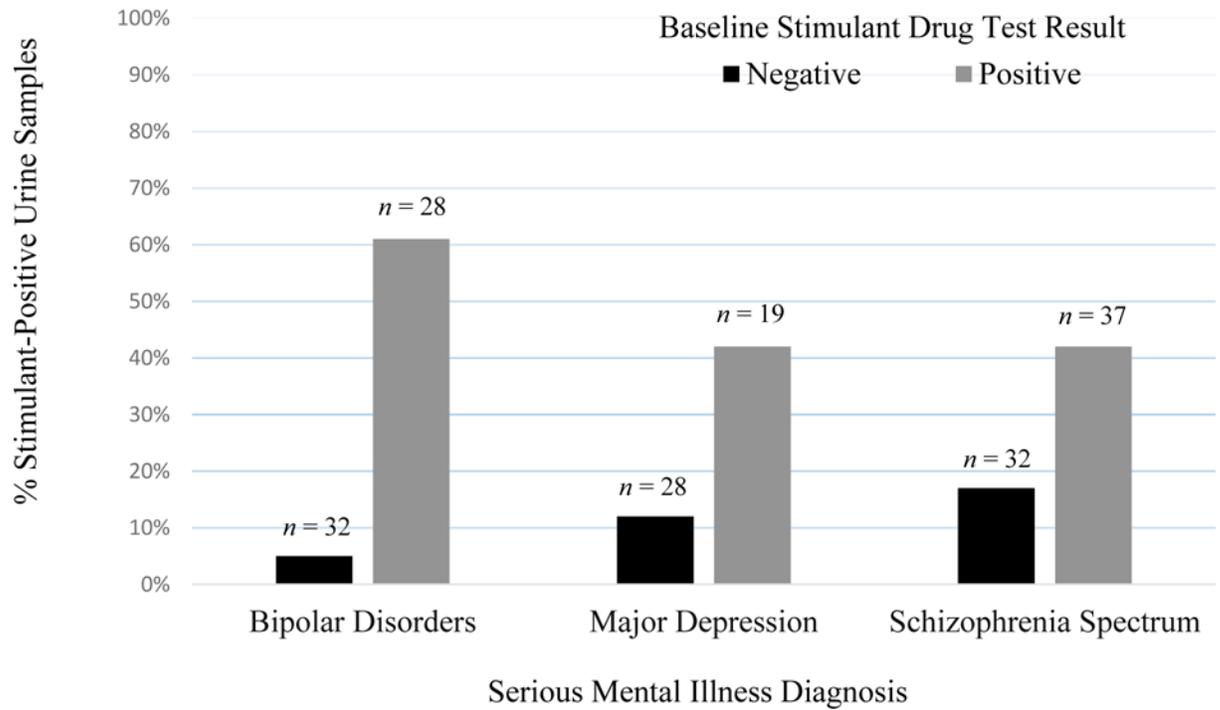- Tailored treatment among individuals with co-occurring disorders is needed.

Figure 1.
Percentage of stimulant-positive urine samples during treatment differs based on the interaction of baseline stimulant use and serious mental illness diagnoses.