

UC San Diego

UC San Diego Electronic Theses and Dissertations

Title

Explaining individual differences in treatment outcome for adults with substance dependence and major depression : mediators and moderators of change

Permalink

<https://escholarship.org/uc/item/5wx71472>

Author

Worley, Matthew J.

Publication Date

2013

Peer reviewed|Thesis/dissertation

UNIVERSITY OF CALIFORNIA, SAN DIEGO

SAN DIEGO STATE UNIVERSITY

Explaining individual differences in treatment outcome for adults with substance
dependence and major depression: Mediators and moderators of change

A dissertation submitted in partial satisfaction of the requirements for the degree Doctor
of Philosophy

in

Clinical Psychology

by

Matthew J. Worley

Committee in charge:

University of California, San Diego

Professor Sandra A. Brown, Chair

Professor Mark G. Myers

Professor Ryan S. Trim

San Diego State University

Professor Georg E. Matt

Professor Scott C. Roesch

The Dissertation of Matthew J. Worley is approved, and it is acceptable in quality and form for publication on microfilm and electronically:

Chair

University of California, San Diego

San Diego State University

2013

TABLE OF CONTENTS

Signature Page	iii
Table of Contents	iv
List of Figures	v
List of Tables	vi
Acknowledgements	vii
Vita	viii
Abstract	xvi
Introduction	1
Study 1	11
Methods	14
Results	18
Discussion	21
Study 2	31
Methods	33
Results	37
Discussion	41
Study 3	50
Methods	54
Results	60
Discussion	63
Study 4	73
Methods	77
Results	83
Discussion	87
Discussion	98
References	113

LIST OF FIGURES

Figure 1. Hypothesized relations between treatment group, 12-step variables, depression, and alcohol/drug use	30
Figure 2. Parallel-process latent growth curve mediation model	48
Figure 3. Group means of 12-step variables and drinking/drug use frequency	49
Figure 4. Percentage of time in controlled contexts and distribution of settings.....	71
Figure 5. Significant interactions between social network variables and controlled context on post-treatment drinking and drug use	72
Figure 6. Significant two-way interactions between neurocognitive impairment and proximal variables on drinking and drug use.....	96
Figure 7. Significant three-way interactions between neurocognitive impairment, 12-step affiliation, and depression on drinking	97

LIST OF TABLES

Table 1. Demographic and clinical characteristics	26
Table 2. 12-step variables, depression, and alcohol/drug use.....	27
Table 3. Results of 12-step variables predicting depression.....	28
Table 4. Mediating effects of depression on alcohol/drug use	29
Table 5. Demographic and clinical characteristics	45
Table 6. Results of unconditional latent growth curve models.....	46
Table 7. Results of conditional latent growth curve models.....	47
Table 8. Post-treatment substance use, self-efficacy, and social network variables.....	68
Table 9. Models predicting self-efficacy, social network variables, and context.....	69
Table 10. Effects of self-efficacy and social network variables on alcohol/drug use.....	70
Table 11. Descriptive statistics of substance use outcomes, proximal variables, and neurocognitive impairment	93
Table 12. Results of models predicting proximal variables from neurocognitive impairment	94
Table 13. Interactions between 12-step affiliation, depression, and neurocognitive impairment	95

ACKNOWLEDGEMENTS

I would like to thank Dr. Sandra A. Brown for her support as my research mentor in graduate school and chair of my dissertation and guidance committees. Her willingness to allow me to explore my specific interests and helpful guidance along the way has increased my enthusiasm for clinical science, and I am forever grateful.

Data utilized in this dissertation was obtained in a clinical trial funded by the Department of Veterans Affairs, Veterans Health Administration, Office of Research and Development, Clinical Sciences Research & Development Merit Review Award to Dr. Sandra A. Brown. This research was supported by National Institute on Drug Abuse fellowship grant (F31DA030861) awarded to Matthew J. Worley.

Study 1 has been accepted for publication in *Addiction*. The dissertation author was the primary author, with Drs. Susan R. Tate and Sandra A. Brown as co-authors.

Study 2 has been accepted for publication in *Substance Abuse*. The dissertation author was the primary author, with Drs. Susan R. Tate, John R. McQuaid, Eric G. Granholm, and Sandra A. Brown as co-authors.

VITA

EDUCATION

- 2008-2013 Ph.D. San Diego State University/University of California, San Diego Joint Doctoral Program in Clinical Psychology, San Diego, CA**
Concentration: Experimental Psychopathology
Dissertation: *Mediators of Outpatient Treatment for Comorbid Substance Use Disorder and Major Depression*
Advisor: Sandra A. Brown, Ph.D.
- 2009-2012 M.P.H. San Diego State University, San Diego, CA**
Concentration: Epidemiology
- 2008-2010 M.S. San Diego State University/University of California, San Diego Joint Doctoral Program in Clinical Psychology, CA**
Master of Science in Psychology
Master's thesis: *Comorbid Depression and Substance Use Disorder: Longitudinal Associations between Symptoms in a Controlled Trial*
- 2001-2005 B.A. Princeton University, Princeton, NJ**
Bachelor of Arts in Psychology

GRANTS AWARDED

1F31DA030861 – Worley (PI)

Mediators of Outpatient Treatment for Comorbid Substance Use Disorder and Major Depression

Date: 1/2011-12/2012

Funding: National Institutes of Health/National Institute on Drug Abuse

The proposed research will conduct longitudinal mediation analyses to examine mediators of substance use and depression outcomes during a randomized, controlled trial of outpatient group therapies for veterans with comorbid substance use disorder and major depression.

AWARDS AND HONORS

- 2012 Research Society on Alcoholism
 Enoch Gordis Predoctoral Award Finalist
- 2012 College of Problems on Drug Dependence
 NIDA Director's Travel Award
- 2011 Research Society on Alcoholism
 Enoch Gordis Predoctoral Award Finalist

2011	College of Problems on Drug Dependence NIDA Director's Travel Award
2010	UCLA Center for Advancing Longitudinal Drug Abuse Research Investigator Travel Award
2009-2010	Inamori Fellowship San Diego State University
2010-2012	Research Society on Alcoholism Student Merit Award
2009-2012	University of California, San Diego Student Travel Award
2009-2011	San Diego State University Student Travel Award

PROFESSIONAL PUBLICATIONS

Peer-reviewed publications

1. Swanson, A., Shoptaw, S., Heinzerling, K., **Worley, M.J.**, Sayers, W.M., & London, E.D. (in press). Up in Smoke? Behavioral and pharmacotherapy interventions for smoking cessation with youth in Los Angeles, California. *Substance Use and Misuse*.
2. **Worley, M.J.**, Tate, S.R., McQuaid, J.R., Granholm, E., & Brown, S.A. (2013). 12-step affiliation and attendance following treatment for comorbid substance dependence and depression: A latent growth curve mediation model. *Substance Abuse*, 34, 43-50.
3. **Worley, M.J.** Tate, S.R., & Brown, S.A. (2012). Mediatlional relations between 12-step meeting attendance, depression, and substance use during treatment for comorbidity. *Addiction*, 107, 532-542. doi: 10.1111/j.1360-0443.2012.03943.
4. Worley, M.J., Trim, R.S., Roesch, S.C., Tate, S.R., Mrnak-Meyer, J.S., & Brown, S.A. (2012). Comorbid depression and substance use disorder: Longitudinal associations between symptoms in a controlled trial. *Journal of Substance Abuse Treatment*, 43, 291-302.
5. Mrnak-Meyer, J., Tate, S.R., Tripp, J.C., **Worley, M.J.**, Jajodia, J., & McQuaid, J.R. (2011). Predictors of suicide-related hospitalization among U.S. veterans receiving treatment for comorbid depression and substance dependence. Who is the riskiest of the risky? *Suicide and Life Threatening Behaviors*, 41, 532-542.
6. Bekman, N.M., Goldman, M.S., **Worley, M.J.**, & Anderson, K.G. (2011). Pre-adolescent alcohol expectancies: Critical shifts and associated maturational processes. *Experimental and Clinical Psychopharmacology*, 19, 420-432.
7. Doran, N., Sanders, P.E., Bekman, N.M., **Worley, M.J.**, Monreal, T.K., McGee, E., Cummins, M.S., & Brown, S.A. (2011). Mediating influences of negative affect and risk perception on the relationship between sensation seeking and adolescent cigarette smoking. *Nicotine and Tobacco Research*, 6, 457-65.

8. **Worley, M.J.**, Trim, R.S., Tate, S.R., Hall, J.S., & Brown, S.A. (2010). Service Utilization During and After Outpatient Treatment for Comorbid Substance Use Disorder and Depression. *Journal of Substance Abuse Treatment*, 39, 124-131.
9. **Worley, M.**, Gallop, R., Connolly Gibbons, M.B., Ring-Kurtz, S., Present, J., Weiss, R. D., & Crits-Christoph, P. (2008). Additional treatment services in a cocaine treatment study: Level of services obtained and impact on outcome. *American Journal on Addictions*, 17, 209-217.
10. Crits-Christoph, P., Connolly Gibbons, M.B., Gallop, R., Ring-Kurtz, S., Barber, J.P., **Worley, M.**, Present, J., & Hearon, B. (2008). Supportive-expressive psychodynamic therapy for cocaine dependence: A closer look. *Psychoanalytic Psychology*, 25, 483-498.
11. Present, J., Crits-Christoph, P., Connolly Gibbons, M.B., Hearon, B., Ring-Kurtz, S., **Worley, M.**, & Gallop, R. (2008). Sudden gains in the treatment of generalized anxiety disorder. *Journal of Clinical Psychology*, 64, 119-126.
12. Forman, R., Crits-Christoph, P., Kaynak, O., **Worley, M.**, Hantula, D.A., Kulaga, A., Rotrosen, J., Chu, M., Gallop, R., Potter, J., Muchowski, P., Brower, K., Strobbe, S., Magruder, K., Chellis, A.H., Clodfelter, T., & Cawley, M. (2007). A feasibility study of a web based performance improvement system for substance abuse treatment providers. *Journal of Substance Abuse Treatment*, 33, 363-371.
13. Crits-Christoph, P., Connolly Gibbons, M.B., Barber, J.P., Hu, B., Hearon, B., **Worley, M.**, & Gallop, R. (2007). Predictors of sustained abstinence during psychosocial treatments for cocaine dependence. *Psychotherapy Research*, 17, 240-252.

Book Chapters

1. Shoptaw, S., Rawson, R.A., **Worley, M.**, Lefkowitz, S., & Roll, J.M. (2009). Psychosocial and behavioral treatment of methamphetamine dependence. In J.M. Roll, R. A. Rawson, W. Ling, & S. Shoptaw (Eds.), *Methamphetamine Addiction: From Basic Science to Treatment* (pp. 185-201). New York, NY: Guilford Press.

Manuscripts in Preparation

1. **Worley, M. J.**, Tate, S.R., Granholm, E.G., & Brown, S.A. *Neurocognitive impairment interacts with 12-step affiliation and depression to predict future drinking in depressed substance users*. Manuscript submitted for publication.
2. **Worley, M. J.**, Tate, S.R., & Brown, S.A. *Self-efficacy, social networks, and the moderating effects of context following treatment for co-occurring substance dependence and depression*. Manuscript submitted for publication.

3. Brown, S.A., **Worley, M. J.**, Stallings, M.C., Hopfer, C.J., & Hewitt, J.K. *Conjoint development of substance use and antisocial behaviors from adolescence into young adulthood*. Manuscript in preparation.
4. **Worley, M. J.**, Brown, S.A., Stallings, M.C., Hopfer, C.J., & Hewitt, J.K. *Transitions in substance use, abuse, and dependence status over time in conduct-disordered adolescents*. Manuscript in preparation.

PROFESSIONAL PRESENTATIONS

1. **Worley, M.J.**, Brown, S.A., Stallings, M.C., Hopfer, C.J., & Hewitt, J.K. (2012). Transitions in substance use, abuse, and dependence status over time in conduct-disordered adolescents. Oral presentation at the annual meeting of the College of Problems on Drug Dependence. La Quinta, CA.
2. **Worley, M. J.**, Tate, S.R., Tapert, S.F., Granholm, E.G., & Brown, S.A.. (2012). Neurocognitive impairment interacts with 12-step affiliation and depression to predict future drinking in depressed, substance-dependent veterans. Oral presentation at the 35th Annual Scientific Meeting of the Research Society on Alcoholism. San Francisco, CA.
3. **Worley, M.J.**, Tate, S.R., Mrnak-Meyer, J., Tonigan, J.S., & Brown, S.A. (2011). Mediation relations between 12-step attendance, depression, and alcohol use during treatment for comorbidity. Oral presentation at the 34th Annual Scientific Meeting of the Research Society on Alcoholism. Atlanta, GA.
4. **Worley, M.J.**, Tate, S.R., Mrnak-Meyer, J., Tonigan, J.S., McQuaid, J.R., & Brown, S.A. (2011). Mediation relations between 12-step attendance, depression, and alcohol use during treatment for comorbidity. Oral presentation at the 2011 Mechanisms of Behavior Change pre-conference Satellite Meeting of the Research Society on Alcoholism. Atlanta, GA.
5. **Worley, M.J.**, Brown, S.A., Stallings, M.C., Hopfer, C.J., & Hewitt, J.K. (2011). Conjoint development of antisocial behaviors and marijuana use from adolescence into young adulthood. Poster session presented at the annual meeting of the College of Problems on Drug Dependence. Hollywood, Fl.
6. Wilkins, K.C., Tomlinson, K., Ramo, D.E., **Worley, M.J.**, & Brown, S.A. (2011). Extending long term outcomes: Comparing adolescents with alcohol use disorders and community adolescents 20 years following treatment. Oral presentation at the 34th Annual Scientific Meeting of the Research Society on Alcoholism. Atlanta, GA.
7. Wilkins, K.C., **Worley, M.J.**, Tomlinson, K., Ramo, D.E., Khoddam, R., & Brown, S.A. (2011). The long term impact of psychiatric comorbidity on adolescent

- alcohol/drug treatment outcomes. Oral presentation at the 34th Annual Scientific Meeting of the Research Society on Alcoholism. Atlanta, GA.
8. **Worley, M. J.,** Bekman, N.M., Doran, N., Monreal, T., Anderson, K.G., & Brown, S. A. (2010, November). *Mediators of the relationship between sensation seeking and marijuana use in adolescence*. Poster session presented at the annual meeting of the Association for Behavioral and Cognitive Therapies. San Francisco, CA.
 9. **Worley, M. J.,** Tate, S. R., Trim, R. S., Glasner-Edwards, S. & Brown, S. A. (2010). Integrated treatment versus 12-step facilitation for depressed substance users. Oral presentation at the 118th annual convention of the American Psychological Association. San Diego, CA.
 10. **Worley, M.J.,** Trim, R.S., Roesch, & Brown, S.A. (2010). *Longitudinal associations between depression and substance use in a comorbid treatment sample*. Poster session presented at the 3rd bi-annual conference of the UCLA Center for Advancing Longitudinal Drug Abuse Research. Marina del Rey, CA.
 11. **Worley, M.J.,** Trim, R.S., Roesch, & Brown, S.A. (2010). *Greater alcohol and substance use is related to time-specific elevations from growth curves of depression*. Poster session presented at the 33rd Annual Scientific Meeting of the Research Society on Alcoholism. San Antonio, TX.
 12. **Worley, M. J.,** Hanson, K.L., Winward, J., Tapert, S.F., & Brown, S.A. (2010). *Dimensional modeling of externalizing behavior and its association with neurocognition in adolescence*. Poster session presented at the annual meeting of the College of Problems on Drug Dependence. Scottsdale, AZ.
 13. **Worley, M. J.,** Cummins, K.C., Trim, R. S., Tate, S. R., Hall, J. E., & Brown, S. A. (2009). *Predicting ancillary service utilization with trajectories of substance use and depression*. Poster session presented at the annual meeting of the Association for Behavioral and Cognitive Therapies. New York, NY.
 14. **Worley, M. J.,** Trim, R. S., Tate, S. R., Hall, J. E., & Brown, S. A. (2009). *Evaluating 18-month service utilization among veterans with comorbid alcohol/drug dependence and depression*. Poster session presented at 32nd Annual Scientific Meeting of the Research Society on Alcoholism. San Diego, CA.
 15. **Worley, M.,** Crits-Christoph, P., Connolly-Gibbons, M.B., Ring-Kurtz, S., Gallop, R., Present, J., & Hearon, B. (2007). *The impact of non-protocol treatment services on the outcome of psychosocial therapy for cocaine dependence*. Poster session presented at the annual meeting of the Society for Psychotherapy Research, Madison, WI.

16. Present, J., Crits-Christoph, P., Connolly-Gibbons, M.B., Gallop, R., Ring-Kurtz, S., Hearon, B., **Worley, M.** (2007). *Predictors of outcome of supportive-expressive therapy for generalized anxiety disorder*. Paper session presented at the annual meeting of the Society for Psychotherapy Research, Madison, WI.
17. Crits-Christoph, P., Connolly-Gibbons, M.B., Ring-Kurtz, S., Gallop, R., **Worley, M.**, Present, J., & Hearon, B. (2007). *Changes in quality of life over the course of psychotherapy*. Paper session presented at the annual meeting of the Society for Psychotherapy Research, Madison, WI.
18. Connolly-Gibbons, M.B., Crits-Christoph, P., Rothbard, A., Farris, K., Hearon, B., Ring-Kurtz, S., Present, J., & **Worley, M.** (2007). *Changes in psychotherapy utilization in the community mental health system*. Poster session presented at the annual meeting of the Society for Psychotherapy Research, Madison, WI.
19. McClure, B., Kulaga, A., Rotrosen, J., Crits-Christoph, P., Ring-Kurtz, S., **Worley, M.**, & Forman, R. (2007). *A randomized, controlled, multi-site study of the effect of patient feedback on rates of attendance and abstinence in outpatient substance abuse treatment programs – An interim progress report*. Poster session presented at the annual meeting for the College on Problems of Drug Dependence, Quebec City, QC.
20. **Worley, M.**, Forman, R., Crits-Christoph, P., & Hearon, B. (2006). *Patient feedback: A preliminary study of a performance improvement system for substance abuse treatment providers*. Paper session presented at the annual meeting of the North American Chapter of the Society for Psychotherapy Research, Burr Oak, OH.
21. Hearon, B., Gibbons, M.B., Crits-Christoph, P., & **Worley, M.** (2006). *Predictors of self-understanding across dynamic and cognitive psychotherapies*. Paper session presented at the meeting of the North American Chapter of the Society for Psychotherapy Research, Burr Oak, OH.
22. Gibbons, M.B., Crits-Christoph, P., Hearon, B., & **Worley, M.** (2006). *Supportive-expressive psychotherapy versus cognitive therapy for panic disorder*. Paper session presented at the meeting of the North American Chapter of the Society for Psychotherapy Research, Burr Oak, OH.
23. Crits-Christoph, P., Newberg, A., Gibbons, M.B., **Worley, M.**, & Hearon, B. (2006). *Neurobiological changes following treatment of cocaine dependence*. Paper session presented at the meeting of the North American Chapter of the Society for Psychotherapy Research, Burr Oak, OH.
24. Kulaga, A., Forman, R., Rotrosen, J., Crits-Christoph, P., & **Worley, M.** (2006). *Patient feedback: A quality improvement study in outpatient settings*. Poster session presented at the meeting on Critical Issues in eHealth Research, Bethesda, MD.

RESEARCH EXPERIENCE

- 2008-2012 University of California, San Diego**
Department of Psychiatry
Graduate Research Assistant
Supervisor: Sandra A. Brown, Ph.D.
- 2007-2008 University of California, Los Angeles, Los Angeles, CA**
Department of Family Medicine
Medications Development Unit for Stimulant Abuse
Research Assistant
Supervisors: Steven Shoptaw, Ph.D.
- 2005-2007 University of Pennsylvania, Philadelphia, PA**
Department of Psychiatry
Center for Psychotherapy Research
Research Assistant
Supervisor: Paul Crits-Christoph, Ph.D., and Sarah Ring-Kurtz, M.A.

CLINICAL EXPERIENCE

- 2011-2012 Operation Enduring Freedom/Operation Iraqi Freedom (OEF/OIF)**
Clinic, VA San Diego Healthcare System
Psychology Trainee
Supervisors: Sonya Norman, Ph.D., Martha Diaz, Ph.D., & Abigail Goldsmith, Ph.D.
- 2010-2011 Alcohol and Drug Treatment Program, VA San Diego Healthcare System**
Psychology Trainee
Supervisors: Tamara Wall, Ph.D, Shoshana Shea, Ph.D., & Abigail Goldsmith, Ph.D.
- 2010-2011 Substance Abuse & Mental Illness Program, VA San Diego Healthcare System**
Psychology Trainee
Supervisors: Susan Tate, Ph.D, & Ryan Trim, Ph.D.
- 2008-2009 San Diego State University Psychology Clinic**
Psychology Trainee
Supervisors: Nader Amir, Ph.D., & Brenda Johnson, Ph.D.

JOURNAL REVIEWER

Journal of Substance Abuse Treatment, invited reviewer

PROFESSIONAL ACTIVITIES

2010- current	American Psychological Association Division 50 (Society for Addiction Psychology) Student Representative to the Executive Board
2010-2011	American Psychological Association Division 50 Taskforce on Empirically-Supported Treatments Coordinator
2011	San Diego State University, University of California, San Diego Joint Doctoral Program Selection Committee Student Reviewer

PROFESSIONAL MEMBERSHIPS

2009- current	Research Society on Alcoholism Student Member
2009- current	College of Problems on Drug Dependence Student Member
2009-2011	American Psychological Association Division 50 (Society for Addiction Psychology) Student Member
2009-2011	Association for Behavioral and Cognitive Therapies Student Member

ABSTRACT OF THE DISSERTATION

Explaining individual differences in treatment outcome for adults with substance dependence and major depression: Mediators and moderators of change

by

Matthew J. Worley

Doctor of Philosophy in Clinical Psychology

University of California, San Diego, 2013
San Diego State University, 2013

Professor Sandra A. Brown, Chair

Background: Among individuals diagnosed with substance dependence, major depressive disorder (MDD) is the most common co-occurring Axis I disorder and is associated with greater treatment costs and poor treatment response. Recently revised models recognize substance use behaviors as a complex interplay of distal risk, proximal risks, intrapersonal processes, and contextual factors but few studies have examined mediators and moderators of change in this population, which would inform the development and delivery of clinical interventions.

Methods: Veterans (N = 209) meeting DSM-IV criteria for substance dependence with recent use and substance-independent MDD with current depressive symptoms received group Twelve-Step Facilitation (TSF) or Integrated Cognitive-Behavioral Therapy (ICBT). Both groups received adjunct pharmacotherapy. Measures were

assessed at baseline and at 3-month intervals during 6 months of treatment and 12 months of follow-up. Outcomes were percent days drinking and percent days using drugs.

Results: In Study 1 TSF had superior improvement in depression during treatment, which was mediated by greater Alcoholics/Narcotics Anonymous (AA/NA) meeting attendance. In both groups the effects of AA/NA attendance on future drinking were mediated through depression. In Study 2 TSF was significantly higher than ICBT on AA/NA attendance and affiliation at end-of-treatment, but during follow-up TSF had greater decreases in AA/NA attendance and affiliation, which mediated greater increases in drinking. In Study 3 greater self-efficacy and lower social network drinking/drug use predicted lower future drinking and drug use. Social network effects were moderated by context, with greater effects of social networks for veterans with less time in constrained environments. In Study 4 greater neurocognitive impairment predicted greater drinking and drug use indirectly through lower self-efficacy, lower AA/NA affiliation, and greater depressive symptoms. Furthermore, AA/NA affiliation interacted with depression and neurocognitive impairment to predict future drinking, such that the effects of 12-step affiliation were strongest for those with severe neurocognitive impairment when they were severely depressed.

Discussion: In adults receiving treatment for co-occurring substance dependence and major depression, negative affect, AA/NA attendance, self-efficacy, and social

network substance use are key proximal factors linked to drinking and drug use outcomes, and severity of neurocognitive impairment impacts treatment through indirect associations with these proximal variables.

Introduction

Prevalence and societal costs of substance use disorders

Substance use disorders (SUDs) are among the most prevalent and costly psychiatric disorders in the United States. The 12-month prevalence of alcohol use disorders among American adults was recently estimated at 8.46%, while the prevalence of drug use disorders was 2.0% (Stinson et al., 2006). Individuals with SUDs often incur greater treatment costs than patients with chronic medical conditions (Garnick, Hendricks, Comstock, & Horgan, 1997) and other behavioral health disorders (Clark, Samnaliev, & McGovern, 2009). They also have an elevated risk of negative psychosocial outcomes, including intimate-partner and non-partner violence (Chermack, Fuller, & Blow, 2000; Murray et al., 2008), incarceration (Erickson, Rosenheck, Trestman, Ford, & Desai, 2008; Slade et al., 2008), and absenteeism from work (El-Guebaly et al., 2007).

Depression is highly prevalent and problematic in SUD populations

Among individuals diagnosed with a SUD, the prevalence of other psychiatric disorders is greater than in the general population. In recent epidemiological research the prevalence of mood disorders among those with SUDs was 20.13%, compared to 8.19% for the non substance-disordered population (Grant et al., 2006). Major depressive disorder (MDD) is the most common co-occurring disorder, with a prevalence of 15.5% among individuals diagnosed with a SUD. Although many types of co-occurring conditions are associated with negative outcomes, the additional burdens associated with MDD have been especially well-characterized. Patients with SUD and MDD incur substantially greater costs in mental health, substance abuse, and medical care (Mark,

2003) and utilize high-cost emergency department and inpatient care more frequently (Curran et al., 2003; O'Toole, Pollini, Ford, & Bigelow, 2007). The annual cost of treating a patient with SUD and MDD has been estimated at \$5,318, compared to \$1,246 for those with a SUD alone (Druss & Rosenheck, 1999). In addition to these excess cost burdens, having MDD in addition to SUD is associated with a multitude of negative psychosocial outcomes, including greater risk of suicide attempts (Bolton, Pagura, Enns, Grant, & Sareen, 2010a; Glasner-Edwards et al., 2008), worse quality of life (Saatcioglu, Yapici, & Cakmak, 2008), and higher rates of social problems and work disability (Olfson et al., 1997), (Wilk, West, Rae, & Regier, 2006b). Pre-treatment levels of problem severity across multiple domains are often worse for patients with SUD and MDD (Leventhal, Mooney, DeLaune, & Schmitz, 2006).

Depression negatively impacts substance treatment outcomes

Perhaps the most important clinical characteristic of adults with SUD and MDD is evidence that they typically have poorer outcomes from treatment for substance use. In naturalistic studies of inpatient alcohol treatment, having MDD at baseline predicted earlier relapse (Greenfield et al., 1998) and greater post-treatment depressive symptoms were associated with a greater risk of relapse (Curran, Flynn, Kirchner, & Booth, 2000). In Project MATCH (Matching Alcoholism Treatment to Client Heterogeneity) greater depressive symptoms predicted poorer drinking outcomes (Gamble et al., 2010; Ilgen & Moos, 2005), and in patients with alcohol and tobacco dependence, depressive symptoms predicted non-abstinence and level of drinking at every follow-up assessment (Kodl et al., 2008). Findings are similar in studies of treatment for users of illicit drugs. Cocaine-dependent patients with MDD have exhibited poorer outcomes from cognitive-behavioral

therapy (Levin et al., 2008a). In the Methamphetamine Treatment Project, greater severity of depressive symptoms predicted poorer adherence and worse treatment outcomes, and patients with MDD had more frequent methamphetamine use and lower odds of abstinence at follow-up (Glasner-Edwards, Marinelli-Casey, Hillhouse, Ang, Mooney, & Rawson, 2009). Among adolescents in marijuana dependence treatment, MDD was associated with a greater likelihood of relapse and more total relapses (White et al., 2004). Adults with SUD and MDD may resist participation in community 12-step activities and derive less benefit from 12-step involvement (Kelly, McKellar, & Moos, 2003). Although some past studies found no relationship between depression and substance use treatment outcomes (Davidson & Blackburn, 1998), there is a growing body of evidence supporting the negative impact of depression on treatments for various substances in a variety of settings.

Optimizing treatments for co-occurring substance dependence and MDD

Historically, those with substance dependence and a co-occurring psychiatric disorder could not receive integrated treatments that simultaneously target both disorders in a single setting (Drake et al., 2001). More recently, researchers have advocated for the evaluation and implementation of integrated treatments that could be superior to treatments that target substance use alone (Zweben, 2000). However, very few well-designed studies have examined the efficacy of integrated treatment for substance dependence and MDD, with a recent meta-analysis identifying only five controlled trials comparing integrated treatment to treatment of substance use alone (Hesse, 2009). Overall, integrated treatments performed significantly better on substance use outcomes, but not on depression or retention. Although early results are promising, integrated

treatments are not fully empirically-supported, suggesting that further research examining core therapeutic processes within this patient population is needed.

Mediators of treatment outcomes

Mediators are intervening variables that statistically explain some association between an independent variable (e.g., treatment condition) and dependent variable (Baron & Kenny, 1986a; MacKinnon, 2008). Within the substance dependence treatment literature, researchers have increasingly stressed the importance of studies that seek to identify the mediators of treatment effects (Finney, 2007; Morgenstern & Longabaugh, 2000) with some noting this needs to be “a first priority” (Morgenstern & Longabaugh, 2000). Within the depression treatment literature a similar movement has occurred in parallel (Garratt, Ingram, Rand, & Sawalani, 2007; Haaga, 2007). By gaining a greater understanding of the specific processes involved in treatment, therapies can be improved and disseminated more easily into practice settings (Kazdin, 2007). However, the search for treatment-specific mediators has often been less than promising, with theoretically-dissimilar therapies often producing equivalent treatment effects or showing no differential change on theory-based mediators (Morgenstern & McKay, 2007), and some recommending a paradigm shift in substance use treatment research (Babor, 2008). However, even studies of alternative treatments with similar effects on mediators and outcomes can provide useful insight into the common mechanisms of treatments, distinct but similarly effective mechanisms, or some combination of both (Longabaugh, 2007).

Previous studies have found that coping skills (Litt, Kadden, Cooney, & Kabela, 2003; Litt, Kadden, & Stephens, 2005), self-efficacy (Finney, Noyes, Coutts, & Moos, 1998), (Crits-Christoph et al., 2003), and social support (Brown, Seraganian, Tremblay,

& Annis, 2002) were common mechanisms of both cognitive-behavioral therapies and comparison interventions, due to similar levels of these variables across treatments and similar magnitude of associations between mechanisms and outcome. While these “null difference” findings are in some ways disappointing (Morgenstern & Longabaugh, 2000), they identify therapeutic processes that generally predict positive outcomes across different treatments. In other studies self efficacy (Brown et al., 2002; Litt et al., 2005) and coping skills (Litt, Kadden, Kabela-Cormier, & Petry, 2008) were treatment-specific mediators of cognitive behavioral interventions, because greater levels or change were attained and were predictive of group superior reductions in substance use, suggesting that under certain conditions, certain treatments do elicit differential change on therapeutic process variables. Some of the more robust treatment-specific mediators have been 12-step attendance and affiliation, with greater increases in these mediators repeatedly found for treatments that explicitly encourage 12-step activities (Brown et al., 2002; Finney et al., 1998; Johnson, Finney, & Moos, 2006; Longabaugh, Wirtz, Zweben, & Stout, 1998; Moos, 2007). In addition, change in social support for abstinence has been specific mediator of outcome in treatments designed to change social networks (Litt, Kadden, Kabela-Cormier, & Petry, 2007; Litt, Kadden, Kabela-Cormier, & Petry, 2009). Mediators of substance use may also relate to other outcomes, as one study found greater 12-step meeting attendance was associated with future drinking but also with lower current depressive symptoms (Kelly, Stout, Magill, Tonigan, & Pagano, 2010). Amid the questionable efficiency in continued reliance on large-scale randomized controlled trials and scrutiny of these designs, further research in proximal variables that mediate

treatment outcomes or predict outcomes across treatment conditions has an important role in the further development of substance dependence interventions.

Limited research on mediational processes for those with co-occurring disorders

Few studies have examined mediators of outcome in patients with substance dependence and psychiatric disorders, and almost none have involved integrated treatments that simultaneously target both disorders. In naturalistic studies of community-based, dual-focus self-help groups, the effects of greater meeting attendance and 12-step affiliation on abstinence were mediated by social support, sociability, internal locus of control, and self-help processes (Laudet, Cleland, Magura, Vogel, & Knight, 2004; Magura, Knight, et al., 2003; Magura, Laudet, et al., 2003). In an observational study of residential treatment, self-efficacy and social support at baseline predicted psychological distress and substance use at follow-up in patients with substance dependence and mixed psychiatric disorders (Warren, Stein, & Grella, 2007b). In one randomized, controlled study, changes in negative mood expectancies predicted long-term alcohol use in patients receiving adjunctive CBT for depression in patients receiving relaxation training (Ramsey, Brown, Stuart, Burgess, & Miller, 2002). In a study of our sample of veterans with substance dependence and MDD, self-efficacy predicted time to relapse and frequency of substance use during treatment (Glasner-Edwards et al., 2007; Tate et al., 2008). None of these studies conducted formal statistical tests for mediation, a necessary criterion for the establishment of an intervening variable as a mechanism of change (Kazdin & Nock, 2003), along with the temporal precedence. There is initial evidence that therapeutic processes involved in substance use treatment and maintenance of

abstinence will translate to those with co-occurring MDD, but this literature is currently lacking in methodologically-sound, longitudinal investigations.

In addition to therapeutic process variables identified in general substance dependence treatment studies, level of negative affect likely plays a large role in the maintenance of substance use for individuals with substance dependence and MDD. Negative affect is frequently a precursor to substance use (Marlatt, 1996) and is dynamically-linked to alcohol and drug use following treatment (Jaffe, Shoptaw, Stein, Reback, & Rotheram-Fuller, 2007; Witkiewitz & Villarroel, 2009). These associations may be even stronger in adults with SUDs and MDD, who likely have stronger urges to “self-medicate” with substances to manage depressive symptoms. In one study comparing SUD-only patients to those with SUDs and psychiatric disorders, those with co-occurring MDD were especially likely to experience depressive symptoms prior to relapse (Tomlinson, Tate, Anderson, McCarthy, & Brown, 2006). Furthermore, changes in depression and substance use during treatment and follow-up were strongly correlated in our sample of veterans with substance dependence and MDD (Worley et al., 2012). In addition to the significance of depression severity as proximal risk factor for substance use, the magnitude of improvement in depression during treatment is a potential mechanism of change for substance use behaviors in this population. Prior research suggests the salutary effects of AA meetings on drinking may be explained, in part, by related improvements in depression (Kelly et al., 2010). Treatment processes or individual characteristics that relate to depression may be especially potent for patients with SUDs and MDD, but prior studies have not examined these effects during or following outpatient treatment for these co-occurring disorders.

Effects of neurocognitive impairment on mediational processes

Models of post-treatment relapse characterize the mediating variables discussed above as critical proximal determinants of substance use (Witkiewitz & Marlatt, 2004) but also emphasize the significance of more “distal” risk variables (e.g., family history of alcoholism). As such, investigations of mediating variables should also consider the impact of such distal risks on the therapeutic process. One relevant factor for patients with substance dependence and MDD is neurocognitive impairment. Despite a strong clinical rationale that patients with neurocognitive deficits will have poorer outcomes from psychological treatments, especially those that engage higher-order cognitive functions (Bates, Bowden, & Barry, 2002), most studies examining this hypothesis have yielded weak and inconsistent results (Alterman, Kushner, & Holahan, 1990; Teichner, Horner, Roitzsch, Herron, & Thevos, 2002; Turner, LaRowe, Horner, Herron, & Malcolm, 2009). More recently, two studies have examined more indirect effects of neurocognitive impairment: as a predictor of mediating variables, and as a moderator of their effects on substance use. Interestingly, both studies found that greater impairment was linked to lower self-efficacy during treatment, and that therapeutic effects of self-efficacy were weaker for impaired patients (Morganstern & Bates, 1999; Bates, Pawlak, Tonigan, & Buckman, 2006). These studies highlight complex interactions between variables at different levels of analysis, which are required to fully elucidate our understanding of individual differences in substance dependence treatment outcome.

Neurocognitive effects on therapeutic change mechanisms could be similar or even more pronounced in patients with co-occurring MDD. Neurocognitive features of MDD share many impairments with substance dependence, including deficits in memory

(Austin et al., 1992), processing speed (Gualtieri, Johnson, & Benedict, 2006) and executive function (Watkins & Brown, 2002). Furthermore, better neurocognitive functioning at baseline has predicted greater reductions in depression for patients with depressive symptoms and hazardous alcohol use (Hunt, Baker, Michie, & Kavanagh, 2009). This finding in particular suggests impairment is related to recovery from depressive symptoms, an important determinant of substance use for patients with substance dependence and MDD (Tomlinson et al., 2006). A prior study of our sample found better substance use outcomes for veterans with poorer cognitive functioning who received integrated CBT as compared to TSF, a result that was somewhat unexpected given the theoretically greater cognitive demands in CBT (Granholm et al., 2011). Given these prior findings, determining whether neurocognitive impairment interrupts therapeutic change mechanisms has important implications for clinical practice, but these questions have not been examined in patients with co-occurring substance dependence and MDD.

Contributions of the current studies

Compared to recently emerging literature examining mediators and moderators of outcome in substance-dependent patients, there is a paucity of research examining these factors in patients with SUDs and co-occurring psychiatric disorders, who are more costly to treat (Druss & Rosenheck, 1999), at greater risk of suicide (Glasner-Edwards et al., 2008), are more disabled (Olfson et al., 1997), and typically have poorer treatment outcomes (Greenfield et al., 1998; Levin et al., 2008a). The proposed series of studies will make significant contributions in this area of need by focusing on the largest group of substance-dependent adults with co-occurring psychiatric disorders, those with MDD.

Results will assist in delineating the specific processes involved in the reduction of both substance use and depressive symptoms over time in this prevalent, chronically disabled, and costly population. The studies will conduct examinations of mediating processes, to explain associations between predictor variables (e.g., treatment type, 12-step attendance) and outcomes (e.g., substance use). These studies will examine whether specific proximal variables are common mechanisms of change, by highlighting whether specific intrapersonal processes (e.g., self-efficacy, social support) are predictive of outcome regardless of treatment orientation. In addition, results may show that processes traditionally targeted to improve substance use may generalize to depressive symptoms, which has direct implications for clinical practice. By including outcomes up to one-year post treatment, these studies will seek to identify key processes involved in the long-term maintenance of symptom improvement. In addition, this study may be the first to elucidate pathways through which neurocognitive impairment impacts outcome in patients with substance dependence and MDD, which will have significant implications for the treatment of patients with neurocognitive impairment.

Study 1

Compared to the general population, mood and anxiety disorders occur at higher rates among individuals with substance use disorders (SUDs), and major depression (MDD) is the most common comorbid Axis I psychiatric disorder (Grant et al., 2004). Comorbid MDD is associated with a more chronic and prolonged course of SUDs (Hasin et al.), higher rates of disability (Wilk, West, Rae, & Regier), greater treatment costs (Curran et al.; O'Toole et al.) and elevated risk of suicide (Bolton et al.; Glasner-Edwards et al.). The prevalence is even greater among those who receive SUD treatment; in some clinical settings over half of patients have MDD (Chi, Satre, & Weisner; Lynskey). These patients often have greater severity of problems at intake (Leventhal et al.) and poorer outcomes from alcohol or drug treatment (Curran et al., 2000; Gamble et al., 2010; Glasner-Edwards, Marinelli-Casey, Hillhouse, Ang, Mooney, Rawson, et al.; Ilgen & Moos, 2005; Levin et al., 2008b). Despite high prevalence and evidence that treatment is less effective, few studies have examined treatment processes within this population. Recent research in SUD interventions has increasingly focused on mechanisms of change, defined as the factors that explain how and why treatments work (Longabaugh, 2007). Studies of mediators, or variables that account for the association between a predictor and outcome (MacKinnon), are a core element of this research (Longabaugh & Magill, 2011). However, these factors have rarely been investigated in patients with SUD and comorbid MDD, which hinders the advancement of interventions for this patient population.

Some of the most frequently-studied mediators of SUD treatment have been variables related to 12-step involvement, including attendance at 12-step meetings and

participation in 12-step activities (e.g., having a sponsor, reading literature). In general SUD samples these variables are consistently associated with reduced alcohol and drug use (Ouimette, Moos, & Finney, 1998; Tonigan, Toscova, & Miller, 1996) and mediated the effects of 12-step psychotherapies in clinical trials (Subbaraman, Kaskutas, & Zmore, 2011; Walitzer, Dermen, & Barrick, 2009). However, among patients with comorbidity studies of 12-step involvement have yielded inconsistent findings. In some studies, patients with psychiatric comorbidity attended similar levels of 12-step meetings (Chi et al., 2006) and experienced similar benefits as those without psychiatric conditions (Bogenschutz, Geppert, & George), but others found reduced benefits of 12-step involvement for patients with comorbid MDD (Kelly et al., 2003). Issues inherent to some community meetings, such as attitudes about psychiatric medication, could interfere with participation (Noordsy, Schwab, Fox, & Drake, 1996). In light of the limited existing research, further studies are needed to evaluate the utility of 12-step involvement in this population.

A more complete understanding of 12-step variables may be achieved by examining mediators of therapeutic effects. Among patients with MDD one potential mediating variable is depressive symptoms. Affect regulation is frequently described in the 12-step literature (Alcoholics-Anonymous, 1953), and 12-step involvement may increase exposure to common therapeutic factors that could reduce depressive symptoms (Laudet et al., 2004). Therapeutic changes in mood could play a key role in substance use outcomes, as negative affect is often implicated in relapse (Zywiak, Connors, Maisto, & Westerberg, 1996) and reductions in depression over time are associated with reduced alcohol and drug use (Jaffe et al.; Stulz, Crits-Christoph, Thase, & Gallop, 2011;

Witkiewitz & Villarroel). In a secondary analysis of Project MATCH (Matching Alcoholism Treatment to Client Heterogeneity), lower depression explained the effects of Alcoholics' Anonymous (AA) attendance on future drinking, but this was mostly attributable to AA's effects on current drinking (Kelly et al., 2010). The relative role of depression in mediating 12-step involvement could be greater for patients with comorbid MDD. Depressive symptoms are a prevalent precipitant of relapse for these patients (Tomlinson et al.), and prior research with this sample found strong correlations between individual changes in depression and substance use (Worley, Tate, & Brown, under review). Thus, improvement in depressive symptoms linked to 12-step involvement could be a key process in the reduction of substance use for patients with SUD and MDD.

The goal of this study was to examine relations between 12-step involvement, depression, and substance use in patients receiving treatment for comorbid SUD and MDD. Veterans with alcohol or drug dependence and MDD received antidepressant pharmacotherapy and 6 months of group psychotherapy with either Twelve-Step Facilitation (TSF) or Integrated Cognitive-Behavioral Therapy (ICBT), a cognitive-behavioral treatment that focused jointly on depression and substance use (Brown et al., 2006). In previously published studies of this sample, the TSF group had greater 12-step affiliation (Glasner-Edwards et al., 2007) and greater reductions in depression compared to ICBT during treatment, while substance use outcomes were similar between groups (Lydecker et al., 2010). For the current study we hypothesized that the superior depression outcomes in the TSF group would be mediated by greater 12-step attendance and affiliation. Furthermore, we predicted that the effects of 12-step attendance and affiliation on future alcohol and drug use would be mediated by depressive symptoms. As

depression often decreases with initial abstinence (Brown, Vik, Patterson, Grant, & Schuckit, 1995), we controlled for past alcohol and drug use in longitudinal models, to test whether the hypothesized relations were independent of prior substance use.

Methods

Subjects

The current study involves secondary analyses of 209 veterans who participated in a trial of outpatient group psychotherapy for comorbid SUD-MDD (Brown et al., 2006; Lydecker et al., 2010). Demographics of the sample are presented in Table 1. Participants met DSM-IV criteria for: (1) lifetime dependence on alcohol, cannabis, or stimulants with use in the past 90 days, and (2) major depressive disorder with ≥ 1 lifetime episode occurring independent of substance use, assessed via the Composite International Diagnostic Interview (Robins et al., 1988). Exclusion criteria included opiate dependence with intravenous administration, bipolar disorder or psychotic disorder, living more than 50 miles from the facility, or severe memory impairment interfering with assessment.

Procedures

The trial was approved by the University of California, San Diego and VA San Diego Healthcare System (VASDHS) Institutional Review Boards. Research staff obtained referrals from the VASDHS dual diagnosis clinic, briefly screened individuals for eligibility, and met with eligible veterans to explain study procedures and obtain informed consent. Participants consented to group psychotherapy, video recording of sessions, monthly psychotropic medication visits, random toxicology screens, and research assessments at baseline and every 3 months. Veterans agreed to participate only

in the assigned form of treatment (except pharmacotherapy and 12-step meetings) for the duration of group psychotherapy. Rates of prescription antidepressant utilization during the group psychotherapy phase were high for both treatment conditions (TSF = 94%, ICBT = 90%).

Group Treatments

Group psychotherapy was initiated via a rolling admission procedure, with start dates scheduled every 2 weeks and alternating assignment of patients to the condition with the next start date. Group sessions occurred twice/week for the first 3 months and weekly for the next 3 months. Session attendance was not significantly different ($M = 22$ of 36 sessions) across groups. Both interventions were co-delivered by senior clinicians and doctoral students trained to criterion via manual review, direct observation, and weekly supervision. Therapists rotated across treatment conditions every 6-12 months and treatment adherence was assessed via client report of content and videotape review. The TSF and ICBT groups did not differ significantly on the demographic and clinical characteristics assessed at baseline (see Table 1).

For the TSF condition we modified TSF (Nowinski, Baker, & Carroll, 2007) from Project MATCH (Group, 1997) to allow focus on multiple substances and group delivery. The three core modules of the TSF protocol covered Steps 1-3, general Twelve-Step topics and literature, and Steps 4-5. Sessions involved discussions of 12-step readings and recovery tasks (e.g., talking to sponsor). Depression was only discussed in the context of 12-Step themes. For ICBT, material was adapted from two empirically-validated treatments: group cognitive-behavioral treatment of depression (Muñoz & Ying, 1993) and cognitive-behavioral therapy from Project MATCH (Kadden, 1995). The three core

modules of ICBT were Thoughts (e.g., challenging cognitions), Activities (e.g., increasing positive activities), and Interpersonal (e.g., communication and assertiveness training).

Measures

All measures were obtained at intake, mid-treatment (Month 3), end-of-treatment (Month 6), and 3-month follow-up (Month 9). Follow-up rates were high (Month 3 = 99%, Month 6 = 94%, Month 9 = 89%). Summary statistics for the following measures, by treatment group and time, are presented in Table 2.

12-step meeting attendance and affiliation. The Alcoholics Anonymous Affiliation Scale (Humphreys, Kaskutas, & Weisner, 1998) was used to measure 12-step meeting attendance and affiliation in the past month. Attendance at 12-step meetings was captured by one ordinal item measuring the number of meetings attended (0 = “None”, .25 = “1 to 10”, .50 = “11-20”, .75 = “21 to 30”, 1 = “More than 30”). Affiliation with 12-step (e.g., having a sponsor, doing service, reading literature, having a spiritual awakening) was measured by a summary score of four binary items (Range 0-4). Given prior differences between 12-step attendance and affiliation in predicting substance use (Weiss et al., 2005), we examined these constructs separately, utilizing the 12-step variables from intake, Month 3, and Month 6.

Depressive symptoms. The Hamilton Depression Rating Scale (Hamilton, 1960), a structured clinical interview previously validated with MDD (Kneesevich, Biggs, Clayton, & Ziegler, 1977) and SUD populations (Willenbring, 1986) was used to assess depressive symptoms in the past week. Reliability of the HAMD ranged from .78 to .85

across all assessments. This study used the HAMD total score (Range 0-60) from intake, Month 3, and Month 6.

Frequency of alcohol and drug use. Alcohol and drug use was assessed with the Timeline Follow-Back (TLFB (Sobell & Sobell, 1992)), a calendar-assisted interview with documented reliability and validity (Maisto, Sobell, & Sobell). We used the TLFB to separately measure the frequency of alcohol and drug use. The primary outcome variables were percent days drinking (PDD) and percent days using drugs (PDDRG) during the previous 90 days. PDD and PDDRG from intake and Months 3, 6, and 9 were utilized in analyses.

Statistical methods

Multilevel analyses. We employed hierarchical linear models (HLMs) to examine the relations between treatment condition, 12-step variables, depression, and alcohol/drug use in multilevel mediation analyses (Krull & MacKinnon, 2001). The use of HLM allows inclusion of multiple time points nested within individuals and both static and time-varying covariates. By examining associations between sets of time-varying predictors and outcomes, these analyses were akin to running multiple models for multiple time points and averaging their effects. We included all available data via maximum likelihood estimation, a preferred method of estimation when the data contain information that is assumed missing-at-random (Schafer & Graham). Analyses revealed no differences on any study variables between individuals with complete data and those with any missing data, supporting this assumption.

Separate HLMs were conducted in Stata 10.1 (StataCorp, 2007) to examine individual paths in each mediation model (see Figure 1). Covariates for each HLM

included treatment group, time, baseline level of outcome, demographics (age, gender, ethnicity, level of education) and post-traumatic stress disorder (PTSD), as these covariates have previously predicted substance use in this sample (Norman, Tate, Wilkins, Cummins, & Brown, 2010) or others (Adamson, Sellman, & Frampton, 2009). Repeated variables were treated as time-varying covariates, with PDD and PDDRG as time-varying covariates in the final HLMs to determine if effects were independent of current alcohol and drug use. Finally, in Model 2 all time-varying covariates were lagged, with prior variables predicting future (3 months later) alcohol and drug use.

Statistical test of mediation. Consistent with current conventions in mediation analysis (MacKinnon, 2008), formal tests to estimate the magnitude, statistical significance, and effect sizes of mediated effects were computed using products-of-coefficients with asymmetric 95% confidence limits, which has more accurate Type I error rates and greater power to detect mediated effects than alternate approaches (MacKinnon, Lockwood, Hoffman, West, & Sheets, 2002). Estimates of mediated effects and confidence limits were obtained using the PRODCLIN program (MacKinnon, Fritz, Williams, & Lockwood, 2007) by importing coefficients and standard errors from the HLMs. Mediated effect size was reported with the proportion of the direct effect explained by the mediated effect (MacKinnon, 2008).

Results

Effects of treatment condition on depression and 12-step variables

Separate HLMs examined the effect of treatment group on depression and 12-step variables during active treatment, controlling for covariates. No covariates significantly predicted 12-step attendance, affiliation, or depression. Consistent with prior reports of

this sample (Lydecker et al., 2010), TSF had significantly lower levels of depression during active treatment as compared to ICBT (see Table 3). The TSF group also had greater 12-step meeting attendance ($b = 0.14, p < 0.001$) and affiliation ($b = 0.54, p < 0.001$).

Effects of 12-step variables on depression

Separate HLMs examined the effects of 12-step attendance and affiliation on depression at Months 3 and 6, controlling for treatment condition, baseline depression, time, and other covariates (see Table 3). Greater 12-step attendance ($b = -7.06, p = 0.001$) and greater 12-step affiliation ($b = -1.23, p = 0.014$) both predicted lower depression, and the effect of treatment condition was no longer statistically significant. When examining the 12-step variables simultaneously, only 12-step meeting attendance independently predicted depression ($p = 0.014$), thus further analyses did not include 12-step affiliation.

A final model included current (Month 3 and 6) PDD and PDDRG as time-varying predictors of depression, to determine if the effects of 12-step meetings on depression were independent of current alcohol and drug use. Lower PDD and PDDRG both significantly predicted lower depression (see Table 3). Controlling for these effects, greater 12-step meeting attendance still predicted lower depression ($p = 0.006$), indicating that relations between meeting attendance and depression were independent of current drinking and drug use.

Multilevel mediation test

To assess the statistical and clinical significance of mediation we obtained an estimate of the mediated effect with asymmetric 95% confidence intervals. In Model 1 this refers to the specific portion of the group difference (TSF vs. ICBT) on depression

that is mediated through 12-step meeting attendance. These results ($b = -0.80$, 95% CI $[-1.59, -0.20]$, $p < 0.05$) indicated that the effect of TSF on depression was mediated through 12-step meeting attendance, with the mediated effect explaining 24.3% of the direct effect of TSF on depression.

Effects of 12-step attendance on future alcohol and drug use

Lagged measures of 12-step attendance at Months 3 and 6 were used to predict future (Month 6 and 9) frequency of drinking and drug use, controlling for covariates, none of which significantly predicted drinking or drug use in the subsequent HLMs. As shown in Table 4, greater 12-step meeting attendance significantly predicted lower future PDD ($p = 0.029$) but not future PDDRG ($p = 0.18$). This indicated individuals with greater 12-step meeting attendance had lower future drinking frequency, but 12-step attendance was not significantly related to future drug use.

Effects of depression on future alcohol and drug use

Support for the predictor-to-mediator path in Model 2 (12-step attendance predicting depression) was previously established in Model 1. To complete Model 2 analyses, we examined the mediator-to-outcome path by testing whether depression at Month 3 and 6 predicted future (Month 6 and 9) alcohol and drug use, controlling for the effects of the predictor (12-step attendance). As shown in Table 4, lower lagged depression significantly predicted lower future PDD ($p < .001$) but not future PDDRG ($p = .75$). The effects of 12-step attendance were no longer statistically significant ($p = .17$).

Given that effects of depression on future drinking could be confounded by current drinking, our final model controlled for the effects of lagged PDD. As shown in Table 4, prior PDD was significantly and strongly related to future PDD ($p < .001$), but

lagged depression was still significantly predictive of future PDD ($p = .017$). In other words, lower month 3 and 6 depression uniquely predicted lower drinking at months 6 and 9, above and beyond the effects of prior drinking.

Multilevel mediation test

In Model 2 the mediated effect refers to the specific portion of the relationship between 12-step meeting attendance and future drinking that is mediated through depressive symptoms. Results ($b = -1.16$, 95% CI $[-2.57, -0.18]$, $p < 0.05$) indicated that the effect of 12-step meeting attendance on future drinking was significantly mediated through depression, explaining 15.7% of the direct effect.

Discussion

In our original trial of ICBT and TSF for adults with SUD and MDD, the ICBT group was expected to have superior reductions in depression symptoms during treatment, but the results were contrary to these expectations (Brown et al., 2006; Lydecker et al., 2010). The current study utilized mediation analyses to examine whether greater engagement in 12-step resources explained lower within-treatment depression for the TSF condition. Greater attendance at community-based 12-step meetings was associated with lower depression and mediated the group difference in depression, providing preliminary evidence for 12-step attendance as a therapeutic mechanism for reductions in depressive symptoms. Others have noted that general therapeutic factors inherent to self-help groups (e.g., social contact) may be especially helpful for SUD patients with psychiatric conditions (Moos, 2008), and patients in TSF likely gained greater exposure to such therapeutic factors through greater community 12-step meeting attendance. Greater meeting attendance could also signal greater behavioral activation, a

component of effective psychotherapy for depression (Dimidjian, Barrera, Martell, Munoz, & Lewinsohn, 2011). While interpersonal and behavioral coping skills were also targeted in ICBT, our findings suggest 12-step meetings could be an important and readily accessible vehicle for general symptom reduction in patients with SUD and MDD. While the ICBT group had less reduction in depression during treatment, our prior report revealed superior post-treatment depressive symptoms and substance use for ICBT (Lydecker et al., 2010), and future studies of this sample may provide insight into the unique vs. common mechanisms that explain differential patterns of symptom change in these alternative treatments.

Consistent with prior studies (Kelly et al., 2010; McCrady, Epstein, & Kahler, 2004) greater 12-step meeting attendance predicted lower future drinking. However, our study was unique in finding this effect was mediated by depression, even when controlling for current drinking. In a similar study of Project MATCH, depressive symptoms were not uniquely related to meeting attendance or future drinking when current drinking was controlled (Kelly et al., 2010). This discrepancy suggests that changes in depressive symptoms linked to 12-step meeting attendance may be an especially critical therapeutic process for patients with comorbid MDD. Other studies suggest negative affect has a large role in the maintenance of substance use for these patients. Individual changes in depression and substance use were highly correlated in this sample (Worley et al., under review), and SUD patients with MDD are more likely to experience depressed mood prior to relapse (Tomlinson et al., 2006). The importance of negative affect was also confirmed in recent work with Project MATCH (Kelly, Hoepfner, Stout, & Pagano, 2012), in which the mediating effects of depression were

significant and independent of other process variables (e.g., social networks, self-efficacy, spirituality) in the aftercare sample, who may be more representative of patients enrolled in our study. In our sample 12-step meeting attendance no longer predicted future drinking when accounting for the mediating effects of depressive symptoms. This suggests that even when treatment processes focus explicitly on substance use, ancillary effects on mood may be an important mechanism of change for patients with comorbid MDD. Conversely, patients with depressive symptoms that persist despite continued abstinence and frequent 12-step meeting attendance may need additional interventions to control depression and prevent future relapse.

Two aspects of our hypotheses were not confirmed and merit discussion. When examined concurrently, 12-step affiliation did not predict depression independent of 12-step meeting attendance. While 12-step meetings may be more instrumental in reducing depressive symptoms due to the positive effects of social interaction and behavioral activation, the lack of effects for affiliation here could also be due to statistical and methodological limitations. The two 12-step variables were highly correlated (.65-.69) at each wave, and this multicollinearity could have biased regression coefficients (Raudenbush & Bryk, 2002). Our measure of 12-step affiliation was brief and basic, and other measures may capture detailed components of affiliation (Klein, Slaymaker, & Kelly, 2011) more predictive of depression. Secondly, future drug use was not predicted by 12-step attendance or depression. We had less power to detect this effect, because fewer patients were drug-dependent or using drugs at intake. Still, the effects of 12-step meetings could be stronger for patients who primarily use alcohol, possibly due to greater availability of specific meetings (e.g., AA). The effects of 12-step meetings have differed

between alcohol and drug users in prior research (Tonigan & Beatty, 2011), so the lack of effects on drug use in this study may be important and deserving of further exploration.

This study has limitations, most notably in the sample's restricted demographic characteristics which limit the generalizability of findings. These results may be applicable to a large proportion of SUD patients due to the high prevalence of comorbid MDD in clinical settings (Chi et al., 2006; Lynskey, 1998), but replication in other samples is needed. Importantly, factors other than 12-step meeting attendance (e.g., antidepressants, psychotherapy content) could have accounted for better initial depression response in TSF, but the groups had similar attendance at group therapy sessions and similar rates of antidepressant medication use. Temporal precedence between 12-step attendance and depression was not explicitly tested here, and more rigorous models could examine lagged effects of 12-step attendance on future depression. Also, our measure of 12-step attendance did not differentiate between different meetings (e.g., AA vs. NA), which may have helped investigate the lack of effects on drug use. Finally, while we controlled for the effects of comorbid PTSD on all outcomes, we did not explore more intricate (e.g., moderating) effects that may be of interest due to the high prevalence of PTSD in this population.

Our study provides preliminary evidence that among patients with SUD and MDD receiving TSF, reduction in depression is mediated by greater 12-step meeting attendance, and that reductions in depression related to 12-step attendance can also occur for patients receiving other (e.g., cognitive-behavioral) forms of therapy. Importantly, reductions in depressive symptoms appear to mediate the effects of 12-step meeting attendance on future drinking outcomes among patients with SUD and MDD, regardless

of treatment condition. Because our lagged analyses controlled for prior substance use, this study provides strong initial support for reduced depression as a mechanism through which 12-step attendance influences future drinking in adults with SUD and comorbid MDD.

Study 1 has been accepted for publication in *Addiction*, as following: Worley, M.J., Tate, S.R., & Brown, S.A. (*in press*). Mediatonal Relations between 12-step Meeting Attendance, Depression, and Substance Use during Treatment for Comorbidity. *Addiction*. The dissertation author was the primary author of this published manuscript.

Table 1. Baseline demographic and clinical characteristics of veterans with substance dependence and major depression (N = 209).

	TSF	ICBT
	<i>n</i> =97	<i>n</i> =112
Male	90.9 %	88.7 %
Caucasian	70.7 %	76.3 %
Mean age (<i>SD</i>)	49.6 (7.6)	48.8 (7.8)
Mean years of education (<i>SD</i>)	13.6 (2.2)	13.4 (2.1)
Employed	21.2 %	15.0 %
Married	17.2 %	8.9 %
Post-traumatic stress disorder	38.4%	41.6%
Alcohol dependence	87.0 %	92.2 %
Stimulant dependence	54.4 %	54.2 %
Cannabis dependence	27.8 %	30.8 %

Note. TSF: Twelve-Step Facilitation; ICBT: Integrated Cognitive-Behavioral Therapy

Table 2. 12-step variables, depression, alcohol use, and drug use at each wave by treatment condition.

		Month			
		Intake	3	6	9
		<i>M (SD)</i>	<i>M (SD)</i>	<i>M (SD)</i>	<i>M (SD)</i>
Past month	TSF	0.50 (.33)	0.49 (.31)	0.44 (.30)	-
12-step attendance ^a	ICBT	0.48 (.31)	0.34 (.31)	0.25 (.27)	-
Past month	TSF	2.26 (1.33)	2.56 (1.33)	2.55 (1.38)	-
12-step affiliation ^b	ICBT	2.15 (1.19)	2.06 (1.34)	1.78 (1.33)	-
HAMDC ^c	TSF	27.81 (11.55)	23.99 (12.81)	19.00 (10.90)	-
	ICBT	29.19 (10.08)	26.04 (12.57)	24.92 (13.5)	-
Percent Days Drinking	TSF	26.36 (24.82)	6.90 (16.50)	8.71 (20.08)	11.78 (23.98)
	ICBT	21.61 (22.49)	8.54 (17.53)	12.35 (23.49)	11.45 (21.19)
Percent Days	TSF	11.58 (21.26)	3.15 (13.21)	4.16 (11.84)	3.60 (13.18)
Using Drugs	ICBT	10.78 (20.26)	2.88 (9.14)	3.94 (12.85)	4.94 (15.27)

Note. TSF: Twelve-Step Facilitation; ICBT: Integrated Cognitive-Behavioral Therapy;
HAMDC: Hamilton Depression Rating Scale.

^aOrdinal scale (0 = “None”, .25 = “1 to 10”, .50 = “11-20”, .75 = “21 to 30”, 1 = “More than 30”). ^bRange = 0-4 affiliation behaviors. ^cRange = 0-60.

Table 3. Hierarchical linear modeling results for 12-step variables (Month 3/6) predicting depression (Month 3/6).

	Direct effect model	Mediator model	Mediator model controlling for substance use
	b (SE)	b (SE)	b (SE)
Baseline HAMD	0.56 (0.06)***	0.54 (0.07)***	0.53 (0.06)***
Treatment group	-3.30 (1.39)*	-2.19 (1.48)	-2.29 (1.42)
Month	-0.94 (0.31)**	-0.86 (0.32)**	-0.90 (0.33)**
12-step attendance	-	-6.16 (2.51)*	-5.69 (2.08)**
12-step affiliation	-	-.38 (.61)	-. ^a
PDD	-	-	0.09 (0.03)*
PDDRG	-	-	0.12 (0.06)*

Note. HAMD: Hamilton Depression Rating Scale; PDD: percent days drinking; PDDRG: percent days using drugs. Non-significant covariates included age, gender, ethnicity, level of education, and post-traumatic stress disorder (coefficients not shown).

^aPredictor was not retained in final model.

* $p < .05$, ** $p < .01$, *** $p < .001$.

Table 4. Hierarchical linear modeling results for lagged 12-step attendance and depression (Month 3/6) predicting future alcohol and drug use (Month 6/9).

	Direct effect model	Mediator model	Mediator model controlling for substance use
	b (SE)	b (SE)	b (SE)
Post-treatment drinking			
Baseline PDD	0.12 (0.06)*	0.13 (0.05)*	-
Treatment group	-0.33 (2.76)	0.53 (2.69)	1.12 (2.11)
Month	0.76 (0.44)	0.94 (0.46)*	0.73 (0.54)
Lagged 12-step attendance	-7.22 (3.39)*	-4.75 (3.43)	-2.50 (3.27)
Lagged HAMD	-	0.31 (0.08)***	0.19 (0.08)*
Lagged PDD			0.49 (0.06)***
Post-treatment drug use			
Baseline PDDRG	0.03 (0.05)	0.03 (0.05)	-
Treatment group	0.74 (1.94)	0.82 (1.97)	-0.75 (1.74)
Month	1.50 (1.03)	1.50 (1.07)	0.36 (0.39)
Lagged 12-step attendance	-3.38 (2.50)	-3.60 (2.60)	-3.34 (2.52)
Lagged HAMD	-	-.02 (0.06)	-.03 (0.06)
Lagged PDDRG			0.39 (0.08)***

Note. HAMD: Hamilton Depression Rating Scale; PDD: percent days drinking; PDDRG: percent days using drugs. Non-significant covariates included age, gender, ethnicity, level of education, and post-traumatic stress disorder (coefficients not shown).

* $p < .05$, ** $p < .01$, *** $p < .001$.

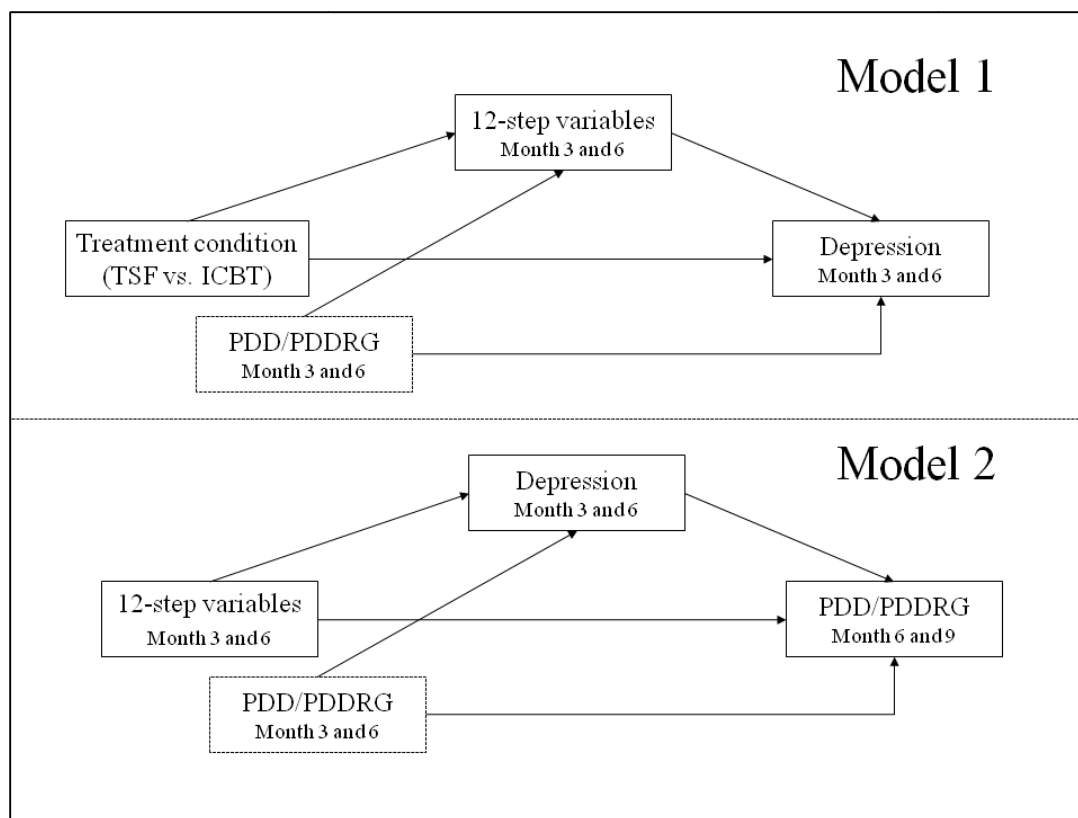


Figure 1. Hypothesized relations between treatment group, 12-step attendance/affiliation, and depression (Model 1), and between 12-step attendance/affiliation, depression, and future alcohol and drug use (Model 2). Final models controlled for current alcohol and drug use. Other covariates include time, gender, ethnicity, level of education, and post-traumatic stress disorder. PDD = Percent Days Drinking; PDDRG = Percent Days using Drugs; TSF = Twelve-Step Facilitation; ICBT = Integrated Cognitive Behavioral Therapy.

Study 2

Among individuals diagnosed with substance dependence, major depressive disorder (MDD) is a common and problematic psychiatric comorbidity, affecting an estimated 22% of persons with alcohol dependence and 40% with drug dependence (Grant et al., 2004). Compared to individuals without comorbidity, those with MDD have a poorer long-term course of substance use (Hasin et al., 2002), greater risk of suicide (Bolton et al., 2010a), and greater treatment costs (Druss & Rosenheck, 1999; Mark, 2003). In clinical settings the prevalence of comorbid MDD is even greater, exceeding 50% in some settings (Chi et al., 2006), and these patients typically have poorer outcomes from inpatient (Curran et al., 2000) or outpatient treatment (Gamble et al., 2010; Glasner-Edwards, Marinelli-Casey, Hillhouse, Ang, Mooney, & Rawson, 2009; Levin et al., 2008b). Given the vast prevalence and complications associated with comorbid substance dependence and MDD, there is a clear need to better understand processes that contribute to long-term outcomes in these chronically-disabled patients, and to develop treatments that better sustain long-term change.

Researchers have recently stressed the importance of identifying mechanisms of behavior change (Longabaugh, 2007; Longabaugh et al., 2005a), the factors that explain why and how treatments work. Some of the most prominent mediating variables in this line of research have been those related to 12-step involvement, such as attendance at 12-step meetings and affiliation with 12-step principles. Greater levels of 12-step affiliation and attendance have been consistently associated with reduced alcohol and drug use in general samples (Ouimette et al., 1998; Tonigan et al., 1996), but fewer studies have examined these relations in patients with psychiatric comorbidity. Similar levels of

participation (Chi et al., 2006) and degree of benefit from 12-step meetings (Bogenschutz et al., 2006) have been found for patients with psychiatric conditions, but other studies found reduced long-term benefits (Kelly et al., 2003) for patients with comorbid MDD. Given the inconsistent and limited body of research, further studies are needed to clarify the importance of post-treatment 12-step affiliation and meeting attendance for patients with comorbid substance dependence and MDD.

The extent to which specific interventions can produce sustained levels of 12-step involvement in comorbid patients is also relatively unknown. Treatments designed specifically to increase 12-step attendance and affiliation can achieve these goals in substance-dependent patients (Timko, Debenedetti, & Billow, 2006; Walitzer et al., 2009), including those with greater psychiatric severity (Subbaraman et al., 2011). Similar results were found in our sample of veterans with comorbid MDD, where patients receiving group Twelve-Step Facilitation (TSF) had increased levels of 12-step affiliation during treatment (Glasner-Edwards et al., 2007). However, it is not known whether comorbid patients can sustain high levels of 12-step participation after the conclusion of TSF therapy, and if any changes in long-term participation will impact substance use. Surprisingly few studies of substance-dependent samples have directly examined post-treatment change in 12-step involvement, but some investigations have found no decline in 12-step attendance or affiliation in the first six months (Kahler et al., 2004) or one year (Walitzer et al., 2009) following treatment. Patients with comorbid MDD could have greater difficulty sustaining 12-step involvement, possibly due to persistent depressive symptoms interfering with meeting attendance, difficulty making social connections with group members, or group resistance to the use of psychotropic medication (Rychtarik,

Connors, Dermen, & Stasiewicz, 2000). Difficulty sustaining 12-step involvement may contribute to the poorer long-term treatment outcomes for patients with comorbid MDD, but to date this question has not been examined empirically.

This study involves secondary analyses of a sample of veterans enrolled in a 6-month trial of group TSF and Integrated Cognitive Behavioral Therapy (ICBT) for treatment of comorbid substance dependence and major depression (Brown et al., 2006; Lydecker et al., 2010). Utilizing latent growth curve models (LGMs) which explicitly model individual patterns of change in specified variables, we had three primary aims related to 12-step involvement and post-treatment substance use during the one-year follow-up period. First, we aimed to describe the post-treatment trajectories of 12-step affiliation and meeting attendance separately for the TSF and ICBT groups. Secondly, we examined if the post-treatment trajectories of 12-step affiliation and meeting attendance differed between TSF and ICBT, hypothesizing that patients in TSF would have difficulty sustaining within-treatment levels of 12-step affiliation and attendance and evince greater decline in these variables during follow-up. Thirdly, we examined if post-treatment change in 12-step affiliation and meeting attendance predicted post-treatment change in drinking and drug use. We hypothesized that greater reductions in 12-step affiliation and meeting attendance would predict greater increases in drinking and drug use, and that these effects would mediate the superior long-term treatment effects observed for the ICBT condition.

Methods

Subjects

The sample for this study includes 201 veterans who participated in a trial of outpatient group psychotherapy for comorbid substance dependence and MDD (Brown et al., 2006; Lydecker et al., 2010). We included all participants from the trial who completed at least one follow-up assessment from end-of-treatment (Month 6) to the one-year follow-up (Month 18). Demographics of the sample are presented in Table 5. Study inclusion criteria were lifetime dependence on alcohol, cannabis, or stimulants with recent (past 90 day) use, and major depressive disorder with at least one episode occurring independently of substance use. Exclusion criteria included opiate dependence with intravenous administration, bipolar or psychotic disorder, residing excessively far ($\geq$ 50 miles) from the research facility, or memory impairments prohibiting accurate recall in study assessments.

Procedures

The procedures for this study were approved by the University of California, San Diego and VA San Diego Healthcare System (VASDHS) Institutional Review Boards. Participant referrals were obtained from the VASDHS dual diagnosis clinic by research study staff, who conducted brief screenings prior to meeting with eligible veterans to explain study procedures and obtain informed consent. Participating veterans consented to 6 months of group psychotherapy, recording of sessions, psychotropic medication management appointments, random urine screens, and research assessments conducted at intake and at 3-month intervals for an 18-month period. Veterans agreed to receive no other formal treatment for substance use or depression for the duration of group psychotherapy. Participation in other formal intervention was allowed during follow-up.

Group Treatments

Group psychotherapy was initiated on a rolling basis, with starts occurring every 2 weeks. After completing the intake assessment participants were sequentially allocated to the treatment condition with the next start date. For Twelve-Step Facilitation (TSF) we modified the TSF protocol from Project MATCH (Group, 1997) to allow group delivery and discussion of multiple substances. For development of Integrated Cognitive-Behavioral Therapy (ICBT), material was adapted from two empirically-supported treatments: group cognitive-behavioral therapy for depression (Muñoz & Ying, 1993) and cognitive-behavioral relapse prevention from Project MATCH (Kadden, 1995). The two treatments were identically structured with a series of three modules, with each module designed to cover a specific 12-step (e.g., Steps 1-3) or cognitive-behavioral (e.g., modifying thoughts) topic. Group sessions occurred twice/week for the first 3 months of group treatment, when each topic was covered in a one-month block. Topics were reviewed in the next 3 months during weekly group sessions. The mean session attendance was similar ($M = 22$ sessions) across groups. Interventions were co-delivered by senior clinicians (e.g., clinical staff or post-doctoral fellows) and doctoral students trained via manual review, direct observation, and weekly supervision. Therapists were rotated across treatment conditions on a regular basis (every 6-12 months), and adherence to protocol was assessed via videotape review.

Measures

Measures utilized in this study were obtained at end-of-treatment (Month 6) and at 3-month intervals until the one-year follow-up (Month 18).

12-step meeting attendance and affiliation. We used the Alcoholics Anonymous Affiliation Scale (Humphreys et al., 1998) to measure 12-step affiliation and

meeting attendance in the past month. Analytical models examined 12-step affiliation and meeting attendance separately, as prior research has found differences in their prediction of substance use (Weiss et al., 2005). The number of 12-step meetings attended in the past month was measured by a single ordinal item, while 12-step affiliation was measured with the sum of four binary items (e.g., having a sponsor, reading literature, doing service, having a spiritual awakening). We utilized the 12-step variables from Months 6, 9, 12, 15, and 18.

Frequency of alcohol and drug use. Alcohol and drug use during the prior 90 days was assessed with the Timeline Follow-Back (TLFB (Sobell & Sobell, 1992)), a reliable and valid calendar-assisted interview (Maisto, Sobell, & Sobell, 1982). In this study the TLFB was utilized to separately examine percent days drinking (PDD) and percent days using drugs (PDDRG) during the previous 90 days. Our analyses included all measures of PDD and PDDRG from end-of-treatment (Month 6) and the 12-month follow-up period (Months 9, 12, 15, and 18).

Statistical methods

Our longitudinal analyses utilized latent growth modeling (LGM) in the structural equation modeling framework. In LGM a series of repeated measures (e.g., PDD at Months 6 through 18) are used to indicate each individual's underlying latent "growth curve" (i.e., trajectory) on one or more variables. This process creates separate growth curves for each individual, described by "growth factors" such as latent intercept (starting level) and latent slope (rate of change over time). Estimates of the sample mean and variance are obtained for each growth factor, and covariates can be used to predict individual differences in the initial level or rate of change over time. One distinct

advantage of LGM is the ability to examine relations between the rates of change in multiple longitudinal processes, as warranted by the aims of this study. Because we were primarily concerned with the 12-month follow-up period, the end-of-treatment (Month 6) time point served as the initial level for each LGM. Thus, in each LGM the latent intercept represents the level at end-of-treatment, while latent slopes represent rates of increase or decrease during the 12 months of follow-up (Month 6 to Month 18).

For each study variable we first fit unconditional (i.e., no predictors) growth models to determine the optimal shape of the growth trajectory, before incorporating treatment group as a predictor in conditional models. This allowed us to test whether treatment condition predicted variability in the intercepts and slopes. In the final LGMs for PDD and PDDRG we specified growth curve mediation models (see Figure 1), to determine if the slope of 12-step affiliation or meeting attendance mediated the relationship between treatment group and the slope of PDD or PDDRG. To test the significance of mediated effects we used asymmetric 95% confidence intervals obtained with the bias-corrected bootstrap procedure (MacKinnon, 2008), which has shown greater power to detect mediated effects than other formal mediation tests (MacKinnon et al., 2002). All LGMs utilized the maximum likelihood procedure, which incorporates all available data from each participant under the assumption of missing at random.

Results

12-step Meeting Attendance and Affiliation

As shown in Figure 2, the ICBT and TSF groups differed in their longitudinal patterns of 12-step meeting attendance and affiliation from Month 6 to Month 18. We used LGMs to estimate the mean pattern of change and variability in 12-step variables

separately for TSF and ICBT. For the TSF group, a quadratic LGM was an excellent fit to the data for 12-step affiliation ($\chi^2(6, N = 91) = 2.76, p = .84, CFI = 1.00, RMSEA < .01$) and attendance ($\chi^2(6, N = 91) = 5.37, p = .50, CFI = 1.00, RMSEA < .01$). At the mean level, the TSF group exhibited a significant decline in 12-step affiliation and meeting attendance from Month 6 to 18, with a significant deceleration in that decline as indicated by a positive, statistically significant quadratic slope (see Table 6). This nonlinear decline was likely due to a steep descent in the first 6 months following treatment (Month 6 to Month 12) with little change thereafter. There was significant individual variability in the intercept, linear slope, and quadratic slope for 12-step affiliation, but variability was significant only in the intercept for 12-step meeting attendance. For the ICBT group, a linear LGM was a good fit to the data for 12-step affiliation ($\chi^2(10, N = 105) = 12.26, p = .27, CFI = 0.99, RMSEA = .05$) and attendance ($\chi^2(10, N = 105) = 8.52, p = .58, CFI = 1.00, RMSEA = .05$). In contrast to TSF, the ICBT group exhibited no significant increase or decrease in 12-step affiliation or meeting attendance, and no significant individual variability in the intercept or slope for either 12-step model (see Table 6).

To examine whether patients in the TSF and ICBT groups differed significantly in their longitudinal patterns of 12-step affiliation and attendance, we conducted conditional LGMs with the full sample, using a dummy-coded treatment group variable (ICBT = 0, TSF = 1) as a predictor of 12-step affiliation and attendance growth factors. The linear LGM was an adequate fit for 12-step affiliation ($\chi^2(13, N = 196) = 36.21, p < .01, CFI = .94, RMSEA = .09$) and a good fit for meeting attendance ($\chi^2(13, N = 196) = 20.65, p = .08, CFI = .98, RMSEA = .06$). Compared to ICBT, individuals in TSF had significantly greater intercepts of 12-step affiliation ($b = .45, SE = .20, p = .02$) and meeting

attendance ($b = .14$, $SE = .04$, $p = .001$). However, TSF also predicted significantly greater decline in 12-step affiliation ($b = -.11$, $SE = .05$, $p = .03$) and attendance ($b = -.04$, $SE = .01$, $p = .003$) from Month 6 to Month 18. These results indicate that while veterans in TSF had greater levels of 12-step involvement at end-of-treatment, their 12-step affiliation and meeting attendance declined to a greater extent than the ICBT group during the 12 months of follow-up.

Alcohol and Drug Use Outcomes

To examine changes in alcohol and drug use, we first estimated separate unconditional LGMs for percent days drinking (PDD) and percent days using drugs (PDDRG) from Month 6 to Month 18. The linear LGM was an excellent fit to the data for PDD ($\chi^2(7, N = 201) = 5.025$, $p < .001$, CFI = 1.00, RMSEA < .01) and PDDRG ($\chi^2(8, N = 201) = 12.85$, $p = .12$, CFI = .98, RMSEA = .06). At the mean level there was a significant increase from Month 6 to Month 18 in PDD but no significant change in PDDRG (see Table 7). The variance estimates for growth factors (e.g., intercept, linear slope) revealed significant individual variability in the intercept and slope for PDD and PDDRG. Thus, while the mean pattern of change was an increase in alcohol use and no change in drug use, there was considerable individual variability in the initial level and change over time in frequency of drinking and drug use.

In the conditional model there were no treatment group differences in PDD intercepts, but TSF predicted significantly greater PDD slopes over time (see Table 7). Treatment group did not significantly predict PDDRG intercepts or slopes. These results indicated that patients in TSF increased in drinking frequency more than patients in ICBT during the year-long follow-up, and that there were no group differences in the end-of-

treatment drinking frequency, end-of-treatment drug use frequency, or rate of change in drug use over time.

Changes in 12-step involvement predicting alcohol and drug use

We then used the LGMs for 12-step and affiliation to predict individual differences in the end-of-treatment level (intercept) and rate of change in alcohol and drug use (linear slope) from Month 6 to Month 18. In separate models the slopes for 12-step affiliation and meeting attendance were utilized as mediating variables between treatment group and the slopes for PDD and PDDRG (see dashed lines in Figure 1), to test whether the greater increases in PDD over time for TSF patients were explained by greater decreases in 12-step variables. Results from these analyses are presented in Table 7. The PDD intercept was significantly and negatively correlated with the intercepts for 12-step affiliation and meeting attendance, indicating that individuals with greater levels of affiliation and meeting attendance at end-of-treatment were also drinking less frequently at end-of-treatment. The PDD intercept was significantly and positively correlated with the slopes for 12-step affiliation and attendance, indicating that individuals with lower PDD at end-of-treatment had greater decreases in their 12-step affiliation and attendance during follow-up. Finally, the slopes for 12-step affiliation and meeting attendance were strongly, negatively predictive of PDD slope. This indicated that individuals with greater decreases in 12-step affiliation and meeting attendance from Month 6 to Month 18 had greater increases in PDD over time. As shown by asymmetric 95% confidence intervals obtained via the bias-corrected bootstrap procedure, the indirect effects of treatment group on PDD through slopes of 12-step affiliation ($ab = 3.30$, 95% CI [.67, 16.54]) and meeting attendance ($ab = 2.41$, 95% CI [.47, 6.47]) were statistically

significant. These results indicate that the greater relative increases in PDD for the TSF patients were mediated by (and possibly attributable to) their greater relative decreases in 12-step affiliation and meeting attendance. There were no significant relations between intercepts and slopes of the 12-step variables and PDDRG (see Table 7), indicating that the end-of-treatment level and change during follow-up for drug use frequency was unrelated to end-of-treatment level or change during follow-up for 12-step affiliation or meeting attendance.

Discussion

This study examined post-treatment change in 12-step affiliation and meeting attendance and related effects on substance use outcomes in a sample of veterans with comorbid substance dependence and major depression who received six months of group treatment with TSF or ICBT. Because fewer studies of mediating variables have focused on substance-dependent patients with psychiatric comorbidity, there is relatively less knowledge about processes that sustain long-term change in their substance use outcomes. This study adds to the existing literature by examining post-treatment trajectories of change in 12-step affiliation and attendance in comorbid patients, determining whether treatment condition predicts individual differences in these trajectories, and reporting the mediational effects of reduced 12-step involvement on long-term substance use outcomes.

Veterans in the TSF condition had greater levels of 12-step affiliation and meeting attendance at end-of-treatment than those in ICBT. This is consistent with prior studies of this sample (Glasner-Edwards et al., 2007; Worley et al., under review) and shows that a professionally-delivered TSF intervention can enable greater levels of 12-step

involvement than other psychotherapies during active treatment. However, veterans in TSF also evinced a significant nonlinear decline in both 12-step affiliation and meeting attendance during the one year follow-up, while those in ICBT had no significant change. Previous studies of non-comorbid patients found no post-treatment decline in affiliation or meeting attendance following 12-step interventions (Kahler et al., 2004; Walitzer et al., 2009). Our contrasting findings suggest comorbid MDD may interfere with continued attendance at 12-step meetings and affiliation with prescribed 12-step behaviors, even when patients are relatively successful at achieving these goals during active TSF. Potential explanatory mechanisms behind this finding are beyond our current scope, but could be related to persistent depressive symptoms and related low motivation, the sudden absence of accountability provided by a formal treatment group, or difficulty in establishing firm social bonds in 12-step meetings for patients with comorbid MDD. Some patients were evidently successful at sustaining 12-step affiliation as revealed by significant individual variance estimates, but modifications to TSF or continued contact may be necessary to achieve the desired long-term results in the majority of patients with comorbid MDD.

Independent of treatment condition, individuals with greater decreases in 12-step affiliation and meeting attendance also had greater increases in drinking frequency during the one-year follow-up. As evidenced by strong standardized coefficients in our latent growth curve models, post-treatment change in 12-step involvement likely plays a large role in determining whether patients with comorbid substance dependence and MDD experience post-treatment increases in drinking. Similar to a prior report of follow-up substance use outcomes in this sample (Lydecker et al., 2010), the current study found

patients in TSF had greater post-treatment increases in drinking frequency than those in the ICBT condition. We also determined this group difference was mediated through reductions in 12-step affiliation and meeting attendance, which provides a possible explanation for the worse outcomes over time for TSF and supports the long-term efficacy of ICBT. During follow-up the ICBT group as a whole did not increase or decrease in 12-step affiliation or meeting attendance, but their mean levels of attendance and affiliation remained consistently greater than zero. Although it was not a prescribed element of treatment, there is apparently a subset of patients in ICBT who continue 12-step involvement. Superior long-term patterns in other mediating variables (e.g., self-efficacy, social support) may have also occurred for the ICBT condition, and future studies will explore other potential factors related to their superior post-treatment drinking outcomes.

Limitations of this study include the restricted demographic characteristics of the veteran sample (e.g., heavily male, mostly Caucasian) which curtails the immediate generalizability of these findings. Because we tested relations between concurrent changes in 12-step involvement and substance use, we cannot make conclusions about causal relationships, but other elements of our design and findings (e.g., mediation testing, dose-response relationship) enhance the plausibility of causal conclusions (Nock, 2007). Our measures did not differentiate between different types of 12-step meetings (e.g., Alcoholics vs. Narcotics Anonymous), which could have helped explain the lack of findings for drug use outcomes, and future work might benefit from more detailed measures of 12-step involvement. Also, because our 12-step measures were relatively brief, there may have been important aspects of these behaviors we did not consider.

Finally, while the results have important implications for the broader population of individuals with substance dependence and MDD, replication in other samples and settings is needed.

Study 2 has been accepted for publication in *Substance Abuse*, as following:

Worley, M.J., Tate, S.R., McQuaid, J.R., Granholm, & Brown, S.A. (*in press*). 12-step Affiliation and Attendance following Treatment for Comorbid Substance Dependence and Depression: A Latent Growth Curve Mediation Model. *Substance Abuse*. The dissertation author was the primary author of this published manuscript.

Table 5. Demographic and clinical characteristics of veterans with substance dependence and major depression (N = 201).

	TSF	ICBT
	<i>n</i> = 113	<i>n</i> = 129
Male	90.4 %	89.7 %
Caucasian	71.3 %	78.5 %
Mean age (<i>SD</i>)	49.2 (7.6)	48.9 (7.8)
Mean years of education (<i>SD</i>)	13.6 (2.2)	13.4 (2.1)
Employed	21.3 %	16.0 %
Married	7.6 %	17.0 %
Alcohol dependence	86.7 %	91.9 %
Stimulant dependence	55.2 %	54.4 %
Cannabis dependence	28.7 %	31.1 %

TSF: Twelve-Step Facilitation; ICBT: Integrated Cognitive-Behavioral Therapy

Table 6. Results from unconditional latent growth curve models of 12-step affiliation and meeting attendance separately for Twelve-Step Facilitation and Integrated Cognitive-Behavioral Therapy.

	TSF		ICBT	
	Mean (SE)	Variance (SE)	Mean (SE)	Variance (SE)
12-step affiliation				
Latent intercept	2.54 (.15)***	1.74 (.46)***	1.86 (.13)***	1.15 (.23)***
Linear slope	-.61 (.15)***	1.11 (.37)**	-.06 (.03)	.01 (.02)
Quadratic slope	.11 (.03)**	.05 (.02)*	-	-
12-step attendance				
Latent intercept	.44 (.03)***	.07 (.02)**	.26 (.03)***	.05 (.01)***
Linear slope	-.13 (.02)***	.006 (.01)	-.002 (.008)	.002 (.001)
Quadratic slope	.02 (.005)***	.000 (.001)	-	-

TSF: Twelve-Step Facilitation; ICBT: Integrated Cognitive-Behavioral Therapy

* $p < .05$, ** $p < .01$, *** $p < .001$.

Table 7. Results from latent growth curve models of percent days drinking and percent days using drugs from Month 6 (End of treatment) to Month 18 for veterans with substance dependence and major depression.

	% Days Drinking		% Days Using Drugs	
	Intercept	Slope	Intercept	Slope
Unconditional model				
Mean	8.70***	0.99*	3.28***	0.46
Variance	217.67***	20.45***	74.78***	5.61***
Conditional models				
	b or r (SE)	b or r (SE)	b or r (SE)	b or r (SE)
Treatment group (TSF vs. ICBT)	-.10	.20*	-.002	.09
12-step affiliation model				
Treatment group (TSF vs. ICBT)	-.10	-.15	-.003	-.07
12-step affiliation intercept	-.40***	.25	-.09	-.03
12-step affiliation slope	.57*	-.93**	.14	-.43
12-step attendance model				
Treatment group (TSF vs. ICBT)	-.10	-.07	-.003	-.08
12-step attendance intercept	-.29**	.10	-.09	-.05
12-step attendance slope	.37*	-.63**	.26	-.42

TSF: Twelve-Step Facilitation; ICBT: Integrated Cognitive-Behavioral Therapy

* $p < .05$, ** $p < .01$, *** $p < .001$.

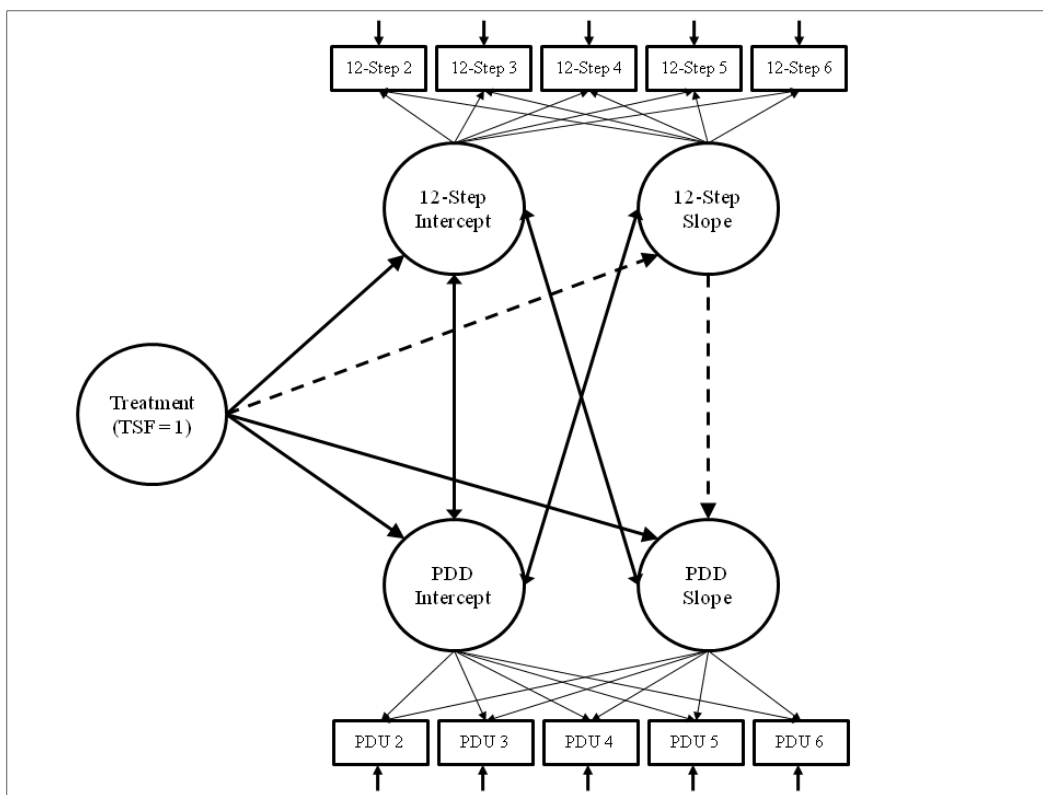


Figure 2. Latent growth curve mediation model with treatment group predicting post-treatment change in 12-step involvement, which in turn predicts post-treatment change in percent days drinking (PDD). Dotted line represents mediation path.

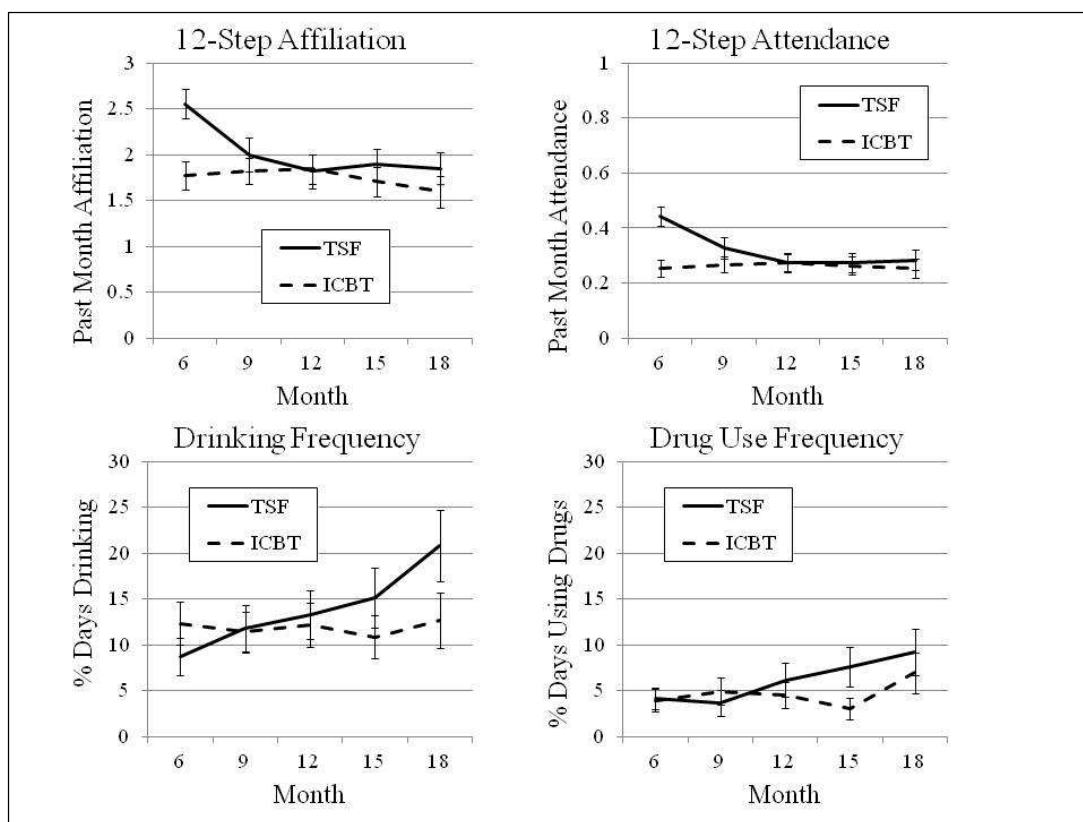


Figure 3. Group means of 12-step affiliation, 12-step attendance, drinking frequency, and drug use frequency for Twelve-Step Facilitation (TSF) and Integrated Cognitive-Behavioral Therapy (ICBT).

Study 3

Among adults with substance use disorders (SUDs) major depressive disorder (MDD) is the most common co-occurring Axis I psychiatric disorder, affecting a large percentage of those diagnosed with alcohol (22%) or drug (40%) dependence (Grant et al., 2004). Individuals with substance dependence and MDD typically have more severe psychopathology as MDD is associated with prolonged course of dependence (Hasin et al., 2002), greater treatment costs (Druss & Rosenheck, 1999; Mark, 2003), and greater risk of suicide (Bolton, Pagura, Enns, Grant, & Sareen, 2010b; Glasner-Edwards et al., 2008). The high prevalence of co-occurring MDD is also reflected in substance dependence treatment settings, with estimates ranging from 26-67% (Lynskey, 1998). Although many adults with co-occurring MDD do benefit from alcohol/drug treatment, they typically have worse outcomes than those without MDD (Curran et al., 2000; Gamble et al., 2010; Glasner-Edwards, Marinelli-Casey, Hillhouse, Ang, Mooney, Rawson, et al., 2009; Ilgen & Moos, 2005). Despite these high prevalence rates and strong evidence of poorer treatment outcomes, few research studies have examined processes that predict post-treatment substance use within this population.

Studies examining mechanisms of substance use treatment outcomes have not typically selected individuals with co-occurring psychiatric conditions, but have identified variables that likely translate to those with SUDs and MDD. As recognized by recent reviews, self-efficacy is a key construct involved in maintenance of abstinence following treatment for substance dependence (Kadden & Litt, 2011), and is one of the most potent predictors of substance use treatment outcomes (Adamson et al., 2009). Typically defined as the confidence/belief that one can resist using substances in high-

risk situations, abstinence self-efficacy has consistently predicted treatment outcomes for both alcohol (Maisto, Connors, & Zywiak, 2000) and drug users (Litt et al., 2005; McKay et al., 2005), in both inpatient/residential and outpatient settings (Allsop, Saunders, & Phillips, 2000; Dolan, Martin, & Rohsenow, 2008; Ilgen, McKellar, & Tiet, 2005; Maisto, Clifford, Stout, & Davis, 2008). Studies also suggest enhanced self-efficacy is a common therapeutic element across treatment models as diverse as Alcoholics Anonymous (Kelly et al., 2012), cognitive-behavioral therapy (Long, Williams, Midgley, & Hollin, 2000), and motivational enhancement therapy (LaChance, Feldstein Ewing, Bryan, & Hutchison, 2009). Overall, these studies indicate self-efficacy has a critical role in long-term treatment outcomes in substance-dependent population.

The role of social network characteristics in managing SUDs following treatment has also received considerable attention. As reducing contacts with users and developing sober relationships is frequently a component of treatment, of particular interest is whether the level of use in one's social network actually predict post-treatment drinking and drug use. This has largely been supported in studies of alcohol users, as the overall frequency of drinking in the network, the proportion of network members abstinent, and the proportion of heavy drinkers in the network have all predicted post-treatment drinking (Bond, Kaskutas, & Weisner, 2003; Litt et al., 2007; Longabaugh, Wirtz, Zywiak, & O'Malley, 2010). Network effects on drug use have not been studied in the context of formal treatment, but observational studies of drug users have had similar findings (Latkin, Knowlton, Hoover, & Mandell, 1999; Schroeder et al., 2001). Overall, these studies suggest social network characteristics could be a critical determinant of post-treatment use for patients with substance dependence and MDD.

Despite extensive study of self-efficacy and social networks in general treatment samples, it is relatively unknown whether these process variables hold the same benefit for patients with SUDs and MDD, or if these patients can sustain self-efficacy and supportive social networks following formal treatment. However, some previous studies generally support the value of self-efficacy and social support among patients with SUDs and co-occurring mental health disorders. Among residential treatment patients with substance dependence and mixed co-occurring disorders including MDD, baseline self-efficacy and general social support predicted six month substance use (Warren, Stein, & Grella, 2007a), and at follow-up self-efficacy was significantly associated with alcohol use (Bradizza et al., 2009). Among participants of dual-focus self-help groups, social support for abstinence mediated relations between greater group attendance and future substance use (Laudet et al., 2004), while greater self-efficacy predicted greater quality of life (Magura, Cleland, Vogel, Knight, & Laudet, 2007). While these findings are promising, no known study has examined longitudinal, prospective effects of self-efficacy or social networks on substance use following outpatient, professional psychotherapy for substance dependence and MDD. Other treatment process variables were found to be less potent or more difficult to sustain for patients with MDD (Kelly et al., 2003), which highlights the need to systematically evaluate effects of self-efficacy and social networks in patients with substance dependence and MDD.

Investigations of treatment outcome should also consider moderators of process variable effects (Kadden & Litt, 2011; Longabaugh & Magill, 2011). Within our sample, a potential moderator is living in environments that explicitly constrain alcohol/drug use, either via restricted access to substances (e.g., prison, inpatient treatment) or strong

contingencies against using (e.g., sober living homes, halfway houses). Studies demonstrate that placement into halfway houses does achieve the intended effects of reducing substance use or achieving treatment milestones (Greenwood, Woods, Guydish, & Bein, 2001; Hitchcock, Stainback, & Roque, 1995; Polcin, 2009). Because substance use is (in principle) more constrained by these environments, intrapersonal and interpersonal mechanisms like self-efficacy and social networks may be less crucial for individuals living in these “controlled contexts”. Investigation of these contextual effects is especially relevant for patients with substance dependence and MDD, who are especially likely to utilize residential or inpatient services (Druss & Rosenheck, 1999). The moderating role of context has scarcely been investigated, but in one prior study the effects of the client-provider relationship on substance use were weaker for those in residential treatment (Shin, Marsh, Cao, & Andrews, 2011). Thus, it is possible that controlled contexts moderate self-efficacy and social network effects, but to our knowledge no previous studies have investigated these relationships.

The overall goal of this study was to examine prospective effects of self-efficacy and social network variables, the effects of controlled context, and their interactions in the prediction of posttreatment substance use for veterans with substance dependence and MDD. Study participants received six months of either group Twelve-Step Facilitation (TSF) or Integrated Cognitive-Behavioral Therapy (ICBT) for treatment of alcohol or drug dependence and MDD. Previous reports of this sample found that both groups increased in substance use during the one-year follow-up, with the ICBT group having comparatively less increase (Lydecker et al., 2010; Worley et al., 2012). Self-efficacy change was similar in both groups and predicted substance use outcomes during

treatment (Glasner-Edwards et al., 2007). This study builds upon those findings by examining group differences and change over time in self-efficacy and substance-specific social network variables over the 12-months following treatment. We hypothesized that better post-treatment substance use outcomes would be predicted by greater self-efficacy and lower network substance use. Furthermore, we hypothesized that greater time in controlled context would be associated with lower alcohol/drug use, and that controlled context would moderate the effects of self-efficacy and network substance use on future drinking and drug use.

Methods

Subjects

This study involved secondary data analysis of veterans participating in a trial of outpatient group psychotherapy for co-occurring substance dependence and MDD (Brown et al., 2006; Lydecker et al., 2010), conducted at the San Diego Veterans Affairs Healthcare System (SDVAHS). Participants met DSM-IV criteria for lifetime dependence on alcohol (92%), cannabis (30%), or stimulants (55%) with recent use, and DSM-IV criteria for MDD with at least one depressive episode occurring during a 3-month period of abstinence from substances. Exclusion criteria included dependence on opiates with intravenous administration, bipolar or psychotic disorder, living excessively far (≥ 50 miles) from the SDVAHS, or severe memory impairments limiting recall in assessments. With our current focus on the post-treatment period, we included all veterans ($N = 201$) completing at least one assessment from end-of-treatment (Month 6) to the one-year follow-up (Month 18).

The sample averaged 49 years of age ($SD = 7.67$) and was mostly (90%) male, with 75% reporting Caucasian ethnicity, 12% African-American, 8% Hispanic, and 4% other ethnicity. At intake few were currently working (18.5%) or married (12%). During the 90 days prior to intake 84% of the sample had used alcohol and 49% had used other drugs, and the average intake Hamilton Depression score was 28, indicative of severe depressive symptoms.

Procedures

The University of California, San Diego and VASDHS Institutional Review Boards approved the procedures for this study, which were explained in greater detail previously (Brown et al., 2006; Glasner-Edwards et al., 2007; Lydecker et al., 2010) and are described briefly here. Study staff received referrals from the VASDHS dual diagnosis clinic, contacted veterans to conduct brief screenings, and met with eligible veterans to explain the procedures and obtain informed consent. Study participants consented to 6 months of group psychotherapy and 12 months of quarterly follow-up assessments, recording of group sessions, psychotropic medication management appointments, random toxicology screens, and review of electronic medical records. All participating veterans consented to receive no additional formal treatment for substance use or depression for the duration of the treatment phase except for the psychotherapy and pharmacotherapy of the study, while participation in other formal interventions was allowed during follow-up. Peer or community based therapeutic activities (e.g., 12-step meetings) were not restricted.

Treatments

Veterans entered into group psychotherapy on a rolling basis, with start dates occurring every 2 weeks. After completing the intake assessment, veterans were sequentially allocated to the treatment condition with the next start date. Both interventions were manualized and were 6 months in duration, with twice-weekly sessions for 3 months followed by weekly sessions for the final 3 months. Group sessions were co-delivered by a senior clinician (e.g., licensed clinical psychologist, post-doctoral fellow) and doctoral trainee who were trained to criterion via manual review, direct observation, and weekly review and supervision. The protocol for Twelve-Step Facilitation (TSF) was modified from TSF in Project MATCH (Group, 1997) for group delivery and targeting both drugs and alcohol. The Integrated Cognitive-Behavioral Therapy (ICBT) intervention was developed by adapting material from two empirically-supported treatments: cognitive-behavioral relapse prevention from Project MATCH (Kadden, 1995) and group cognitive-behavioral therapy for depression (Muñoz & Ying, 1993). Both treatments were identically structured with a series of three modules, with each module covering a broad content area specific to 12-step (e.g., Steps 1-3) or cognitive-behavioral (e.g., modifying thoughts) principles. Each topic was introduced over a one-month block for the first 3 months of treatment, with review occurring in the final 3 months. Mean session attendance was not significantly different between TSF and ICBT ($M = 22$ of 36 possible sessions). All veterans were offered pharmacotherapy management with VA physicians. Nearly all (99.5%) utilized medication management, with a mean attendance of 4.61 visits during treatment and 4.79 visits during follow-up.

Measures

Except for demographic and clinical covariates obtained at intake, all measures utilized in this study were obtained at end-of-treatment (Month 6) and at 3-month intervals until the one-year follow-up (Month 18). Summary statistics for each variable at each time point are provided in Table 8.

Frequency of alcohol and drug use. We assessed substance use with the Timeline Follow-Back (TLFB (Sobell & Sobell, 1992), a reliable and valid calendar-assisted interview (Maisto et al., 1982) which was modified to include eight drug types. At each quarterly assessment the TLFB was used to separately measure alcohol and drug use during the prior 90 days. Primary outcome variables derived from the TLFB were percent days drinking (PDD) and percent days using drugs (PDDRG).

Self-efficacy. Self-efficacy for coping with high-risk situations was measured with the Drug-Taking Confidence Questionnaire (Sklar, Annis, & Turner, 1997), a 50-item self-report measure of perceived ability to resist using alcohol or drugs across a variety of situations (e.g., negative emotions, pleasant times, social pressure to use). On each item respondents rated their perceived confidence on an ordinal scale (0 = 0%, 1 = 20%, 2 = 40%, 3 = 60%, 4 = 80%, 5 = 100%), and the average across all items was used as the self-efficacy score.

Social network variables. Social network variables were assessed with the Social Support Questionnaire (Sarason, Levine, Basham, & Sarason, 1983), modified with supplementary questions to assess the use patterns of each support. Respondents identified members of their social support system (e.g., romantic partners, friends, family) and reported the alcohol and drug use pattern of each member on an ordinal scale (1 = Nonuser/abstainer, 2 = Infrequent user, 3 = Regular use, 4 = Possible abuser, 5 =

Abuser). Variables utilized in this study were mean network use (average use across all network members), the proportion of network abstinent, and the proportion of network regularly using. Each of these variables have previously been utilized in studies of social network effects (Bond et al., 2003; Litt et al., 2007; Longabaugh et al., 2010) and were computed separately for alcohol and drugs.

Controlled context. A structured interview captured the veterans' specific living environment for each assessment period, which was supplemented with information from VA electronic medical records. Controlled contexts were defined as environments restricting access to alcohol/drugs, and included all inpatient admissions, jails, crisis homes, and recovery homes. The variable used in analyses was the percentage of each three-month assessment period spent in controlled contexts.

Statistical Analysis

We utilized hierarchical linear modeling (HLM) to examine process variables, controlled context, and their interaction in the prediction of post-treatment alcohol and drug use. The use of HLM was preferred for this study due to inclusion of multiple time points nested within individuals, use of both static and time-varying covariates/predictors, and inclusion of all available data via maximum likelihood estimation. Maximum likelihood estimation is preferred when data contain missing values assumed missing-at-random (Schafer & Graham, 2002), and no significant differences were found any study variables between those with complete data and those with any missing data, supporting this assumption. With the exception of group and time effects, all predictor variables were grand-mean centered prior to inclusion in analyses. All statistical analyses were performed in Stata 10.1 (StataCorp, 2007).

In preliminary models we examined static predictors of PDD and PDDRG to control for potential confounding variables (e.g., baseline severity, demographics), and then tested effects of treatment group, time, and the group x time interaction to model group differences in these outcomes. To examine group differences and time effects for self-efficacy, social network, and controlled context, these variables were analyzed as outcomes in HLM with group, time, and group x time as predictors. To examine prospective relations between process variables and substance use, lagged (prior wave) self-efficacy and each social network variable were used as time-varying predictors of PDD and PDDRG in HLM. Each social network variable was substance-specific (e.g., percent-network drinking to predict PDD, percent-network using drugs to predict PDDRG). For these longitudinal analyses with time-varying covariates, the repeated measures contain confounded information about between-person and within-person differences, and disaggregation of these effects has been recommended when dictated by substantive interest (Curran & Bauer, 2011). In this study, both effects were of interest: between-person differences (e.g., persons greater in self-efficacy generally) or within-person differences (e.g., spikes/drops in self-efficacy within persons) could predict future substance use. To disaggregate the between- and within-person effect, raw scores were de-composed into two variables representing the person-mean (between-effect) and time-specific deviations from the person mean (within-effect), and both variables were included in HLM to examine independence of these effects. To examine effects of controlled context, the controlled context variable was entered as a time-varying covariate of current PDD and PDDRG. The final HLMs examined interactions of lagged process variables (between- and within-effects) with concurrent controlled context, to

examine whether controlled context moderated effects of lagged process variables on PDD and PDDRG.

Results

Substance use outcomes over time

Prior to testing core hypotheses, preliminary HLMs examined intake covariates of post-treatment PDD and PDDRG. Greater years of education predicted lower PDD ($b = -2.71, p < .001$), being employed predicted lower PDDRG ($b = -0.90, p = .04$), and pretreatment frequency of use predicted PDD ($b = 0.28, p < .001$) and PDDRG ($b = 0.21, p < .001$). Models examining effects of treatment group, time, and the group x time interaction revealed that PDD and PDDRG increased significantly following treatment, independent of treatment group. Furthermore, the group x time interaction was statistically significant for PDD, replicating the previous findings of relatively greater increase in substance use in the TSF group during follow-up (Lydecker et al., 2010; Worley et al., 2012). All subsequent models of PDD and PDDRG accounted for these significant covariate effects.

Group differences and change over time in process variables and context

By testing effects of treatment group, time, and the group x time interaction in HLM, the next series of models examined group differences in mean levels, change over time, and group differences in change over time in self-efficacy, social network variables, and controlled context during the 12-month post-treatment follow-up. As shown in Table 9, estimates of variance components revealed significant variability at both the between-individual and within-individual level for self-efficacy and social network variables, justifying the use of HLM and disaggregation of these effects. A significant group x time

interaction was found for social support for drug use ($b = 0.02$, $SE = 0.008$, $p < .05$), percent-network abstinent from drugs ($b = -0.75$, $SE = 0.31$, $p < .05$), and percent-network using drugs ($b = 0.54$, $SE = 0.25$, $p < .05$). Inspection of means revealed that at month 6 the TSF group had relatively greater percent-network abstinent from drugs, with lower levels of mean network drug use and percent-network using drugs. However, during follow-up the ICBT group had relatively greater increases in percent-network abstinent, and greater decreases in mean-network drug use and percent-network using drugs. Effects of group, time, and group $\times$ time were not statistically significant for self-efficacy or the remaining social network variables. Overall the two treatment groups had few differences on process variables, with the exception of social network drug use. Finally, the effect of time was negative and statistically significant for controlled context ($b = -1.18$, $SE = 0.19$, $p < .001$), indicating an overall decrease over time in the proportion of time spent in controlled contexts, a trend that did not differ between treatment groups.

Relations between process variables, controlled context, and substance use

We then examined whether self-efficacy and social network variables prospectively predicted post-treatment alcohol and drug use. Separate HLMS for each process variable tested associations with substance use outcomes (PDD, PDDRG), controlling for previously mentioned covariates. Each time-varying predictor was lagged (e.g., prior wave score) and decomposed into two distinct variables (the person-mean and within-person deviations) to disaggregate between-person and within-person effects on PDD and PDDRG. Social network variables were substance-specific, with network drinking predicting PDD and network drug use predicting PDDRG. Results of these

models are displayed in Table 10. With one exception (percent-network abstinent from drugs), all between-person effects were statistically significant. Individuals who had greater levels of self-efficacy had lower PDD and PDDRG during follow-up. Moreover, individuals with social networks characterized by lower mean use and a lower percentage of regular users had lower PDD and PDDRG during follow-up, and those with greater percent-network abstinent from drinking had lower PDD. For within-person effects, greater mean network drinking and greater percent-network drinking predicted PDD, indicating that fluctuations from the person- mean in these variables predicted drinking in the next 3 months.

We then determined whether the amount of time spent in controlled contexts was associated with post-treatment substance use. These HLMs tested the time-varying effect of controlled context on concurrent PDD and PDDRG, controlling for identical covariates as previous models. The results, displayed in Table 10, indicate that a greater proportion of time spent in controlled contexts was associated with significantly lower PDD and PDDRG during these same periods. At month 18 (12 months after treatment) veterans with 0% days controlled had an estimated PDD of 18.19. Estimated PDD was lower (15.96) for those at the mean of controlled context (19% days), and even lower (11.75) for those 1 standard deviation above the mean (55.96% days). These results confirmed that the percentage of time spent in controlled contexts was significantly and negatively associated with frequency of current substance use.

Final models included interactions between lagged process variables (between and within effects) and controlled context, to test hypotheses that percent-days in controlled context would moderate the effects of lagged process variables on PDD and

PDDRG. As displayed in Table 10, between-person effects for each social network drinking variable interacted significantly with controlled context to predict future PDD. Also, between-person effects for mean network drug use and percent-network regularly using drugs interacted with controlled context to predict future PDDRG. As displayed in Figure 1, social network effects on future PDD and PDDRG were weaker when time in controlled context was high. Controlled context did not significantly moderate self-efficacy or within-person effects. Overall, these results indicate that social network characteristics of veterans with substance dependence and MDD predicted future drinking and drug use, but these predictive effects were weakened when veterans lived in controlled contexts for extended periods of time.

Discussion

Prior studies of determinants of post-treatment substance use have not typically focused on individuals with SUDs and co-occurring psychiatric disorders, despite high rates of these co-occurring disorders in many clinical settings (Chi et al., 2006; Lynskey, 1998). Co-occurring MDD is particularly common, and individuals with SUD and MDD typically have poorer outcomes following treatment (Gamble et al., 2010; Glasner-Edwards et al., 2009; Mark Ilgen & Moos, 2005) and may receive less benefit from therapeutic mechanisms of change (Kelly et al., 2003). Because they represent a large proportion of patients receiving substance dependence treatment and have a greater risk of poor outcomes, it is critically important to examine determinants of post-treatment substance use within this population. In a sample of veterans who had received group outpatient psychotherapy for substance dependence and MDD, we examined self-efficacy

and network substance use, the effects of controlled contexts, and their interaction in the prediction of post-treatment drinking and drug use.

In this sample with substance dependence and MDD, individuals with greater self-efficacy had lower future drinking and drug use during the year following treatment. Self-efficacy has predicted post-treatment use across various substances and treatment settings (Kadden & Litt, 2011), and our study extends these findings to patients with substance dependence and MDD. By separating the between-person and within-person components of self-efficacy, we demonstrated that generally maintaining higher self-efficacy was protective against future substance use, while time-specific fluctuations in self-efficacy were less critical. Prior studies with this sample revealed that baseline self-efficacy predicted time to relapse (Brown et al., 2006) and self-efficacy increased significantly during treatment (Glasner-Edwards et al., 2007). Our results were encouraging in finding that during the year following treatment, self-efficacy did not decrease significantly and continued to predict substance use. Moreover, post-treatment self-efficacy was similar between ICBT and TSF, suggesting that self-efficacy can be sustained similarly following cognitive-behavioral or professionally-led, 12-step based interventions, replicating prior research (Finney et al., 1998). Our results support the value of abstinence self-efficacy for patients with substance dependence and MDD, and provide a strong rationale for investigating factors related to increasing self-efficacy within this population.

Substance-specific social network variables were also predictive of post-treatment substance use. For both alcohol and drugs, future frequency of use was lower for individuals who generally had 1) lower average network use and 2) a lower proportion of

regular users in their network. Furthermore, having a network with a greater density of nondrinking individuals predicted lower future drinking. These social network characteristics have previously predicted drinking outcomes in alcohol-dependent samples (Bond et al., 2003; Litt et al., 2007; Longabaugh et al., 2010), but our study is first to demonstrate these findings in patients with substance dependence and MDD. Social network effects at the within-person level were also predictive of substance use. More specifically, when individuals had increases from their own norm of average network drinking or proportion of regular drinkers, they drank more frequently in the future. It is likely that these interpersonal factors operate in multiple ways to influence future drinking (Hunter-Reel, McCrady, & Hildebrandt, 2009). The presence of alcohol or other drinkers represent conditioned cues that elicit craving or other precipitants to drinking, and associating with drinkers may increase exposure to substances or undermine patients' sobriety efforts via changes in outcome expectancies. Treatment protocols designed explicitly to change social networks have demonstrated long term efficacy in the treatment of alcohol dependence (Litt et al., 2007; Litt et al., 2009). These interventions have not been tested in patients with co-occurring psychiatric disorders, and our study suggests these interventions could be effective in patients with substance dependence and MDD.

This study also found that post-treatment substance use depended on the level of constraint in the living environment. During follow-up over half of our sample (56%) had some time in "controlled contexts" (e.g., sober living homes, inpatient treatment, jail) at an average of 39% of days in these environments. As hypothesized, when patients spent a greater percentage of time in controlled contexts defined by limited access to substances

or negative consequences for use, they had lower frequency of drinking and drug use. Moreover, controlled context acted as a moderator, such that social network influences were more predictive of future alcohol and drug use when the environment did not restrict. Social network effects were attenuated for veterans at the highest levels of controlled context, suggesting these contexts do assist in buffering against the maladaptive influence of substance use within the network. Research indicates that patients with substance dependence and MDD are especially likely to utilize inpatient/residential services (Druss & Rosenheck, 1999). The role of environment is rarely examined in treatment outcome studies, which is surprising given theoretical interest in considering intrapersonal and interpersonal processes within environmental context (Witkiewitz & Marlatt, 2004). Our results suggest the level of constraint in the environment is an important construct to consider in future studies. While some controlled contexts may have resulted from adverse events (e.g., arrests, suicide attempts), the most common contexts utilized were residential sober living facilities. Our results suggest patients with substance dependence and MDD who cannot sustain more protective social networks may benefit most from these constrained environments.

While this study has important research and clinical implications, its limitations should be noted. The immediate generalizability of these findings is limited due to the demographic characteristics of this veteran sample, which was heavily comprised of Caucasian males. While this is a common limitation of many clinical trials of treatments for addictive disorders (Kelly et al., 2010), replication in more diverse samples is needed before broader generalizations can be made. Our social network measure did not capture important features of social support examined in prior studies (Litt et al., 2007), such as

whether network members were supportive of our patients' abstinence efforts. Furthermore, network members' use patterns were reported as perceived by study participants, and may not be a completely accurate assessment of their substance use patterns. While the effects of controlled contexts were in the expected direction, context alone may not fully explain our findings as this variable could be confounded with other unmeasured characteristics (e.g., recent acute medical event, arrest or parole) that are also strong determinants of abstinence. While this study identified variables that predict post-treatment substance use in adults with co-occurring substance dependence and MDD, underlying mechanisms have not yet been identified, which would explain how patients sustained greater levels of self-efficacy and lower levels of network substance use. As such, it will be important for future studies to explore whether specific processes of treatment assist patients in maintaining greater levels of these proximal variables following the conclusion of formal intervention.

Study 3 has been submitted for publication in *Alcoholism: Clinical and Experimental Research*, as following: Worley, M.J., Tate, S.R., & Brown, S.A. Self-efficacy, social networks, and the moderating effects of context following treatment for co-occurring substance dependence and depression. The dissertation author was the primary author of this manuscript under review.

Table 8. Descriptive statistics of substance use, self efficacy, and social network variables following treatment of veterans with substance dependence and major depression (N = 201).

	Month				
	6	9	12	15	18
	M (SD)	M (SD)	M (SD)	M (SD)	M (SD)
Percent days drinking					
TSF	3.70 (1.03)	3.63 (1.21)	3.64 (1.19)	3.58 (1.27)	3.42 (1.30)
ICBT	3.63 (1.20)	3.68 (1.20)	3.64 (1.24)	3.55 (1.33)	3.57 (1.31)
Percent days using drugs					
TSF	3.70 (1.03)	3.63 (1.21)	3.64 (1.19)	3.58 (1.27)	3.42 (1.30)
ICBT	3.63 (1.20)	3.68 (1.20)	3.64 (1.24)	3.55 (1.33)	3.57 (1.31)
Self-efficacy					
TSF	3.70 (1.03)	3.63 (1.21)	3.64 (1.19)	3.58 (1.27)	3.42 (1.30)
ICBT	3.63 (1.20)	3.68 (1.20)	3.64 (1.24)	3.55 (1.33)	3.57 (1.31)
Average network drinking ^a					
TSF	2.35 (0.91)	2.41 (0.96)	2.43 (1.08)	2.50 (1.11)	2.26 (0.99)
ICBT	2.34 (1.01)	2.43 (1.07)	2.44 (1.08)	2.43 (1.03)	2.34 (1.01)
Average network drug use ^a					
TSF	1.90 (0.50)	1.84 (0.48)	1.86 (0.71)	1.86 (0.56)	1.88 (0.73)
ICBT	2.03 (0.98)	1.96 (0.85)	1.84 (0.69)	1.93 (0.76)	1.93 (0.54)
Network abstinent from alcohol (%)					
TSF	65.12 (36.00)	59.52 (36.23)	65.41 (37.54)	63.38 (37.72)	63.84 (37.79)
ICBT	64.44 (34.78)	60.78 (35.30)	61.97 (37.20)	63.02 (35.53)	67.72 (35.08)
Network abstinent from drugs (%)					
TSF	93.34 (15.89)	95.39 (17.19)	94.61 (16.47)	95.51 (13.73)	90.82 (21.55)
ICBT	87.69 (26.97)	90.02 (20.95)	95.85 (15.17)	91.54 (23.23)	94.83 (14.74)
Network regularly drinking (%)					
TSF	21.55 (29.05)	21.32 (30.24)	25.70 (35.11)	26.74 (36.57)	20.83 (32.22)
ICBT	20.88 (31.10)	22.41 (28.12)	21.74 (31.89)	21.75 (29.12)	18.58 (29.12)
Network regularly using drugs (%)					
TSF	3.46 (9.61)	1.16 (6.47)	4.08 (15.31)	4.49 (13.73)	4.20 (14.79)
ICBT	9.44 (24.62)	6.71 (16.79)	3.28 (14.14)	6.59 (22.36)	4.45 (13.71)

Note. TSF: Twelve-Step Facilitation; ICBT: Integrated Cognitive-Behavioral Therapy.

^a 1 = Nonuser/abstainer, 2 = Infrequent user, 3 = Regular use, 4 = Possible abuser, 5 = Abuser.

Table 9. Effects of treatment group, time, and group x time interactions on self-efficacy, social network variables, and controlled context.

	Unconditional Model		Model 1		Model 2		
	σ^2 - between	σ^2 -within	Group	Time (months)	Group	Time (months)	Group X Time
Self-efficacy	0.74***	0.73***	0.03	- 0.01	0.18	-0.003	- 0.01
Average network use							
Drinking	0.38***	0.32***	0.03	- 0.002	- 0.09	- 0.007	0.01
Drug use	0.18***	0.16***	- 0.07	- 0.008	- 0.29*	- 0.02**	0.02*
Percent of network abstinent							
Drinking	690.06***	623.81***	-1.64	0.17	3.32	0.37	- 0.42
Drug use	125.81***	257.71***	1.95	0.24	10.71**	0.60**	-0.75*
Percent of network using regularly							
Drinking	526.94***	478.17***	3.02	- 0.02	- 4.54	- 0.33	0.65
Drug use	123.17***	157.88***	- 2.67	- 0.15	- 9.09**	- 0.42*	0.55*
Controlled context	802.07***	585.12***	- 2.28	- 1.18***	6.13	- 0.85**	- 0.71

^a Ordinal scale (1 = Nonuser/abstainer, 2 = Infrequent user, 3 = Regular use, 4 = Possible abuser, 5 = Abuser).

* p < .05, ** p < .01, *** p < .001.

Table 10. Main effects of time-varying, lagged self-efficacy and social network variables and interactions with controlled context in predicting post-treatment alcohol and drug use.

	PDD		PDDRG	
	b (SE)	b (SE)	b (SE)	b (SE)
Lagged process variables	Between	Within	Between	Within
Self-efficacy	- 6.31 (1.33)***	- 1.65 (0.88)	- 2.71 (0.83)***	-0.35 (0.78)
Average network use ^a	6.19 (1.98)**	3.37 (1.44)*	3.83 (1.65)*	2.37 (1.73)
% of network abstinent	- 0.11 (0.05)*	- 0.05 (0.03)	- 0.09 (0.05)	- 0.05 (0.04)
% of network regularly using	- 0.17 (0.05)**	0.09 (0.04)*	0.13 (0.06)*	0.06 (0.05)
Controlled context × lagged:				
Self-efficacy	0.05 (0.03)	0.01 (0.02)	0.02 (0.02)	0.02 (0.02)
Average network use ^a	- 0.13 (0.04)**	0.01 (0.04)	- 0.15 (0.06)**	0.04 (0.06)
% of network abstinent	0.003 (0.001)**	- 0.001 (0.001)	0.003 (0.002)	-0.001 (0.001)
% of network regularly using	- 0.003 (0.001)**	0.0004 (0.001)	- 0.004 (0.002)*	0.001 (0.002)

^a Ordinal scale (1 = Nonuser/abstainer, 2 = Infrequent user, 3 = Regular use, 4 = Possible abuser, 5 = Abuser).

* p < .05, ** p < .01, *** p < .001.

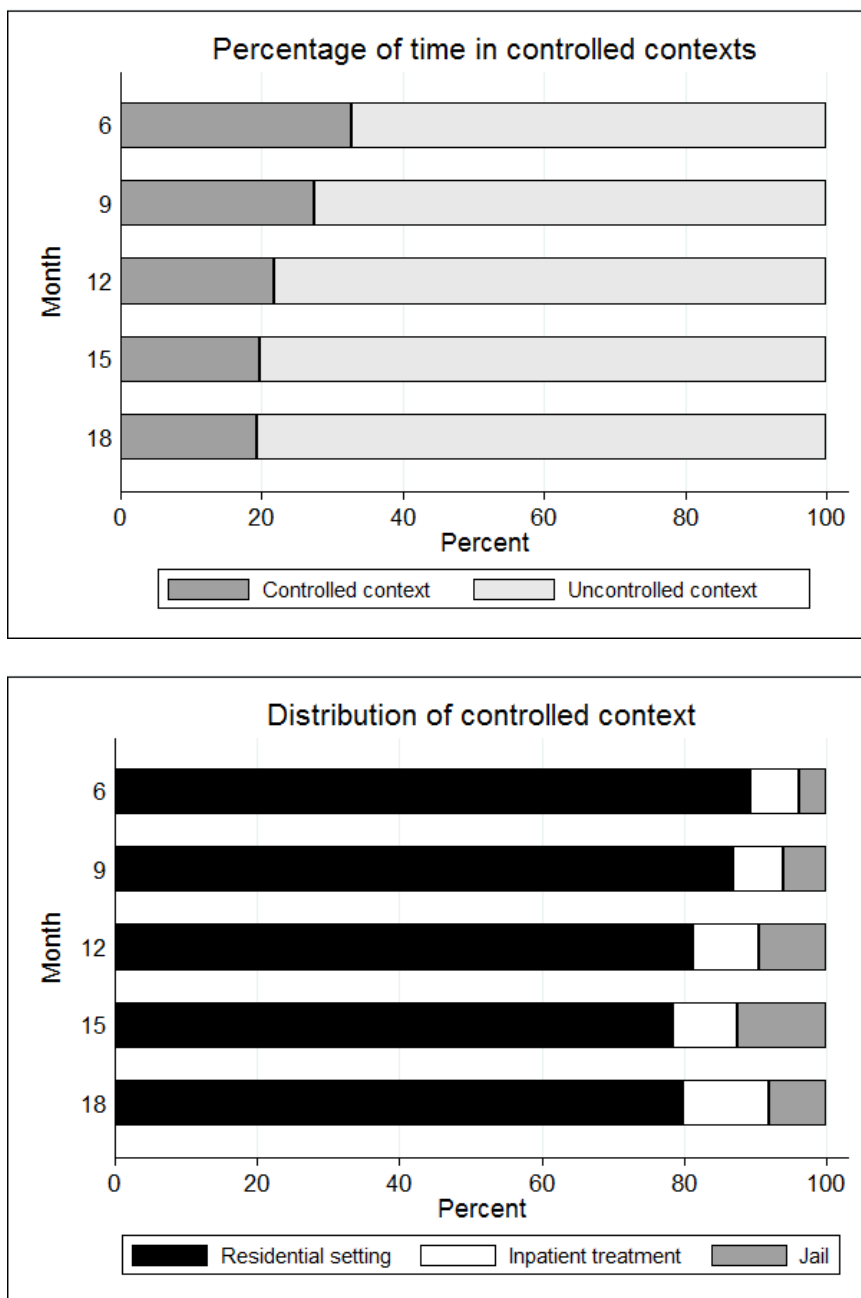


Figure 4. Percentage of time in controlled contexts and distribution of controlled settings at each month of follow-up.

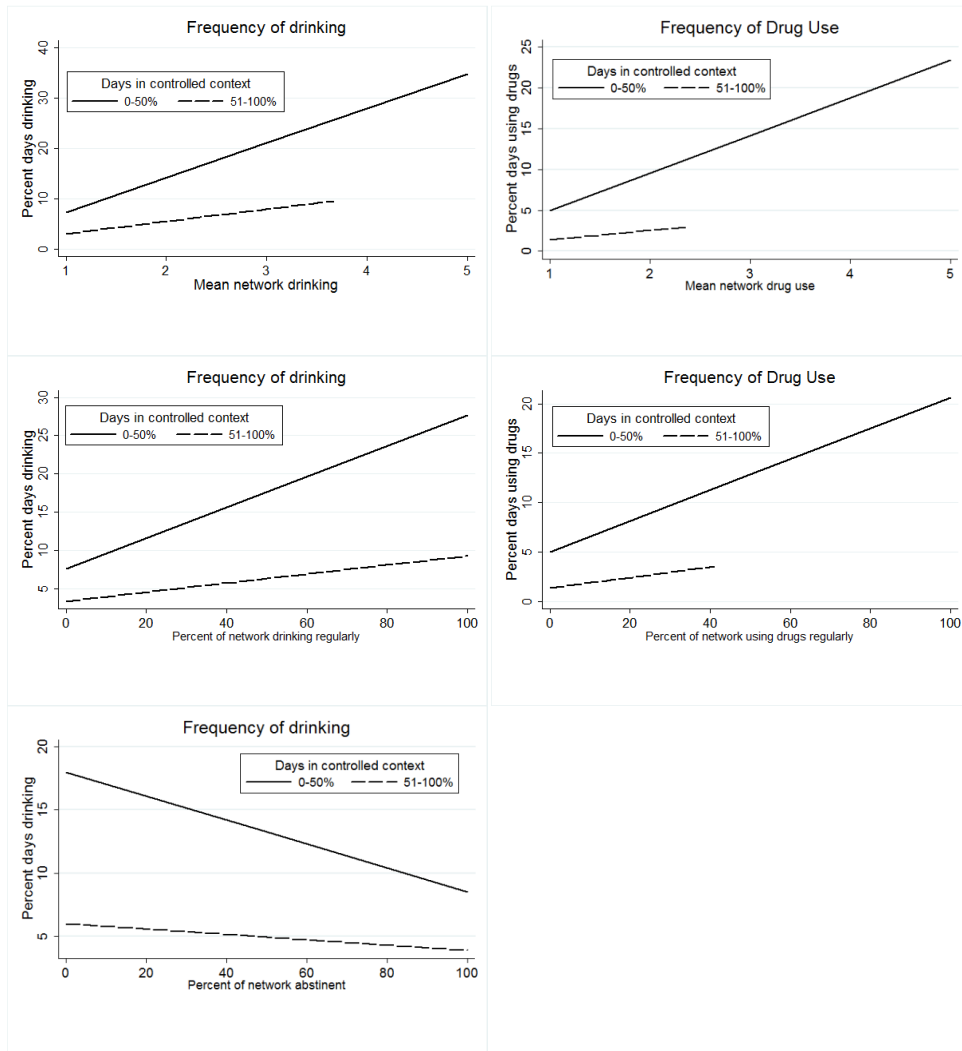


Figure 5. Significant interactions between social network variables and controlled context predict frequency of drinking and drug use during post-treatment follow-up.

Study 4

Many individuals with alcohol or drug dependence have deficits in neurocognitive abilities such as executive functioning and problem solving (Beatty, Tivis, Stott, Nixon, & Parsons, 2000; Tucker et al., 2004; Whitlow et al., 2004), verbal or non-verbal memory (Dawson & Grant, 2000; Lamers, Bechara, Rizzo, & Ramaekers, 2006), cognitive efficiency (Nixon, Paul, & Phillips, 1998), and attention (Solowij, Michie, & Fox, 1995; Solowij et al., 2002), whether these deficits are due to the neurotoxic effects of substance use, preexisting characteristics, or some combination of both (Adams et al., 1993; Braun & Richer, 1993). In clinical settings these deficits are especially prevalent as 30-80% of patients enter treatment with some neurocognitive impairment (Martin, Adinoff, Weingartner, Mukherjee, & Eckardt, 1986; Meek, Clark, & Solana, 1989; Omalley, Adamse, Heaton, & Gawin, 1992). Although modest recovery in neurocognition is possible, these changes are often not clinically significant (Bates et al., 2004; Bates, Voelbel, Buckman, Labouvie, & Barry, 2005) and many deficits do not remit even after periods of extended abstinence (Parsons, 1998). Because neurocognitive impairment is so common and persistent, there is a strong rationale for examining whether impairment relates to treatment outcomes within the substance-dependent population.

Another factor that may compound these neurocognitive deficits is the presence of other psychiatric conditions. Comorbid psychiatric disorders are common in the substance-dependent population (Grant et al., 2004), especially among patients in treatment settings (Chi et al., 2006; Lynskey, 1998). Major depression (MDD) is recognized as the most common Axis I condition, and patients with comorbid MDD typically have poorer outcomes from treatment for alcohol or drug dependence (Curran et

al., 2000; Gamble et al., 2010; Glasner-Edwards, Marinelli-Casey, Hillhouse, Ang, Mooney, Rawson, et al., 2009; Ilgen & Moos, 2005). Importantly, MDD is also associated with deficits in working memory, attention, verbal memory, verbal fluency, and processing speed (Elgamal, Denburg, Marriott, & MacQueen, 2010; Landro, Stiles, & Sletvold, 2001). Consequently, the joint effects of substance dependence and MDD on cognition may be worse than in either disorder alone, as with comorbid substance dependence and bipolar disorder (Levy, Monzani, Stephansky, & Weiss, 2008). Despite the prevalence of comorbid substance dependence and MDD and the deficits associated with both conditions, the effects of neurocognitive impairment in patients receiving treatment for substance dependence and MDD have not previously been examined.

Psychological treatments for substance dependence often require patients to learn and retain new information, inhibit prepotent responses, engage in future-oriented behavior, and plan behavioral coping strategies. Theoretically, patients with neurocognitive deficits would be less adept at internalizing and engaging in these skills, leading to poorer outcomes from psychotherapy. Some studies support this hypothesis, as patients with poorer cognitive functioning had greater substance use or lower retention in cognitive-behavioral therapy (Aharonovich, Brooks, Nunes, & Hasin, 2008; Aharonovich, Nunes, & Hasin, 2003; Jaffe et al., 1996). However, these effects have not been consistent across studies, as many investigations failed to find associations between neurocognition and substance use during or following treatment (Aharonovich et al., 2006; Teichner et al., 2002; Turner et al., 2009). While some methodological differences exist between these studies (e.g., measures of neurocognition), it is equivocal whether

cognitively-impaired patients have poorer outcomes from substance dependence treatment.

An important distinction within this literature is whether neurocognitive impairment is best examined as a direct predictor of outcome, or whether different model specifications are more ideal for testing relations with substance use (Bates et al., 2002). This notion is supported by studies demonstrating that impairment does not predict outcomes directly, but impacts substance use indirectly through therapeutic mechanisms of change. In independent studies lower self-efficacy was correlated with neurocognitive impairment (Morgenstern & Bates, 1999) and mediated the effects of impairment on drinking (Bates, Pawlak, Tonigan, & Buckman, 2006). Impairment also moderated the effects of self-efficacy and Alcoholics Anonymous (AA) affiliation, such that these variables were less predictive of substance use for impaired patients. Other studies support a moderating role of impairment (albeit in seemingly opposite direction), as the protective influence of frequent, positive social support at baseline was greater for patients with executive impairment (Buckman, Bates, & Cisler, 2007; Buckman, Bates, & Morgenstern, 2008). Each these studies employed “threshold” models of impairment as opposed to continuous measures, which may more sensitive to the level of cognitive disturbance required to significantly impact the process of psychotherapy. Our previous studies (Studies 1, 2, and 3 here) found that 12-step affiliation and self-efficacy predicted drinking in patients with substance dependence and MDD, but it is not known whether neurocognitive impairment relates to individual differences in these well-established therapeutic process variables, or moderates their effects on substance use for patients with psychiatric comorbidity.

Previous research also indicates negative affect is an important correlate of post-treatment substance use (Witkiewitz & Villarroel, 2009), especially for patients with comorbid MDD (Tomlinson et al., 2006; Worley et al., 2012). If neurocognitive deficits impact the course of depressive symptoms in patients with substance dependence and MDD, this is another pathway through which neurocognitive impairment may impact substance use. Previous research supports this pathway, as depression severity was linked to executive functioning (Taylor, Wagner, & Steffens, 2002), and fluid reasoning ability predicted reductions in depression among depressed, hazardous drinkers (Hunt et al., 2009). Also of interest is whether impairment moderates the effects of depressive symptoms on substance use. In studies of non-clinical samples the effect of depression on drinking was moderated by impulsivity (King, Karyadi, Luk, & Patock-Peckham, 2011) and distress tolerance (Buckner, Keough, & Schmidt, 2007), other neurobehavioral constructs that could relate to neurocognitive impairment in more severe, treatment-seeking patients. We previously found that greater depressive symptoms predicted greater future drinking in the current sample (Worley et al., under review). If impaired patients have worse acquisition of self-efficacy and coping skills as suggested in prior studies (Bates et al., 2006; Kiluk, Nich, & Carroll, 2011; Morgenstern & Bates, 1999), they may have exaggerated risk for drinking and drug use following periods of increased negative affect.

The overall goal of this study was to explore the impact of neurocognitive impairment on substance use treatment outcomes in patients with comorbid substance dependence and MDD. These aims are guided, in part, by recent models suggesting that substance use is a complex interplay of distal risk, proximal risks, intrapersonal

processes, and contextual factors (Witkiewitz & Marlatt, 2004), and that thorough investigations of therapeutic processes should examine intricate inter-relationships between these factors (Wirtz, 2007). Based on the literature reviewed thus far, we hypothesized that the effects of neurocognitive impairment on future drinking and drug use would be mediated by lower self-efficacy, lower 12-step affiliation and greater depressive symptoms. We also tested interactions between these proximal factors and neurocognitive impairment, expecting that impairment would moderate prospective relations between these variables and future substance use, and that moderating effects would be strongest during periods of increased negative affect.

Methods

Participants

This study included 197 veterans who completed neurocognitive testing prior to participation in a controlled trial of outpatient group psychotherapy for comorbid substance dependence and MDD (Brown et al., 2006; Lydecker et al., 2010). Inclusion criteria included a diagnosis of lifetime dependence on alcohol (91%), cannabis (29%), or stimulants (53%) with use in the past 90 days, and DSM-IV diagnosis of MDD, with at least one depressive episode occurring independently of substance use. Participants were excluded if they were using opiates with intravenously, had bipolar or other psychotic disorder, lived excessively far (> 50 miles) from the SDVAHS, or had severe memory impairments prohibiting accurate recall in assessments. The current sample averaged 49.3 years of age ($SD = 7.87$) and was mostly (90%) male and Caucasian (75%). At intake very few participants were working (17.9%) or married (12%). In the three months preceding the study 85% of the sample had used alcohol, with an average of 15.07 ($SD =$

13.56) drinks per drinking day, and 47% had used drugs. The average intake Hamilton Depression score was 28.35 ($SD = 10.65$), indicative of severe depressive symptoms.

Procedures

The procedures for this study were approved by the University of California, San Diego and VASDHS Institutional Review Boards and have been described in greater detail in prior publications (Brown et al., 2006; Glasner-Edwards et al., 2007; Lydecker et al., 2010) and are explained briefly here. Initial referrals from the VASDHS dual diagnosis clinic were first reviewed for eligibility. Research staff contacted veterans to conduct brief screenings before meeting with eligible veterans to explain procedures and obtain informed consent. Veterans consented to random allocation to group psychotherapy, assessment visits every three months during 6 months of treatment and 12 months of follow-up, recording of group sessions, random toxicology screens, psychotropic medication consultation, and review of electronic medical records. After completing the baseline assessment veterans were sequentially allocated to TSF or ICBT on an alternating, two-week rotation. For the duration of the group intervention provided in the study, veterans agreed to receive no other formal treatment for substance use or depression, while participation in other formal interventions was allowed during follow-up.

Because treatment group differences in long-term outcomes and process variables are not a focus of this study and have previously been published (Brown et al., 2006; Glasner-Edwards et al., 2007; Lydecker et al., 2010; Worley et al., under review), the treatments are described only briefly here. The manual for TSF (Group, 1997) was modified to allow group delivery and targeting both drugs and alcohol, while Integrated

Cognitive-Behavioral Therapy (ICBT) was developed by integrating cognitive-behavioral relapse prevention (Kadden, 1995) and group cognitive-behavioral therapy for depression (Muñoz & Ying, 1993). Group sessions occurred twice/week for three months and weekly thereafter (maximum of 36 sessions). Co-therapists were trained via manual review, direct observation, and weekly supervision, and rotated across conditions every 6-12 months. All participants scheduled pharmacotherapy appointments with VA physicians, and nearly all (99.4%) utilized medication management.

Measures

Measures utilized in this study include variables assessed at intake (Month 0) and at each 3-month interval until the one-year follow-up (Month 18). Rates of follow-up were generally high, decreasing from Month 3 (99%) to Month 18 (75%). Summary statistics for each variable at each time point are provided in Table 11.

Frequency of drinking and drug use. Alcohol and drug use was assessed with the Timeline Follow-Back (TLFB (Sobell & Sobell, 1992), a reliable and valid structured interview (Maisto et al., 1982). At each assessment the TLFB was used to separately capture alcohol and drug use since the prior assessment (90 day window). Outcome variables used in this study were percent days drinking (PDD) and percent days using drugs (PDDRG).

Self-efficacy. Self-efficacy for maintaining abstinence was measured with the Drug-Taking Confidence Questionnaire (Sklar et al., 1997), a 50-item self-report measure of confidence that one can resist the use of alcohol or drugs across a variety of high-risk situations. On each item respondents rate their perceived confidence on an ordinal scale

(0 = 0%, 1 = 20%, 2 = 40%, 3 = 60%, 4 = 80%, 5 = 100%), and the average across all items was used as the self-efficacy score Range = 0 – 5).

12-step affiliation. The Alcoholics Anonymous Affiliation Scale (Humphreys et al., 1998) was used to measure 12-step affiliation in the past month. A single ordinal item captures the number of 12-step meetings attended (0 = Zero, .25 = 1-10, .50 = 11-20, .75 = 21-20, 1 = $\geq$ 30), while 12-step behaviors are measured with four binary items (e.g., having a sponsor, reading literature, doing service, having a spiritual awakening). The 12-step affiliation score was the sum of the single attendance indicator and the 4 12-step behavior items (Range = 0-5).

Depressive Symptoms. Severity of depressive symptoms in the past week was assessed with the Hamilton Depression Rating Scale (Hamilton, 1960), a structured clinical interview previously validated with MDD (Knesevich et al., 1977) and substance-dependent populations (Willenbring, 1986). Reliability of the HAMD ranged from .78 to .85 across all assessments. The total of the 23-item measure was used as the depressive symptom score.

Neurocognitive Impairment. Our index of neurocognitive impairment was modeled after previous studies examining similar relationships in substance-dependent samples (Bates et al., 2006; Morgenstern & Bates, 1999). At the intake assessment participants were tested using neurocognitive measures with known sensitivity to common deficits in chronic, heavy substance users (Knight & Longmore, 1994; Weinstein & Shaffer, 1993). Neurocognitive tests and scores used were the Wechsler Adult Intelligence Scale III (WAIS-III) Digit Symbol and Block Design subtests (Wechsler, 1997), Halstead-Reitan Trail Making A and B subtest time to completion

(Heaton, Grant, & Matthews, 1991), Golden Stroop Color and Word test color-word interference score (Golden, 1978), Wisconsin Card Sorting Test perseveration errors (Heaton, Chelune, Talley, Kay, & Curtiss, 1993), California Verbal Learning Test II long delay recall (Delis, Kaplan, Kramer, & Ober, 2000), and Rey-Osterrieth Complex Figure test 30-minute delay (Rey, 1941). This general neurocognitive battery, while not fully comprehensive, assessed a broad array of neurocognitive domains including executive functioning, processing speed, and both verbal and non-verbal memory. For each of these eight tests raw scores were converted to *T*-scores on the basis of normative data adjusted for age (and gender and education when available). In our threshold model of “severe impairment”, performance on each test was designed as impaired when the score fell at least 1.5 standard deviations below the demographic-adjusted mean. The overall neurocognitive impairment score was the total number of tests on which performance was severely impaired (Range = 0-8).

Statistical Analysis

Analyses were structured to address our two overarching research questions: (1) whether effects of neurocognitive impairment on substance use were mediated by self-efficacy, 12-step affiliation, or depressive symptoms, and (2) whether impairment moderated relationships between these process variables and substance use outcomes. Hierarchical linear models (HLMs) are ideally suited for examining these questions in longitudinal data. By allowing random effects (e.g., intercepts and slopes) multiple time points nested within individuals can be analyzed in one analysis. Repeated measures of process variables can be included as time-varying predictors, and cross-level interactions can be specified to examine cross-level interactions between predictors at the between-

individual (impairment) and within-individual (self-efficacy) levels. All available data was included via maximum likelihood estimation, a preferred method for handling missing data when assumed missing-at-random (Schafer & Graham, 2002). Although in practice this assumption cannot be fully confirmed, we found no significant differences on study variables between participants with complete data vs. those with any missing data, supporting this assumption. With the exception of group and time effects, all predictor variables were grand-mean centered prior to inclusion in analyses. All statistical analyses were performed in Stata 10.1 (StataCorp, 2007).

Prior to mediation and moderation analyses, we examined static predictors of PDD and PDDRG in preliminary models to identify any statistically significant covariate effects, including demographics, therapy attendance, baseline severity of PDD/PDDRG, group, time (linear and quadratic), and the group by time interaction. To examine the effects of neurocognitive impairment on substance use outcomes and process variables (i.e., self-efficacy, 12-step affiliation, and depressive symptoms), each variable was analyzed separately in HLM with impairment as an individual-level predictor, controlling for effects of time, group, and the group by time interaction. For each process variable predicted by neurocognitive impairment, we then examined the variable's effect on future substance use by including it as a time-varying, lagged predictor of PDD/PDDRG. While these sequential steps detect likely presence of mediation, formal statistical tests are better indicators of mediated effects. Consistent with current conventions in mediation (MacKinnon, 2008), we examined the statistical significance of mediated effects using the products-of-coefficients with asymmetric 95% confidence limits (MacKinnon et al., 2007). This method has more accurate Type I error rates and greater power to detect

mediated effects than alternate approaches (MacKinnon et al., 2002), and is appropriate for the analysis of nested data structures (Krull & MacKinnon, 2001).

In the final models we tested whether neurocognitive impairment moderated the strength of association between process variables and future drinking/drug use. After estimating the covariate model, a main effects model was estimated that simultaneously tested the effects of all process variables and neurocognitive impairment on PDD/PDDRG. To test the moderating effects of impairment, three cross-level interaction terms were created, one for each process variable. To reduce nonessential multicollinearity, all predictor variables were grand-mean centered prior to creation of interaction terms (Kreft, Deleeuw, & Aiken, 1995). In separate HLMs each interaction term was added to the main effects model to test the statistical significance of moderation. For any significant two-way interaction terms, we also tested three-way interactions with other process variables, to determine whether these interactions were further moderated by other treatment processes.

Results

Overall Neurocognitive Impairment

The mean neurocognitive impairment score was 1.05 ($SD = 1.15$), indicating that on average patients had severe impairment on at least one of the eight neurocognitive measures. Less than half of the sample (37.06%) had zero impairment, while 36.55 % were impaired on one measure, 16.75% on two, and the remaining 9.63% were impaired on three or more neurocognitive measures.

Preliminary Substance Use Models

To identify significant covariates before examining primary hypotheses, preliminary HLMS tested the effects of demographic variables, baseline frequency of use, group therapy attendance, group (coded TSF = 1, ICBT = 0), time, time-squared, and the group by time interaction on drinking and drug use. In the PDD model age ($b = 0.39, p < 0.01$), years of education ($b = -1.09, p < 0.05$), baseline PDD ($b = 0.19, p < 0.001$), sessions attended ($b = -0.77, p < 0.001$), group ($b = -5.97, p < 0.05$) and the group x time interaction ($b = 0.57, p < 0.05$) were significantly related to frequency of drinking. In the PDDRG model only sessions attended ($b = -0.24, p < 0.01$) and baseline PDDRG ($b = 0.16, p < 0.001$) were related to frequency of drug use. To maintain consistency across analyses of drinking and drug use outcomes, all subsequent models of PDD and PDDRG included each of these covariate effects.

Effects of Neurocognitive Impairment on Outcomes and Mediating Variables

In the next series of analyses we tested the effects of baseline neurocognitive impairment on substance use outcomes and mediating variables. In mediation terminology these analyses would test for the presence of significant relations between the predictor (impairment) and outcome (PDD/PDDRG) and for significant effects of the predictor on mediators, namely self-efficacy, 12-step affiliation, and depression. Neurocognitive impairment did not significantly predict PDD ($b = 0.76, SE = 0.91, p = 0.41$), or PDDRG ($b = -0.57, SE = 0.57, p = 0.32$). However, as displayed in Table 12, impairment did significantly predict self-efficacy, 12-step affiliation, and depressive symptoms, in the hypothesized directions. Thus, while individuals with greater impairment, on average, did not drink or use drugs more frequently, they did have lower

self-efficacy, lower 12-step affiliation, and greater depressive symptoms during the course of the study.

With the first presumptive paths for mediation supported, the next analyses examined whether self-efficacy, 12-step affiliation, and depression predicted future drinking and drug use. Each process variable was tested as time-varying predictor in separate HLMs for PDD and PDDRG, which controlled for previously mentioned covariates and neurocognitive impairment. Future PDD was significantly predicted by self-efficacy, 12-step affiliation, and depressive symptoms, and future PDDRG was also predicted by each of these process variables, supporting the second presumptive path for mediation. These results indicated that individuals with greater self-efficacy, greater 12-step affiliation, and lower depressive symptoms had greater future drinking and drug use frequency.

Statistical Mediation Tests

While results thus far provided presumptive support for mediation, current conventions in mediation analysis recommend obtaining precise estimates of the mediated effect and joint standard error for determining statistical significance of mediation (MacKinnon, 2008). Using the results obtained in HLM, we obtained estimates of each mediated effect and associated 95% confidence intervals, which would indicate whether neurocognitive impairment was significantly related to future drinking and drug use through the mediating variables. For PDD, effects of neurocognitive impairment were significantly mediated through self-efficacy ($b = 0.33$, 95% CI [0.10, 0.64], $p < 0.05$), 12-step affiliation ($b = 0.32$, 95% CI [0.02, 0.69], $p < 0.05$) and depressive symptoms, ($b = 0.29$, 95% CI [0.08, 0.58], $p < 0.05$). Similarly, effects of neurocognitive impairment

on PDDRG were significantly mediated by self efficacy, ($b = 0.28$, 95% CI [0.08, 0.53], $p < 0.05$), 12-step affiliation ($b = 0.15$, 95% CI [0.005, 0.35], $p < 0.05$), and depressive symptoms, ($b = 0.19$, 95% CI [0.03, 0.41], $p < 0.05$), indicating that neurocognitive impairment was related to PDD and PDDRG indirectly through these hypothesized mediating variables.

Neurocognitive Impairment as a Moderator of Mediators

Further analyses were conducted to determine whether neurocognitive impairment moderated relations between these process variables and future substance use. In contrast to analyses conducted thus far, the next set of HLMs specified and tested cross-level interactions between neurocognitive impairment and process variables in the prediction of PDD and PDDRG. To proceed in a parsimonious fashion given the large number of potential interactions, separate models tested each impairment by process variable interaction separately, before building significant terms into a full model with potential three-way interactions. Results for PDD indicated that effects of lagged self-efficacy ($b = -0.13$, $SE = 0.47$, $p = 0.78$) and lagged depressive symptoms ($b = -0.05$, $SE = 0.05$, $p = 0.22$) were not moderated by impairment, but that impairment significantly moderated effects of lagged 12-step affiliation on PDD ($b = -0.88$, $SE = 0.37$, $p < 0.05$). The relationship between 12-step affiliation and future PDD was greater for patients with greater impairment (see Figure 1). As displayed in Table 4, the interaction of impairment and 12-step affiliation was statistically significant in the full model controlling for all process variable main effects and other interactions. Moreover, this interaction was further qualified by a significant 3-way interaction between impairment, affiliation, and depression, ($b = -0.07$, $SE = 0.03$, $p < 0.05$). As depicted in Figure 2, the effect of 12-

step affiliation on PDD was strongest for impaired patients when levels of depressive symptoms were high. Overall, these results suggest that in our sample the benefits of 12-step affiliation on future drinking were greatest for patients with greater levels of neurocognitive impairment, especially when they were severely depressed.

Separated analyses examined identical relationships in the prediction of drug use. Impairment did not moderate the effects of lagged self-efficacy ($b = 0.48$, $SE = 0.35$, $p = 0.17$) or lagged 12-step affiliation ($b = -0.16$, $SE = 0.27$, $p = 0.55$), but impairment did moderate the effects of depressive symptoms ($b = -0.09$, $SE = 0.03$, $p < 0.01$). As displayed in Figure 1, depressive symptoms predicted PDDRG to a greater extent in patients with lower impairment. However, this interaction was no longer statistically significant when controlling for lagged self-efficacy and 12-step affiliation. Results indicated that, contrary to predictions, more severe depressive symptoms predict greater future drug use to a lesser extent among patients with greater cognitive impairment, but these effects were not independent of prior levels of self-efficacy and 12-step affiliation.

Discussion

Despite strong clinical rationale that neurocognitive deficits will negatively impact the outcome of psychotherapy for treatment of substance dependence, a number of studies have not found worse outcomes for patients with neurocognitive functioning (Aharonovich et al., 2006; Teichner et al., 2002; Turner et al., 2009). More recent investigations suggest that neurocognitive impairment impacts substance use outcomes through more indirect mechanisms: by influencing treatment process variables like self-efficacy and AA affiliation, or by moderating the strength of relations between these variables on substance use (Bates et al., 2006; Morgenstern & Bates, 1999). These studies

also suggest that measures of exceptionally poor performance are perhaps better indicators of impairment than continuous performance scores or dichotomous classifications of samples based on arbitrary cutpoints. Despite evidence that patients with psychiatric comorbidity comprise the majority of patients in clinical settings (Chi et al., 2006; Lynskey, 1998) and have greater neurocognitive deficits than patients with substance dependence only (Levy et al., 2008) previous studies have not explored the impact of neurocognitive impairment on treatment outcomes for patients with comorbidity. The current study addresses this area of need by examining the effects of neurocognitive impairment on substance use outcomes in patients treated for substance dependence and MDD.

Greater neurocognitive impairment at baseline predicted lower self-efficacy and lower 12-step affiliation, and our analyses confirmed that these proximal variables mediated the effects of impairment on future drinking and drug use. Previous studies found similar relationships between impairment and self-efficacy (Bates et al., 2006; Morgenstern & Bates, 1999), and our study extends these findings to patients with comorbid MDD. Self-efficacy is typically defined as the confidence to abstain from substance use in high-risk situations, and patients with greater impairment apparently had lower confidence they could manage these situations without using substances. The specific mechanisms underlying these effects are unclear, but it is possible that impaired patients engaged less fully in TSF and ICBT or experienced less perceived benefit from therapy sessions. In one recent study poorer cognitive ability predicted lower acquisition of coping skills in CBT (Kiluk et al., 2011). Future studies might explore whether

reduced coping skills or difficulty engaging in other aspects of group treatment explain lower self-efficacy for cognitively impaired patients.

Patients with greater impairment had lower levels of 12-step affiliation, suggesting they had greater difficulty engaging in 12-step practices that common in both therapy conditions but were only specifically targeted in TSF. This may help explain why patients with poorer neurocognitive functioning had better long-term substance use in ICBT than in TSF (Granholm et al., 2011). While it was originally hypothesized that patients with poorer neurocognitive functioning would fare worse in ICBT due to the cognitive demands of the treatment, the current study shows that impaired patients had difficulty frequently attending 12-step meetings or engaging in 12-step behaviors. The direction of this finding contradicts those of previous studies, which found that levels of AA affiliation were significantly greater for impaired patients (Bates et al., 2006; Morgenstern & Bates, 1999). It is possible that for patients with substance dependence and MDD, neurocognitive impairment represents an additional and especially disabling risk factor leading to limited engagement in 12-step practices.

Patients with greater neurocognitive impairment were also found to have greater depressive symptoms during the course of the study. Similar results were found in a sample of depressed, hazardous drinkers, as patients with better cognitive functioning had greater reductions in depressive symptoms during CBT (Hunt et al., 2009). We hypothesized that neurocognitive effects on depressive symptoms would impact substance use outcomes, given that negative affect is a frequent precursor to relapse in patients with comorbid MDD (Tomlinson et al., 2006), and is consistently tied to substance use over time (Witkiewitz & Villarroel, 2009; Worley et al., 2012), suggesting

that greater depression severity within these patients is frequently a potential trigger for future substance use. This hypothesis was confirmed by mediation analyses demonstrating that greater depressive symptoms predicted greater future alcohol and drug use and mediated the effects of neurocognitive impairment on these outcomes. Our previous work tied reductions in depression during treatment to 12-step meeting attendance (Worley et al., under review), and it is possible that reduced engagement in 12-step contributed to greater depression for cognitive impaired patients. Alternatively, these patients may have had difficulty with other elements of treatment (e.g., pharmacotherapy compliance, cognitive coping skills) that limited their improvement in depressive symptoms.

Investigation of neurocognitive impairment as a moderator revealed complex interactions with therapeutic process variables in the prediction of drinking and drug use. Greater 12-step affiliation predicted lower future drinking to a greater extent for impaired patients. Although the direction of this finding is contrary to effects observed in previous, similar studies (Bates et al., 2006; Morgenstern & Bates, 1999), other research found the effects of baseline social support on future drinking were greater for impaired patients (Buckman et al., 2007; Buckman et al., 2008). Our sample differed from these studies in that all patients had comorbid MDD, and our results suggest at greater levels of depression severity, the benefits of engaging with external sources of support are especially useful. That is, 12-step affiliation was most predictive of future drinking for patients with severe impairment, especially when they were severely depressed. Although prior research has found relatively reduced benefits of AA practices for patients with MDD (Kelly et al., 2003), our results suggest the opposite may be true for patients with

neurocognitive impairment, as they may experience relatively greater benefits from 12-step affiliation.

Neurocognitive impairment also moderated the effects of depression on future drug use, but in the opposite direction than expected: relations between depressive symptoms and future drug use were stronger for patients with less impairment. Although rates of drug use in the sample were low overall, patients with little or no impairment had a greater tendency to use drugs frequently following periods of more severe depressive symptoms. Because previous studies of neurocognitive effects on treatment have largely focused on alcohol users without MDD or depressive symptoms, the mechanisms underlying this unexpected finding are unclear. Others have speculated that cognitively impaired patients may be relatively less capable of the planning required to re-initiate substance use (Morgenstern & Bates, 1999). Relations between depression and drinking were not moderated by impairment, suggesting this could be the case for drug use but not necessarily for alcohol. This interaction was also less robust, as it was not statistically significant when controlling for prior self-efficacy and 12-step affiliation. Future studies are needed to determine whether this finding is consistent in other samples of drug-dependent patients, with or without comorbid MDD.

Limitations of this study should be noted. The results may not be immediately generalizable to the broad population of patients with psychiatric comorbidity, as we only studied patients with MDD, and our sample was comprised of veterans who were predominantly male and Caucasian. Clinical trials of treatment for alcohol and drug dependence frequently suffer these demographic limitations, and replication of these findings in a wider range of patients is needed before broader generalizations can be

made. Although we examined complex mediated and moderated pathways to substance use, there are untested relationships among the variables in this study that merit further exploration. Greater self-efficacy has been associated with greater 12-step affiliation, which could be one factor explaining lower self-efficacy for patients with greater neurocognitive impairment. Because the effects of mediating variables were examined in separate HLMs, we did not test whether each variable relates independently to future substance use, which can be examined in “multiple mediator” models that help demonstrate which mediating processes may be most crucial for limiting future substance use. Although this study met several conceptual criteria for examining mechanisms of change (e.g., statistical mediation, temporal precedence), further criteria are required to conclude with greater confidence that these process variables are mechanisms of change (Nock, 2007) or casual factors for limiting long-term substance use.

Study 4 has been submitted for publication in *Journal of Consulting and Clinical Psychology*, as following: Worley, M.J., Tate, S.R., Tapert, S.F., Granholm, E.G., & Brown, S.A. Neurocognitive impairment interacts with 12-step affiliation and depression to predict future drinking in depressed, substance-dependent veterans. The dissertation author was the primary author of this manuscript under review.

Table 11. Descriptive statistics of substance use outcomes, process variables, and neurocognitive impairment for veterans with substance dependence and major depressive disorder (N = 197).

	Month						
	0	3	6	9	12	15	18
PDD							
M	23.63	7.57	10.65	11.89	13.09	12.99	15.92
SD	23.63	16.71	22.08	22.69	24.11	25.79	29.73
PDDRG							
M	10.04	2.66	3.95	4.48	5.34	4.87	7.34
SD	19.56	10.36	12.17	14.65	15.66	14.28	18.92
Self-efficacy							
M	3.24	3.64	3.65	3.64	3.64	3.58	3.52
SD	1.16	1.11	1.13	1.22	1.21	1.29	1.31
12-step affiliation							
M	2.67	2.70	2.45	2.17	2.10	2.01	1.96
SD	1.48	1.61	1.65	1.74	1.74	1.71	1.71
HAMD							
M	28.35	24.94	22.02	22.03	21.51	22.61	21.30
SD	10.65	12.50	12.69	13.71	12.19	12.74	12.48

Note. PDD: percent days drinking; PDDRG: percent days using drugs; HAMD: Hamilton Depression Rating Scale.

Table 12. Results of hierarchical linear models predicting hypothesized mediators from covariates and neurocognitive impairment.

	Self-efficacy	12-step affiliation	Depression severity
	b (SE)	b (SE)	b (SE)
Group (TSF vs. ICBT)	0.17 (0.14)	0.48 (0.20)*	- 2.51 (1.38)
Month	0.07 (0.02)	- 0.05 (0.02)**	- 0.93 (0.16)***
Month ²	- 0.003 (0.0001)	0.001 (0.001)	0.04 (0.01)***
Group x month	- 0.01 (0.01)	- 0.02 (0.01)	- 0.10 (0.11)
Therapy sessions	0.03 (0.008)**	0.01 (0.01)	- 0.24 (0.08)**
Age	0.001 (0.01)	- 0.02 (0.01)	- 0.09 (0.08)
Years of education	0.05	0.06 (0.04)	- 0.33 (0.30)
Neurocognitive Impairment	- 0.15 (0.05)**	- 0.17 (0.08)*	1.93 (0.54)***

Note. TSF: Twelve-Step Facilitation; ICBT: Integrated Cognitive-Behavioral Therapy.

* $p < .05$, ** $p < .01$, *** $p < .001$.

Table 13. Results of hierarchical linear models examining interactions between 12-step affiliation, depression, and neuropsychological impairment in the prediction of future drinking or drug use.

	Alcohol use		Drug use
	b (SE)	b (SE)	b (SE)
	2-way interactions	3-way interactions	2-way interactions
Constant	8.80 (2.40)	8.72 (2.38)	4.32 (3.52)
Month	0.17 (0.48)	0.19 (0.48)	- 0.75 (0.69)
Month ²	0.005 (0.02)	0.004 (0.02)	0.05 (0.03)
Group (TSF vs. ICBT)	- 3.58 (2.39)	- 3.95 (2.37)	0.10 (3.23)
Group x month			0.31 (0.28)
Group sessions	- 0.64 (0.12)***	- 0.63 (0.12)***	- 0.27 (0.11)*
Age	0.31 (0.13)*	0.31 (0.13)*	0.03 (0.12)
Years of education	- 0.73 (0.44)	- 0.75 (0.44)	0.03 (0.39)
Baseline PDD/PDDRG	0.14 (0.04)***	0.13 (0.04)***	0.09 (0.04)*
Lagged HAMD	0.08 (0.06)	0.07 (0.06)	- 0.008 (0.07)
Lagged 12-step affiliation	- 1.72 (0.45)***	- 1.60 (0.45)***	- 1.29 (0.54)*
Lagged self-efficacy	- 1.53 (0.57)**	- 1.55 (0.57)**	- 1.86 (0.69)**
Impairment score	0.73 (0.88)	0.49 (0.88)	0.54 (0.93)
Impairment x 12-step	-1.09 (0.39)**	-1.03 (0.39)**	- 0.37 (0.53)
Impairment x HAMD	- 0.05 (0.04)	- 0.03 (0.04)	0.003 (0.04)
12-step x HAMD	0.0009 (0.03)	- 0.005 (0.03)	0.01 (0.04)
Impairment x 12-step x HAMD	-	- 0.07 (0.03)*	-

Note. TSF: Twelve-Step Facilitation; ICBT: Integrated Cognitive-Behavioral Therapy; PDD: percent days drinking; PDDRG: percent days using drugs; HAMD: Hamilton Depression Rating Scale.

* $p < .05$, ** $p < .01$, *** $p < .001$.

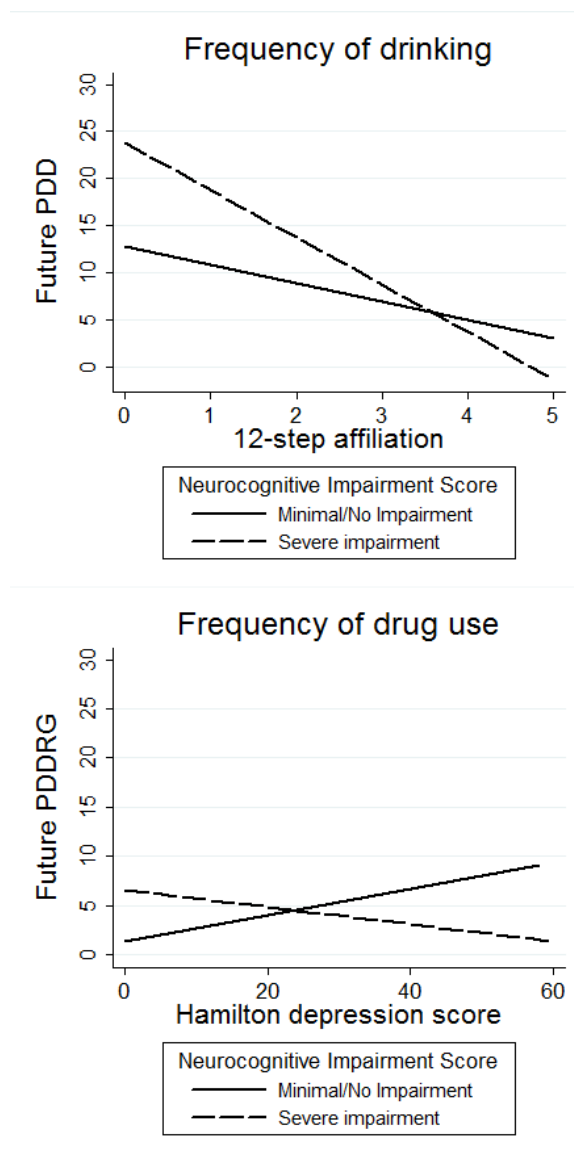


Figure 6. Significant interactions between impairment and 12-step affiliation on percent days drinking (PDD), and between impairment and depression on percent days using drugs (PDDRG).

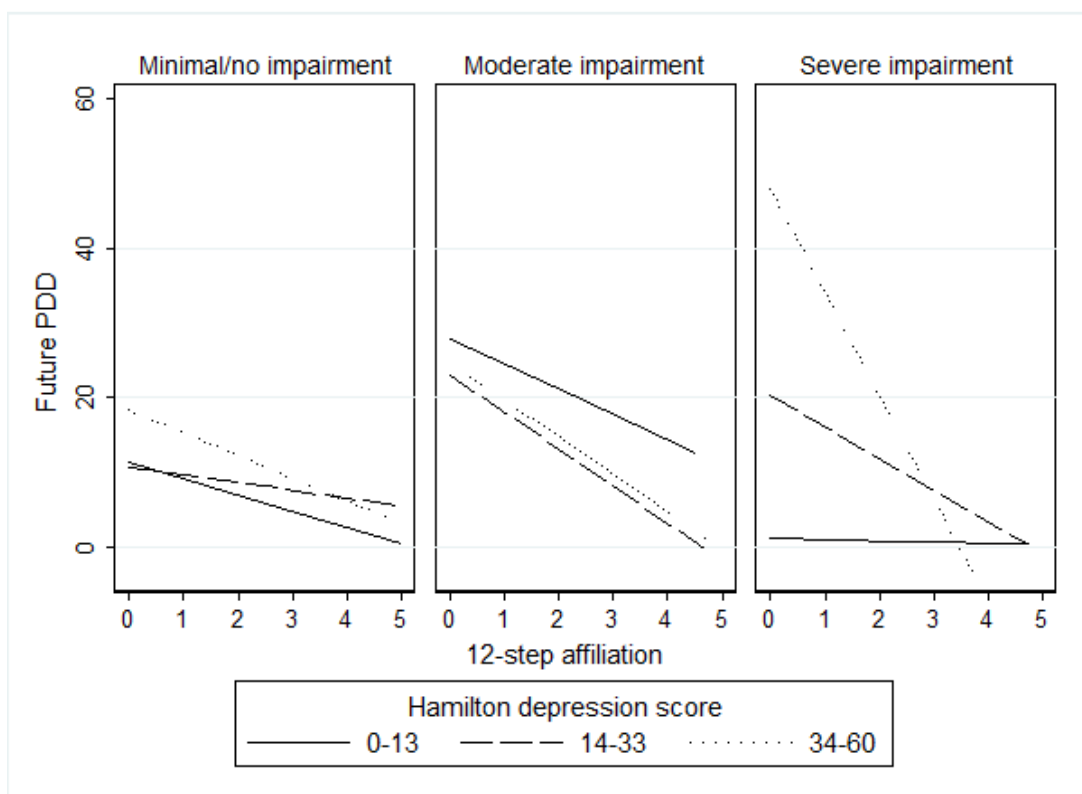


Figure 7. Significant three-way interaction between impairment, 12-step affiliation, and depression in the prediction of future percent days drinking (PDD).

Discussion

The Importance of Process-Oriented Treatment Research

Despite decades of clinical research developing and testing behavioral interventions for substance dependence, evidence-based interventions are only moderately effective, with a substantial number of patients returning to substance use following treatment (Longabaugh & Magill, 2011). Furthermore, many of the largest randomized trials have found equivalent outcomes across distinct treatment conditions (Crits-Christoph et al., 1999; Project Match Research Group, 1997), and theoretically-distinct treatments often fail to produce differential change on hypothesized mechanisms of action (Morgenstern & Longabaugh, 2000), suggesting we may know little about the underlying mechanisms of change within addiction treatment. Consequently, researchers have increasingly turned towards process-focused investigations aimed at identifying how treatments work, for whom they are effective, and which modifiable factors are most integral for maintaining positive change (Finney, 2007), with hopes of improving the overall likelihood that substance dependence treatment will result in long-term change.

The past decade has seen vast growth in process-oriented studies in the general addictions treatment field (Apodaca & Longabaugh, 2009; Finney, 2007; Longabaugh et al., 2005b). However, very little of this work has involved samples of patients with other psychiatric disorders, despite evidence that these patients comprise the majority in many treatment settings (Chi et al., 2006; Lynskey, 1998). Among individuals with substance dependence, major depression (MDD) is the most common co-occurring Axis I disorder in the general population and in treatment settings (Grant et al., 2006). Patients with co-occurring MDD typically cost more to treat (Druss & Rosenheck, 1999) and have poorer

treatment outcomes than patients without this MDD (Curran et al., 2000; Gamble et al., 2010; Glasner-Edwards, Marinelli-Casey, Hillhouse, Ang, Mooney, & Rawson, 2009; Greenfield et al., 1998; Ilgen & Moos, 2005; Kodl et al., 2008; Levin et al., 2008a), suggesting it is especially important to identify core therapeutic processes within these patients. However, because little process-oriented research has involved patients with substance dependence and MDD, it is not known whether previous findings generalize to this highly prevalent, costly, and disrupted population.

Studies of mediators of treatment outcome are essential to the general area of “treatment process” research. Mediators are third variables that statistically explain an association between a predictor and outcome (Baron & Kenny, 1986b; MacKinnon, 2008). Within treatment studies, investigations of mediators typically examine an intermediate factor (e.g., coping skills) that may explain the effect of treatment “dose” (e.g., number of sessions, experimental intervention) on a clinical outcome (e.g., substance use). These studies have the potential to inform the development of more efficient and portable interventions by identifying the skills or behaviors targeted by interventions that are most responsible for producing positive change. In previous studies examining mediation, lower marijuana use in CBT + contingency management compared to contingency management alone was mediated by enhanced self-efficacy (Litt et al., 2008), and better abstinence rates in TSF were explained by greater commitment to abstinence (Longabaugh et al., 2005b). Importantly, statistical mediation is only one of several conditions to be met before declaring a variable is a mechanism of change, as temporal precedence, specificity, and experimental manipulation of the variable must also be demonstrated (Kazdin & Nock, 2003; Nock, 2007). In practice these criteria are rarely

met, as many interventions have failed to produce differential change on theoretical mediators (Apodaca & Longabaugh, 2009; Morgenstern & Longabaugh, 2000).

However, these “failed” investigations of mediating variables can still be informative about common therapeutic processes, because they still identify modifiable characteristics that explain individual differences in substance use treatment outcome (Longabaugh, 2007).

Our research provides examples of both specific and common mediators in veterans treated for substance dependence and MDD. In Study 1 we found that greater 12-step meeting attendance for veterans in TSF mediated their superior within-treatment depression outcomes, while Study 2 found that greater reductions in 12-step meeting attendance and affiliation following treatment mediated poorer post-treatment drinking outcomes in the TSF group. Both of these findings highlight the impact of differential levels of engagement with community, self-help resources that were specifically tied to the TSF condition. Independent of treatment group, levels of self-efficacy and substance use in the social network predicted future alcohol and drug use in the year following treatment, suggesting these variables were common determinants of substance use in both treatment conditions. These studies also highlighted the value of investigating mediating variables with respect to individual differences in distal risk factors, by finding that neurocognitive impairment impacted substance use indirectly through self-efficacy, 12-step affiliation, and depression. We demonstrated that mediation analyses can assist in explaining the positive impact of specific therapeutic processes, by finding that the impact of greater attendance at 12-step meetings on future drinking were explained by lower levels of depressive symptoms. Altogether these studies provided new information

with respect to explaining how treatment processes or individual characteristics relate to differences in substance use outcomes, highlighting the value of examining mediating processes in persons receiving treatment for substance dependence and MDD.

Process-oriented research also includes investigations of moderating variables (Morgenstern & McKay, 2007). In the presence of moderation (i.e., interaction), the magnitude of association between two variables depends on the level of a third variable (Baron & Kenny, 1986b; Kraemer, Wilson, Fairburn, & Agras, 2002). While studies of mediators typically ask *how* or *why*, studies of moderators are perhaps best suited to determine *for whom* or *under what conditions* treatments are most effective. Treatment-related studies of moderators typically examine if a preexisting characteristic (e.g., psychiatric severity) influences effects of treatment on substance use outcomes. In previous examples of moderation, TSF was the most effective therapy for patients with social networks supportive of drinking (Longabaugh et al., 1998), and CBT was more effective for cocaine users with greater severity at intake (Carroll, Rounsaville, & Gawin, 1991). In tune with the shift towards examining therapeutic process variables, there is perhaps greater current interest in identifying moderators that influence relations between process variables and substance use (Kadden & Litt, 2011). Statistical recommendations for testing moderated mediation, or “conditional mediation” are now available (Muller, Judd, & Yzerbyt, 2005), with clinical examples published in recent literature (Bates et al., 2006). These studies help illustrate heterogeneous pathways to recovery, because the magnitude of benefits conferred by a proximal variable (e.g., 12-step attendance) may depend on some other distal risk factors. Because certain distal characteristics (e.g., neurocognitive impairment) are prevalent and relatively intractable in substance-

dependent patients, it is critical to explore these complex relationships in the context of addictions treatment.

Investigations of such moderators provided further information about the complex associations between therapeutic process variables and treatment outcome for individuals with substance dependence and MDD. While social network characteristics were predictive of future substance use in the sample at-large, moderation analyses revealed these effects were attenuated for certain individuals. More specifically, the predictive effects of social network variables were reduced for veterans who resided in controlled contexts for longer periods of time. Neurocognitive impairment was also found to moderate process variable effects, as veterans with greater impairment experienced relatively stronger benefits from 12-step affiliation, especially when they were severely depressed. These findings are significant as they reveal the benefits or risks conferred by certain processes are not similar across all recipients of treatment, and that certain contextual factors (e.g., living environment) or individual characteristics (e.g., impairment) impact the relations between these processes and substance use outcomes.

Significant Contributions

The series of studies conducted herein represent some of the most substantial and informative process-oriented studies of treatment outcomes involving patients with substance dependence and MDD. In addition to illustrating the utilization of methods that are likely applicable to studies of process of psychotherapy for a variety of conditions, the resulting findings have a number of important implications for future research and clinical practice.

Research Implications. The major goal in process-oriented research is frequently to discover factors that explain group differences, especially with respect to differences between treatment conditions. Whether group differences are consistent or inconsistent with hypotheses, studies of mediating variables can provide useful and potentially explanatory information, and our studies provide several examples of this type of contribution. In perhaps the most surprising finding of our controlled trial, the TSF group had superior reductions in depression during treatment, as compared to ICBT which targeted both depressive symptoms and substance use (Lydecker et al., 2010). While reductions in depression during follow-up were greater for ICBT, it was still perplexing that the “addiction-focused” treatment performed better (initially) than an intervention designed to target depression. Results of Study 1 provided some insight, suggesting that greater reductions in depression for TSF were likely attributable to greater attendance at community 12-step meetings. In fact, when controlling for meeting attendance, TSF and ICBT were similar on depression. In another unexpected finding, patients with poorer neurocognitive functioning had better substance use outcomes if assigned to ICBT (Granholm et al., 2011). Patients with poorer cognitive functioning were expected to do worse in ICBT, because CBT is theoretically more cognitively-demanding. A key finding of Study 4 here was that patients with greater neurocognitive impairment had lower 12-step affiliation, suggesting that the poorer outcomes in TSF were likely attributable to difficulties engaging in TSF’s principal therapeutic targets: attendance at 12-step meetings and engagement with prescribed 12-step behaviors.

These studies also illustrate that both dynamic, contextual factors and static, distal factors can moderate the effects of therapeutic process variables on treatment outcomes.

In Study 3 we examined “controlled contexts”, environments where patients had restricted access to substances (e.g., inpatient admissions, sober living homes, jail), and found these contexts moderated social network effects. If more time was controlled, having a greater density of network drinking was less predictive of one’s own drinking. For other populations in which utilization of these controlled contexts is fairly common, studies that ignore these moderating contextual effects might underestimate associations between mediating variables and clinical outcomes. Furthermore, our findings demonstrate that effects of certain contextual variables (e.g., social networks) may depend on other contextual factors (e.g. controlled environment) in predicting substance use or other maladaptive behaviors. In Study 4 the effects of 12-step affiliation on future drinking were moderated by neurocognitive impairment, with stronger effects for the neurocognitively impaired. This interaction was further modified by depression: among patients with greater impairment, having more severe depressive symptoms increased the influence of 12-step affiliation on future drinking. This finding, in particular, reinforces the value of examining proximal variables in conjunction with distal risks and other dynamic processes in the prediction of complex behaviors such as substance use (Witkiewitz & Marlatt, 2004). Study 4, in particular, illustrates there are specific times (feeling depressed) for particular patients (cognitively impaired) at which certain self-regulatory behaviors (12-step affiliation) are especially powerful, and elucidating these complex relationships is an important goal for future clinical research in addictions and other conditions.

The strengths of repeated, frequent measurement of variables and specification of appropriate longitudinal models were also illustrated by this series of studies.

Establishment of temporal precedence is one of many criteria for identifying a mechanism of change (Nock, 2007). In our studies time-varying predictors were used in a lagged fashion, with prior levels of process variables predicting future substance use outcomes. While these tests are not sufficient for indication of causation, establishing temporal precedence increases confidence that adjusting/altering the predictor will result in changes in the outcome variable (Kraemer, Stice, Kazdin, Offord, & Kupfer, 2001). Compared to correlational tests, our methods provided stronger evidence that changing 12-step affiliation, negative affect, self-efficacy, and social network variables could alter substance use in patients with substance dependence and MDD. This is an important distinction that strengthens the rationale to target these specific processes in therapy or to design treatments around these goals. Furthermore, we were able to estimate individual patterns of change in process variables and examine associations with changes in outcomes. Many psychological constructs change over time, and this is typically the goal of psychological treatments: to change an adverse condition. However, process variables and outcomes are often studied without consideration of change over time, which can produce biased or distorted results (Maxwell & Cole, 2007). By modeling within-individual change in Study 2, we have stronger support to conclude that within-individual change in 12-step involvement is an important determinant of changes in post-treatment drinking.

Clinical Implications. Adults with substance dependence and MDD historically have poor outcomes from substance use treatment, and are responsible for disproportionate levels of treatment costs and disability. Because these individuals are so commonly represented in SUD treatment settings but have rarely been the focus of

treatment outcome or process research, we considered it paramount to explore clinically-relevant determinants of substance use within this population. Our sample, in particular, was characterized by low levels of occupational and social functioning, with low rates of employment and marriage. The average participant in our sample had multiple prior inpatient treatments for substance dependence and multiple inpatient episodes for psychiatric problems, highlighting the debilitating and refractory nature of these co-occurring conditions. However, it was encouraging to find that, in general, the therapeutic processes with empirically-validated benefits in patients without co-occurring disorders also appeared to confer therapeutic benefits in our sample of adults with substance dependence and MDD. Because the current studies elucidated relationships between a variety of coping-oriented behaviors, contextual processes, and individual characteristics in the prediction of alcohol and drug use, the clinical implications of these studies are numerous.

Several of our findings suggest facilitating 12-step involvement can be a useful component of interventions for patients with substance dependence and MDD. In Study 1 patients in TSF had greater reductions in depression that were mediated by 12-step meeting attendance. Furthermore, greater attendance at 12-step meetings had unique effects on depressive symptoms (independent of current drinking), which in turn predicted lower future drinking. It has been suggested that patients with co-occurring psychiatric problems may receive amplified benefits from social interaction inherent to self-help meetings, perhaps due to greater severity of social problems and isolation (Moos, 2008), which may have contributed to improved depression and drinking in our sample. During post-treatment follow-up (Study 2), maintaining greater 12-step

attendance and affiliation over time predicted less increase in drinking, suggesting that continued involvement in 12-step practices can be a beneficial post-treatment maintenance strategy for patients with co-occurring depression. However, one unfavorable finding was that patients in TSF had difficulty sustaining high levels of 12-step meeting attendance and affiliation after conclusion of the formal intervention phase. This suggests that patients with substance dependence and MDD may need some level of ongoing, therapeutic support to continue high levels of 12-step engagement, perhaps through the use of brief motivational/facilitation interventions (Timko et al., 2006).

These studies were also helpful in elucidating the impact of negative affect in the maintenance of substance use for patients with substance dependence and MDD. We previously found that changes in depressive symptoms and substance use were highly correlated in this sample (Worley et al., 2012). The current studies built upon that work by highlighting more specific and unique roles of depressive symptoms. We found that reduced depressive symptoms during treatment (1) were predicted by greater 12-step meeting attendance, independent of current drinking, and (2) mediated the relation between meeting attendance and future drinking. Patients with substance dependence and MDD can likely experience reductions in depressive symptoms by attending 12-step meetings frequently, and these mood changes may help buffer against future drinking. Our findings also suggest that patients who are attending meetings frequently and fail to improve in depression should receive additional intervention or alteration to ongoing treatments to avoid future drinking. Results of Study 4 also indicated that greater depressive symptoms represent a distinct exacerbation of risk for cognitively impaired

patients, during which they should engage in greater levels of protective behaviors (e.g., attending meetings, contacting sponsor) to reduce the odds of increased drinking.

Studies also confirmed significant roles of self-efficacy and social network substance use in the maintenance of abstinence in adults treated for substance dependence and MDD. During post-treatment follow-up, individuals who were generally at higher levels of self-efficacy had lower drinking and drug use. Self-efficacy has predicted good outcomes in a variety of studies (Kadden & Litt, 2011) and increased significantly during treatment in our sample (Glasner-Edwards et al., 2007). Our results only suggest that following the conclusion of formal treatment, patients with low confidence in their ability to abstain from substance use in risky situations are at greater risk for increased frequency of use in the future and may benefit from higher levels of care. Our study of social network effects confirms that adults with SUD and MDD will likely benefit from efforts to restructure their social networks by (1) increasing the number of abstinent/nonusing supports and (2) decreasing the number of contacts who use substances regularly. Results also suggested that both (1) regular maintenance of positive social networks and (2) avoiding momentary shifts that increase the density of regular users are likely important for avoiding future increases in drinking. For individuals who are unable to enact sustained changes in social networks, our research suggests that placement into constrained environments (e.g., sober living) can assist in attenuating the negative influence of a social network comprised of greater numbers of substance abusers.

Limitations

While this series of studies makes important research and clinical contributions, especially with respect to the treatment and long-term recovery of patients with substance dependence and MDD, overall limitations should be noted. Perhaps most notable among these limitations are the restricted demographic characteristics of our sample (e.g., heavily male, mostly Caucasian) which curtails the immediate generalizability of these findings. This is a common limitation of clinical trials of treatments for addictive disorders (Kelly et al., 2010), and while these results may be widely applicable due to the high prevalence of MDD in substance use treatment settings (Chi et al., 2006; Lynskey, 1998), replication in other samples is needed before generalizing these findings to a population with a wider range of demographic characteristics. Many of our patients (approximately 40%) also had post-traumatic stress disorder. While we tested effects of PTSD on substance use outcomes, we did not explore more intricate (e.g., moderating) effects that are of interest due to the high prevalence of PTSD in this population. Temporal precedence between variables was not always tested (e.g., effects of 12-step attendance on depression in Study 1), and even models demonstrating temporal precedence did not fulfill all criteria for examining mechanisms of change (Nock, 2007). There is still some debate as to whether some of the process variables we studied (e.g., self-efficacy, 12-step affiliation) are true mechanisms, or just risk markers of some underlying characteristics that better enable patients to limit drinking and drug use (Kadden & Litt, 2011; Kelly, Magill, & Stout, 2009).

Regardless of these distinctions, our studies make important contributions to the literature because these variables have not been studied extensively in patients with SUDs and co-occurring psychiatric disorders, but further research is needed to demonstrate

these processes can be manipulated in ways that improve the effectiveness of interventions. Because these studies involved secondary analyses of existing data, we were somewhat limited by characteristics of measures utilized in the original clinical trial. Our measures of 12-step attendance and affiliation were brief and did not differentiate between different meetings (e.g., AA vs. Narcotics Anonymous), which may have allowed better investigation of disparate findings with respect to alcohol vs. drug use. Our social network measure did not capture features of social support examined in prior studies, such as whether network members actively supported patients' abstinence efforts (Litt et al., 2007). Furthermore, although we examined complex mediating and moderating effects on long-term substance use, there are potential relationships among mediating variables that we did not investigate. Previous studies of substance-dependent patients demonstrate that process variables such as 12-step attendance, social support, and self-efficacy often influence each other (Kelly et al., 2012; Magura et al., 2007; Magura, Knight, et al., 2003), and further investigations in this sample or others are needed to fully elucidate the pathways to long-term recovery in patients with substance dependence and co-occurring psychiatric disorders.

Future Directions

Considering the results of these four studies in the context of prior research in substance-dependence samples, there are numerous interesting lines of research for future inquiry. While we found that impairment predicted overall levels of 12-step affiliation, we did not test whether impairment relates to specific 12-step behaviors or impacts rates of post-treatment changes in 12-step attendance or affiliation. Because the rate of change in 12-step affiliation may be especially important, as demonstrated in Study 2, future

research might further investigate the role of impairment on changes in 12-step affiliation in patients with substance dependence and MDD. Prior studies also found that neurocognitive functioning moderated social network effects (Buckman et al., 2007; Buckman et al., 2008), and given that social networks predicted substance use (Study 3) and impairment moderated the effects of other contextual variables (Study 4), this question is worth exploring in patients with substance dependence and co-occurring psychiatric disorders. Studies have demonstrated that patients' pre-existing social network characteristics may moderate the effects of certain interventions, such that treatments specializing in altering the structure of social networks (e.g., TSF) are especially useful for patients with networks comprised primarily of substance users (Longabaugh et al., 1998; Wu & Witkiewitz, 2008). It is currently unknown whether social networks or many other baseline characteristics impacted whether patients in our sample had better outcomes from TSF or ICBT, which may help guide decisions about the appropriateness of certain interventions for patients with substance dependence and psychiatric disorders. Further work is needed to determine if particular aspects of psychosocial therapy are responsible for initiating change in mediating or moderating variables, and how to optimally package interventions for dissemination. A prior study of alcohol-dependent patients found that receiving a specific craving module moderated relations between negative mood and drinking (Witkiewitz, Bowen, & Donovan, 2011). Given that patients in our study received distinct modules that focused on different aspects of coping, and depression predicted future substance use, it may be worth investigating whether receipt of certain therapy modules had intended effects on reducing "self-medicating" patterns of drinking. Homework compliance has been found to predict

outcomes in CBT for cocaine dependence and may be an important mechanism of intervention effects on substance use (Carroll, Nich, & Ball, 2005), suggesting that compliance with group therapy homework may have influenced therapeutic process variables in our sample. By identifying modifiable variables that predict future substance use (e.g., self-efficacy, 12-step affiliation, negative affect, social networks), our research identifies important proximal targets for newly developed interventions or modifications to existing therapies. Since the publication of the short and long-term results of our trial, there is somewhat stronger evidence for the efficacy of integrated psychosocial therapies (Baker et al., 2010; Hides et al., 2010), but given the historically poor treatment outcomes for patients with substance dependence and MDD, further development and refinement of interventions is necessary to improve the long-term treatment outcomes within this population.

REFERENCES

- Adams, K. M., Gilman, S., Koeppe, R. A., Kluin, K. J., Brunberg, J. A., Dede, D., Kroll, P. D. (1993). Neuropsychological Deficits Are Correlated with Frontal Hypometabolism in Positron Emission Tomography Studies of Older Alcoholic Patients. *Alcoholism-Clinical and Experimental Research*, 17, 205-210.
- Adamson, S. J., Sellman, J. D., & Frampton, C. M. (2009). Patient predictors of alcohol treatment outcome: a systematic review. *J Subst Abuse Treat*, 36, 75-86.
- Aharonovich, E., Brooks, A. C., Nunes, E. V., & Hasin, D. S. (2008). Cognitive deficits in marijuana users: Effects on motivational enhancement therapy plus cognitive behavioral therapy treatment outcome. *Drug Alcohol Depend*, 95, 279-283.
- Aharonovich, E., Hasin, D. S., Brooks, A. C., Liu, X., Bisaga, A., & Nunes, E. V. (2006). Cognitive deficits predict low treatment retention in cocaine dependent patients. *Drug Alcohol Depend*, 81, 313-322.
- Aharonovich, E., Nunes, E., & Hasin, D. (2003). Cognitive impairment, retention and abstinence among cocaine abusers in cognitive-behavioral treatment. *Drug Alcohol Depend*, 71, 207-211.
- Alcoholics-Anonymous. (1953). *Twelve steps and Twelve Traditions* ([1st ed.]. New York, NY: Alcoholics Anonymous Publishing.
- Allsop, S., Saunders, B., & Phillips, M. (2000). The process of relapse in severely dependent male problem drinkers. *Addiction*, 95, 95-106.
- Alterman, A. I., Kushner, H., & Holahan, J. M. (1990). Cognitive functioning and treatment outcome in alcoholics. *J Nerv Ment Dis*, 178, 494-499.
- Apodaca, T. R., & Longabaugh, R. (2009). Mechanisms of change in motivational interviewing: a review and preliminary evaluation of the evidence. *Addiction*, 104, 705-715.
- Austin, M. P., Ross, M., Murray, C., O'Carroll, R. E., Ebmeier, K. P., & Goodwin, G. M. (1992). Cognitive function in major depression. *J Affect Disord*, 25, 21-29.
- Babor, T. F. (2008). Treatment for persons with substance use disorders: mediators, moderators, and the need for a new research approach. *International Journal of Methods in Psychiatric Research*, 17, S45-S49.

- Baker, A. L., Kavanagh, D. J., Kay-Lambkin, F. J., Hunt, S. A., Lewin, T. J., Carr, V. J., & Connolly, J. (2010). Randomized controlled trial of cognitive behavioural therapy for coexisting depression and alcohol problems: Short-term outcome. *Addiction, 105*, 87-99.
- Baron, R. M., & Kenny, D. A. (1986a). The moderator-mediator variable distinction in social psychological research: conceptual, strategic, and statistical considerations. *J Pers Soc Psychol, 51*, 1173-1182.
- Baron, R. M., & Kenny, D. A. (1986b). The Moderator Mediator Variable Distinction in Social Psychological-Research - Conceptual, Strategic, and Statistical Considerations. *J Pers Soc Psychol, 51*, 1173-1182.
- Bates, M. E., Barry, D., Labouvie, E. W., Fals-Stewart, W., Voelbel, G., & Buckman, J. F. (2004). Risk factors and neuropsychological recovery in clients with alcohol use disorders who were exposed to different treatments. *J Consult Clin Psychol, 72*, 1073-1080.
- Bates, M. E., Bowden, S. C., & Barry, D. (2002). Neurocognitive impairment associated with alcohol use disorders: Implications for treatment. *Experimental and clinical psychopharmacology, 10*, 193-212.
- Bates, M. E., Pawlak, A. P., Tonigan, J. S., & Buckman, J. F. (2006). Cognitive impairment influences drinking outcome by altering therapeutic mechanisms of change. *Psychol Addict Behav, 20*, 241-253.
- Bates, M. E., Voelbel, G. T., Buckman, J. F., Labouvie, E. W., & Barry, D. (2005). Short-term neuropsychological recovery in clients with substance use disorders. *Alcohol Clin Exp Res, 29*, 367-377.
- Beatty, W. W., Tivis, R., Stott, H. D., Nixon, S. J., & Parsons, O. A. (2000). Neuropsychological deficits in sober alcoholics: Influences of chronicity and recent alcohol consumption. *Alcoholism-Clinical and Experimental Research, 24*, 149-154.
- Bogenschutz, M. P., Geppert, C. M., & George, J. (2006). The role of twelve-step approaches in dual diagnosis treatment and recovery. *American Journal on Addictions, 15*, 50-60.
- Bolton, J. M., Pagura, J., Enns, M. W., Grant, B., & Sareen, J. (2010a). A population-based longitudinal study of risk factors for suicide attempts in major depressive disorder. *Journal of Psychiatric Research, 44*, 817-826.

- Bolton, J. M., Pagura, J., Enns, M. W., Grant, B., & Sareen, J. (2010b). A population-based longitudinal study of risk factors for suicide attempts in major depressive disorder. *J Psychiatr Res*, 44, 817-826.
- Bond, J., Kaskutas, L. A., & Weisner, C. (2003). The persistent influence of social networks and alcoholics anonymous on abstinence. *J Stud Alcohol*, 64, 579-588.
- Bradizza, C. M., Maisto, S. A., Vincent, P. C., Stasiewicz, P. R., Connors, G. J., & Mercer, N. D. (2009). Predicting post-treatment-initiation alcohol use among patients with severe mental illness and alcohol use disorders. *J Consult Clin Psychol*, 77, 1147-1158.
- Braun, C. M. J., & Richer, M. (1993). A Comparison of Functional Indexes, Derived from Screening-Tests, of Chronic-Alcoholic Neurotoxicity in the Cerebral-Cortex, Retina and Peripheral Nervous-System. *Journal of studies on alcohol*, 54, 11-16.
- Brown, S. A., Glasner-Edwards, S. V., Tate, S. R., McQuaid, J. R., Chalekian, J., & Granholm, E. (2006). Integrated cognitive behavioral therapy versus twelve-step facilitation therapy for substance-dependent adults with depressive disorders. *Journal of Psychoactive Drugs*, 38, 449-460.
- Brown, S. A., Vik, P. W., Patterson, T. L., Grant, I., & Schuckit, M. A. (1995). Stress, vulnerability and adult alcohol relapse. *Journal of Studies on Alcohol*, 56, 538-545.
- Brown, T. G., Seraganian, P., Tremblay, J., & Annis, H. (2002). Process and outcome changes with relapse prevention versus 12-Step aftercare programs for substance abusers. *Addiction*, 97, 677-689.
- Buckman, J. F., Bates, M. E., & Cisler, R. A. (2007). Social networks and their influence on drinking behaviors: differences related to cognitive impairment in clients receiving alcoholism treatment. *J Stud Alcohol Drugs*, 68, 738-747.
- Buckman, J. F., Bates, M. E., & Morgenstern, J. (2008). Social support and cognitive impairment in clients receiving treatment for alcohol- and drug-use disorders: a replication study. *J Stud Alcohol Drugs*, 69, 738-746.
- Buckner, J. D., Keough, M. E., & Schmidt, N. B. (2007). Problematic alcohol and cannabis use among young adults: the roles of depression and discomfort and distress tolerance. *Addict Behav*, 32, 1957-1963.

- Carroll, K. M., Nich, C., & Ball, S. A. (2005). Practice makes progress? Homework assignments and outcome in treatment of cocaine dependence. *J Consult Clin Psychol*, 73, 749-755.
- Carroll, K. M., Rounsaville, B. J., & Gawin, F. H. (1991). A comparative trial of psychotherapies for ambulatory cocaine abusers: relapse prevention and interpersonal psychotherapy. *Am J Drug Alcohol Abuse*, 17, 229-247.
- Chermack, S. T., Fuller, B. E., & Blow, F. C. (2000). Predictors of expressed partner and non-partner violence among patients in substance abuse treatment. *Drug and alcohol dependence*, 58, 43-54.
- Chi, F. W., Satre, D. D., & Weisner, C. (2006). Chemical dependency patients with cooccurring psychiatric diagnoses: service patterns and 1-year outcomes. *Alcoholism: Clinical and Experimental Research*, 30, 851-859.
- Clark, R. E., Samnaliev, M., & McGovern, M. P. (2009). Impact of Substance Disorders on Medical Expenditures for Medicaid Beneficiaries With Behavioral Health Disorders. *Psychiatric Services*, 60, 35-42.
- Crits-Christoph, P., Gibbons, M. B., Barber, J. P., Gallop, R., Beck, A. T., Mercer, D., . . . Frank, A. (2003). Mediators of outcome of psychosocial treatments for cocaine dependence. *J Consult Clin Psychol*, 71, 918-925.
- Crits-Christoph, P., Siqueland, L., Blaine, J., Frank, A., Luborsky, L., Onken, L. S., . . . Beck, A. T. (1999). Psychosocial treatments for cocaine dependence: National Institute on Drug Abuse Collaborative Cocaine Treatment Study. *Arch Gen Psychiatry*, 56, 493-502.
- Curran, G. M., Flynn, H. A., Kirchner, J., & Booth, B. M. (2000). Depression after alcohol treatment as a risk factor for relapse among male veterans. *Journal of Substance Abuse Treatment*, 19, 259-265.
- Curran, G. M., Sullivan, G., Williams, K., Han, X. T., Collins, K., Keys, J., & Kotrla, K. J. (2003). Emergency department use of persons with comorbid psychiatric and substance abuse disorders. *Annals of Emergency Medicine*, 41, 659-667.
- Curran, P. J., & Bauer, D. J. (2011). The disaggregation of within-person and between-person effects in longitudinal models of change. *Annual Review of Psychology*, 62, 583-619.

- Davidson, K. M., & Blackburn, I. M. (1998). Co-morbid depression and drinking outcome in those with alcohol dependence. *Alcohol and Alcoholism*, 33, 482-487.
- Dawson, L. K., & Grant, I. (2000). Alcoholics' initial organizational and problem-solving skills predict learning and memory performance on the Rey-Osterrieth Complex Figure. *Journal of the International Neuropsychological Society*, 6, 12-19.
- Delis, D. C., Kaplan, E., Kramer, J. H., & Ober, B. A. (2000). *California Verbal Learning Test-II (CVLT-II) Manual*. San Antonio, TX: The Psychological Corporation.
- Dimidjian, S., Barrera, M., Martell, C., Munoz, R. F., & Lewinsohn, P. M. (2011). The Origins and Current Status of Behavioral Activation Treatments for Depression. *Annual Review of Clinical Psychology*, 7, 1-38.
- Dolan, S. L., Martin, R. A., & Rohsenow, D. J. (2008). Self-efficacy for cocaine abstinence: pretreatment correlates and relationship to outcomes. *Addict Behav*, 33, 675-688.
- Drake, R. E., Essock, S. M., Shaner, A., Carey, R. B., Minkoff, K., Kola, L., . . . Rickards, L. (2001). Implementing dual diagnosis services for clients with severe mental illness. *Psychiatric Services*, 52, 469-476.
- Druss, B. G., & Rosenheck, R. A. (1999). Patterns of health care costs associated with depression and substance abuse in a national sample. *Psychiatric Services*, 50, 214-218.
- El-Guebaly, N., Currie, S., Williams, J., Wang, J. L., Beck, C. A., Maxwell, C., & Patten, S. B. (2007). Association of mood, anxiety, and substance use disorders with occupational status and disability in a community sample. *Psychiatric Services*, 58, 659-667.
- Elgamal, S., Denburg, S., Marriott, M., & MacQueen, G. (2010). Clinical factors that predict cognitive function in patients with major depression. *Can J Psychiatry*, 55, 653-661.
- Erickson, S. K., Rosenheck, R. A., Trestman, R. L., Ford, J. D., & Desai, R. A. (2008). Risk of incarceration between cohorts of veterans with and without mental illness discharged from inpatient units. *Psychiatric Services*, 59, 178-183.

- Finney, J. W. (2007). Treatment processes and mediators of substance use disorders treatment effects: the benefits of side road excursions. *Alcohol Clin Exp Res*, 31, 80s-83s.
- Finney, J. W., Noyes, C. A., Coutts, A. I., & Moos, R. H. (1998). Evaluating substance abuse treatment process models: I. Changes on proximal outcome variables during 12-step and cognitive-behavioral treatment. *J Stud Alcohol*, 59, 371-380.
- Gamble, S. A., Conner, K. R., Talbot, N. L., Yu, Q., Tu, X. M., & Connors, G. J. (2010). Effects of pretreatment and posttreatment depressive symptoms on alcohol consumption following treatment in Project MATCH. *Journal of Studies on Alcohol and Drugs*, 71, 71-77.
- Garnick, D. W., Hendricks, A. M., Comstock, C., & Horgan, C. (1997). Do individuals with substance abuse diagnoses incur higher charges than individuals with other chronic conditions? *J Subst Abuse Treat*, 14, 457-465.
- Garratt, G., Ingram, R. E., Rand, K. L., & Sawalani, G. (2007). Cognitive processes in cognitive therapy: Evaluation of the mechanisms of change in the treatment of depression. *Clinical Psychology-Science and Practice*, 14, 224-239.
- Glasner-Edwards, S., Marinelli-Casey, P., Hillhouse, M., Ang, A., Mooney, L. J., & Rawson, R. (2009). Depression among methamphetamine users: association with outcomes from the Methamphetamine Treatment Project at 3-year follow-up. *Journal of Nervous and Mental Disease*, 197, 225-231.
- Glasner-Edwards, S., Marinelli-Casey, P., Hillhouse, M., Ang, A., Mooney, L. J., Rawson, R., & Project, M. T. (2009). Depression Among Methamphetamine Users Association With Outcomes From the Methamphetamine Treatment Project at 3-Year Follow-Up. *Journal of Nervous and Mental Disease*, 197, 225-231.
- Glasner-Edwards, S., Mooney, L. J., Marinelli-Casey, P., Hillhouse, M., Ang, A., & Rawson, R. (2008). Risk factors for suicide attempts in methamphetamine-dependent patients. *American Journal on Addictions*, 17, 24-27.
- Glasner-Edwards, S., Tate, S. R., McQuaid, J. R., Cummins, K., Granholm, E., & Brown, S. A. (2007). Mechanisms of action in integrated cognitive-behavioral treatment versus twelve-step facilitation for substance-dependent adults with comorbid major depression. *Journal of Studies on Alcohol and Drugs*, 68, 663-672.
- Golden, C. J. (1978). *Stroop Color and Word Test*. Chicago, IL: Stoelting Company.

- Granholm, E., Tate, S. R., Link, P. C., Lydecker, K. P., Cummins, K. M., McQuaid, J., . . . Brown, S. A. (2011). Neuropsychological functioning and outcomes of treatment for co-occurring depression and substance use disorders. *Am J Drug Alcohol Abuse*, 37, 240-249.
- Grant, B. F., Stinson, F. S., Dawson, D. A., Chou, P., Dufour, M. C., Compton, W., . . . Kaplan, K. (2004). Prevalence and co-occurrence of substance use disorders and independent mood and anxiety disorders: Results from the national epidemiologic survey on alcohol and related conditions. *Archives of General Psychiatry*, 61, 807-816.
- Grant, B. F., Stinson, F. S., Dawson, D. A., Chou, S. P., Dufour, M. C., Compton, W., . . . Kaplan, K. (2006). Prevalence and co-occurrence of substance use disorders and independent mood and anxiety disorders - Results from the National Epidemiologic Survey on Alcohol and Related Conditions (reprinted from *Archives of General Psychiatry*, vol 61, pg 807, 2004). *Alcohol Research & Health*, 29, 107-120.
- Greenfield, S. F., Weiss, R. D., Muenz, L. R., Vagge, L. M., Kelly, J. F., Bello, L. R., & Michael, J. (1998). The effect of depression on return to drinking: A prospective study. *Archives of General Psychiatry*, 55, 259-265.
- Greenwood, G. L., Woods, W. J., Guydish, J., & Bein, E. (2001). Relapse outcomes in a randomized trial of residential and day drug abuse treatment. *J Subst Abuse Treat*, 20, 15-23.
- Group, P. M. R. (1997, Jan). Matching Alcoholism Treatments to Client Heterogeneity: Project MATCH posttreatment drinking outcomes. *Journal of Studies on Alcohol*, 58, 7-29.
- Gualtieri, C. T., Johnson, L. G., & Benedict, K. B. (2006). Neurocognition in depression: patients on and off medication versus healthy comparison subjects. *J Neuropsychiatry Clin Neurosci*, 18, 217-225.
- Haaga, D. A. F. (2007). Could we speed this up? Accelerating progress in research on mechanisms of change in cognitive therapy of depression. *Clinical Psychology-Science and Practice*, 14, 240-243.
- Hamilton, M. (1960). A rating scale for depression. *Journal of Neurology, Neurosurgery, and Psychiatry*, 23, 56-62.

- Hasin, D., Liu, X., Nunes, E., McCloud, S., Samet, S., & Endicott, J. (2002). Effects of major depression on remission and relapse of substance dependence. *Archives of General Psychiatry*, 59, 375-380.
- Heaton, R. K., Chelune, G. J., Talley, J. L., Kay, G. G., & Curtiss, G. (1993). *Wisconsin Card Sorting Test Manual: Revised and Expanded*. Odessa, FL: Psychological Assessment Resources.
- Heaton, R. K., Grant, I., & Matthews, C. G. (1991). *Comprehensive norms for Expanded Halstead-Reitan Battery: Demographic corrections, research findings, and clinical applications*. Odessa, FL: Psychological Assessment Resources, Inc.
- Hides, L., Carroll, S., Catania, L., Cotton, S. M., Baker, A., Scaffidi, A., & Lubman, D. I. (2010). Outcomes of an integrated cognitive behaviour therapy (CBT) treatment program for co-occurring depression and substance misuse in young people. *J Affect Disord*, 121, 169-174.
- Hitchcock, H. C., Stainback, R. D., & Roque, G. M. (1995). Effects of halfway house placement on retention of patients in substance abuse aftercare. *Am J Drug Alcohol Abuse*, 21, 379-390.
- Humphreys, K., Kaskutas, L. A., & Weisner, C. (1998). The Alcoholics Anonymous Affiliation Scale: Development, reliability, and norms for diverse treated and untreated populations. *Alcoholism: Clinical and Experimental Research*, 22, 974-978.
- Hunt, S. A., Baker, A. L., Michie, P. T., & Kavanagh, D. J. (2009). Neurocognitive profiles of people with comorbid depression and alcohol use: implications for psychological interventions. *Addict Behav*, 34, 878-886.
- Hunter-Reel, D., McCrady, B., & Hildebrandt, T. (2009). Emphasizing interpersonal factors: an extension of the Witkiewitz and Marlatt relapse model. *Addiction*, 104, 1281-1290.
- Ilgen, M., McKellar, J., & Tiet, Q. (2005). Abstinence self-efficacy and abstinence 1 year after substance use disorder treatment. *J Consult Clin Psychol*, 73, 1175-1180.
- Ilgen, M., & Moos, R. (2005). Deterioration Following Alcohol-Use Disorder Treatment in Project MATCH. *Journal of Studies on Alcohol*, 66, 517-525.
- Jaffe, A., Shoptaw, S., Stein, J. A., Reback, C. J., & Rotheram-Fuller, E. (2007). Depression ratings, reported sexual risk behaviors, and methamphetamine use:

- Latent growth curve models of positive change among gay and bisexual men in an outpatient treatment program. *Experimental and Clinical Psychopharmacology*, 15, 301-307.
- Jaffe, A. J., Rounsaville, B., Chang, G., Schottenfeld, R. S., Meyer, R. E., & O'Malley, S. S. (1996). Naltrexone, relapse prevention, and supportive therapy with alcoholics: an analysis of patient treatment matching. *J Consult Clin Psychol*, 64, 1044-1053.
- Johnson, J. E., Finney, J. W., & Moos, R. H. (2006). End-of-treatment outcomes in cognitive-behavioral treatment and 12-step substance use treatment programs: Do they differ and do they predict 1-year outcomes? *J Subst Abuse Treat*, 31, 41-50.
- Kadden, R. M. (1995). *Cognitive-behavioral coping skills therapy manual : a clinical research guide for therapists treating individuals with alcohol abuse and dependence*. Rockville, Md.: U.S. Dept. of Health and Human Services, Public Health Service, National Institutes of Health, National Institute on Alcohol Abuse and Alcoholism.
- Kadden, R. M., & Litt, M. D. (2011). The role of self-efficacy in the treatment of substance use disorders. *Addict Behav*, 36, 1120-1126.
- Kahler, C. W., Read, J. P., Ramsey, S. E., Stuart, G. L., McCrady, B. S., & Brown, R. A. (2004). Motivational enhancement for 12-step involvement among patients undergoing alcohol detoxification. *Journal of Consulting and Clinical Psychology*, 72, 736-741.
- Kazdin, A. E. (2007). Mediators and mechanisms of change in psychotherapy research. *Annu Rev Clin Psychol*, 3, 1-27.
- Kazdin, A. E., & Nock, M. K. (2003). Delineating mechanisms of change in child and adolescent therapy: methodological issues and research recommendations. *J Child Psychol Psychiatry*, 44, 1116-1129.
- Kelly, J. F., Hoepfner, B., Stout, R. L., & Pagano, M. (2012). Determining the relative importance of the mechanisms of behavior change within Alcoholics Anonymous: a multiple mediator analysis. *Addiction*, 107, 289-299.
- Kelly, J. F., Magill, M., & Stout, R. L. (2009). How Do People Recover from Alcohol Dependence? A Systematic Review of the Research on Mechanisms of Behavior Change in Alcoholics Anonymous. *Alcoholism-Clinical and Experimental Research*, 33, 48a-48a.

- Kelly, J. F., McKellar, J. D., & Moos, R. (2003). Major depression in patients with substance use disorders: Relationship to 12-Step self-help involvement and substance use outcomes. *Addiction*, 98, 499-508.
- Kelly, J. F., Stout, R. L., Magill, M., Tonigan, J. S., & Pagano, M. E. (2010). Mechanisms of behavior change in alcoholics anonymous: does Alcoholics Anonymous lead to better alcohol use outcomes by reducing depression symptoms? *Addiction*, 105, 626-636.
- Kiluk, B. D., Nich, C., & Carroll, K. M. (2011). Relationship of cognitive function and the acquisition of coping skills in computer assisted treatment for substance use disorders. *Drug Alcohol Depend*, 114, 169-176.
- King, K. M., Karyadi, K. A., Luk, J. W., & Patock-Peckham, J. A. (2011). Dispositions to rash action moderate the associations between concurrent drinking, depressive symptoms, and alcohol problems during emerging adulthood. *Psychol Addict Behav*, 25, 446-454.
- Klein, A. A., Slaymaker, V. J., & Kelly, J. F. (2011). The 12 Step Affiliation and Practices Scale: Development and initial validation of a measure assessing 12 step affiliation. *Addictive Behaviors*, 36, 1045-1051.
- Knesevich, J. W., Biggs, J. T., Clayton, P. J., & Ziegler, V. E. (1977). Validity of the Hamilton Rating Scale for depression. *Br J Psychiatry*, 131, 49-52.
- Knight, R. G., & Longmore, B. E. (1994). *Clinical neuropsychology of alcoholism*. Hove (UK) ; Hillsdale (USA): L. Erlbaum.
- Kodl, M. M., Fu, S. S., Willenbring, M. L., Gravely, A., Nelson, D. B., & Joseph, A. M. (2008). The impact of depressive symptoms on alcohol and cigarette consumption following treatment for alcohol and nicotine dependence. *Society for Research on Nicotine and Tobacco*, Feb 2007, Austin, TX, US; This work was presented at the aforementioned conference., 32, 92-99.
- Kraemer, H. C., Stice, E., Kazdin, A., Offord, D., & Kupfer, D. (2001). How do risk factors work together? Mediators, moderators, and independent, overlapping, and proxy risk factors. *Am J Psychiatry*, 158, 848-856.
- Kraemer, H. C., Wilson, G. T., Fairburn, C. G., & Agras, W. S. (2002). Mediators and moderators of treatment effects in randomized clinical trials. *Arch Gen Psychiatry*, 59, 877-883.

- Kreft, I. G. G., Deleeuw, J., & Aiken, L. S. (1995). The Effect of Different Forms of Centering in Hierarchical Linear-Models. *Multivariate Behavioral Research*, 30, 1-21.
- Krull, J. L., & MacKinnon, D. P. (2001). Multilevel modeling of individual and group level mediated effects. *Multivariate Behavioral Research*, 36, 249-277.
- LaChance, H., Feldstein Ewing, S. W., Bryan, A. D., & Hutchison, K. E. (2009). What makes group MET work? A randomized controlled trial of college student drinkers in mandated alcohol diversion. *Psychol Addict Behav*, 23, 598-612.
- Lamers, C. T. J., Bechara, A., Rizzo, M., & Ramaekers, J. G. (2006). Cognitive function and mood in MDMA/THC users, THC users and non-drug using controls. *Journal of Psychopharmacology*, 20, 302-311.
- Landro, N. I., Stiles, T. C., & Sletvold, H. (2001). Neuropsychological function in nonpsychotic unipolar major depression. *Neuropsychiatry Neuropsychol Behav Neurol*, 14, 233-240.
- Latkin, C. A., Knowlton, A. R., Hoover, D., & Mandell, W. (1999). Drug network characteristics as a predictor of cessation of drug use among adult injection drug users: a prospective study. *Am J Drug Alcohol Abuse*, 25, 463-473.
- Laudet, A. B., Cleland, C. M., Magura, S., Vogel, H. S., & Knight, E. L. (2004). Social support mediates the effects of dual-focus mutual aid groups on abstinence from substance use. *American Journal of Community Psychology*, 34, 175-185.
- Leventhal, A. M., Mooney, M. E., DeLaune, K. A., & Schmitz, J. M. (2006). Using addiction severity profiles to differentiate cocaine-dependent patients with and without comorbid major depression. *American Journal on Addictions*, 15, 362-369.
- Levin, F. R., Bisaga, A., Raby, W., Aharonovich, E., Rubin, E., Mariani, J., . . . Nunes, E. V. (2008a). Effects of major depressive disorder and attention-deficit/hyperactivity disorder on the outcome of treatment for cocaine dependence. *J Subst Abuse Treat*, 34, 80-89.
- Levin, F. R., Bisaga, A., Raby, W., Aharonovich, E., Rubin, E., Mariani, J., . . . Nunes, E. V. (2008b). Effects of major depressive disorder and attention-deficit/hyperactivity disorder on the outcome of treatment for cocaine dependence. *Journal of Substance Abuse Treatment*, 34, 80-89.

- Levy, B., Monzani, B. A., Stephansky, M. R., & Weiss, R. D. (2008). Neurocognitive impairment in patients with co-occurring bipolar disorder and alcohol dependence upon discharge from inpatient care. *Psychiatry Res*, *161*, 28-35.
- Litt, M. D., Kadden, R. M., Cooney, N. L., & Kabela, E. (2003). Coping skills and treatment outcomes in cognitive-behavioral and interactional group therapy for alcoholism. *Journal of consulting and clinical psychology*, *71*, 118-128.
- Litt, M. D., Kadden, R. M., Kabela-Cormier, E., & Petry, N. (2007). Changing network support for drinking: initial findings from the network support project. *J Consult Clin Psychol*, *75*, 542-555.
- Litt, M. D., Kadden, R. M., Kabela-Cormier, E., & Petry, N. M. (2008). Coping skills training and contingency management treatments for marijuana dependence: exploring mechanisms of behavior change. *Addiction*, *103*, 638-648.
- Litt, M. D., Kadden, R. M., Kabela-Cormier, E., & Petry, N. M. (2009). Changing network support for drinking: network support project 2-year follow-up. *J Consult Clin Psychol*, *77*, 229-242.
- Litt, M. D., Kadden, R. M., & Stephens, R. S. (2005). Coping and self-efficacy in marijuana treatment: Results from the marijuana treatment project. *Journal of consulting and clinical psychology*, *73*, 1015-1025.
- Long, C. G., Williams, M., Midgley, M., & Hollin, C. R. (2000). Within-program factors as predictors of drinking outcome following cognitive-behavioral treatment. *Addict Behav*, *25*, 573-578.
- Longabaugh, R. (2007). The search for mechanisms of change in behavioral treatments for alcohol use disorders: a commentary. *Alcoholism: Clinical and Experimental Research*, *31*, 21s-32s.
- Longabaugh, R., Donovan, D. M., Karno, M. P., McCrady, B. S., Morgenstern, J., & Tonigan, J. S. (2005a). Active ingredients: How and why evidence-based alcohol behavioral treatment interventions work. *Alcoholism: Clinical and Experimental Research*, *29*, 235-247.
- Longabaugh, R., Donovan, D. M., Karno, M. P., McCrady, B. S., Morgenstern, J., & Tonigan, J. S. (2005b). Active ingredients: how and why evidence-based alcohol behavioral treatment interventions work. *Alcohol Clin Exp Res*, *29*, 235-247.

- Longabaugh, R., & Magill, M. (2011). Recent Advances in Behavioral Addiction Treatments: Focusing on Mechanisms of Change. *Current Psychiatry Reports*, 13(5), 382-389.
- Longabaugh, R., Wirtz, P. W., Zweben, A., & Stout, R. L. (1998). Network support for drinking, Alcoholics Anonymous and long-term matching effects. *Addiction*, 93, 1313-1333.
- Longabaugh, R., Wirtz, P. W., Zywiak, W. H., & O'Malley, S. S. (2010). Network support as a prognostic indicator of drinking outcomes: the COMBINE Study. *J Stud Alcohol Drugs*, 71, 837-846.
- Lydecker, K. P., Tate, S. R., Cummins, K. M., McQuaid, J., Granholm, E., & Brown, S. A. (2010). Clinical outcomes of an integrated treatment for depression and substance use disorders. *Psychology of Addictive Behaviors*, 24, 453-465.
- Lynskey, M. T. (1998). The comorbidity of alcohol dependence and affective disorders: treatment implications. *Drug and Alcohol Dependence*, 52, 201-209.
- MacKinnon, D. P. (2008). *Introduction to statistical mediation analysis*. New York: Lawrence Erlbaum Associates.
- MacKinnon, D. P., Fritz, M. S., Williams, J., & Lockwood, C. M. (2007). Distribution of the product confidence limits for the indirect effect: program PRODCLIN. *Behavioral Research Methods*, 39, 384-389.
- MacKinnon, D. P., Lockwood, C. M., Hoffman, J. M., West, S. G., & Sheets, V. (2002). A comparison of methods to test mediation and other intervening variable effects. *Psychological Methods*, 7, 83-104.
- Magura, S., Cleland, C., Vogel, H. S., Knight, E. L., & Laudet, A. B. (2007). Effects of "dual focus" mutual aid on self-efficacy for recovery and quality of life. *Adm Policy Ment Health*, 34, 1-12.
- Magura, S., Knight, E. L., Vogel, H. S., Mahmood, D., Laudet, A. B., & Rosenblum, A. (2003). Mediators of effectiveness in dual-focus self-help groups. *Am J Drug Alcohol Abuse*, 29, 301-322.
- Magura, S., Laudet, A. B., Mahmood, D., Rosenblum, A., Vogel, H. S., & Knight, E. L. (2003). Role of self-help processes in achieving abstinence among dually diagnosed persons. *Addict Behav*, 28, 399-413.

- Maisto, S. A., Clifford, P. R., Stout, R. L., & Davis, C. M. (2008). Factors mediating the association between drinking in the first year after alcohol treatment and drinking at three years. *J Stud Alcohol Drugs*, 69, 728-737.
- Maisto, S. A., Connors, G. J., & Zywiak, W. H. (2000). Alcohol treatment, changes in coping skills, self-efficacy, and levels of alcohol use and related problems 1 year following treatment initiation. *Psychology of Addictive Behaviors*, 14, 257-266.
- Maisto, S. A., Sobell, L. C., & Sobell, M. B. (1979). Comparison of alcoholics' self-reports of drinking behavior with reports of collateral informants. *Journal of Consulting and Clinical Psychology*, 47, 106-112.
- Maisto, S. A., Sobell, M. B., & Sobell, L. C. (1982). Reliability of self-reports of low ethanol consumption by problem drinkers over 18 months of follow-up. *Drug and Alcohol Dependence*, 9, 273-278.
- Mark, T. L. (2003). The costs of treating persons with depression and alcoholism compared with depression alone. *Psychiatric Services*, 54, 1095-1097.
- Marlatt, G. A. (1996). Taxonomy of high-risk situations for alcohol relapse: evolution and development of a cognitive-behavioral model. *Addiction*, 91 Suppl, S37-49.
- Martin, P. R., Adinoff, B., Weingartner, H., Mukherjee, A. B., & Eckardt, M. J. (1986). Alcoholic Organic Brain Disease - Nosology and Pathophysiologic Mechanisms. *Prog Neuropsychopharmacol Biol Psychiatry*, 10, 147-164.
- Maxwell, S. E., & Cole, D. A. (2007). Bias in cross-sectional analyses of longitudinal mediation. *Psychol Methods*, 12, 23-44.
- McCrary, B. S., Epstein, E. E., & Kahler, C. W. (2004). Alcoholics anonymous and relapse prevention as maintenance strategies after conjoint behavioral alcohol treatment for men: 18-month outcomes. *Journal of Consulting and Clinical Psychology*, 72, 870-878.
- McKay, J. R., Foltz, C., Stephens, R. C., Leahy, P. J., Crowley, E. M., & Kissin, W. (2005). Predictors of alcohol and crack cocaine use outcomes over a 3-year follow-up in treatment seekers. *J Subst Abuse Treat*, 28, S73-S82.
- Meek, P. S., Clark, H. W., & Solana, V. L. (1989). Neurocognitive Impairment - the Unrecognized Component of Dual Diagnosis in Substance Abuse Treatment. *Journal of psychoactive drugs*, 21, 153-160.

- Moos, R. H. (2007). Theory-based active ingredients of effective treatments for substance use disorders. *Drug and alcohol dependence*, 88, 109-121.
- Moos, R. H. (2008). Active ingredients of substance use-focused self-help groups. *Addiction*, 103, 387-396.
- Morgenstern, J., & Bates, M. E. (1999). Effects of executive function impairment on change processes and substance use outcomes in 12-step treatment. *J Stud Alcohol*, 60, 846-855.
- Morgenstern, J., & Longabaugh, R. (2000). Cognitive-behavioral treatment for alcohol dependence: a review of evidence for its hypothesized mechanisms of action. *Addiction*, 95, 1475-1490.
- Morgenstern, J., & McKay, J. R. (2007). Rethinking the paradigms that inform behavioral treatment research for substance use disorders. *Addiction*, 102, 1377-1389.
- Muller, D., Judd, C. M., & Yzerbyt, V. Y. (2005). When moderation is mediated and mediation is moderated. *J Pers Soc Psychol*, 89, 852-863.
- Muñoz, R. F., & Ying, Y.-W. (1993). *The Prevention of Depression: Research and Practice*. Baltimore: Johns Hopkins University Press.
- Murray, R. L., Chermack, S. T., Walton, M. A., Winters, J., Booth, B. M., & Blow, F. C. (2008). Psychological Aggression, Physical Aggression, and Injury in Nonpartner Relationships Among Men and Women in Treatment for Substance-Use Disorders. *Journal of Studies on Alcohol and Drugs*, 69, 896-905.
- Nixon, S. J., Paul, R., & Phillips, M. (1998). Cognitive efficiency in alcoholics and polysubstance abusers. *Alcoholism-Clinical and Experimental Research*, 22, 1414-1420.
- Nock, M. K. (2007). Conceptual and design essentials for evaluating mechanisms of change. *Alcoholism: Clinical and Experimental Research*, 31, 4s-12s.
- Noordsy, D. L., Schwab, B., Fox, L., & Drake, R. E. (1996). The role of self-help programs in the rehabilitation of persons with severe mental illness and substance use disorders. *Community Mental Health Journal*, 32, 71-81.

- Norman, S. B., Tate, S. R., Wilkins, K. C., Cummins, K., & Brown, S. A. (2010). Posttraumatic stress disorder's role in integrated substance dependence and depression treatment outcomes. *J Subst Abuse Treat*, 38, 346-355.
- Nowinski, J., Baker, S., & Carroll, K. (2007). *Twelve step facilitation therapy manual : a clinical research guide for therapists treating individuals with alcohol abuse and dependence*. Rockville, Md.: U.S. Dept. of Health and Human Services, Public Health Service, National Institutes of Health, National Institute on Alcohol Abuse and Alcoholism.
- O'Toole, T. P., Pollini, R. A., Ford, D. E., & Bigelow, G. (2007). The effect of integrated medical-substance abuse treatment during an acute illness on subsequent health services utilization. *Medical Care*, 45, 1110-1115.
- Olfson, M., Fireman, B., Weissman, M., Leon, A. C., Sheehan, D. V., Kathol, R. G., . . . Farber, L. (1997). Mental disorders and disability among patients in a primary care group practice. *The American Journal of Psychiatry*, 154, 1734-1740.
- Omalley, S., Adamse, M., Heaton, R. K., & Gawin, F. H. (1992). Neuropsychological Impairment in Chronic Cocaine Abusers. *American Journal of Drug and Alcohol Abuse*, 18, 131-144.
- Ouimette, P. C., Moos, R. H., & Finney, J. W. (1998). Influence of outpatient treatment and 12-step group involvement on one-year substance abuse treatment outcomes. *Journal of Studies on Alcohol*, 59, 513-522.
- Parsons, O. A. (1998). Neurocognitive deficits in alcoholics and social drinkers: a continuum? *Alcohol Clin Exp Res*, 22, 954-961.
- Polcin, D. L. (2009). A model for sober housing during outpatient treatment. *J Psychoactive Drugs*, 41, 153-161.
- Project Match Research Group, U. S. (1997). *Matching alcoholism treatments to client heterogeneity: Project MATCH Posttreatment drinking outcomes*. (0096-882X). US: Alcohol Research Documentation
- Ramsey, S. E., Brown, R. A., Stuart, G. L., Burgess, E. S., & Miller, I. W. (2002). Cognitive variables in alcohol dependent patients with elevated depressive symptoms: changes and predictive utility as a function of treatment modality. *Subst Abus*, 23, 171-182.

- Raudenbush, S. W., & Bryk, A. S. (2002). *Hierarchical linear models : Applications and data analysis methods* (2nd ed.). Thousand Oaks: Sage Publications.
- Rey, A. (1941). Psychological examination of traumatic encephalopathy. *Archives de Psychologie*, 28, 286-340.
- Robins, L. N., Wing, J., Wittchen, H. U., Helzer, J. E., Babor, T. F., Burke, J., . . . et al. (1988). The Composite International Diagnostic Interview. An epidemiologic Instrument suitable for use in conjunction with different diagnostic systems and in different cultures. *Arch Gen Psychiatry*, 45, 1069-1077.
- Rychtarik, R. G., Connors, G. J., Dermen, K. H., & Stasiewicz, P. R. (2000). Alcoholics Anonymous and the use of medications to prevent relapse: an anonymous survey of member attitudes. *Journal of Studies on Alcohol*, 61, 134-138.
- Saatcioglu, O., Yapici, A., & Cakmak, D. (2008). Quality of life, depression and anxiety in alcohol dependence. *Drug and Alcohol Review*, 27, 83-90.
- Sarason, I. G., Levine, H. M., Basham, R. B., & Sarason, B. R. (1983). Assessing social support: The social support questionnaire. *Journal of Personality and Social Psychology*, 44, 127-139.
- Schafer, J. L., & Graham, J. W. (2002). Missing data: Our view of the state of the art. *Psychological Methods*, 7, 147-177.
- Schroeder, J. R., Latkin, C. A., Hoover, D. R., Curry, A. D., Knowlton, A. R., & Celentano, D. D. (2001). Illicit drug use in one's social network and in one's neighborhood predicts individual heroin and cocaine use. *Ann Epidemiol*, 11, 389-394.
- Shin, H. C., Marsh, J. C., Cao, D., & Andrews, C. M. (2011). Client-Provider relationship in comprehensive substance abuse treatment: differences in residential and nonresidential settings. *J Subst Abuse Treat*, 41, 335-346.
- Sklar, S. M., Annis, H. M., & Turner, N. E. (1997). Development and validation of the drug-taking confidence questionnaire: a measure of coping self-efficacy. *Addict Behav*, 22, 655-670.
- Slade, E. P., Stuart, E. A., Alkever, D. S. S., Karakus, M., Green, K. M., & Ialongo, N. (2008). Impacts of age of onset of substance use disorders on risk of adult incarceration among disadvantaged urban youth: A propensity score matching approach. *Drug and alcohol dependence*, 95, 1-13.

- Sobell, L. C., & Sobell, M. B. (1992). Timeline follow-back: A technique for assessing self-reported alcohol consumption. In R. Z. Litten & J. P. Allen (Eds.), *Measuring alcohol consumption: Psychosocial and biochemical methods* (pp. 41-72). Totowa, NJ: Humana Press.
- Solowij, N., Michie, P. T., & Fox, A. M. (1995). Differential Impairments of Selective Attention Due to Frequency and Duration of Cannabis Use. *Biol Psychiatry*, 37, 731-739.
- Solowij, N., Stephens, R. S., Roffman, R. A., Babor, T., Kadden, R., Miller, M., . . . Res, M. T. P. (2002). Cognitive functioning of long-term heavy cannabis users seeking treatment. *Jama-Journal of the American Medical Association*, 287, 1123-1131.
- StataCorp. (2007). *Stata Statistical Software: Release 10*. College Station, TX: StataCorp LP.
- Stinson, F. S., Grant, B. F., Dawson, D. A., Ruan, W. J., Huang, B. J., & Saha, T. (2006). Comorbidity between DSM-IV alcohol and specific drug use disorders in the United States - Results from the National Epidemiologic Survey on Alcohol and Related Conditions (Reprinted from Drug and Alcohol Dependence, vol 80, pg 105-116, 2005). *Alcohol Research & Health*, 29, 94-106.
- Stulz, N., Crits-Christoph, P., Thase, M. E., & Gallop, R. (2011). Psychosocial treatments for cocaine dependence: The role of depressive symptoms. *Drug and Alcohol Dependence*, 114, 41-48.
- Subbaraman, M. S., Kaskutas, L. A., & Zemore, S. (2011). Sponsorship and service as mediators of the effects of Making Alcoholics Anonymous Easier (MAAEZ), a 12-step facilitation intervention. *Drug and Alcohol Dependence*, 116, 117-124.
- Tate, S. R., Wu, J., McQuaid, J. R., Cummins, K., Shriver, C., Krenek, M., & Brown, S. A. (2008). Comorbidity of substance dependence and depression: role of life stress and self-efficacy in sustaining abstinence. *Psychol Addict Behav*, 22, 47-57.
- Taylor, W. D., Wagner, H. R., & Steffens, D. C. (2002). Greater depression severity associated with less improvement in depression-associated cognitive deficits in older subjects. *Am J Geriatr Psychiatry*, 10, 632-635.
- Teichner, G., Horner, M. D., Roitzsch, J. C., Herron, J., & Thevos, A. (2002). Substance abuse treatment outcomes for cognitively impaired and intact outpatients. *Addict Behav*, 27, 751-763.

- Timko, C., Debenedetti, A., & Billow, R. (2006). Intensive referral to 12-Step self-help groups and 6-month substance use disorder outcomes. *Addiction, 101*, 678-688.
- Tomlinson, K. L., Tate, S. R., Anderson, K. G., McCarthy, D. M., & Brown, S. A. (2006). An examination of self-medication and rebound effects: Psychiatric symptomatology before and after alcohol or drug relapse. *Addictive Behaviors, 31*, 461-474.
- Tonigan, J. S., & Beatty, G. K. (2011). Twelve-step program attendance and polysubstance use: interplay of alcohol and illicit drug use. *Journal of Studies on Alcohol and Drugs, 72*, 864-871.
- Tonigan, J. S., Toscova, R., & Miller, W. R. (1996). Meta-analysis of the literature on Alcoholics Anonymous: sample and study characteristics moderate findings. *Journal of Studies on Alcohol, 57*, 65-72.
- Tucker, K. A., Potenza, M. N., Beauvais, J. E., Browndyke, J. N., Gottschalk, P. C., & Kosten, T. R. (2004). Perfusion abnormalities and decision making in cocaine dependence. *Biol Psychiatry, 56*, 527-530.
- Turner, T. H., LaRowe, S., Horner, M. D., Herron, J., & Malcolm, R. (2009). Measures of cognitive functioning as predictors of treatment outcome for cocaine dependence. *J Subst Abuse Treat, 37*, 328-334.
- Walitzer, K. S., Dermen, K. H., & Barrick, C. (2009). Facilitating involvement in Alcoholics Anonymous during out-patient treatment: a randomized clinical trial. *Addiction, 104*, 391-401.
- Warren, J. I., Stein, J. A., & Grella, C. E. (2007a). Role of social support and self-efficacy in treatment outcomes among clients with co-occurring disorders. *Drug Alcohol Depend, 89*, 267-274.
- Warren, J. I., Stein, J. A., & Grella, C. E. (2007b). Role of social support and self-efficacy in treatment outcomes among clients with co-occurring disorders. *Drug and alcohol dependence, 89*, 267-274.
- Watkins, E., & Brown, R. G. (2002). Rumination and executive function in depression: an experimental study. *J Neurol Neurosurg Psychiatry, 72*, 400-402.
- Wechsler, D. (1997). *Wechsler Adult Intelligence Scale* (Third ed.). San Antonio, TX: The Psychological Corporation.

- Weinstein, C. S., & Shaffer, H. J. (1993). Neurocognitive Aspects of Substance-Abuse Treatment - a Psychotherapists Primer. *Psychotherapy*, 30, 317-333.
- Weiss, R. D., Griffin, M. L., Gallop, R. J., Najavits, L. M., Frank, A., Crits-Christoph, P., . . . Luborsky, L. (2005). The effect of 12-step self-help group attendance and participation on drug use outcomes among cocaine-dependent patients. *Drug and Alcohol Dependence*, 77, 177-184.
- White, A. M., Jordan, J. D., Schroeder, K. M., Acheson, S. K., Georgi, B. D., Sauls, G., . . . Swartzwelder, H. S. (2004). Predictors of Relapse During Treatment and Treatment Completion among Marijuana-Dependent Adolescents in an Intensive Outpatient Substance abuse Program. *Substance Abuse*, 25, 53-59.
- Whitlow, C. T., Liguori, A., Livengood, L. B., Hart, S. L., Mussat-Whitlow, B. J., Lamborn, C. M., . . . Porrino, L. J. (2004). Long-term heavy marijuana users make costly decisions on a gambling task. *Drug and alcohol dependence*, 76, 107-111.
- Wilk, J., West, J. C., Rae, D. S., & Regier, D. A. (2006a). Relationship of comorbid substance and alcohol use disorders to disability among patients in routine psychiatric practice. *American Journal on Addictions*, 15, 180-185.
- Wilk, J., West, J. C., Rae, D. S., & Regier, D. A. (2006b). Relationship of comorbid substance and alcohol use disorders to disability among patients in routine psychiatric practice. *Am J Addict*, 15, 180-185.
- Willenbring, M. L. (1986). Measurement of depression in alcoholics. *Journal of Studies on Alcohol*, 47, 367-372.
- Wirtz, P. W. (2007). Advances in causal chain development and testing in alcohol research: mediation, suppression, moderation, mediated moderation, and moderated mediation. *Alcohol Clin Exp Res*, 31, 57s-63s.
- Witkiewitz, K., Bowen, S., & Donovan, D. M. (2011). Moderating effects of a craving intervention on the relation between negative mood and heavy drinking following treatment for alcohol dependence. *J Consult Clin Psychol*, 79, 54-63.
- Witkiewitz, K., & Marlatt, G. A. (2004). Relapse prevention for alcohol and drug problems: that was Zen, this is Tao. *Am Psychol*, 59, 224-235.

- Witkiewitz, K., & Villarroel, N. A. (2009). Dynamic association between negative affect and alcohol lapses following alcohol treatment. *Journal of Consulting and Clinical Psychology, 77*, 633-644.
- Worley, M. J., Tate, S. R., & Brown, S. A. (under review). Mediation Relations between 12-step Meeting Attendance, Depression, and Substance Use during and after Treatment for Comorbidity.
- Worley, M. J., Trim, R. S., Roesch, S. C., Mrnak-Meyer, J., Tate, S. R., & Brown, S. A. (2012). Comorbid depression and substance use disorder: Longitudinal associations between symptoms in a controlled trial. *J Subst Abuse Treat.*
- Wu, J., & Witkiewitz, K. (2008). Network support for drinking: an application of multiple groups growth mixture modeling to examine client-treatment matching. *J Stud Alcohol Drugs, 69*, 21-29.
- Zweben, J. E. (2000). Severely and persistently mentally ill substance abusers: Clinical and policy issues. *Journal of psychoactive drugs, 32*, 383-389.
- Zywiak, W. H., Connors, G. J., Maisto, S. A., & Westerberg, V. S. (1996). Relapse research and the Reasons for Drinking Questionnaire: a factor analysis of Marlatt's relapse taxonomy. *Addiction, 91 Suppl*, S121-130.