The Treatment of Patients with Co-occurring Bipolar Disorder and Substance Use Disorder

Roger D. Weiss, MD

Chief, Division of Alcohol and Drug Abuse, McLean Hospital

Professor of Psychiatry, Harvard Medical School

Belmont, Massachusetts USA

rweiss@mclean.harvard.edu

The Scope of the Problem

NESARC: Lifetime Prevalence rate of Substance Use Disorders (SUDs) in Bipolar Disorder (BD)

- Alcohol Use Disorder 58%
- Drug Use Disorder 38%
- Nicotine Use Disorder 44%

NESARC Odds Ratios of SUDs in Persons with Bipolar Disorder

- Alcohol Dependence 5.7
- Drug Dependence 13.9

Influence of Substance Use on Bipolar Disorder

- BD has a higher prevalence of co-occurring SUD than any other psychiatric illness
- Co-morbidity is associated with more severe course of BD
    - Earlier onset
    - More frequent episodes
    - More aggressive behavior
    - Legal problems
    - Suicide

Swann et al., 2010

The Influence of Specific Substances on Bipolar Disorder:

Cannabis, Tobacco, Alcohol

Bipolar Disorder and Cannabis Use

Cannabis use in BD associated with

- Less medication adherence
- Poorer social functioning
- More severe mood episodes
- Greater likelihood of psychosis
- Poorer treatment outcome

First-Episode Psychosis: the Implications of Cannabis Use

- Three categories
  - Used cannabis beforehand and stopped
  - Used cannabis beforehand and continued use
  - Never used cannabis beforehand
- Best outcomes for those who used cannabis beforehand and stopped
- Worst outcomes for those who continued cannabis use

Gonzales-Pinto et al., 2011; Stone et al., 2014

The Clinical Significance of Smoking Tobacco in Bipolar Disorder

Graff et al., 2008

61 patients with BD and SUD receiving group therapy weekly x 12 weeks

- Study to predict likelihood of dropout (i.e., missing ≥ 4 consecutive groups)
- Lower education and recent mood episode predicted dropout
- Best predictor of dropout was cigarette smoking (odds ratio 11.5)

The Clinical Significance of Smoking Tobacco in Bipolar Disorder

Ostacher et al., 2006

- 399 patients with BD evaluated, 39% were daily smokers
- Daily smoking was associated with
  - Earlier age of onset of first episode
  - Lower Global Assessment of Functioning scores
  - Lifetime other substance dependence
  - Lifetime suicide attempt (47% vs. 25%)

Alcohol Use Disorder as a Risk Factor of Suicidal Behavior in Bipolar Disorder

- 1,643 individuals with BD
  - 54% also had dx of AUD
  - Individuals with BD & AUD were more likely to report suicide attempts (25% vs. 15% in the BD-only group

Oquendo et al. 2010

Neurocognitive effects of Bipolar Disorder & Alcohol Use Disorder

- Three groups with Bipolar I disorder, admitted due to manic episode-
  - BD & current AUD (n=13), BD & AUD in remission for over 1 year (n=9), BD only with no history of SUD (n=41)

  Those with BD & current AUD were significantly more impaired in visual and verbal memory measures than BD only
- Both BD + AUD groups performed significantly worse than BD-alone patients on executive function measures

Levy et al. 2008

Treatment of Patients with SUD and Bipolar Disorder

- Pharmacotherapy
- Psychosocial treatment

Pharmacotherapy

Valproate for Alcohol Dependence & BD

- 24-week trial of valproate vs. placebo in 59 pts on lithium
- Valproate patients had:
  - Fewer heavy drinking days
  - Less drinking on heavy drinking days
  - No differences in manic, depressive sx

Salloum et al., 2005

Quetiapine for Alcohol Abuse or Dependence & BD:

- 12-week trial of quetiapine add-on Rx (N=115), titrated up to 600 mg/day over 6 weeks
  - No difference between quetiapine and placebo on alcohol use measures or Young Mania Rating Scale
  - Depressive sx reduced more in quetiapine Ss, esp. in first 6 weeks

Brown et al., 2008

Citicoline in SUDs

- Citicoline: increases incorporation of phospholipids into membranes and enhances the synthesis of structural phospholipids.
- Sold over the counter
- May have neuroprotective and cognitive enhancing properties
- Used in some countries for Parkinson disease, traumatic head injury, stroke, vascular dementia

Benefits- May improve cognitive functioning, may weaken the neurotoxic effects of the drugs abused

Citicoline for Cocaine Dependence & BD

- 12-week trial of citicoline vs. placebo (N=130)
- Citicoline started at 500mg/day and increased to 2 g/d
- Citicoline patients had:
  - A decrease in cocaine use based on urine screens
  - No significant difference in manic or depressive symptoms
- Effects of citicoline in reducing cocaine use appeared quickly and declined during the study

Brown, et al. 2015

Lifetime Medication Adherence in Patients with BD and SUD

100% Adherence

Lithium*	22%
Valproate	48%
BZs	36%
Neuroleptics	37%
TCAs	63%
SSRIs	46%

*Lithium vs. Valproate $p < .03$

Reasons for Med Non-Adherence

Lithium	24% Physical effects
N = 29	21% Saw no need
	10% Wanted to use
Valproate	31% Hassle to take
N = 13	15% Forgot to take
	15% Wanted to use
BZs	29% Took more to get “high”
N = 21	29% Impatience, took more
	10% Couldn’t think clearly

Reasons for Med Non-Adherence

Nlptcs	37%	Physical effects (EPS)
N = 19	26%	Impatience, modify sub. use, get high
	11%	Saw no need
TCAs	40%	Impatience, took more
N = 10	20%	Saw no need
	10%	Meds not working, took less
SSRIs	18%	Wanted to use
N = 17	12%	Felt manic
	12%	Meds not working, took less

Psychosocial Treatment

Types of Behavioral Treatments for patients with BD and co-occurring & SUD

- Individual counseling
  - Early Recovery Adherence Therapy (ERAT)
  - Individual cognitive-behavioral treatment (CBT)
- Integrated Group Therapy (IGT)

Early Recovery Adherence Therapy (ERAT)

- Design- Increase medication and treatment adherence during early phases of recovery from an acute episode
- Integrated principles- motivational enhancement, relapse prevention strategies
- 34 patients with BD & AUD given either ERAT or 12-step intervention over 12-week period
- Individuals participating in ERAT compared to 12-step:
  - Decrease in alcohol consumption
  - Decrease in depressive symptoms

Salloum, et al 2008

Individual Cognitive-Behavioral Approach

- Medication monitoring and 16 individual cognitive-behavioral sessions
- Schmitz et al 2002
  - 46 individuals with BD & SUD randomly assigned either medication monitoring (MM) alone or medication monitoring plus individual cognitive behavioral treatment (MM+CBT)
  - The group given MM + CBT had better medication adherence and fewer depressive symptoms compared to MM alone.
  - Both groups had no difference in substance use outcome

Integrated Group Therapy (IGT): Core principles

- Cognitive-behavioral model focuses on parallels between the disorders in recovery/relapse thoughts and behaviors
- Stresses the interaction between the disorders
- The single disorder paradigm: “bipolar substance abuse”
- The central recovery rule: “No matter what, don’t use drugs, don’t use alcohol, and take your medication as prescribed, no matter what”

What is “integrated” about Integrated Group Therapy?

- Check-in focuses on mood, substance use, and medication adherence
- Topics relevant to both disorders (e.g., “Dealing with depression without using alcohol or drugs”)
- Patients seen as having a single disorder: “bipolar substance abuse”
- Relationship & similarities between the disorders & the recovery process stressed

Findings of IGT research

- 3 studies funded by U.S. National Institute on Drug Abuse (NIDA)
- Compared IGT to either treatment as usual or standard manualized Group Drug Counseling
- All 3 studies showed significantly greater likelihood of abstinence in IGT patients
- Fewer differences in mood outcomes
- Cited by NIDA as one of only 5 “examples of promising behavioral therapies for adult patients with comorbid conditions”

Parallels in the recovery and relapse processes

- The abstinence violation effect vs. stopping medication when depressed
- “May as well thinking” vs. “It matters what you do” to combat layers of hopelessness

IGT vs. Group Drug Counseling

Patients

- 61 patients: 31 IGT & 30 GDC
- Current BD & substance dependence
- Substance use in the past 60 days
- A mood stabilizer regimen that had been in place for ≥ 2 weeks

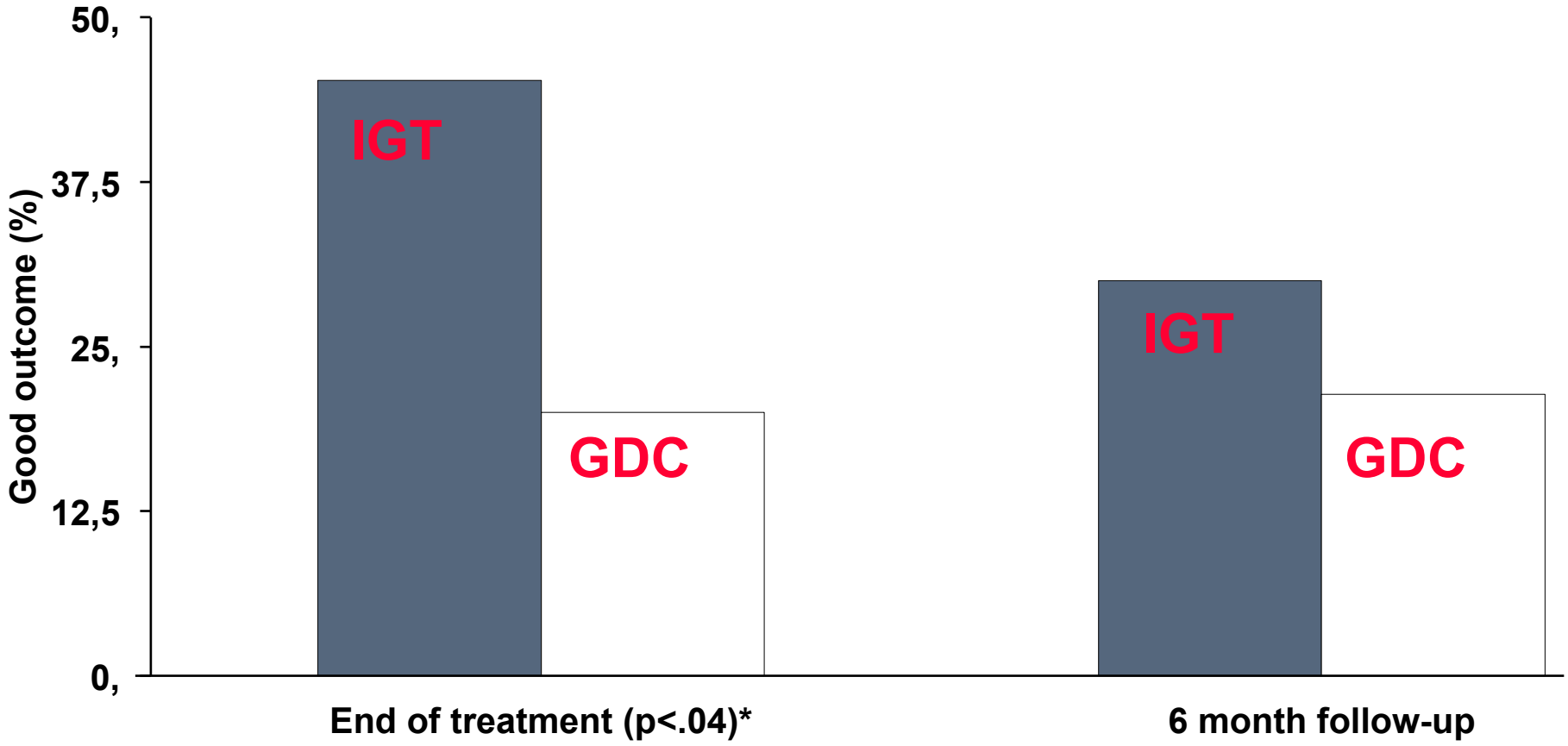
Results: Mood (p<.10)

Outcome Variables	IGT (n=31)			GDC (n=30)		
	Baseline	End of Tx	3-mo f/u	Baseline	End of tx	3-mo f/u
Mood episode (% yes)	52	20	27	57	30	37
Depressive episode	35	20	20	40	23	22
Manic episode	16	0	7	17	7	15

Abstinence: IGT vs. GDC

- ≥1 month abstinent: 71% vs. 40 %, p<.02
- Abstinent throughout treatment (3 mos.): 36% vs. 13%, p<.05

“Good clinical outcome” by treatment condition: Abstinent & no mood episodes in last month



Current status of IGT

- Has been adapted for patients with psychotic illness and mood disorders as well
- In use in multiple clinical settings at McLean Hospital, and has been adapted to different settings: inpatient, residential, forensic
- Currently in use in multiple clinical research and correctional settings in U.S. and other countries
- Can be adapted to different settings
- Book published in 2011 by Guilford Press
- App currently in development

Integrated Group Therapy for Bipolar Disorder and Substance Abuse

Roger D. Weiss and Hilary Smith Connery