Adapting and implementing sleep and circadian treatment for mental illness and for community mental health settings

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Plan

- Treatment development to implementation science
- Disorder-focused (bipolar disorder) to transdiagnostic (severe mental illness, broadly defined)
- Use of the process of clinical science
- Change of context: university clinic to community mental health
- Sleep tips and tricks
Bipolar Disorder

- Typically alternate between episodes of mania (or hypomania) and depression (APA, 2000)
- The lifetime prevalence of Bipolar I, II, NOS is 2.6% and 6.5%, respectively (Merikangas et al., 2011)
- Each episode lasts between 2 and 7 months
- High rates of suicide (Isometa, 1993)
- Ranked in the top 10 leading causes of disability worldwide (World Health Organization, 2001)
- Sleep symptoms are prominent correlates of episodes and inadequate recovery (Harvey, 2008; Plante & Winkelman, 2008; Wehr, 1990)
Is Sleep Disturbance Epiphenomenal?


Sleep disturbance is the most common prodrome of mania and the sixth most common prodrome of depression (Jackson et al., 2003)

Sleep loss is highly correlated with daily manic symptoms (Barbini et al., 1996) and negative affect (Talbot et al., 2012; Gershon et al., 2012)

Induced sleep deprivation triggers hypomania or mania in a proportion of patients (Colombo et al., 1999)
Bi-Directional Escalating Vicious Cycle

Mood Regulation Difficulty

Sleep Disturbance

Inter-episode dysfunction

Vulnerability to relapse
Step-BD

- N = 2,024 patients diagnosed with bipolar disorder
- Variability in sleep/wake times across one week: 
  - 2.78 hours (SD = 3.02)

Dr. June Gruber

Gruber, J., Harvey, AG., Wang, PW., Brooks, JO., Thase, ME., Sachs, GS., Ketter, TA. 
Step-BD

• N = 2,024 patients diagnosed with bipolar disorder

• Variability in sleep/wake times across one week:
  – 2.78 hours (SD = 3.02)  

• Variability in sleep is associated with more past and current depressive episodes
  – sleep efficiency (r=0.50, p<.05)
  – total wake time (r=0.56, p<.005)
  – sleep onset latency (r=0.70, p<.05)

Step-BD

Hypersomnia in Inter-Episode Bipolar Disorder

- Rate = 25%

- Total Sleep Time (TST) or Time In Bed (TIB) ?
  - 4% TST > 9 hrs
  - 53% TIB > 9 hrs
  - TIB (av $r=0.55$) more highly correlated with all other measures of hypersomnia than TST (av $r=0.38$)

More complex than we expected

- Insomnia
- Hypersomnia (TIB problem)
- Short sleepers
- Irregular bed and wake times
- And more!

R34 to adapt CBT-I for bipolar disorder …
Recruited patients with bipolar disorder & insomnia
Did not exclude hypersomnia or delayed sleep phase
A Modifiable Pathway?

- Mood Regulation Difficulty
- Sleep Disturbance
- Inter-episode dysfunction
- Vulnerability to relapse
Inter-episode, Bipolar 1 Disorder + Insomnia

Included hypersomnia & delayed sleep phase

Screening & Baseline

Randomization

Treatment As Usual + 8 Sessions of ...

CBTI-BD (n = 30)

Psychoeducation (n = 28)

No Study Treatment Follow-up (6 months)

Insomnia Severity Index

Time X Condition Pre-Post $\beta=-6.64$, $p<0.001$

Time X Condition Pre-Follow-up $\beta=-5.64$, $p<0.01$

Standard error is depicted
Sheehan Disability Scale - Mood

Time Pre-Post $\beta = -1.97$, $p < 0.001$
Time Pre-Follow-up $\beta = -1.88$, $p < 0.01$
Standard error is depicted
Relapse: 6 Month Follow-up

- Depression
- Mania or Hypomania
- Any Recurrence

CBTI-BP (N=22) vs PE (N=19)

- Depression: ns
- Mania or Hypomania: p = 0.036
- Any Recurrence: ns
Days Spent in Episodes: 6 Mth Follow-up

![Bar chart showing days spent in episodes for depression, mania or hypomania, and any recurrence. Red and blue bars represent CBTI-BP (N=22) and PE (N=19), respectively.](image)

- Depression: CBTI-BP (n=2) vs. PE (n=19)
- Mania or Hypomania: CBTI-BP (n=2) vs. PE (n=19)
- Any Recurrence: CBTI-BP (n=2) vs. PE (n=19)

$p = 0.028$

Standard errors depicted.
Convergence

Sleep intervention improves sleep and symptoms of comorbid mental disorder

- Bipolar disorder (Harvey et al., 2015; R34MH080958)
- Depression: Youth (Clarke et al., 2015; R34MH082034)
- Schizophrenia (Myers et al., 2011)
- Depression: Adults (Manber et al., 2008)
- PTSD (Germain et al., 2009)
- And others including meta-analyses (e.g., Geiger-Brown et al., 2015)

Disorder-focused (on insomnia) but real life sleep and circadian problems are not so easily categorized (clinical or subclinical features of hypersomnia, delayed phase, irregular sleep & wake times)
How do we deal with the complexity?

• Do we continue to develop multiple disorder-focused treatments?

‘Too many empirically supported treatments problem’ (p. 68) (Weisz, Ng & Bearman, 2014)

Burden on clinicians, who must learn multiple disorder-focused protocols, with common theoretical underpinnings
Current Direction

Could one treatment be devised that is helpful ...  
• Across the various sleep and circadian disturbances  
• Across mental illnesses (physical health)  
• Across (some phases of) development (?)

Advantageous for dissemination: Substantial cost advantage to training providers in one treatment that covers multiple problems (McHugh & Barlow, 2010)

Transdiagnostic Intervention for Sleep and Circadian Dysfunction (TranS-C)  
(Harvey & Buysse, 2017, Guilford Press)
Sources for TranS-C

Transdiagnostic Intervention for Sleep and Circadian Dysfunction (TranS-C)

Cognitive Behavior Therapy for Insomnia (CBT-I)
- Stimulus control and sleep restriction
- Cognitive therapy

Chronotherapy
- Light exposure
- Regular sleep schedules

Interpersonal and Social Rhythms Therapy (IPSRT)
- Stabilize bedtime, wake time, meal times, socializing, exercise, etc.

Sources:
- de Bruin et al., 2014; Schlarb et al. 2010; Gradisar et al., 2011; Pain & Gradisar, 2011; Morin et al., 2006; Frank, Swartz, & Kupfer, 2000; Frank et al., 2005; Wirz-Justice et al., 2009
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Sleep and Circadian Basic Science

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Sleep Health Framework (Buysse, 2014)

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What is this complexity doing ...

- Insomnia
- Hypersomnia (or Too much time in bed)
- Delayed phase
- Irregular bed and wake times
- And other complexities
Implications for the Biological Orchestra of Clocks: Desynchrony!

- There are clocks in every cell in the body
  - Central clock: Suprachiasmatic nucleus (SCN) controls the circadian system and is responsive to light and dark
  - Clocks in the muscle, liver and lung synchronize to a variety of stimuli at their own rates but interact with all the other clocks

- Double desynchronization can occur:
  - between internal (SCN) and external time
  - between different clocks and organs in the body itself

Logan & McClung, 2018; Wirz-Justice, 2003; 2006
Sleep System vs. Circadian System

• Separate systems

• They interact

• We do not know the specific contribution of the two systems to the sleep problems experienced by people with a mental illness

Borbely, 1982
Open System
Exogenous Inputs

Modifiable

- Social rhythms
- Light
- Temperature
- Meal times
- Sleep deprivation
- Arousal
- Stress/Emotions
- Locomotor activity
Sources for TranS-C

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Glimpse of CBT-I

• Go to bed only when sleepy

• Awaken at the same time every morning

• Use the bed mainly for sleeping – no reading, watching TV, or eating in bed
  – Maladaptive conditioning or learned association between wakefulness and the bedroom

Why don’t we just use CBT-I?

• TranS-C incorporates CBT-I

• And addresses a broader range of sleep and circadian dysfunctions common to mental illness
  • Chronotherapy approaches and rise-up routines for delayed phase
  • CPAP adherence approaches for OSA
  • Negotiating sleep in a complex environment

• A notable proportion of SMI patients exhibit sleep efficiency >85% or their sleep efficiency is corrected by regularizing bed and wake times (Kaplan & Harvey, 2013, AJP)

• Safety: stimulus control and sleep restriction can involve partial sleep deprivation and SMI relapse (Columbo et al., 1999)
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TranS-C: A modular treatment

<table>
<thead>
<tr>
<th>Cross-Cutting Modules</th>
<th>Common Transdiagnostic Sleep-Circadian Problems</th>
<th>Treatment Module</th>
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<td>Case Formulation</td>
<td>Establishing regular sleep-wake times</td>
<td>Core Module 1</td>
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<tr>
<td>Education</td>
<td>Learning a wind-down routine</td>
<td>Core Module 1</td>
</tr>
<tr>
<td>Behavior Change &amp; Motivation</td>
<td>Learning a wake-up routine</td>
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<td>Goal Setting</td>
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<td>Correcting unhelpful sleep-related beliefs</td>
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<tr>
<td></td>
<td>Improving sleep efficiency</td>
<td>Optional Module 1</td>
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<td></td>
<td>Reducing time in bed</td>
<td>Optional Module 2</td>
</tr>
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<td></td>
<td>Dealing with delayed or advanced phase</td>
<td>Optional Module 3</td>
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<td></td>
<td>Reducing sleep-related worry/vigilance</td>
<td>Optional Module 4</td>
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<td>Promoting compliance with CPAP/exposure therapy</td>
<td>Optional Module 5</td>
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<td>for claustrophobic reactions to CPAP</td>
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<td>Negotiating sleep in a complicated environment</td>
<td>Optional Module 6</td>
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<td>Reducing nightmares</td>
<td>Optional Module 7</td>
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<td></td>
<td>Maintenance of behavior change</td>
<td>Core Module 4</td>
</tr>
</tbody>
</table>
Change of context

• Representativeness of the samples
  • In a highly diverse location
  • 50%+ with graduate level degrees
  • Difficulty recruiting ethnic and racial minority group members

• Who is not comfortable attending a university clinic for treatment?
• What are the barriers for those people?
Community Mental Health Centers

- “Unique national asset”
- 1960’s “War on Poverty” to eliminate health disparities
- SMI (serious mental illness)
- Serves 29 million Americans. No one is turned away: 40% uninsured, 36% Medicaid, 63%+ racial or ethnic minority, 91% low-income (200% Federal poverty level or below)
- Publicly funded providers
- Seriously under-resourced
- Providers carry a heavy, complex and comorbid caseload
- Providers may not receive training or supervision in EBTs

(Aarons et al., 2012; Adashi et al. 2010; Bruns et al., 2015; Chin et al., 2010; Drake et al., 2001; Garland et al., 2010; Lefkowitz et al., 2005; Rodríguez et al., 2014; Prosner, 2005; Weissman et al., 2006)
Snapshot of patient demographics (n=121)

- Av personal income $12,751 per yr
- 68% single
- 2% attended graduate school
- 80% not currently employed
- 55% living in a supported living environment
- 43% African American / Black

SMI diagnosis
- 50% Schizophrenia spectrum disorder
- 18% Bipolar disorder
- 32% MDD
(anxiety disorders & substance use often comorbid)
Alameda County, CA

**UC Berkeley providers delivering the treatment in CMHCs**
Mean PROMIS-Sleep Disturbance

- TranS-C (N = 61) vs. UC-DT (N = 60)

Pre-post, $p < .001$

Pre-6FU, $p < .001$

ns
The bar graph shows the mean Sheehan Disability Scale Total Score for two groups: TranS-C (N = 61) and UC-DT (N = 60). The x-axis represents different time points: Pre, Post, and 6FU. The y-axis represents the score range from 0 to 16.

- **Pre**:
  - TranS-C: 12 (ns)
  - UC-DT: 13

- **Post**:
  - TranS-C: 11
  - UC-DT: 12

- **6FU**:
  - TranS-C: 10
  - UC-DT: 11

A significant difference is indicated with **Pre-post, p < .05**. Additionally, the graph notes **Pre-6FU, NS**.
Secondary Outcomes

TranS-C, relative to usual care, reduction on: Psychotic Symptom Rating Scales (PSYRATS)

Total Wake Time
Wake Time Variability
Earlier Bedtime

Improvement on:
Sleep Efficiency

Sleep Health Composite (Buysse, 2014; Dong et al., 2019)

7-day sleep diary
New Project

- **CMHCs we are working with**
- **FQHCs we are working with**

Map of California highlighting counties.
New Project

- Funded by NIMH
- Patients n = 624; CMHC Providers n = 104
- Does TranS-C improve sleep and mental health and reduce substance use?
- Implementation science questions:
  - Can TranS-C can be effectively delivered by providers within CMHCs?
  - The implementation process (facilitation: Kirchner and PARIHS)
  - Supervision and fidelity
  - Training e.g., train-the-trainer
May I offer some sleep tips and tricks?
Look for 8+ tweaks to your sleep

Cut out checking the clock (bright light & arousal)
Cut down on caffeine & alcohol
Regular bedtimes
Regular waketimes (most important)
Accept that poor night’s of sleep will happen
Consider timeframe
‘Romantic’ lighting before bedtime
Rid bedroom of all light pollution
Ensure bedroom is very dark so the summer morning light doesn’t wake you
Cont...

Be aware of liquid intake before bedtime
Increase exercise
Perception of sleep: we often get more sleep than we think
Watch for vicious ‘racing mind’ cycles

‘I’m never going to get back to sleep’
‘I won’t cope tomorrow’
‘I will get sick’
Vs.
‘It’s so nice to be comfy here’
‘I feel so warm and calm’
Summary

- Disorder focused – Transdiagnostic
- TranS-C: Behavior change approach
  - Generated from sleep and circadian science
  - Generated from existing evidence-based treatments
  - Simple, short … disseminable
  - Promising initial results for sleep & the comorbid mental illness
- Advantages for dissemination, particularly in under resourced settings (e.g., CMHCs)
- Challenge ahead: Scaling of sleep treatment within many other contexts and populations …
Our community partners

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