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Actigraphy And Symptom Changes With A Social Rhythm Intervention In Young Persons With Mood Disorders

Gabriela De Queiroz Campos

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Actigraphy and Symptom Changes with a Social Rhythm Intervention in Young Persons with Mood Disorders

A Thesis Submitted to the Yale University School of Medicine in Partial Fulfillment of the Requirements for the Degree of Doctor of Medicine

By

Gabriela de Queiroz Campos

2024
Abstract

ACTIGRAPHY AND SYMPTOM CHANGES WITH A SOCIAL RHYTHM INTERVENTION IN YOUNG PERSONS WITH MOOD DISORDERS

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Irregularities in rest and activity patterns are being increasingly recognized to play important roles in symptoms of major mood disorders, such as bipolar disorder (BD) and major depressive disorder (MDD). Passive measures obtained from digital wearable actigraph devices have potential to provide scalable methods sensitive to behavioral and symptom changes that could be informative in identifying worsening and assessing effects of interventions. Use in younger individuals can be particularly helpful for identifying targets for early detection, allowing for potential reduction of disorder progression. Through this investigation, we aimed to assess changes in actigraphic measures of rest and activity patterns and mood disorder symptoms in adolescents and young adults with and at familial risk for a mood disorder receiving a telehealth social rhythm therapy (SRT) that provides individuals strategies to regularize their daily routines. Further, we aimed to assess for any associations between these changes in symptoms and actigraphic measures.

Seven adolescents and young adults with and at risk for a mood disorder, ages 14-29 years, participated in a protocol that included measures of behaviors and clinical symptoms (i.e., social rhythm stability, depressive symptoms, and suicide propensity),
Actigraphic recording generating measures of daily rest and activity patterns (i.e. interdaily stability [IS] and relative amplitude [RA]), and a 12-week telehealth SRT intervention through the Brain Emotion circuitry targeted Self-Monitoring and Regulation Therapy for daily rhythm regularization (BE-SMART-DR). Daily rhythm stability was assessed using the self-administered Brief Social Rhythm Scale (BSRS), as well as the BSRS items exclusively pertaining to stability of sleep and wake times (BSRS4). Symptoms of depression were assessed by the investigator-rated Hamilton Depression Rating Scale (HAMD), and suicide propensity was assessed using the self-reported Concise Health Risk Tracking Scale (CHRT). Actigraphic recording was done using GENEActiv actigraphy watch-like devices during the first two and last two weeks of BE-SMART-DR. The GGIR RStudio processing package was used to collect data on IS and RA. Changes in symptom and behavioral ratings and actigraphy measures pre- and post-BE-SMART-DR intervention, and associations among these changes were assessed.

It was hypothesized that participants would show improvement in social rhythm stability, depression, and suicide propensity, as well as actigraphic measures of IS and RA. Further, it was also hypothesized that improvements in actigraphy measures would be associated with those in behaviors and symptoms. Namely, improvements in RA and IS would be associated with improvement in depression, and improvement in IS would be associated with improvement in BSRS4.

Following intervention with BE-SMART-DR, participants showed significant improvements in BSRS (p<0.05), HAMD (p<0.01), and CHRT (p<0.05). There were improvements in BSRS4, IS, and RA over the intervention, but these did not reach statistical significance. While associations did not reach statistical significance in this
sample, associations of percent increases in IS and percent decrease in HAMD were of strong (Pearson correlation $r = -0.65$), and of medium effect size with percent decrease in BSRS4 (Pearson correlation $r = -0.34$).

The findings of this preliminary investigation suggest that telehealth-administered SRT, BE-SMART-DR, can reduce social rhythm irregularities, depressive symptoms, and suicide propensity in adolescents and young adults with and at risk for mood disorders. Actigraphic measures of daily rest and activity pattern stability may provide a way to collect data in a passive and scalable way about pattern regularity that may also reflect improvements in depression. While findings of this study in this modest sample did not reach significance, effect sizes suggest promise in this ongoing investigation.
Acknowledgements

First and foremost, I would like to thank my thesis advisor, Dr. Hilary Blumberg. I could not have completed this project without her excellent mentorship and guidance. I have her to thank for being a phenomenal mentor throughout my time at Yale School of Medicine and for creating a space where I could develop my voice in the field of academic research on mood disorders. I learned valuable lessons that I will take with me in my future career as a psychiatrist.

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Finally, I would like to thank my family, my partner, and my friends for all of their love, support, and encouragement throughout my time at Yale School of Medicine and as I completed this project. Thank you for the endless joy! I wouldn’t be where I am today without you.
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**Introduction**

Disruptions in sleep and activity patterns are central features in the symptomatology of mood disorders such as major depressive disorder (MDD) and bipolar disorder (BD). Notably, based on the American Psychiatry Association’s (APA) Diagnostic and Statistical Manual of Mental Disorders Fifth Edition (DSM-5), changes in sleep and activity patterns are included in the very diagnostic criteria for both MDD and BD.¹ Specifically, for MDD, the DSM-5 outlines both insomnia and hypersomnia in the list of assessable symptoms for diagnosis of the disorder. For BD, on the other hand, both a decreased need for sleep during a manic episode, or hypersomnia or insomnia during a depressive episode, are assessable symptoms for diagnosis. Given how relevant changes in patterns of rest and activity are to these disorders’ presentations and diagnoses, understanding these patterns provides an important lens through which to understand them.

**Actigraphy**

Digital technologies are important tools employed to better understand the sleep and activity signatures of mood disorders.² Notably, actigraphy has been an increasingly popular technology in elucidating activity patterns in these disorders,³⁻⁵ as its features allow for longitudinal monitoring over weeks-long periods, and provide high temporal resolution and ability to capture objective data passively. Even as we continue to make advances in the field of psychiatry with respect to different diagnostic tools and approaches, there still remains an opportunity to increase the number of objectively measurable phenomena that can be correlated with diagnosis or symptom severity in
psychiatric illness. Actigraphy is a tool that can offer new variables to be considered for detection, diagnosis, or treatment targets.\

Actigraphs are wrist-worn, watch-like devices which collect continuous, time-stamped data on gross motor activity through accelerometers that detect acceleration speed. This data can then be processed through actigraphy-specific software to determine both periods of activity and periods of rest during the recording window. Given that the data collected by these devices is anchored to time of day, it is possible to reconstruct an individual’s rest and activity patterns for the duration of actigraph wear-time. Table 1 below outlines and defines some of the variables that can be extracted from GENEActiv actigraphy watches with GGIR processing software, which will be employed in this investigation, as well as other variables commonly referenced in actigraphic literature.

<table>
<thead>
<tr>
<th>Actigraphic Variable Name</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Sleep Time (TST)</td>
<td>Estimated time between sleep onset and sleep offset, minus time awake after sleep onset</td>
</tr>
<tr>
<td>Wake After Sleep Onset (WASO)</td>
<td>Total time awake between sleep episode onset and sleep offset</td>
</tr>
<tr>
<td>Sleep Efficiency (SE)</td>
<td>Percentage of time asleep during sleep episode</td>
</tr>
<tr>
<td>Sleep Latency</td>
<td>Total time between reported bedtime and sleep onset</td>
</tr>
<tr>
<td>M10</td>
<td>Activity levels over the greatest 10 hours of activity in given 24-hour period</td>
</tr>
<tr>
<td>L5</td>
<td>Activity levels over the lowest 5 hours of activity in given 24-hour period</td>
</tr>
</tbody>
</table>
Intradaily Variability (IV)  A marker of the difference in patterns within days, as indicated by transitions between rest and active states

Interdaily Stability (IS)  A marker of stability in rest and activity patterns across days, as indicated by consistency in timing of transitions between rest and active states

Relative Amplitude (RA)  Measure of differentiation between the activity during the most active ten hours in a 24-hour period (M10) and the least active five hours (L5) in a 24-hour period

While “rest” as determined through actigraphic recording has been, in previous literature, referred to as “sleep,” it is important to emphasize that the “rest” periods classified by actigraphy software are, more accurately, just a proxy marker for sleep. Actigraphs, unlike polysomnography (PSG), are not capable of obtaining information via electroencephalogram (EEG), electrooculogram (EOG), and electromyogram (EMG) for sleep stage classification and confirmation. Therefore, they cannot be used to estimate sleep with absolute certainty. In this investigation, we will refer to “rest” determined from actigraphic recording as such, with the exception of reference to prior literature, where the language used in the original study will be mirrored instead, in order to maintain accurate citation.

While PSG remains the gold standard for sleep estimation studies, the ability to collect activity data in naturalistic, noninvasive, and longitudinal manner in the ambulatory setting poses an important advantage of actigraphy. Other features that make actigraphy an advantageous, easy-to-implement research tool include its cost-

3
effective nature and watch-like appearance, which decreases the burden of wear for research participants. Though we emphasize that actigraphy can only provide a proxy marker for sleep, the reliability of these devices should also be underscored. Actigraphy has been deemed a reliable alternate for PSG in ambulatory settings, showing an agreement rate of sleep-wake scoring with PSG of 91-93%. Notably, in order to provide reliable estimates of rest-activity behavior, actigraphs must be worn for an estimated minimum of 3-6 nights, according to studies in both children and adults.

Another notable misnomer in research employing actigraphic recording is that of referring to 24-hour activity patterns as circadian rhythmicity. While actigraphs are able to estimate rest-activity patterns in the 24-hour period through measures such as IS, IV, and RA, they are not able to measure endogenous circadian function and should not be interpreted as such. While these variables can provide information about rest-activity timing, which in turn is a proxy for circadian function, they should not be used to claim effects such as definitive circadian phase delays or advances without being coupled with other measures of endogenous function. The sleep-wake cycle is one of many components of circadian function, and its disruption as estimated with actigraphy should not be equated with true circadian dysfunction.

**Actigraphy and Mood Disorders**

Actigraphy has been a longstanding monitoring technology for tracking rest and activity, and its application extends into gaining insight into mood disorders such as MDD and BD. Different approaches to this exploration have included attempting to understand unique actigraphic signatures of these disorders, the symptom
correlates of actigraphic variables, as well as differences in actigraphic variables before and after therapeutic interventions.\textsuperscript{21}

Previous investigations seeking to clarify actigraphic features in individuals with BD exhibit notable heterogeneity in methods and results; nonetheless, there is convergence in certain findings across these studies.\textsuperscript{20} In euthymic subjects with BD, the current literature aligns on the primary actigraphic features of the disorder being longer sleep latency, longer sleep duration, and greater variability in sleep timing when compared to healthy controls.\textsuperscript{22–27} A study by Jones et al. also found that individuals with BD also had lower IS than controls.\textsuperscript{28} Though Jones’ study did not show a difference in RA between those with BD and health controls (HC), other studies done in both young adult and adult populations, have found individuals with BD and those at-risk for BD to have lower RA than their HC counterparts.\textsuperscript{22,27} Symptoms of mania have also been associated with decreased RA and decreased IS in young adults.\textsuperscript{29,30}

A systematic review and meta-analysis by Tazawa et al. explored the actigraphic signatures of depression. Their investigation revealed that individuals with MDD have lower activity counts, as measured by actigraphy, as well as increased wake after sleep onset.\textsuperscript{21} Individuals with MDD were also found to have lower IS than individuals without a diagnosis of MDD.\textsuperscript{31} Other studies study aiming to better understand symptom correlates of actigraphy found that lower RA is also associated with MDD.\textsuperscript{32,33} Similarly, a study of individuals undergoing electroconvulsive therapy (ECT) for MDD found that those achieving disorder remission had significantly greater increases in RA following treatment.\textsuperscript{34}
As outlined above, in both MDD and BD, past meta-analyses of actigraphy studies have shown the following similar actigraphic signatures: increased total sleep time, increased sleep latency, decreased sleep efficiency, decreased RA, and decreased IS. Given that depressive symptoms, albeit in different forms, are present in both BD and MDD, we will focus on exploring their specific relationship with actigraphic variables in this investigation.

When assessing actigraphic correlates of symptoms of depression, we find that there are a few salient relationships to highlight, both from studies in individuals with BD and MDD. An investigation aimed at understanding the rest-activity rhythm profiles of individuals with manic-hypomanic or depressive symptoms revealed that those with lower IS as well as later chronotypes measured by actigraphy, had greater lifetime depression and manic-hypomanic symptoms. A study by Luik et al. also found that symptoms of depression were associated with lower IS. Dampening of rest-activity cycles, as evidenced by lowered RA, has also been found to be an indicator of depression. Another study also identified an association between negative affect, as per the Clinician-Rated Inventory of Depressive Symptomatology, and greater sleep disruption, evidenced by increased periods of wake after sleep onset, greater sleep latency, and lower sleep efficiency.

In summary, noteworthy actigraphic findings have been identified in both MDD and BD. Lowered IS and diminished RA have consistently emerged as linked to increased symptoms of depression, as evidenced by current literature, and will therefore be the focus of this exploration. Building upon this foundation, our investigation seeks to deepen the understanding of these relationships. Namely, we aim to unravel intricate
actigraphic differences and their corresponding symptomatologic correlates both before and after the implementation of a targeted social rhythm therapy (SRT) intervention designed for individuals with mood disorders. By delving into the nuanced dynamics of these associations, we strive to contribute valuable insights to the evolving landscape of mood disorder interventions and their impact on actigraphic profiles.

**Social Rhythm Therapy**

Based on the actigraphy data outlined above, daily rhythm instabilities are a notable feature of both MDD and BD. That is, in these individuals, there is less similarity in activity patterns between subsequent days, as evidenced by the findings of decreased IS in both populations. A key explanation for these findings is the social zeitgeber theory of mood disorders. This theory posits that disruptions to daily rhythms are caused by instability in social routines, and that these rhythm disruptions in and of themselves lead to a greater propensity of relapsing into a mood episode.\(^{36}\) This claim presents the hypothesis that social rhythms – that is, the timing of individuals’ habitual activities such as sleeping, eating meals, exercising, and interacting with others– can entrain to natural 24-hour cycles.\(^{37}\) According to the theory, social activities also act as zeitgebers (timekeepers), exerting influence on circadian rhythm synchronization, similarly, albeit to a lesser extent, to light. It is the lack of day-to-day timing consistency of these activities, therefore, that leads to rhythmic disruptions captured by actigraphy and, in turn, to increased likelihood of mood episodes.\(^{38}\)

The social zeitgeber theory of mood disorders has been demonstrated in studies showing that depressed individuals have more irregular social rhythms. Namely, both the
presence of MDD and increased symptoms of depression were associated with decreased
stability in daily social activities.\textsuperscript{39-42} Furthermore, the increased propensity to mood
episode relapse following social rhythm disruptions was exemplified in a study by
Malkoff-Schwartz et al. In this study of college-aged students with BD, the investigators
found that life events leading to social rhythm disruptions, as measured by a scale
designed by their research team, were strongly associated with onset of manic episodes
within an 8-week period.\textsuperscript{43}

While medication is an effective approach to treating mood disorders such as
MDD and BD,\textsuperscript{44,45} other effective, often adjunct, therapeutic approaches exist.
Psychosocial interventions, for example, are a commonplace approach to mood disorders
in both youths and adults.\textsuperscript{46} Therefore, a promising avenue through which to stabilize
daily rhythm disruptions and potentially curb mood episodes is through a psychosocial
therapy that aims to regularize social rhythms.

Interpersonal and social rhythm therapy (IPSRT) is a psychotherapeutic approach
in which the SRT component is specifically designed to address these daily rhythm
disruptions, in addition to the IP component that addresses participants’ interpersonal
relationships.\textsuperscript{47} Therapeutic targets for SRT include mealtimes, social and physical
activities, as well as wake and bedtimes. Through regularization of the timing of these
activities, this psychotherapeutic approach aims to stabilize participants’ daily rhythms
and, therefore, decrease relapse of mood episodes, as per the social zeitgeber theory.
IPSRT approaches, moreover, also provide psychoeducation about mood disorders and
aim to address participants’ interpersonal problems related to mood symptoms.\textsuperscript{47} IPSRT
provides a promising therapeutic intervention for MDD and BD. In studies of patients
with either disorder, this psychotherapeutic intervention has been shown to reduce mood symptoms.\textsuperscript{48–50}

The social rhythm therapy component of IPSRT focuses on teaching behavioral strategies aimed at not only forming but also maintaining healthy, regular daily schedules.\textsuperscript{38} SRT aims to re-entrain the 24-hour social rhythm cycle and, therefore, curb rhythmic disruptions and their resultant mood consequences. The SRT component of IPSRT is not often investigated separately to the IP component, but studies have shown successful response to SRT in both MDD and BD.\textsuperscript{37,51,52} Furthermore, Crowe et al. conducted a qualitative study of young adults with BD who had received different psychotherapeutic interventions for the disorder five years prior, in order to explore strategies that they had found to be helpful in managing their BD. The investigators found that identifying and keeping daily routines was a prominent theme in participants’ descriptions of helpful tactics for staying well in those who had received an SRT intervention, showing that this therapy can have lasting positive effects.\textsuperscript{53}

An additional benefit to SRT’s aim of regularizing daily rhythms, especially as it focuses on stabilizing daily sleep and wake times, is targeting a risk factor for suicide. In a study exploring the sleep and circadian rhythm markers associated with suicide attempts in euthymic individuals with BD, circadian rhythm instability was linked to increased suicidal thoughts and behaviors.\textsuperscript{54} Therefore, employing a psychotherapeutic approach that targets daily rhythm instability may not only be an effective tool in managing BD and MDD symptoms, but may also provide benefit to patients by addressing this important risk factor for suicide.
This investigation was conducted as part of the Brain Emotion circuitry-targeted Self-Monitoring and Regulation Therapy (BE-SMART) program of psychotherapeutic intervention research. Specifically, we will be utilizing the version of this therapy called BE-SMART-DR, where DR stands for ‘Daily Rhythm.’ BE-SMART-DR is a version of SRT\textsuperscript{38} modified specifically for telehealth delivery. The main goal of this therapy is to provide participants strategies to regularize the patterns of their daily activities in order to stabilize their daily rhythms. This regularization makes their subsequent days more similar in parameters such as bedtime, wake-up time, mealtimes, and time of first social interaction. BE-SMART-DR will be the specific SRT used for intervention in this study’s participant cohort.

One approach of assessing the effect of SRT on regularizing daily rhythms is through self-report questionnaires addressing the regularity with which individuals perform their daily tasks. One such instrument is the Brief Social Rhythm Scale (BSRS),\textsuperscript{55} which contains a list of questions used to measure irregularities in responders’ social rhythms.\textsuperscript{42} More specifically, the first four items of the BSRS refer to regularity of sleep and wake times, while the remaining items focus on mealtimes and social interactions. These first four items, focused on sleep and wake times, are therefore most closely aligned with the primary actigraphic variable of IS. For that reason, they will be used as its more appropriate variable for comparison, rather than using BSRS in its entirety. To our knowledge, there are no existing investigations into the relationship between BSRS questionnaires and actigraphic variables. As part of this investigation, we will assess the relationship between the first four items of the BSRS and IS, as both are measures that address daily sleep and wake times regularity.
Statement of Purpose

Digital technologies, particularly actigraphy, have potential to play a crucial role in understanding the rest and activity patterns associated with mood disorders in psychiatry. Further, passive measures obtained from actigraphy can be sensitive to symptom changes and could be informative in identifying potential targets for early detection of disease and markers for intervention outcomes in adolescents and young adults. Current literature in actigraphy in MDD and BD, reveal the following actigraphic features shared by both disorders: lowered IS and reduced RA. Further, both lowered IS and reduced RA have also been found to correlate with increased symptoms of depression in BD and MDD. The social zeitgeber theory of mood disorders suggests that these actigraphy-detected disturbances are caused by disruptions in social rhythms and contribute to mood episode relapse. Social rhythm therapies, aimed at regularizing these daily social routines, provide a promising psychotherapeutic approach for both BD and MDD. This forms the basis for a nuanced investigation into symptom and actigraphic differences and their associations before and after a targeted SRT intervention in adolescents and young adults with and at-risk for mood disorders.

Aims

Assess changes in behaviors and clinical symptoms (i.e., self-reported social rhythm stability, depressive symptoms, and suicide propensity), and actigraphic measures (i.e., IS and RA), in adolescents and young adults with and at-risk for mood disorders receiving SRT intervention, BE-SMART-DR, focused on regularization of daily routines.
Further, assess the associations between changes in symptoms/behaviors and actigraphic measures.

**Hypotheses**

(1) Adolescents and young adults with and at-risk for mood disorders who receive BE-SMART-DR will improve in measures of social rhythm stability, depressive symptoms, and suicide propensity.

(2) Adolescents and young adults with and at-risk for mood disorders who receive BE-SMART-DR will improve in actigraphic measures of IS and RA.

(3) Improvements in both IS and RA following BE-SMART-DR will be associated with improvement in clinician-rated depressive symptoms, and improvements in IS will be correlated with improvements in self-reported daily regularity of sleep and wake times.

**Methods**

*Student’s Contributions*

I contributed directly to the execution of this ongoing project as part of the Yale Mood Disorders Research Program (MDRP). My initial contribution was as a co-author of a comprehensive, published systematic review of the current literature for which I assisted in analyzing, summarizing, and interpreting studies that employed actigraphy to understand rest and activity rhythms in individuals with BD. This systematic review partially prompted the symptom and behavioral targets and hypotheses of this investigation. Throughout the completion of this investigation, I also took part in
meetings with research clinicians reviewing videorecorded SRT sessions of the participants’ BE-SMART-DR meetings. Further, I was also responsible for processing the raw actigraphy data collected from subjects both presented here and individuals participating in other BE-SMART projects within the MDRP. I contributed to discussions and decisions regarding actigraphy processing algorithms and establishing and implementing the actigraphy data processing and analysis methods of this investigation. This included conversations with other Yale, as well as national and international, research groups utilizing actigraphy that resulted in optimization of our raw data processing pipeline. I also formulated the scope of the investigation presented here, designing its specific aims, hypotheses, subject group, and statistical approach for analyses. I was responsible for conducting the statistical analysis, which included creating all tables and figures. I also continue to be responsible for ongoing data collection and processing as this project continues to progress.

*Ethics Statement & Human Subject Research Information*

This investigation was conducted in accordance with the Yale School of Medicine Human Investigation Committee Institutional Review Board and the Declaration of Helsinki as revised in 2013. Written informed consent was obtained from all participants ages ≥ 18 years, while written participant assent and permission from guardians was obtained from minors ages <18 years, before enrollment in the study. Participants were clearly communicated that they could withdraw participation at any point.
Participants

Participant recruitment for this investigation was done in a large, urban academic medical center and through study advertisement in the surrounding community. Recruitment efforts for the current sample spanned from 2020 to 2023. The participants included in this study were selected from a larger program of study of BE-SMART that included other treatment and control arms. Participants selected included all who received BE-SMART-DR, had sufficient actigraphy data, and met criteria for bipolar I disorder (BD I), bipolar II disorder (BD II), MDD, or were at-risk for BD. Participants who were deemed to be at-risk for BD were those with a parent with a history of BD, which was determined through parental report of own medical history. Seven participants ages 14-29 years (mean±SD age = 21.1 ± 5.5 years; BD I n = 2, BD II n = 1, MDD n = 3, at-risk for BD n = 1) were included in this investigation. Three participants identified as female, two as male, and two participants identified as non-binary.

The presence or absence of psychiatric disorder diagnoses, as well as any history of psychosis, were determined through a structured clinical research interview evaluation conducted by interviewers trained to reliability based on criteria defined in the DSM-5. Clinical interviews followed both the Structured Clinical Interview for DSM Disorders Research Version (SCID-5-RV) format, for adult participants, and the Kiddie Schedule for Affective Disorder and Schizophrenia (KSADS) format, for participants under the age of 18 years. The participant classified as at-risk for BD had a parent with a reported diagnosis of BD on interview and presented with sub-diagnostic mood symptoms at their baseline evaluation visit. More detailed clinical characteristics of the sample can be found in Table 2 below.
Exclusion criteria for study participation were major medical and neurological disorders and conditions that could affect brain tissue (including loss of consciousness $\geq 5$ minutes); moderate to severe substance or alcohol use disorders within the prior 6 months (though both lifetime substance use disorder history and current mild use disorder were allowed); IQ $< 70$ as determined by the Wechsler Abbreviated Scale of Intelligence\textsuperscript{58} (WASI); currently receiving structured interpersonal and social rhythm, cognitive-behavioral, dialectical behavior, or family therapies; current psychosis; being too symptomatic to participate according to the clinical judgment of a licensed clinician; and having active suicidal intent or homicidal ideation. All participants were inquired about previous suicide attempts using the Columbia-Suicide Severity Rating Scale (C-SSRS),\textsuperscript{59} though past suicidal attempts or ideation were not criteria for exclusion.

**Symptom and Behavioral Assessment Scales**

To assess for changes in daily rhythm regularity, reflecting the “active” ingredient in SRT, the BSRS\textsuperscript{55} was used. The BSRS is a self-report measure of irregularities in social rhythms comprised of 10 items. Each questionnaire item is rated on a 6-point scale, ranging from 1, very regularly, to 6, very irregularly. Total BSRS scores can range from 0 to 60, where greater scores indicate more irregular social rhythms. As previously mentioned, the first four items of the BSRS refer to the regularity of sleep and wake times only. For the purposes of this investigation and having an appropriate comparator to the actigraphic variable of IS, analyses were performed on both total BSRS scores and scores calculated from the sum of the first four items of the BSRS, hereafter referred to as BSRS4. Total
scores on the BSRS4 can, therefore, range from 0-24, where higher scores indicate more self-reported irregularity in sleep and wake times.

Participants’ mood symptoms were assessed by raters trained to reliability and blind to each participant’s treatment arm. Depressive symptoms were assessed using the 29-item Hamilton Depression Rating Scale (HAMD). This scale contains items that assess both typical and atypical symptoms of depression and each of the 29 items is scored on a 3-, 4-, or 5-point Likert Scale. Total scores on the HAMD scale can range from 0 to 90, where higher scores indicate more severe depressive symptoms. Manic symptoms were assessed using the Young Mania Rating Scale (YMRS). The YMRS is comprised of 11 items, four of which are rated on an 8-point Likert scale and seven of which are rated on a 4-point Likert scale. Therefore, scores can range from 0-60, where higher scores signify more severe symptoms of mania. As participants primarily had depressed symptoms, HAMD scores were the chosen mood scale used for analysis.

Risk for suicide was assessed using the Concise Health Risk Tracking Scale (CHRT) self-report questionnaire. The version of the CHRT used in this investigation is a 13-item scale where each item includes a statement that participants respond to on a scale from 0, strongly disagree, to 4, strongly agree. Total scores on the CHRT were used for analyses. Total scores on the CHRT range from 0-52, where higher scores indicate a greater risk for suicide. Clinical relevance of these scores is further supported by a report stating that 10-point increases in baseline CHRT score correspond to a 76% increase in the hazard of a suicidality-related serious adverse event.

All clinician-rated (HAMD, YMRS) and self-report (BSRS, CHRT), scales were administered before and after BE-SMART intervention (see Figure 1 for detailed protocol
timeline in the Actigraphy subsection below). Assessment points occurred during the first BE-SMART-DR session (session 1; pre-intervention) and then again after completing the intervention at the last BE-SMART-DR session (session 12; post-intervention).

| Table 2: Demographic and clinical characteristics of study participants (N=7) |
|------------------------|-----------------|-----|
| Characteristic         | N               | %   |
| Age (mean ± SD)        | 21.1 ± 5.5      |     |
| Gender (F/M/non-binary)| 3/2/2           |     |
| Diagnosis              |                 |     |
| Bipolar Disorder I     | 2               | 28.6% |
| Bipolar Disorder II    | 1               | 14.3% |
| Major Depressive Disorder | 3         | 42.9% |
| At-risk for Bipolar Disorder | 1        | 14.3% |
| Lifetime psychosis     | 1               | 14.3% |
| History of suicide attempt | 2             | 28.6% |
| Psychiatric comorbidities (current) |           |     |
| Generalized Anx. Dis. | 2               | 28.6% |
| Social Anx. Dis.       | 1               | 14.3% |
| Panic Disorder         | 1               | 14.3% |
| ADHD                   | 2               | 28.6% |
| Current medications    |                 |     |
| Anticonvulsants        | 3               | 42.9% |
| SSRIs                  | 2               | 28.6% |
| Atypical Antidepressants | 2         | 28.6% |
| Benzodiazepines        | 1               | 14.3% |
| Antihistamines         | 1               | 14.3% |
| Lithium                | 0               | 0.0%  |
| Antipsychotics         | 0               | 0.0%  |
| Stimulants             | 0               | 0.0%  |
| Substance use          |                 |     |
| Cannabis (mild)        | 2               | 28.6% |
| Rating Scale Scores    |                 |     |
| BSRS Score (mean ± SD) | 38.9 ± 10.1     |     |
### Table 2

<table>
<thead>
<tr>
<th>Measure</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>BSRS4 Score</td>
<td>13.6 ± 6.9</td>
</tr>
<tr>
<td>HAMD Score</td>
<td>22.7 ± 7.6</td>
</tr>
<tr>
<td>YMRS Score</td>
<td>3.6 ± 6.2</td>
</tr>
<tr>
<td>CHRT Score</td>
<td>21.7 ± 12.2</td>
</tr>
</tbody>
</table>

Legend: F – female; M – male; Anx. – Anxiety; Dis. – Disorder; ADHD – Attention-deficit/Hyperactivity Disorder; SSRI – Selective Serotonin Reuptake Inhibitors; Atypical Antidepressants included bupropion and trazodone.

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**BE-SMART-DR**

The SRT intervention used for all participants in this investigation was BE-SMART-DR, as outlined above. BE-SMART-DR, delivered by one of two trained licensed therapists, consists of twelve one-on-one weekly sessions between a therapist and a participant. Participants were also asked to complete assignments that were reviewed and discussed with the therapist in subsequent sessions. Table 3 below outlines the content of each of the twelve BE-SMART-DR sessions. All therapy sessions were conducted using a secure video platform, with the exception of the first, middle, and last sessions, where participants were seen in person. With consent of participants, sessions were audio or video recorded for supervision and fidelity ratings. The content of these sessions was specifically focused on daily rhythm regularity, though it also included time for clinicians to establish therapeutic alliances with participants, provide them psychoeducation about mood disorders, termination, and planning for future mood episodes or increases in symptom severity. While focusing on the same intervention aim, sessions were also tailored specifically to each participant’s circumstances, such as work or school schedules. For example, clinicians used language and frames that were pertinent to each subject (e.g., waking up at the same time every day for school or for work).
Table 3: BE-SMART-DR Intervention Session-by-Session Content Outline

<table>
<thead>
<tr>
<th>Session Number</th>
<th>Session Content</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-2</td>
<td>Provide psychoeducation about participant’s diagnosis and circadian rhythms</td>
</tr>
<tr>
<td>3-5</td>
<td>Develop participant’s understanding of relationships between social rhythms and disturbances in mood and sleep</td>
</tr>
<tr>
<td>6-8</td>
<td>Work on regularization of sleep and other daily activities that impact daily rhythms</td>
</tr>
<tr>
<td>9-10</td>
<td>Develop self-awareness of symptoms and rhythm disruptors</td>
</tr>
<tr>
<td>11-12</td>
<td>Identify early warning signs of mood episodes, create a relapse prevention plan, and discuss therapy termination</td>
</tr>
</tbody>
</table>

**Actigraphy**

All actigraphic recordings were done using GENEActiv triaxial accelerometer devices worn on participants’ non-dominant wrists throughout recording time. Actigraphs provided continuous recording of motor activity throughout the wear period. Data were analyzed from two distinct time frames: two weeks’ time during the first two weeks and the last two weeks of the BE-SMART-DR intervention. See Figure 1 below for an outline of the experimental design timeline.
All raw actigraphy data was processed using the GGIR processing package on RStudio. The GGIR processing package is used to calculate several actigraphic variables from the raw accelerometry files. In this investigation, GGIR was used to extract an IS value and an RA value for each participant over device wear-time. IS is a stability marker of activity patterns across subsequent days. The IS measure can range from 0-1, where greater values signify greater stability of rhythm across days. Greater stability in rhythms is synonymous with greater consistency of rest-activity patterns. Therefore, individuals who wake up and rest at the same time every day, for example, will have a calculated IS value closer to 1 than those with less consistent schedules. RA, on the other hand, is a measure of differentiation between the average activity during the ten hours of highest activity in a 24-hour period (M10) and the average activity during the five hours of lowest activity in a 24-hour period (L5). This measure is calculated by dividing the difference between M10 and L5 by their sum. RA can range from 0-1, with scores closer to 1.
signifying greater difference in average activity between resting periods and most active periods.

Statistical Analysis

All data analyses were conducted using RStudio statistical package software and visual data representations were created using Microsoft Excel’s graphing feature. Differences in BSRS, BSRS4, HAMD, and CHRT scores from pre- to post-intervention were assessed using paired, two-tailed t-tests at an alpha level of 0.05. Differences in both IS and RA values between pre- and post-intervention actigraphic recording were also assessed using paired, two-tailed t-tests at an alpha level of 0.05. Assessment of associations between changes in actigraphic variables and symptom and behavioral outcomes utilized percent change in scores over the intervention. Associations between the following measures: percent change in HAMD and percent change in IS; percent change in HAMD and percent change in RA; and percent change in BSRS4 and percent change in IS, were evaluated using a Pearson correlation regression model also at an alpha level of 0.05. The specific comparisons for linear regression analysis were chosen according to the predetermined hypotheses based on existing literature.

Results

Symptom and Behavioral Ratings Pre- and Post-Intervention

Before BE-SMART-DR intervention, participants had BSRS scores ranging from 26-52 (mean±SD = 38.9 ± 10.1), BSRS4 scores ranging from 4-24 (mean±SD =13.6 ± 6.9), HAMD scores ranging from 6-28 (mean±SD = 22.7 ± 7.6), and CHRT scores
ranging from 8-38 (mean±SD = 21.7 ± 12.2). After BE-SMART-DR, at the post-intervention mark, participants had BSRS scores ranging from 18-37 (mean±SD = 26.4 ± 8.3), BSRS4 scores ranging from 5-14 (mean±SD = 9.7 ± 3.7), HAMD scores ranging from 5-19 (mean±SD = 11.0 ± 5.3), and CHRT scores ranging from 5-39 (mean±SD = 17.4 ± 12.2). The average symptom/behavioral scale scores pre- and post-intervention with BE-SMART-DR can be seen in Figure 2 below.

![Figure 2: Average symptom/behavioral scale scores and respective standard error bars pre- and post-intervention with BE-SMART-DR. Statistically significant changes with p<0.05 and p<0.01 are signified with a * and a †, respectively.](image)

There were statistically significant improvements in BSRS (t-test: df=6, p<0.05), HAMD (t-test: df=6, p<0.01), and CHRT (t-test: df=6, p<0.05) over the BE-SMART-DR intervention. The average percent decrease in BSRS scores was of 30.0%. The average percent decrease in HAMD was 46.8%, and the average percent decrease in CHRT was 21.0%. Though there was an average percent decrease of 15.1% in BSRS4 over the
intervention, t-test results did not yield a significant difference between pre- and post-intervention BSRS4 values (t-test: df=6, p=0.12).

Actigraphy

Subjects wore the actigraph in the pre-intervention recording period for 12.9 ± 3.9 days (mean±SD) and for 14.2 ± 3.2 days (mean±SD) in the post-intervention recording period. Actigraphy was recorded continuously for the duration of watch wear time. No subject wore the actigraph for less than 5 days, rounded up to the nearest full day, during either time period. In total, the number of days of actigraphy recording across all subjects and conditions was 190. The IS for all subjects in the pre-intervention recording period ranged from 0.07 to 0.49 (mean±SD = 0.35 ± 0.22); for post-intervention the range was 0.12 to 0.92 (mean±SD = 0.35 ± 0.21). The RA for all subjects in the pre-intervention recording period ranged from 0.49 to 0.86 (mean±SD = 0.67 ± 0.14); for post-intervention the range was 0.57 to 0.92 (mean±SD = 0.71 ± 0.13).

The average percent change in IS over the BE-SMART-DR intervention was an increase of 8.7% and the average percent change in RA was an increase of 8.8%. However, these measures did not change significantly over the intervention (p’s > 0.46). Figure 3 below illustrates the average percent change in both IS and RA over BE-SMART-DR.
Changes in Symptom and Behavioral Ratings and Actigraphy

Pearson correlation regression analyses did not reveal any significant findings. Associations between percent change in HAMD scores and percent change in IS were negative, in the direction hypothesized ($r = -0.65$, $p = 0.12$). While this relationship was not statically significant, it yielded a Pearson $r$ absolute value greater than 0.5, denoting a large effect size. The linear relationship between percent change in HAMD and IS is depicted below in Figure 4. There was no significant association found between the percent change in RA and percent change in HAMD ($r = 0.16$, $p = 0.72$). As hypothesized, here was a negative association between the percent change in BSRS4 and percent change in IS ($r = -0.34$, $p = 0.44$), however this association also did not reach significance and showed a medium effect size with a Pearson $r$ absolute value greater than 0.3.

![Figure 3: Average percent change in IS and RA over intervention with BE-SMART-DR.](image-url)
Discussion

The current investigation on actigraphic and symptomatologic changes and their correlations in adolescents and young adults with and at-risk for mood disorders following BE-SMART-DR shed light on the potential effects of SRT and how they are reflected in actigraphic measures. In this modest sample, we found that BE-SMART-DR significantly improved self-report measures of daily social rhythm regularity, though this improvement was not statistically significant for the items in the questionnaire assessing stability of sleep and wake times only. Moreover, clinician-rated symptoms of depression, as well as a self-reported suicide risk significantly improved following the SRT intervention. There were also associations found between improvements in actigraphic measures of daily rhythm stability (IS) and improvements in depressive symptoms. While
this association did not reach statistical significance, it had a large effect size. This is an important finding, and it supports current literature linking actigraph-assessed daily rhythm stability to mood disorder symptoms. Findings also included a medium effect size association between improvements in IS and daily rhythm stability assessed by the BSRS4, though this association was also not statistically significant. No associations between changes in RA and depressive symptoms were found in this investigation.

These results provide preliminary evidence for the effects of SRT in improving core symptoms of both MDD and BD. Despite the small sample presented in this investigation, there was robust improvement in clinician-assessed depressive symptoms and self-rated suicide propensity. These findings support the current literature outlined above that psychotherapy aimed to regularize daily rhythms may comprise an effective treatment approach for individuals with mood disorders.\textsuperscript{48–50} It is particularly important to highlight that this therapy resulted in improvement in suicide risk. Given the high rates of suicide in individuals with BD specifically,\textsuperscript{66} uncovering therapies that decrease the risk of this outcome is of utmost importance in clinical research. According to the social zeitgeber theory of mood disorders, the social rhythm regularization aspect of BE-SMART-DR, evidenced by significant improvement in BSRS, is likely responsible for the effects described here. However, these effects could also be attributable to other factors. For example, it is also possible that the constant of a weekly therapy session where participants could discuss their week and share their frustrations, could be the active therapeutic factor. Comparing BE-SMART-DR to a control therapy condition in future studies will be crucial in parsing apart what is its “active ingredient” for improving depressive symptoms and suicide propensity.
Notably, while there was a significant improvement in self-rated daily social rhythm stability, as hypothesized, this was not seen when only the questionnaire items that pertained to sleep and wake times were analyzed. The most likely explanation for this discrepancy is the decreased variance in scores, caused by including less items on the scale, leading to decreased statistical power to detect differences in samples. However, this discrepancy also raises the question of whether it is appropriate to consider that BE-SMART-DR therapy regularizes rhythms with particular emphasis on the more social timekeepers such as time of first social interaction and mealtimes, which are reflected in BSRS but not BSRS4 scores. This could also provide an explanation to why there was no change seen in the actigraphic variable of IS over the intervention, as it is only sensitive to rest versus activity rather than more specific daily social functions. In order to better ascertain if this is the case, future explorations of BE-SMART-DR and other SRT’s should compare measures of social rhythmicity and sleep-related rhythmicity.

Growing supportive findings of SRT in research support implementation of this psychotherapeutic modality in the clinical setting. BE-SMART-DR presents several advantages that increase its feasibility for clinical delivery. A notable advantage is that it can be delivered through telehealth platforms, especially given the recent COVID-19 pandemic and the pressures it placed on healthcare providers to rely on digital formats to deliver care. Additionally, telehealth delivery also increases access to care for patients with limited access to transportation and limited time. The use of videoconferencing platforms therefore makes BE-SMART-DR particularly accessible to both patients and clinicians. Notably, a systematic review of telepsychiatry interventions found that not
only was this method of care delivery efficient in reducing suicide rates and reattempts, but it also was found to be well-tolerated and to have high retention rates.67

Furthermore, we also explored the actigraphic changes over the BE-SMART-DR intervention and their correlations with symptom changes. While, on average, both objectively measured IS and RA improved over the intervention, as hypothesized, the pre- and post-intervention values were not significantly different. It is possible that these changes occur at a slower rate than changes in BSRS, for example, and that full effect of the intervention is seen later, after the 12-week intervention period. It is also possible to consider that, given that disruptions in IS and RA are seen in individuals with mood disorders even when euthymic,22 that these disruptions may not normalize robustly over interventions, regardless of their success in symptom reduction. Given that this investigation provides only a preliminary, first exploration into actigraphic correlates of SRT, future explorations of these relationships are warranted to reach more concrete conclusions. This is an ongoing study and, as more participants are included, better defined relationships, may emerge between SRT and actigraphic variables.

Though there were no significant changes observed in the IS parameter, there was an association of large effect size between increased actigraph-recorded stability of daily rhythms and decreases in clinician-rated symptoms of depression. The direction of this association indicated that, as rhythms became more stable, symptoms of depression decreased. This is further supported by the associations between decreased IS and increased depressive symptoms described in actigraphy literature and outlined above.5,17,31 depression. Given the large effect size of this association, it is likely that the reason this relationship did not reach significance was due to being statically
underpowered. As this study continues to progress with more participants, the relationship between changes in IS and HAMD should continue to be explored. Though this current analysis does not provide sufficient evidence for this purpose, future explorations of this relationship may begin to uncover what features of SRT make it efficient in decreasing mood symptoms. Future results may also shed light on an objectively and passively measured variable that can eventually be used to assess symptom changes and efficacy of therapy. The aim of uncovering objective markers of symptom changes is to have an easily, remotely accessible parameter for patient assessment. While conclusions cannot be definitively drawn from these results, we suggest this relationship should continue to be explored in this ongoing study as well as future investigations of actigraphy and mood disorders.

As hypothesized, there was also a medium effect size relationship between increase in daily rhythm stability (IS) and an increase in self-rated stability of sleep and wake times only, as assessed by the BSRS4. This finding provides direction for future investigation of objective actigraphic correlates of subjective, self-reported daily rhythm measures. While studies have found discrepancies between objectively- and subjectively-assessed sleep and wake estimations in populations with mood disorders,\textsuperscript{30,68} this is the first investigation to use a BSRS-derived measure for comparison to actigraphy. Though it is not possible to determine that BSRS4 and IS are decisively correlated from the results presented here, we suggest, based on these results, that future explorations of this relationship are warranted.

Moreover, contrary to our proposed hypothesis, no significant associations were found between changes in RA over BE-SMART-DR intervention and changes symptoms
of depression. While studies on mood disorders and actigraphy suggests a relationship between increased depression and decreased RA, this was not reflected in our findings. Prior studies have associated RA from one period of recording with depressive symptoms during that time. However, in this investigation, we analyzed the association in percent change of these variables over two time points across the SRT intervention. It is possible that, while RA and depression can be associated at specific timepoints, they do not change together at the same rate, and analyses over time may not capture their relationship. It can also be considered, based on the findings of this present investigation, that these variables are independent. However, this is less likely given the current literature, and this claim would also warrant further investigation in order to be assertively made.

Limitations and Challenges

An important limitation of this investigation, which must be emphasized, is the small sample size presented here. With a total of seven participants, there were issues of power and, given the heterogeneity among individuals with and at-risk for mood disorders, there were limitations to drawing conclusions about the relationships uncovered through our data analysis. It is important to emphasize that this investigation is ongoing, and as more individuals complete the research protocol, we anticipate the data will converge in more definitive patterns. One important challenge of conducting longitudinal research that relies on wearables is ensuring that participants remain compliant with the recording protocol. There was variation in the number of days each participant wore the watch for in each recording period. While all participants wore the
watch for at least the minimum number of days required to provide reliable estimates for
the variables collected,12,13 one of the challenges we face is determining whether data
from each participant is comparable to others. For example, a participant who wore the
watch for fourteen days may have, on average, a more representative characterization of
their activity patterns than someone who wore the watch for seven days, yet, comparing
the samples assumes that these measures are equivalent. Future investigations based on
larger samples of data may employ more stringent criteria on variance of watch wear
time. Further, future investigations may also explore relationships between actigraphic
variables and length of recording time.

Another challenge of conducting research utilizing actigraphy exists in the
heterogeneity of methods used across the literature. Different research groups use
different recording devices, different raw data processing algorithms, and can choose to
present data on similar but not equivalent variables (e.g., sleep time vs. L5 onset). These
differences make it difficult to determine what “normal” values are for each actigraphic
variable. For example, knowing the average IS value for age-matched HC’s would
provide important information in assessing the average IS of this investigation’s
participants. However, this information would require identical methods of recording and
processing raw data. Future efforts in this field of research should focus on creating a
gold standard for actigraphic recording and open databases of reference values to be used
as points of comparison. Further, as part of this investigation, we contacted multiple
national and international research groups that collect actigraphy in both patient
populations and HC’s and found that actigraphy data on young adults with BD and MDD
is still exceedingly rare in the field. Therefore, continuing to collect data on this
population is an important undertaking in the ongoing effort to understand their rest and activity patterns.

There also exists the challenge of grouping together individuals with different mood disorders for analyses. While a more heterogenous sample is more representative of the diversity that exists within mood disorder presentations, including participants with different primary and comorbid diagnoses prohibits us from making inferences about any specific mood disorder. Given the small sample at hand, we chose to group these individuals together and assess symptoms along a continuum, rather than compare traits of either disorder. Future explorations of this data, as the sample continues to grow, will benefit from analyzing and comparing actigraphic signatures of BD and MDD, separately, in order to better differentiate the actigraphic profile of either diagnosis. Moreover, using a symptom, rather than a diagnosis, as a correlate of actigraphic data also poses a challenge for data interpretation. This investigation is focused on symptoms of depression in individuals with MDD and BD, and how these symptoms respond to SRT. However, we cannot make claims about the effects of this intervention on symptoms of depression in either disorder individually. As more participants are included for analysis, future studies may explore how associations between changes in depressive symptoms and actigraphy differ between MDD and BD.

An argument can also be made that, given the age of the participant sample, it is possible that some individuals diagnosed with MDD as part of this investigation, were in fact experiencing a first mood episode of BD. Considering that the large majority of cases of BD present first as an episode of depression and have and average onset between 15-25 years of age, it is possible the diagnosis of some participants will eventually evolve.
This diagnostic ambiguity presents an advantage to grouping individuals with these diagnoses together in our analyses.

Another challenge in interpreting data from this sample is the heterogeneity in age of participants. The young adult age range of 14-29 years was purposefully chosen given that the age of onset of both BD and MDD is in adolescence to young adulthood, and future aims of this ongoing study include attempting to elucidate actigraphic signatures for early detection of BD and MDD. However, this is also an age where it can be difficult to ascertain whether disturbances in actigraphic patterns are due to presence of psychiatric illness or if these disturbances are attributable to adolescents’ more erratic sleep and wake patterns. The influence of developmental stage on actigraphic data has been previously demonstrated in youth and studies have found that, as adolescents transition to adulthood, there is both overall decreased and greater intra-individual variability in sleep duration. The effect of these changes cannot be disregarded in this sample. Future analyses using larger sample sizes can stratify participants by age group or pubertal status, in order to determine if the effects observed are specific to age or developmental stage. Alternatively, future investigations can also assess for any associations between actigraphic measures and age, across greater age ranges.

Taking psychiatric medication was not part of the exclusion criteria for participants in this investigation. One challenge of conducting research in populations with psychiatric disorders is choosing whether to exclude those taking medications, as medications have an impact on disorder presentation, may confound true effects of interventions, and can have their own effects on rest and activity patterns. Part of the reason one may choose to include medicated individuals in a sample is wanting to recruit
a group that represents the spectrum of severity of these disorders. Not excluding those that require medication allows investigators to include more severe cases, providing a more representative sample of true spectrum of illness. Further, there are significant ethical concerns in requesting that participants stop taking their current medications, and this option was not considered.

Of note, several participants included in the sample were taking medications, and one participant started taking psychiatric medications during the course of the study, representing a potential confound in assessing effects of the intervention. Aside from heterogeneity in some participants taking medications and others not, there was also wide range in medication choice. Notably, this could be considered a strength, as the efficacy of SRT was seen both in medicated and unmedicated participants, suggesting that it holds benefits to both groups. Moreover, BE-SMART-DR was designed to be used as adjunctive to other treatments. Therefore, studying its effects as an adjunctive treatment to existing medication regimens, rather than on its own, is most representative to its intended use. If future, larger participant samples allow for needed degree of granularity, analyses of the effects of individual medications and SRT may elucidate if specific medication-therapy combinations are more effective than others.

A strength of the investigation presented here is the wide distribution of HAMD scores represented in the pre-intervention sample. This range is evidence that individuals throughout the depression severity spectrum were represented in the sample. On the other hand, there was very low variation in mania scores at baseline. Many participants presented with a score of zero on the YMRS, and therefore, there was not enough variation in the data to perform meaningful statistical analyses related to symptoms of
mania. This illustrates a key challenge in conducting research on individuals with BD, which is recruiting and maintaining those experiencing mania to protocol completion in a research study that involves regular participant contact. While active mania can deem research participation difficult, it is important to our understanding of BD to study the effects of SRT in acutely ill patients. Future study efforts can include more accommodating protocols to those experiencing mania by, for example, being completed partially within the inpatient setting. This both ensures participant safety and inclusion of acutely ill patients in the research protocol.

While we compared pre- and post-intervention samples of a specific therapy, it will be important to compare the effects of different types of therapies in order to determine if it is the SRT component of BE-SMART-DR that is assuredly responsible for the changes observed. It is a notable limitation that, if the social rhythm regularization component of SRT is what is making it effective, one could argue that having habitual therapy sessions in and of itself is a regularization of rhythms independent of therapy session content. Ongoing investigations in our research group are utilizing both a psychoeducational control and a version of BE-SMART therapy focused on providing explicit emotional regulation skills, rather than daily rhythm regularization. Future analyses of the resulting data will focus on comparing the effects of each therapy and their actigraphic correlates to determine the efficacy and change characteristics of each. Therefore, these investigations will allow us to better determine whether it is SRT itself or regularization of rhythms through regular therapy sessions, that is causing the observed changes.
Dissemination

The information presented in this investigation has been disseminated to communities of interest. Firstly, we have published a systematic review of current literature on BD and actigraphy, which has served as part of the introduction to this work, in *Frontiers in Psychiatry*. Additionally, the findings presented in this investigation have been shared with members of the Yale Mood Disorders Research Program who have participated in study protocols for collection of the data presented here. Portions of this work have also been presented in the form of a poster by a member of the research group at the annual Society for Neuroscience (SfN) conference, which took place in Washington, DC, in November of 2023. Lastly, the BE-SMART-DR psychotherapeutic intervention in and of itself was shared with participants, who are members of the community who have benefited from receiving this therapy.

Conclusions

The present investigation provides an initial exploration of the symptom and actigraphic correlates of a 12-week SRT intervention in adolescents and young adults with and at-risk for mood disorders. The findings of this preliminary investigation suggest that SRT is a psychotherapeutic approach that can improve regularity of daily social rhythms, depressive symptoms, and risk of suicide in this population. Notably, there was a strong association between improvement in IS and improvement in depressive symptoms. We suggest that actigraphic measures may provide a way to collect data in a passive and scalable way about pattern regularity that may also reflect
improvements in depression. While findings of this study did not reach significance, effect sizes suggest promise in this ongoing investigation, as the small number of participants is supplemented with collection of additional data. Future investigations based on this work will compare BE-SMART-DR to other therapeutic interventions and will investigate MDD and BD separately to identify individual signatures of each disorder.
References


