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Cognitive-Behavioral Treatment of Insomnia and Depression in Adolescents: A Pilot Randomized Trial

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Abstract

We tested whether augmenting conventional depression treatment in youth by treating sleep issues with cognitive behavioral therapy for insomnia (CBT-I) improved depression outcomes. We randomized youth 12–20 years of age to 10 weekly sessions of a sleep hygiene control condition (SH) combined with CBT for depression (CBT-D) (n=20), or an experimental condition consisting of CBT-I combined with CBT-D (n=21).

We assessed outcomes through 26 weeks of follow-up and found medium-large effects favoring the experimental CBT-I arm on some sleep outcomes (actigraphy total sleep time and Insomnia Severity Index "caseness") and depression outcomes (higher percentage recovered, faster time to recovery), but little effect on other measures. Total sleep time improved by 99 minutes from baseline to week 12 in the CBT-I arm, but not in the SH arm. In addition, our pilot yielded important products to facilitate future studies: the youth-adapted CBT-I program; the study protocol; estimates of recruitment, retention, and attrition; and performance and parameters of candidate outcome measures.

Keywords

depression; insomnia; CBT; adolescents; treatment

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INTRODUCTION

Unipolar depression is a common clinical disorder in adolescence and is marked by frequent recurrence and considerable impairment (Zalsman, Brent, & Weersing, 2006). Early-onset depression is a potent predictor of lifelong recurrent depression (Carballo et al., 2011), suggesting that aggressive treatment of youth-onset depression might ameliorate future risk. Unfortunately, conventional treatments (e.g., antidepressants, cognitive behavioral therapy [CBT], combination treatment) have produced outcomes that are modest at best (March et al., 2004; Weersing & Brent, 2006; Weisz, McCarty, & Valeri, 2006).

We sought to augment depression-focused treatment with an additional intervention to address an associated but distinct condition—insomnia—that interferes with depression recovery, and/or contributes to residual problems. Specifically, we focused on improving sleep in youth depression using cognitive behavioral treatment for insomnia (CBT-I).

There is good rationale for addressing insomnia to improve depression outcomes. First, there is high comorbidity between youth depression and insomnia (Liu et al., 2007; Wolfson & Carskadon, 1998). Second, longitudinal studies indicate that teen insomnia typically precedes depression and predicts its onset (Johnson, Breslau, Roehrs, & Roth, 1999; Johnson, Roth, & Breslau, 2006; Roberts, Roberts, & Chen, 2002) suggesting that insomnia may contribute to depression onset. Third, concurrent insomnia is associated with poorer response to treatment for depression in adults (Emslie et al., 2001; Thase, Simons, & Reynolds, III, 1996). Moreover, residual insomnia is a major component of incompletely remitted depression in both youth and adults (Kennard et al., 2006; Becker, 2006; Smith, Huang, & Manber, 2005) and increases risk of depression recurrence in adults (Dombrovski et al., 2008). Finally, there are now several trials demonstrating that psychological and pharmacological treatments for insomnia markedly improve depression in adults beyond the effects of traditional depression treatments (Fava et al., 2006; Krystal et al., 2007; Manber et al., 2008; Watanabe et al., 2011).

However, the lack of a well-tested insomnia treatment for youth has stymied research in this area. While results from several positive trials of insomnia treatments in depressed adults are encouraging, developmental differences between youth and adult insomnia argue for youth-specific treatments (Clarke & Harvey, 2012). Previous pilots of youth CBT-I, though promising, have lacked a randomized control condition (Bootzin & Stevens, 2005; Schlarb, Liddle, & Hautzinger, 2011). Therefore, we conducted a pilot randomized trial among adolescents with insomnia and unipolar depression. Youth were randomized to either a sleep hygiene control condition (SH) combined with CBT for depression (CBT-D), or an experimental condition consisting of CBT-I combined with CBT-D. This feasibility pilot was not powered for formal hypothesis testing. Nonetheless, we predicted that that youth randomized to CBT-I would have better sleep and depression outcomes than those in the SH control arm. Other important products of this pilot were estimates of recruitment, retention, and intervention and study protocols.

METHODS

Participants

Enrolled youth (n=41) were ages 12 to 20 years old. While various definitions of adolescence exist, we adopted the official NIH policy (www.grants.nih.gov/grants/funding/children/pol_children_qa.htm) in order to determine the feasibility of CBT-I with the widest adolescent developmental span. Participants and were required at intake to have both a Research Diagnostic Criteria diagnosis of insomnia obtained via the Duke Structured Interview for Sleep Disorders (DSISD) (Edinger et al., 2006) <u>and</u> a Diagnostic and Statistical Manual (DSM IV) diagnosis of unipolar depression (major depression N=39, depressive disorder not otherwise specified N=2) obtained via the Children's Schedule for Affective Disorders and Schizophrenia (KSADS) psychiatric interview (Kaufman et al., 1997). Individuals with comorbid psychiatric problems were not excluded because selecting 'pure' cases would have reduced the representativeness of the sample, as insomnia and depression are commonly comorbid with a range of psychiatric disorders. Table 1 details the demographic and baseline characteristics of participants.

Exclusion criteria at baseline included: regular use of medications known to alter sleep (e.g., zolpidem, steroids); bipolar or psychotic diagnoses; physical or neurological diseases (e.g., COPD, multiple sclerosis) that could affect sleep; clinical diagnosis of sleep apnea, restless leg syndromes, or periodic limb movement disorder; mental retardation, autism spectrum disorder, or other significant pervasive developmental disorder; or ≥6 sessions of CBT for insomnia or depression in the past year. The rationale for the latter criteria is that a failure to respond to a prior reasonable dose of the same treatment may denote a subgroup whose inclusion would create a confound. Individuals receiving supportive, non-CBT psychotherapy ≤ once per month were not excluded. Stable dose (≥ 8 weeks) antidepressants were allowed, as long as youth met criteria for major depression at baseline. After enrollment all youth were retained in the sample consistent with intent-to-treat (ITT) principles, even if they initiated new treatment as usual (TAU) healthcare services.

Recruitment and Enrollment

Youth were recruited via different methods at the two study sites, but otherwise all procedures were identical. At Kaiser Permanente Northwest (KPNW) in Portland Oregon, potentially eligible youth were identified by querying the KPNW electronic medical record (EMR) chart system for a depression and/or insomnia diagnosis. Providers who made the index mood or sleep diagnoses gave permission to recruit; 32 (9.0%) refused. Mailed invitation letters were followed by a staff phone call several days later.

Youth at the University of California at Berkeley Golden Bear Sleep and Mood Research Clinic were identified through community referrals, radio and newspaper advertising, and pediatricians. At both sites, interested participants were administered a brief screening interview, followed by a full baseline assessment.

Screening and Randomization

Randomization was conducted centrally for all eligible youth across both sites (n=41), stratified by site and baseline depression severity (CDRS-R <40 vs. 40). The randomization program generated permuted blocks of varying size within strata; 21 youth were randomized to the CBT-I+CBT-D condition, and 20 to the SH+CBT-D condition.

Assessment

Assessments were conducted at baseline (Week 0), and at 12- and 26-week follow-up, by independent evaluators blinded to randomization status.

Depression

The 17-item Children's Depression Rating Scale-Revised (CDRS-R) (Poznanski, Freeman, & Mokros, 1984) is a continuous measure of unipolar depression symptomatology frequently used in youth depression RCTs (March et al., 2004; Brent et al., 2008). At each follow-up we administered the KSADS and the Longitudinal Interval Follow-Up Evaluation (LIFE) (Keller, Shapiro, Lavori, & Wolfe, 1982) to obtain weekly Psychiatric Status Ratings (PSRs) since the previous interview for the index depression diagnosis.

Insomnia

For two weeks at each assessment youth wore an actiwatch (Models AWS64 or AWS) to record frequency and intensity of nighttime movements. Computer-scored actigraphy sleep parameters are well validated against gold-standard polysomnography (Lichstein et al., 2006). We used the Philips Respironics Actiware version 6.0.1 scoring program. Youth completed a daily Sleep Diary and recorded bedtime, estimated time to sleep onset, number/duration of waking periods, etc. From Sleep Diary and actiwatch data we calculated total sleep time (TST), wake after sleep onset (WASO), total wake time (TWT), and sleep efficiency (SE) (Morgenthaler et al., 2007). Interviewers administered the DSISD to obtain sleep-disorder diagnoses including insomnia, as well as a screen for sleep apnea, restless leg syndromes, and periodic limb movement disorder. Participants also completed the 7-item selfreport Insomnia Severity Index (ISI) (Morin, 1993), The ISI has been recently validated with adolescents, with a total score of 8 optimally identifying clinical diagnoses of insomnia (Chung, Kan, & Yeung, 2011).

Credibility, Expectancy, Satisfaction

The 6-item Credibility-Expectancy Questionnaire (CEQ) (Devilly & Borkovec, 2000) yielded ratings of treatment credibility, acceptability/satisfaction, and expectations for success. The CEQ addresses participant willingness to recommend treatment as an indicator of perceived usefulness or credibility ("How confident would you be in recommending this sleep treatment to a friend who experiences similar problems?") as well as expectations for improvement ("At the end of treatment how much improvement in your sleep do think will occur?"). Other CEQ items ask participants how logical the treatment seems, and at post-treatment how satisfied they had been with their sleep treatment.

Functional, Adjustment Status

Interviewers rated youth overall functioning on the Children's Global Adjustment Scale (CGAS) (Shaffer et al., 1983). Scores range from 1–100; more than 70 indicates normal adjustment, and below 60 indicates serious impairment.

Interviewers rated the Clinical Global Improvement (CGI-I) and Severity (CGI-S) scales (Guy, 1976); CGI-I 2 represents response since baseline.. The CGI-I is a subjective and relatively simple rating, but it has satisfactory validity relative to other measures of improvement (Berk et al., 2008) and has been sensitive to clinical improvement in other youth depression trials (Kennard et al., 2006; Emslie et al., 1997; March et al., 2004; Wagner et al., 2004).

Interventions

In both arms, the target duration for the combined sleep and depression interventions was 10 weekly sessions completed within a 12 week window. Either SH or CBT-I was delivered over the initial 3 to 4 sessions. Starting between sessions 3 to 5, both study arms transitioned to delivering 4 to 6 CBT-D sessions, althoughsleep issues continued to be reviewed as relevant during the CBT-D portion of the program. Testing the CBT-D program was not an aim of this study; the program was held constant across both arms. The same therapist delivered both interventions to a given participant.

CBT-Insomnia

We developed our youth CBT-I program using several sources. The core of the CBT-I program consisted of an age-appropriate modification of sleep restriction and stimulus-control treatments originally developed for adults (Bootzin & Stevens, 2005; Manber et al., 2008). While parents were generally informed of treatment progress and could be asked to assist (e.g., with difficult morning waking), adolescents were considered the primary agent for changing their own sleep habits. Other developmental adaptations to CBT-I included a greater focus on limiting bedtime electronics such as cell phones; illustrating treatment elements with age-appropriate vignettes and cartoons; and a focus on adverse impacts of poor sleep on outcomes important for youth, such as academics and peer relationships. Other key elements included cognitive restructuring to address unrealistic beliefs regarding consequences of insomnia (Harvey, Sharpley, Ree, Stinson, & Clark, 2007; Morin, 1993), and regularizing day/night schedules (Clarke & Harvey, 2012). Youth also engaged in savoring techniques to help counteract anxieties and tensions that interfere with sleep onset (McMakin, Siegle, & Shirk, 2011). Savoring is the practiced recollection of past positive experiences, such as a favorite vacation, or anticipation of positive future experiences.

Sleep Hygiene Control Condition

Sleep hygiene (SH) was selected as the control comparison condition based on evidence in the adult literature that SH is minimally effective for insomnia (Morin et al., 2006; Edinger et al., 2009), yet has face validity due to its focus on sleep improvement. The SH materials focus on sleep environment, avoiding stimulating activities or substances (e.g., caffeine), and education about normal sleep needs and habits. CBT techniques for insomnia were specifically prohibited in the SH condition.

CBT-Depression

Youth in both study arms received a brief CBT-D treatment which had demonstrated positive effects in previous and ongoing trials (Clarke et al., 2005; Clarke, Gullion, Dickerson, & Lynch, 2010) and was modified from the Adolescent Coping with Depression Course (Clarke, Rohde, Lewinsohn, Hops, & Seeley, 1999; Lewinsohn, Clarke, Hops, & Andrews, 1990). CBT-D content addressed cognitive restructuring for unrealistic thinking contributing to depressed mood, and increasing pleasant activities.

Therapists

The same therapists delivered CBT-I and SH across both study conditions, to control for therapist effects. Training and supervision focused on high quality delivery of both interventions, as well as limiting the delivery of any CBT-I content in the SH condition.

All therapists had a degree in psychology (one Masters degree and one PhD in Berkeley, and two Master degrees in Portland), experience delivering CBT for depression and/or insomnia, and were state licensed, license-eligible, or certified. Prior to initial study training Berkeley therapists had approximately 2 years of CBT-I experience, and Portland therapists had between 10 to 12 years' experience with CBT-D. All staff participated in a 2-day training led by Drs. Clarke and Harvey, followed by bi-weekly telephone supervision addressing implementation and differentiation of CBT-I, SH (particularly the limits of what was permissible in SH), and CBT-D.

Intervention Delivery

The same therapist delivered both the sleep treatment (either CBT-I or SH) and the subsequent CBT-D sessions to each participant. Both sleep and depression issues may have been addressed in the same session, especially in the middle to later sessions where the sleep focus was reducing and depression focus was increasing, and/or where a therapy technique might be employed for both targets (e.g., cognitive therapy).

Sessions ranged from 1 to 10 for the CBT-I+CBT-D condition (M=7.00, SD=3.3) and ranged from 2 to 11 sessions for the SH+CBT-D condition (M=7.89, SD=2.8). Mean total treatment time was similar for the CBT-I+CBT-D arm (398.3 minutes, SD=198.9) and the SH+CBT-D arm (424.0 minutes, SD=177.8). Neither total time nor number of sessions appeared to be different across conditions. However, the CBT-I condition received more minutes of *sleep* treatment than the SH control condition (189.0 mins (SD=67.6) vs. 125.5 mins (SD=45.9)), and the SH control group received slightly more *depression* CBT (244.7 mins, SD=136.4 vs. 169.6 mins, SD=125.0). Because CBT-D was meant to be constant across arms in this design, minutes of CBT-D was employed as a covariate in all outcomes analyses.

Data Analysis

We entered participant event progression and assessment results into a tracking and data-entry system hosted at CHR, reducing likelihood of site protocol or data variability. The primary outcome analysis used the intent-to-treat (ITT) sample. Our primary sleep outcome was actigraphy and diary TST. Our depression outcomes were three binary measures of

improvement (CGI-I<2, CDRS-R<28), and recovery from baseline DSM diagnosis of major depression or dysthymia.

For the continuous outcomes with at least three timepoints (all actigraphy and diary sleep outcomes, SII, CDRS-R), we tested for differences in trajectories across time between arms using two-level hierarchical linear models (HLMs) (Bryk & Raudenbush, 2002). We tested the binary outcomes (CDRS-R<28, ISI 8) with a generalized form of the HLM, using a logit link and the binomial distribution. HLM uses direct maximum likelihood for handling missing data, and yields valid inferences when data are missing at random (Enders, 2010).

In all HLMs, the first level of the model, which represents within-person variation, included time as a predictor (number of weeks elapsed since baseline). The second level of the model, which represents between-person variation, included a dummy variable for arm, site and depression therapy duration as predictors for the intercept and slope parameters of the first level. The coefficient for arm on the slope of time indicates the difference in the trajectories for each week across time for each arm. Given the small sample size, we graphed the result of each HLM to determine whether the estimated trajectories for each arm were consistent with the hypothesized pattern. We analyzed the CDRS-R 50% and CGI-I 2 with chi-square comparing the arms within each of the two timepoints (weeks 12 and 26). We also analyzed the CGI-S by comparing group within each timepoint with independent-samples t-tests.

As a secondary analysis, we also performed an analysis using "completer" cases with data at all timepoints. For continuous measures effect size (ES), estimates are Cohen's *d* derived from the unadjusted observed data or unstandardized regression coefficients in adjusted and ITT models. For dichotomous variables, the effect size metric is number needed to treat (NNT) (Kraemer & Kupfer, 2006) or odds ratios in adjusted and ITT models. An NNT of 5 means that for every five treated youth, one has received a benefit; smaller NNTs are better. A recent review found an NNT of 10 for antidepressants in adolescent depression (Bridge et al., 2007) providing a reasonable comparison for our results.

RESULTS

Retention, Attrition, Bias

Retention was good, with 88% (*n*=36/41) completing the final week-26 follow-up assessment; 95% (*n*=39/41) had at least one post-baseline assessment. There was no interaction between study condition and retention.

Treatment Expectancies, Credibility

We found no apparent differences on the CEQ between the control (*M*=7.24, *SD*=1.05) and intervention groups (*M*=6.95, *SD*=1.61), indicating that youth perception of the credibility of the two study arms was indistinguishable with respect to perceived effectiveness for sleep and depression.

Sleep Outcomes

Actigraphy—Using the ITT approach (Table 2) there was no apparent time×condition effect for most major actigraphy sleep parameters. However, in the completer sample (*n*=21)

there was a short-term (baseline to week 12) advantage for CBT-I on TST, with an ES *d*=1.12.

Sleep Diary—We did not find effects for any of the Sleep Diary variables (Table 2).

Insomnia Severity Index (ISI)—There were no apparent differences between conditions for the ISI total score over either time period (Table 2).

We did not find large differences between groups on an ISI "insomnia caseness" variable using a youth cut-off score of ISI 8 (Chung et al., 2011) at either week 12 (Cramer's V=.17) or Week 26 (Cramer's V=.25). However, the NNT was favorable for the CBT-I condition, with NNT=3.2 at week 12, and NNT=4.8 at week 26.

Depression Outcomes

Child Depression Rating Scale Revised (CDRS-R)—We did not find any apparent between condition effects for the CDRS-R in either the ITT or completers analysis (Table 2).

Depression Diagnosis Recovery—Figure 2 presents the survival curve for diagnostic recovery from the index depression diagnosis. Recovery was defined as 8 or more weeks of "well time;" e.g., one or no symptoms and little or no impairment (Frank et al., 1991), represented by a score of 1 or 2 on weekly diagnostic severity ratings (DSR) from the LIFE interview. There was not strong evidence for a difference in rates of recovery between the CBT-I and SH conditions. However, there was a trend favoring the CBT-I condition with an adjusted NNT of 4.1. A higher percentage of CBT-I participants recovered (84.2%) during study follow-up compared to SH youth (66.7%). Among those who recovered, SH control participants had an average of 23.0 weeks (*SD*=25.7; median=10 wks) until recovery from the index episode, compared to an average of 18.7 weeks (*SD*=18.5; median=11.5 wks) for CBT-I youth.

Other Clinical Outcomes

CGI-Improvement (CGI-I)—Similar to other youth depression trials (Brent et al., 2008; March et al., 2004) we generated a dichotomous measure where CGI-I scores 2 were considered an indication of treatment response. We did not find evidence for a group difference at either week 12 NNT=12) or week 26 follow-up points NNT=6).

DISCUSSION

We conducted this feasibility study knowing that our small sample size was insufficient to firmly establish an effect for the CBT-I condition. This was especially true given that the control condition included a weak sleep treatment, sleep hygiene (Morin et al., 2006; Edinger et al., 2009), and active depression treatment (CBT-D). Importantly, we do not view this as evidence of a negative trial. Instead, this feasibility study is valuable for two reasons. First, we found trends with medium-large effects favoring the experimental CBT-I arm on several but not all sleep and depression outcomes—justification for a future adequately powered trial, and consistent with the treatment development approach advocated by Onken

and colleagues (Onken, Carroll, Shoham, Cuthbert, & Riddle, 2014). Second, this pilot yielded important products that will facilitate future studies: the youth-adapted CBT-I program; the study protocol; estimates of recruitment, retention, and attrition; and the performance and parameters of candidate outcome measures.

A key lesson from this study is that CBT-I can be effectively delivered directly to adolescents rather than through parent intermediaries. Although parent involvement and support is important, the developmental tasks of adolescent individuation and separation from parents argue for the youth-mediated approach we have taken. Also, adolescents viewed the two sleep interventions (CBT-I and SH) as similar in terms of expectancies and credibility—important for maintaining equipoise between conditions. We also found that the ISI, a frequently employed outcome measure in adult sleep research but with little previous use in adolescents, was able to detect trends favoring the experimental condition— suggesting it may be a viable outcome in future youth insomnia trials. We also learned that we could readily identify and enroll depressed youth with clinically significant insomnia, and retain nearly all of them (90.2%) through final follow-up. Finally, actigraphy TST improved in the CBT-I arm by 99 minutes at week 12. Increases in objective TST are rarely reported in adult trials of CBT-I. We are unable to identify any particular CBT-I element or instruction that might account for this. Perhaps for most adolescents insomnia has been of relatively brief duration and has not yet become entrenched, and may yet be more malleable to treatment than is the case with chronic insomnia in adults.. Regardless of the reasons for the acute post-treatment benefits, at the 26 week follow-up CBT-I youth were sleeping 40 minutes more on average relative to baseline. While this still remains a good outcome, the loss of improved sleep over follow-up underscores a potential need for booster sessions or other methods to improve adherence.

There was a moderate effect size result for actigraphy WASO (baseline to week 26) in the opposite direction from expected; i.e., minutes awake increased for the CBT-I youth but not the SH participants. Unfortunately, we have no clear hypotheses for why this might be so.

This study had several limitations other than the small sample. First, relatively low numbers of racial and ethnic minority youth hamper study generalizability. However, the sample was more *clinically* representative than samples in many CBT trials because many enrolled youth had been diagnosed as clinically depressed by their treatment as usual (TAU) provider, and in many cases were receiving TAU healthcare services. Thus, all effects observed were above and beyond benefits imparted by TAU healthcare. Second, we failed to find much between condition difference on the sleep diary. This may have a genuine lack of difference, or may be accounted for partially by poor youth compliance in completing the sleep diary. While youth were shown how to complete the sleep diary at both intake and during treatment sessions, there were many missed entries, as well as AM/PM confusion and other entry errors. We corrected errors when possible, but in many cases we had reduced confidence in the diary results. However, the sleep diary is an essential CBT-I tool (Carney et al., 2012), and therefore future studies must find a way to address this issue. One possible solution we are now testing is a mobile device-accessible sleep diary with built-in reminders and error checking.

Another limitation was the differential time spent on CBT-D in the two conditions. While the introductory educational content of the SH materials was roughly equivalent to that in the CBT-I materials, fewer minutes of contact were required in the middle sessions to implement and refine the relatively simple SH plan, compared to the more clinically complicated CBT-I plan. Therefore, the SH youth transitioned from the sleep focus into the depression focus earlier than youth in the CBT-I arm – even though the overall minutes of therapy were not different across study arms.

In sum, several medium-to-large effect sizes favoring the CBT-I arm suggest that treating comorbid insomnia may be a viable approach to improving depression outcomes—and that well-powered confirmatory trials are merited.

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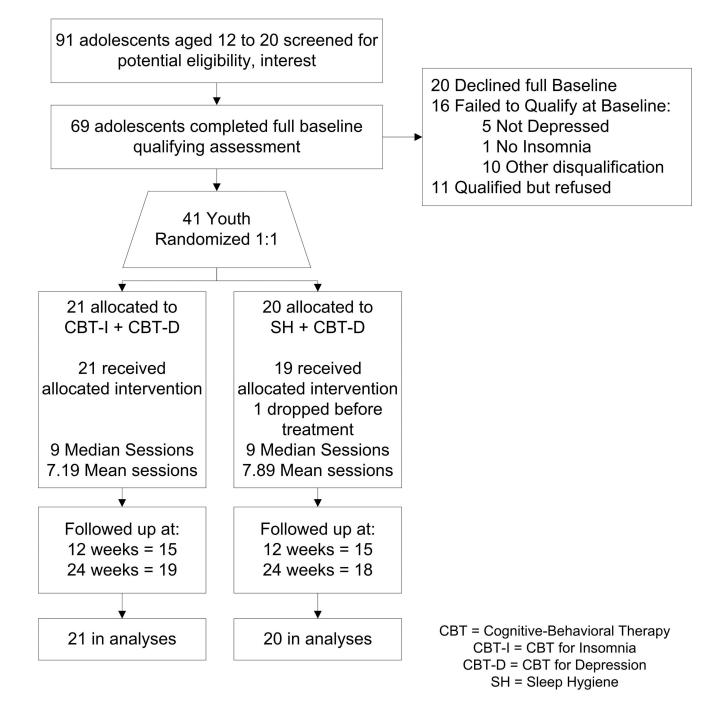
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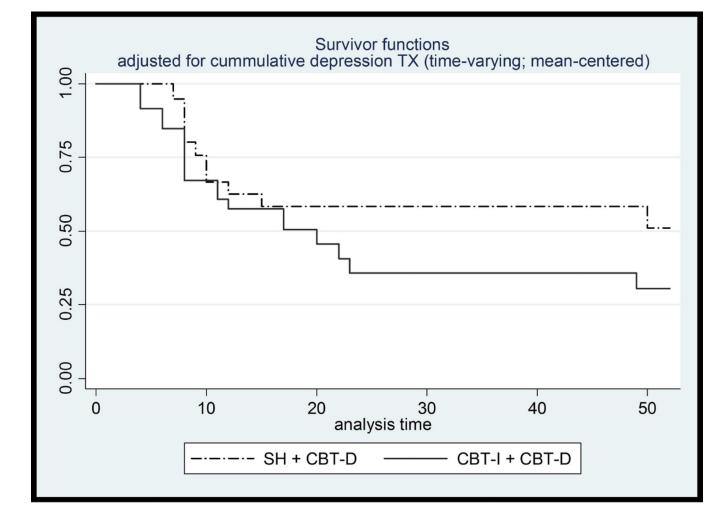## Highlights

- Unipolar depression is a common and impairing disorder in adolescence

- Insomnia is commonly comorbid with depression

- Adding CBT for insomnia to CBT for depression, improved sleep and depression outcomes with medium to large effect sizes

Figure 1.
CONSORT diagram for study events

Figure 2.
Survival curves by condition for recovery from baseline depression diagnosis.

Table 1

Youth baseline demographics and diagnostic status by study arm.

	CBT-I+CBT-D (*experimental*)	SH+CBT-D (*control*)
Youth randomized to arm	21	20
Female N (%)	14 (66.7%)	12 (60.0%)
Mean age in years *(SD)*	16.5 (1.9)	15.9 (1.7)
White N (%)	11 (52.4%)	9 (45%)
Hispanic N (%)	2 (9.5%)	3 (15.0%)
Sleep Diagnosis		
Insomnia	21 (100%)	20 (100%)
Depression Diagnosis		
Major Depression	21 (100%)	18 (90.0%)

Table 2

Depression, sleep and general functioning outcomes by randomization condition and assessment week.

	CBT-I+CBT-D (experimental; n=21)		SH+CBT-D (control; n=20)		Effect Size	95% CI for Effect Size
	Mean or N	(SD or %)	Mean or N	(SD or %)		
CDRS-R					−0.01[a]	−0.34, 0.32
Baseline	54.2	7.8	55.6	10.5		
Wk 12	31.2	9.7	33.1	11.6		
Wk 26	26.1	8.0	28.8	10.1		
CDRS-R > 50% Improvement from baseline						
Wk 12	5	33.3%	5	33.3%	2.03[b]	0.33, 12.47
Wk 26	13	68.4%	10	55.6%	1.35[b]	0.32, 5.58
CDRS-R < 28					0.98[c]	0.87, 1.11
Baseline	0	0%	0	0%		
Wk 12	6	40.0%	7	46.7%		
Wk 26	12	63.2%	11	61.1%		
CGI-I <=2						
Baseline						
Wk 12	10	71.4%	9	60.0%	3.73[b]	0.45, 11.50
Wk 26	14	77.8%	11	61.1%	2.27[b]	0.45, 11.50
CGAS						
Baseline					−0.10[a]	−0.28, 0.08
Wk 12	2.1	1.4	2.2	1.5	−.33[a]	−1.31, 0.65
Wk 26	1.5	1.0	2.3	1.5	−.71[a]	−1.55, 0.13
Insomnia Severity Index (ISI)						
Baseline	17.3	4.3	16.2	3.7		
Wk 12	6.9	4.5	7.8	3.5		
Wk 26	6.6	4.1	8.0	5.5		

	CBT-I+CBT-D (experimental; n=21)		SH+CBT-D (control; n=20)		Effect Size	95% CI for Effect Size
	Mean or N	(SD or %)	Mean or N	(SD or %)		
Insomnia caseness (ISI>=8)					0.94[b]	0.81,1.08
Baseline	0	100%	0	100%		
Wk 12	6	40.0%	8	57.1%		
Wk 26	6	31.6%	9	56.3%		
Actigraphy TST					2.52[a]	−1.71, 6.75
Baseline	365.7	62.4	407.5	47.2		
Wk 12	465.1	186.0	389.9	44.4		
Wk 26	406.9	58.5	406.6	22.3		
Actigraphy SE					0.02[a]	−0.29, 0.33
Baseline	73.2	9.3	76.4	9.0		
Wk 12	74.4	11.9	73.5	8.7		
Wk 26	74.5	7.9	78.5	2.5		
Actigraphy WASO					0.51[a]	−1.06, 2.08
Baseline	69.4	42.6	69.2	33.4		
Wk 12	84.8	61.4	74.8	33.2		
Wk 26	87.0	36.6	69.0	14.9		
Sleep Diary TST					−0.30[a]	−3.18, 2.58
Baseline	419.1	84.3	439.4	96.0		
Wk 12	449.3	52.6	487.2	71.8		
Wk 26	439.6	76.7	467.3	50.2		
Sleep Diary SOL					0.24[a]	−1.15, 1.63
Baseline	49.3	36.1	62.1	49.1		
Wk 12	31.4	30.6	37.0	40.3		
Wk 26	30.0	14.4	28.8	22.0		
Sleep Diary SE					0.09[a]	−0.30, 0.48
Baseline	91.1	6.4	91.3	9.1		
Wk 12	91.8	3.7	93.6	4.1		

	CBT-I+CBT-D (experimental; n=21)		SH+CBT-D (control; n=20)		Effect Size	95% CI for Effect Size
	Mean or N	(SD or %)	Mean or N	(SD or %)		
Wk 26	84.2	12.7	86.6	15.0		
Sleep Diary WASO					-0.27[a]	-1.45, 0.91
Baseline	21.8	37.8	18.8	16.7		
Wk 12	10.5	11.7	6.1	9.3		
Wk 26	9.0	10.4	5.7	3.7		

[a] HLM Coefficient for the effect of the intervention on the slope of time

[b] Odds ratio

[c] Odds ratio for the effect of the intervention on the slope of time based on HLM

Note: Results in Mean or N and (SD or %) columns are based on unadjusted, complete data. Results in effect size and CI columns reflect the magnitude for the effect of the intervention after adjusting for depression therapy duration and site, as well as in most cases using all available data via direct maximum likelihood from the HLM analysis (i.e., ITT).