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Innovations in Practice: The relationship between sleep disturbances, depression, and interpersonal functioning in treatment for adolescent depression

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Background: Sleep disturbance is frequently comorbid with depression and sleep complaints are the most common residual symptoms after treatment among adolescents with depression. The present analyses investigated the effect of sleep disturbance in depressed adolescents treated with interpersonal psychotherapy for adolescents (IPT-A) versus treatment as usual (TAU) in school-based mental health clinics. Method: Sixty-three adolescents participated in a randomized clinical trial of IPT-A versus TAU for adolescent depression. Participants were diagnosed with a DSM-IV depressive disorder and assessed for symptoms of depression, interpersonal functioning, and sleep disturbance. Measures were assessed at baseline, session 4 and 8 of treatment, and session 12 for postacute treatment follow-up. Hierarchical linear modeling was used to model change in depression, interpersonal functioning, and sleep disturbance. Results: Ongoing sleep disturbance was significantly associated with worse depression scores as rated by clinician (γ = 1.04, SE = .22, p < .001) and self-report (γ = 1.63, SE = .29, p < .001), as well as worse interpersonal functioning across the course of treatment (γ = 0.09, SE = .02, p < .001). Treatment condition did not predict change in sleep disturbance (γ = −0.13, SE = .14, p = ns). Conclusions: For all patients in the study, sleep disturbance was a predictor of depression and interpersonal functioning for depressed adolescents. Sleep disturbance predicted more depression and interpersonal stress across treatments and led to a slower improvement in depression and interpersonal functioning. These data suggest that sleep disturbance should be a target for future treatment development research among depressed adolescents.

Key Practitioner Message
- Sleep disturbance is a precursor to the onset of depression among adolescents.
- Residual sleep difficulties are a major component of persistent depressive symptoms after acute treatment and further increase the risk of depression episode relapse.
- This study found that sleep disturbance was significantly associated with worse depression scores across the course of a treatment trial as rated by clinician and adolescent self-report.
- This study highlights the importance of addressing sleep disturbance during treatment in order to improve psychotherapy outcomes for depressed adolescents.

Keywords: Depression; sleep disorders; child; adolescent; clinical trials; treatment

Introduction
While substantial progress in treatment for adolescent depression has been made, even the best treatments achieve 50–70% response rates, leaving much room for improvement (Weisz, McCarty, & Valeri, 2006). Interpersonal psychotherapy for depressed adolescents (IPT-A; Mufson et al., 2004) is an evidence-based psychotherapy that aims to reduce adolescents’ depressive symptoms by helping them improve their relationships. Identifying factors that further enhance IPT-A outcomes may help guide clinicians in treatment planning and focus.

The accumulated evidence makes a strong case for the relevance of sleep difficulties in adolescent depression treatment. Depression and insomnia are highly comorbid (Wolfson & Carskadon, 1998). Adolescent insomnia typically precedes a major depressive episode and predicts its onset in longitudinal studies (Lovato & Grados, 2014). Insomnia that is concurrent with a major depressive episode is associated with poorer response to treatment for active depression in adults (Thase, Simons, & Reynolds, 1996) and in adolescents treated with medication (Emalie et al., 2012). Finally, residual insomnia is a major component of persistent depressive symptoms after acute treatment in both adolescents (Kennard et al., 2006) and adults (Becker, 2006), and further increases the risk of depression relapse (Dombrowski et al., 2008).

Recent evidence suggests that interpersonal distress is associated with more sleep complaints and greater insomnia severity (Gunn, Troxel, Hall, & Buysse, 2014). Sleep difficulties are not directly targeted in IPT-A; however, given the interpersonal targets of IPT-A, sleep may...
be a mediator of positive IPT-A response. To our knowledge, no previous literature has examined sleep disturbance as a mediator of IPT-A.

The goal of this secondary data analysis was to examine sleep as a potential mechanism by which IPT-A works to improve adolescent depression. This question was examined using data from a school-based, randomized controlled trial of IPT-A versus treatment as usual for adolescent depression (TAU; Mufson et al., 2004). We sought to determine if there is a reduction in reported sleep disturbance over the course of treatment for adolescent depression and whether this reduction is greater in IPT-A relative to TAU. The hypothesis was that improvements in depression resulting from IPT-A would be partially mediated by improvements in sleep.

Method

Participants

Participants were 63 depressed adolescents (12–18 years old) participating in a clinical trial examining the effectiveness of IPT-A compared to TAU for the treatment of depression (Mufson et al., 2004). The sample had a mean age of 15.1 years (SD, 1.9 years), and was 84% female and 71% Hispanic. Comorbid diagnoses were 20 patients (32%) with anxiety disorders, 5 (8%) with oppositional defiant disorder, 10 (16%) with substance use, and 4 (6%) with attention-deficit/hyperactivity disorder. Adolescents were referred for treatment in five school-based health clinics in New York City. The study was approved by the institutional review boards for the three hospitals that sponsored the five school-based mental health clinics and by the New York City Board of Education. Informed consent and assent was required for participation. See Mufson et al. (2004) for a complete description of the trial and the Consolidated Standards of Reporting Trials (CONSORT) flowchart.

Treatment

Adolescents were randomized to receive IPT-A or TAU. IPT-A is a 12-session, evidence-based psychotherapy that aims to decrease depressive symptoms by helping adolescents improve their relationships and interpersonal interactions (Mufson et al., 2004). TAU was whatever psychological treatment adolescents normally would have received in the school-based clinic.

Procedures and measures

A psychologist or social worker blind to the youth’s treatment conducted assessments at baseline, weeks 4, 8, and 12; or at early termination. The Schedule for Affective Disorders and Schizophrenia for School-Age Children (KASADS; Kaufman et al., 1997) was used to assess current diagnoses on the basis of DSM-IV diagnostic criteria (American Psychiatric Association, 1994). Depressive symptoms were assessed using the Hamilton Rating Scale for Depression (HRSD; Hamilton, 1967) and the Beck Depression Inventory (BDI-II; Beck, Steer, & Carbin, 1988). In the current analyses, sleep items were removed from the HRSD and BDI and their scores were summed without these items. Interpersonal functioning was assessed with the Social Adjustment Scale-Self-Report (SAS-SR; Weissman & Bothwell, 1976), Cronbach’s alphas for the HRSD, BDI, and SAS-SR were .74, .88, and .67, respectively (Table 1).

Symptoms of sleep disturbance were assessed via three items from the clinician-rated HRSD (Hamilton, 1967). The three items were 0–2 ratings of: (a) difficulty falling asleep, (b) difficulty staying asleep, and (c) waking too early and not being able to fall back to sleep. Higher ratings indicated more severe sleep difficulties. Items were summed to create a composite sleep score at each assessment point. Previous work indicates that the HRSD sleep items are highly correlated with sleep diary reports of insomnia symptoms (Manber et al., 2005).

Data analytic strategy

We analyzed data using growth curve modeling in STATA 12 SE software (STATA version 12; Texas Corp., College Station, TX). A series of models were fit to the HRSD data (sleep items removed), the BDI data (sleep item removed) and the SAS-SR data to determine the shape of the trajectory of patients’ change in depression and interpersonal functioning throughout treatment.

Missing data

A high response rate was achieved. The final data set consisted of 236 sleep disturbance measurements (94% of the possible total of 252), 228 HRSD measurements (91% of the possible total of 252), 236 BDI measurements (94% of the possible total of 252), and 236 SAS-SR measurements (94% of the possible total of 252). There were no differences between treatment groups in the mean number of measurements. If one or more of the measurements had a missing value, that observation was omitted from the model analysis.

Results

At baseline, 65% of trial participants reported nightly sleep difficulties over the previous 2 weeks (a score of two or at least one of the three HRSD sleep items). For the HRSD, BDI, and SAS-SR, the quadratic model was a significantly better fit to the data than the linear model based on chi-square comparison (HRSD $\chi^2(4, N = 63) = 18.49, p < .001$; BDI $\chi^2(4, N = 63) = 9.46, p < .01$, SAS-SR $\chi^2(4, N = 63) = 2.73, p < .05$), thus the quadratic model was selected for all subsequent analyses. Next, treatment condition (IPT-A vs. TAU) was added to the model. The effect of treatment was significant for the HRSD, but not for the BDI and SAS-SR. However, the treatment condition variable significantly improved the model fit over the baseline quadratic model for the HRSD, BDI, and SAS-SR (HRSD $\chi^2(4, N = 63) = 9.65, p < .01$, BDI $\chi^2(4, N = 63) = 8.25, p < .05$, SAS-SR $\chi^2(4, N = 63) = 9.10, p < .01$; See Table 2). Together, these findings indicate that depression symptomatology over the course of treatment was effected by the type of treatment a patient received.

Sleep disturbance as a predictor of depressive symptoms and interpersonal functioning

The sleep disturbance variable was added as a time-varying predictor to the model. There were significant effects of reported sleep disturbance; over the course of treatment, sleep disturbance was associated with increases in HRSD, BDI, and SAS-SR scores (See Table 2). These models were a better fit to the data than those with treatment condition alone (HRSD $\chi^2(4, N = 63) = 28.19, p < .001$; BDI $\chi^2(4, N = 63) = 44.14, p < .001$, SAS-SR $\chi^2(4, N = 63) = 30.04, p < .001$).

Model of treatment condition predicting change in sleep disturbance

Quadratic change in reported sleep disturbance was modeled as a function of treatment group membership in order to further test our hypothesis that IPT-A would have a more significant effect on sleep disturbance than TAU. The linear and quadratic fixed effects were not significant, indicating that sleep disturbance did not significantly change over the course of treatment for either treatment condition. Moreover, treatment condition was not a significant predictor of changes in sleep disturbance scores over the course of treatment (See Table 2).
Discussion

This study aimed to assess the role of reported sleep disturbance in treatment outcome for depressed adolescents undergoing 12 weeks of psychotherapy (IPT-A vs. TAU) in school-based health clinics. Contrary to our prediction, neither treatment condition led to changes in sleep over the course of treatment. However, sleep disturbance over the 12 weeks of treatment was associated with more depression and interpersonal stress at each assessment point for both conditions. The results from this analysis suggest that although sleep does not mediate IPT-A treatment outcome, changes in sleep are indeed related to improvement in adolescents receiving psychotherapy for depression, regardless of type of treatment. It is possible that sleep disturbance may signal a more severe form of depression in teens given that these symptoms also appear to be more resistant to treatment. Although evidence suggests that interpersonal distress is associated with both depression (Rudolph et al., 2000) and poor sleep (Gunn et al., 2014), it is likely that in order for sleep to consistently improve during treatment, a specific focus on the relationship between interpersonal stress and sleep should be addressed. Our results suggest that sleep disturbance functions independently of current treatment targets in IPT-A, which is consistent with evidence that sleep does not improve in other evidence-based treatments for adolescent depression (Kennard et al., 2006). This trial was not designed to target sleep disturbance. However, given that both treatment condition and sleep disturbance independently were predictors of treatment outcome for depression symptoms and interpersonal functioning difficulties, it seems likely that addressing sleep disturbance in the context of interpersonal stress may lead to more robust treatment outcomes for adolescent depression. A greater focus on sleep disturbance and its underlying mechanisms in the context of treatments for depression will be an important area for future research, particularly among adolescents where sleep disturbance is prevalent and the mechanisms of its effect on depression are complex (Wolson & Carskadon, 1998).

We also found that sleep disturbance predicted more depression and interpersonal stress over the course of treatment. This evidence further suggests the need to support new adaptations of current treatments for
adolescent depression to target both depression and sleep disturbance. A recent pilot study found support for such an adaptation. Clarke et al. (2015) found that combining Cognitive Behavior Therapy for youth depression (CBT-D) with CBT for insomnia versus CBT-D alone resulted in medium-large effects of the combined treatment for improving sleep and depression outcomes. The current study lends additional support for conducting larger scale trials combining depression and sleep treatments for adolescents with depression.

Several limitations are important to consider. First, the relatively small sample size may have limited statistical power. Second, gold standard measurements of sleep variables were not used in this study. However, the use of the HRSD clinician administered questions on sleep has been done in previous studies on the impact of sleep disturbance on treatment outcomes (McCall, Reboussin, & Cohen, 2000) and previous work in depression has found that the HRSD sleep items are highly correlated with sleep diary parameters (Manber et al., 2005). Nonetheless, a follow-up study should attempt to use gold standard sleep measures to replicate results.

Conclusion
The results support the hypothesis that sleep disturbance is strongly predictive of treatment outcome for adolescent depression. However, IPT-A is not mediated by changes in sleep. These findings suggest that sleep disturbance should be a target for future treatment development research in adolescent depression. An important next step will also be to examine the long-term effects of continued sleep disturbance after acute treatment for depression and whether offering additional sessions focused on treating the sleep disturbance could enhance long-term outcomes.

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Supporting information
Additional Supporting Information may be found in the online version of this article.

References

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