The Complex Role of Sleep in Adolescent Depression

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Abstract

Psychological and pharmacological treatments for youth depression yield post-acute response and remission rates that are modest at best. Improving these outcomes is an important long-term goal. To that end, in this paper, the authors examine the possibility that a youth CBT insomnia intervention may be employed as an adjunct to traditional depression-focused treatment with the aim of improving depression outcomes. This “indirect route” to improving youth depression treatment outcomes is based on research indicating that the risk of depression is increased by primary insomnia, that sleep problems interfere with depression treatment success, and on emerging adult depression RCT results. The authors describe the protocol they developed for treating insomnia in depressed youth.

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Unipolar depression is one of the most common disorders in adolescence, with point prevalence estimated at 3% to 8%, and episodes typically last 6 to 8 months.1,2 It has a chronic, episodic course marked by frequent recurrence and considerable impairment.3,4 An estimated 20% of adolescents will have had a depressive episode by age 182 with as many as 75% experiencing a second episode within 5 years.5,6 Depression is associated with substantial impairment in school, interpersonal relationships, and occupational adjustment; tobacco and substance abuse; suicide attempts; and a 30-fold increased risk of completed suicide.3,7–9 The diagnostic criteria for major depression are presented in Table 1.

Inadequacy of Treatments for Youth Depression

The critical need to augment traditional depression treatments is evident. Even in the largest, highly controlled clinical trial of youth depression treatment (TADS),10 the maximally effective condition (CBT+ fluoxetine) yielded a 3 month remission (full recovery) rate of only 37%11 and response rates no greater than 71%.10 (response includes both recovered and partially improved youth). The need for improvement is reinforced by several recent meta-analyses and reviews12–14 indicating only modest effects for traditional youth depression treatments such as CBT and antidepressants. Less is known about treatments for pre-pubertal depressed children, but similar inadequacies are generally presumed to be evident for this younger age range as well. Nonetheless, we will focus on adolescents as our research focuses on these older youth.
Improving Suboptimal Teen Depression Treatment Outcome

Given the unsatisfactory outcomes of conventional treatments for youth depression, various strategies are being pursued to improve outcomes (e.g., improving the adherence-fidelity-duration of existing depression treatments; developing novel depression treatments; combining multiple depression-focused treatments—e.g., antidepressants and CBT). In this paper we describe the reason we are pursuing another strategy: we hypothesize that the concurrent treatment of depression and insomnia in depressed youth will improve both sleep and depression outcomes, even beyond the effects of traditional depression treatment. We next review the specific evidence pointing to the promise of this program of research.

Sleep in the Adolescent Years

Magnitude of Youth Insomnia Problem

Although improved depression is our primary goal, improved sleep is an important intermediary target. Researchers have increasingly identified an epidemic of sleep deprivation in youth. An estimated 25% of adolescents have some form of sleep disturbance. Sleep deprivation of varying severity is reported by 10% to 40% of high school youth. This is a persistent problem for many; 12.4% of adolescents in another study reported insomnia symptoms nearly every day of the past month, with higher rates for girls and lower SES youth. Lifetime prevalence of DSM-IV insomnia (see Table 2 for the diagnostic criteria) through age 18 has been reported as 10.7%, with an increased risk among girls after the onset of menses. Community rates of adolescent DSM-IV insomnia have been reported as 4.7% one-month prevalence and approximately 4% point prevalence. Rates of insomnia are even higher in depressed adolescents, our target population.

Sleep disturbance and behavioral problems

Sleep deprivation has significant and severe adverse impacts. Studies suggest a strong link between sleep disturbance and behavioral problems in youth, in part because sleep deprivation undermines emotion regulation the following day. Sleep problems are similarly associated with increased risk of suicidality. Across multiple studies conducted in various countries using different methodologies, insomnia in teens has been associated with suicidal ideation, suicide attempts and suicide completion (the latter was established using a psychology autopsy method). Adolescent insomnia/sleep deprivation also contributes to school absenteeism and dropout. Academic performance also declines, along with impaired cognitive performance and attention, consistent with the emerging neuroscience findings demonstrating the importance of sleep for learning and memory.

Sleep disturbance and medical problems

Persons with insomnia also have more medical problems, more physician visits, are hospitalized more often, use more medication, have higher absenteeism, more problems at work, and more workplace accidents. Sleep deprivation is associated much higher rates of accidents, particularly motor vehicle accidents (MVAs), one of the leading causes of death among young men and adolescents. All of these incur significant direct and indirect costs for individuals, families, health care delivery systems, and for society. The combined annual direct and indirect costs for insomnia have been estimated between $92-$107B billion (1994 US dollars), with indirect costs (e.g., medical comorbidities and care, reduced workplace productivity, MVAs, other accidents) accounting for $77-$92B. Similarly, the average annual per-person direct and indirect costs were $5,010 for individuals with insomnia syndrome, $1,431 for individuals presenting with symptoms, and $421 for good sleepers. There may be even greater, as-yet underestimated costs associated with lower
educational attainment resulting from youth sleep disorder, which may in turn reduce lifetime income.

**Insomnia versus sleep disorders**

Our current work is focusing on youth *insomnia* rather than the broad span of all sleep disorder in youth; e.g., delayed sleep phase syndrome [DSPS] and hypersomnia. Our rationale is twofold. First, studies suggest insomnia is the most prevalent of sleep disorders in community youth samples.19,23–25 Hence, an insomnia treatment will have the broadest applicability. Second, CBT treatments for insomnia, including our youth program, are better established and better evaluated than treatments for other sleep disorders such as DSPS. For these reasons we have been focusing exclusively on the youth insomnia population.

**Insomnia and Depression**

**Insomnia: a Possible Causal and/or Treatment-Interfering Role in Depression?**

This line of research is also motivated by the research priorities developed at the NIH state-of-the-science conference on insomnia47: that insomnia is not just a symptom or by-product of depression, but in many patients insomnia contributes to depression onset and/or maintenance, complicates and attenuates the effectiveness of depression treatment, and is the most common residual symptom when depression is incompletely remitted.48,49 Thus, direct treatment of insomnia seems likely to improve depression outcomes, or even prevent initial onset of depression.50–52 In the sections that follow, we review the evidence for these assertions.

**Insomnia is Comorbid with Depression**

Sleep disturbances are frequently comorbid with depression and anxiety,35,53,54 and there is evidence that these conditions have bidirectional, mutually maintaining influences.55,56 In a recent study of 553 youth with major depression, 72.7% also reported a sleep disturbance, mostly insomnia; these youth (ages 7.3 to 14.9) were also more severely depressed.26 While this association would be expected if insomnia were simply a symptom of depression, a recent review examined the epidemiological, sleep-EEG, neuroendocrine, and immune research and found distinct differences between depression and insomnia, suggesting these are separate but highly associated disorders with bidirectional impacts.57 Convergent evidence from neuroimaging research with healthy individuals and with animals shows that sleep deprivation undermines emotion/mood regulation the following day28 and, at the neural systems level, circuits involved in emotion regulation and circuits involved in sleep regulation interact in bidirectional ways.56 The mechanisms underlying these effects are currently under investigation.

**Insomnia Contributes to Depression Risk**

Evidence has steadily accrued indicating that insomnia is an independent risk factor for first and recurrent episodes of depression.59–64 A recent review estimated that patients with persistent insomnia have a 3.5 fold increased risk for depression relative to individuals without insomnia;50 another recent meta-analysis similarly found a 2 fold risk.65 This pattern of findings holds across the lifespan in older adults,66,67 adults in the middle years68–70 and in young adults.71,72 Insomnia may also be an independent predictor of suicidal behavior in depressed patients.73

Similar results are reported in adolescents. Community residing youth (N=4,500) who reported frequent trouble sleeping were more likely than normal-sleeping controls to report anxiety or depression (odds ratio = 22.7).74 A similar study of 1,014 teens found that chronologically-primary insomnia significantly predicted future depression (hazard rate=
3.8) but that primary depression did not predict subsequent insomnia. Insomnia symptoms also predicted subsequent depression in another large adolescent community panel, elevated insomnia at Wave 1 predicted greater depression severity at Wave 2 even when controlling for Wave 2 insomnia. Insomnia has also been found to predict adolescent hospitalization for suicide attempt.

**Insomnia Interferes with Depression Treatment**

Thase found that depressed adults with polysomnogram (PSG) profiles indicative of sleep disorder had a less favorable response to depression CBT than patients with normal sleep. Similar results have been reported in depressed youth, with decreased sleep efficiency and delayed sleep onset predicting depression recurrence following treatment. Sleep abnormality may impair depression CBT response. The mechanism seems to be via increased hypothalamic-pituitary-adrenocortical (HPA) activity, which is thought to predict poor depression treatment response.

**Residual Insomnia is a Major Component of Incompletely-Remitted Depression**

Insomnia was the most common residual symptom among depressed youth in the TADS study who had responded to treatment but had not yet progressed to full remission. Similar residual insomnia has been reported in incompletely-recovered depressed adults. Persistent residual insomnia may significantly reduce the likelihood of full depression remission by 10–12 fold in patients with major depression or dysthymia, and increase the risk of depression recurrence. While our current focus is on insomnia treatment simultaneous with depression treatment, other important targets are likely to include residual insomnia remaining after depression treatment, thereby converting additional youth to full depression remission status, similar to studies with adults.

**Our Hypothesis: Improved Youth Sleep Will Contribute to Improved Youth Mood**

The review in the previous section suggests that treating sleep disorder promises to improve depression outcomes. Therefore, we have hypothesized that treating youth insomnia simultaneously with depression treatment may improve both sleep and mood outcomes.

**Adult Trials Treating Sleep to Improve Depression**

Three studies with adults highlight the promise of the proposed research. Manber et al found higher rates of depression and insomnia remission (61%, 50%, respectively) when an antidepressant was combined with CBT for insomnia (CBT-I), versus 33% depression and 7% insomnia remission rates in a control condition consisting of an antidepressant plus sleep hygiene (SH), considered a less potent sleep intervention. Fava et al compared an antidepressant plus placebo versus antidepressant plus the sleep agent eszopiclone in adults with both major depression and insomnia. The joint insomnia-depression treatment condition was associated with significantly more depression response (59% vs. 48%) and remission (42% vs. 32%). Similar advantages were observed in clinician-rated depression, improvement at work, and all major sleep outcomes. A third trial found similar results for refractory insomnia in residual depression in adults, comparing behavioral treatment (BT) for insomnia and treatment as usual (TAU) versus a TAU-only control group. The BT+TAU arm demonstrated significantly improved sleep as well as depression outcomes.

Several of these adult trials examined pharmacological treatments for either depression and/or insomnia. In contrast, our focus has been CBT psychotherapy for both conditions. We have elected to focus on CBT-I and CBT-Depression (CBT-D) because surveys indicate that youth and families strongly favor CBT and other psychotherapies over pharmacotherapies,
as do adult patients.\textsuperscript{89,90} ADs are also concerning to many families because of increased suicidal ideation and suicide attempts risk in youth.\textsuperscript{91,92} For sleep medications, there have been no controlled trials of these agents in youth other than exogenous melatonin,\textsuperscript{93–96} and at present neither melatonin nor any other sleep agent has FDA approval for pediatric insomnia.\textsuperscript{55,97–99} Finally, while both CBT and medications are effective short-term treatments for adult insomnia, following discontinuation of active treatment, CBT’s benefits persist while medication’s benefits often fade quickly.\textsuperscript{100,101}

**Youth Insomnia Treatment**

The *adult* insomnia CBT treatment literature is relatively well established, with numerous clinical trials conducted over the past few decades. The evidence base for CBT for adults with insomnia has been summarized in multiple meta analyses\textsuperscript{102–104} and two practice parameters papers commissioned by the American Academy of Sleep Medicine.\textsuperscript{105,106} The clear conclusion is that CBT for insomnia produces reliable and durable changes in sleep. In contrast, outcome literature on *youth* insomnia treatment is very slim—reinforcing the necessity for treatment research in this area. Bootzin and Stevens (2005) conducted the first uncontrolled trial of a CBT insomnia treatment in a sample of sleep-disordered, substance-abusing adolescents. All 55 enrolled youth received the CBT-I protocol. Compared to non-completers, treatment completers showed significant improvements on multiple sleep outcomes. Self-reported drug use declined for the completers at follow-up evaluations while continuing to increase for the non-completers. Improved sleep was associated with decreased aggression.\textsuperscript{107} Another small (n=18) uncontrolled pilot\textsuperscript{108} of a 6-session insomnia behavioral therapy (BT-I) found improvement in numerous sleep parameters. While both of these trials have been limited by the lack of a randomized control condition, the generally positive results encourage us to continue this line of research.

To the best of our knowledge, there are no other published RCTs of CBT or any other psychological treatment for youth insomnia. We have found a few small trials of melatonin supplementation for childhood insomnia,\textsuperscript{93–96} though most of these were with children younger than the age range of interest to us, namely adolescents. Also, as noted earlier, depressed youth and their parents favor psychotherapy over pharmacotherapy,\textsuperscript{88} and CBT appears to be superior to sleep medication in the longer term.\textsuperscript{100,101} Reaffirming the need for more research, this neardearth of youth insomnia treatment development and evaluation is especially surprising given the consistent recent literature on youth insomnia prevalence and associated morbidity.

**There is need for an Adolescent-Specific Developmentally Adapted Insomnia Treatment**

Given the adult trials cited above, readers might ask whether it is really necessary to test an adolescent insomnia intervention. Couldn’t the insomnia interventions from these adult studies be directly employed with depressed, sleep-disordered youth? We believe that separate investigation of the joint treatment of youth insomnia and depression is warranted, for two reasons:

1. *Adult insomnia treatments may be inappropriate for use with youth, without modification.* Our experiences with youth highlights the necessity for age-appropriate adaptations of CBT and psycho-educational materials, examples, exercises, homework, and so on, geared to the unique adolescent psycho-social environment (living with parents; reduced independence; school and peer demands), and to the differing intellectual, emotional regulation and “executive decision-making” capacities of adolescents.\textsuperscript{27,109} As will become evident below, our CBT-I intervention program, developed and pilot tested with NIMH funding (R34 MH82034)\textsuperscript{1}, illustrate the type and extent of developmental adaptations we have made.
2. While insomnia disorder in adults and youth shares several key features, it is also sufficiently different in presentation and maintaining factors that treatments must take these distinctions into account. For example, the number of hours of normative sleep is greater for adolescents than for adults, likely because of dramatic maturational and brain changes during adolescence, such as neuronal pruning. Similar hours of sleep deprivation may therefore result in a greater deficit in adolescents compared to adults. Other developmental differences contributing to the need for a youth-specific insomnia treatment are:

- developmentally normative but often subclinical delayed sleep onset (going to bed later) during adolescence
- cultural and peer pressures for late night socializing
- need to include parents to help scaffold the motivation for change and adolescent independence from parents is in transition, leading to changing parental role with regards to monitoring and enforcing regular sleep habits

In summary, the need for age-appropriate intervention content as well as the divergent nature of insomnia in the different ages argues for a separate investigation of the joint treatment of youth insomnia and depression, rather than relying simply on the similar adult trials.

Effects beyond Depression

Although our primary aim is to improve youth depression, successful treatment of youth insomnia may improve outcomes in other domains as well. These include improved educational attainment; reduced dropout rates; and improved classroom performance. Successful youth insomnia treatment might also reduce rates of sleep deprivation-induced motor vehicle accidents (particularly nighttime accidents) and other accidental injuries. Finally, insomnia has a possible contributing role in obesity, metabolic syndrome or diabetes, and immune system dysfunction. Successful treatment of youth insomnia could ultimately be beneficial in these domains as well.

CBT-Insomnia for Youth

Our CBT-I approach is based on adult CBT-I protocols developed by Manber, Bootzin, and Harvey and their colleagues, as well as the adolescent protocol piloted by Bootzin and Stevens. The core components of this CBT-I protocol are stimulus control (SC), sleep restriction (SR), and sleep-focused cognitive therapy (CT). We have also added elements of motivational enhancement therapy (MET) to improve youth therapy participation. Collectively, we refer to this therapy approach as insomnia CBT (CBT-I). While the primary focus of these techniques is directly on sleep improvement, therapists may use elements of these therapy approaches to address related problems; e.g., CT for anxiety that may be contributing to insomnia. Sleep hygiene, while not a core component, may be incidentally included.

Stimulus Control and Sleep Restriction to Regularize Sleep-Wake Cycle

Stimulus control (SC) and sleep restriction (SR) are the most established of all the behavioral sleep disorder interventions. We developmentally adapted existing protocols. Both stimulus control and sleep restriction aim to regularize the sleep-

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wake cycle and strengthen the association between the bed and sleeping by limiting sleep-incompatible behaviors in the bedroom environment (watching TV, computer use), while developing a consistent sleep-wake schedule. Stimulus control involves:

a. Use the bed only for sleep—i.e., no TV watching or talking on cell phones.

b. Go to bed only when sleepy.

c. Get out of bed and go to another room when unable to fall asleep or return to sleep within approximately 15 to 20 minutes and return to bed only when sleepy again.

d. Arise in the morning at the same time each day (no later than plus 2 hours on weekends)

In terms of sleep restriction, also review the sleep diary for the past week. If sleep efficiency (% of time in bed spent asleep) is lower than 85% we discuss the possibility of implementing sleep restriction therapy with the youth and his/her parent. The goal is to gradually move toward a regular schedule 7 days a week. To achieve steps (a) and (d) we use the standard stimulus control methods which provide a rationale, set goals for bedtime and wake-time, use a daily sleep diary to monitor progress toward goals (also required for outcomes assessment), and review the diary at weekly therapy sessions. For difficulty falling asleep we supplement the traditional stimulus control instruction (get up out of bed) with training in imagery and relaxation techniques with the goal of reducing arousal and promoting sleep onset. The goal is to lower the potential for youth to become engaged in rewarding and arousing activities (e.g., using electronics) should they arise when unable to sleep.

**Cognitive Therapy to address Dysfunctional Sleep Beliefs and Bedtime Rumination**

Cognitive therapy is a treatment for insomnia as well as a well established treatment for depression. Difficulty getting to sleep is often related to excessive worry, rumination, and negative cognitions, and dysfunctional beliefs about sleep. Typical unhelpful beliefs about sleep include: “There is no point going to bed earlier because I won’t be able to fall asleep.” “If I don’t fall asleep soon I will be a wreck tomorrow,” and “Getting more sleep doesn’t help me.” The intervention for dysfunctional beliefs involves a four-step process:

1. identifying dysfunctional thoughts
2. guided discovery and Socratic questioning to challenge beliefs
3. individualized experiments to test the validity and utility of dysfunctional beliefs and to collect data on new beliefs
4. identification and dropping of safety behaviors that prevent disconfirmation of dysfunctional beliefs.

We teach patients to evaluate worry and rumination, diary writing or scheduling a ‘worry period’ to process worries several hours prior to bedtime, creating a ‘to do’ list prior to getting into bed to reduce worry about future plans/events, training to disengage from pre-sleep worry and redirect attention to pleasant, distracting imagery, identifying the adverse consequences of thought suppression in bed and scheduling a pre-sleep ‘wind down’ period prior to bedtime to promote disengagement from daytime concerns. Therapists may also employ cognitive therapy to address some common comorbidities (e.g., general anxiety) if these comorbidities interfere with sleep and/or depression recovery.
Motivational Enhancement

This component is critical given that youth sleep disturbance is associated with poor self-regulation.\textsuperscript{144}, which may undermine adherence to the treatment. A recent meta-analysis\textsuperscript{145} found that motivational enhancement significantly increases client motivation. Motivational enhancement involves a straightforward review of perceived pros and cons of change\textsuperscript{146} recognizing that many sleep-incompatible/interfering behaviors used by youth are rewarding (e.g., text messaging with friends).

Conclusion

In this discussion we had two related goals. First, it is clear that insomnia is a significant problem in adolescence. Successful treatment of insomnia is an important goal in its own right. However, the primary goal in our recent research, consistent with NIMH’s focus on mental disorders and the future research priorities from the NIH State-of-the-Science conference on insomnia,\textsuperscript{47} has been to improve the treatment of youth depression beyond the modest effects achieved with depression-focused interventions. We hypothesize that joint treatment of sleep and mood disorder, with treatment elements specific to each, may increase depression response and remission rates. This approach is suggested by insomnia’s high comorbidity with depression, by the emerging indications that sleep disturbances may play a causal role in the onset of many (but not all) depressive episodes, by preliminary adult outcome trials in which treatment of insomnia also improved depression outcomes and by other uncontrolled pilots of youth insomnia treatment. There is also evidence that insomnia interferes with patients’ ability to benefit from depression-focused CBT, suggesting that insomnia CBT might enable depression CBT to be more successful. Overall, our approach is also consistent with the “primary prevention of secondary disorders” model advocated by several researchers in other clinical contexts\textsuperscript{147–149} and specifically in the case of insomnia and mood disorder.\textsuperscript{51,52,61}

Developmental timing may be important too. Animal and human research suggests that puberty is a unique period for establishing future behavioral patterns and habits;\textsuperscript{150} intervening in this developmental period may assist youth to establish healthy patterns that will serve them well into the future. If we find that this novel intervention improves outcomes across a broad range of critical and prevalent adverse outcomes for teens (e.g., depression, suicidality, insomnia, educational attainment, and others), the public health implications will be large. Even perhaps more startling public health implications, and a fascinating domain for future research, is to treat insomnia as a prevention for youth depression.

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### Table 1

**Diagnostic and Statistical Manual (DSM-IV) Criteria for Major Depression**

At least five of the nine symptoms below for two weeks or more, for most of the time almost every day, representing a change from prior functioning. One of the symptoms must be either (a) depressed mood, or (b) loss of interest.

- **a.** Depressed mood. For children and adolescents, this may be irritable mood.
- **b.** A significantly reduced level of interest or pleasure in most or all activities.
- **c.** Significant loss or gain of weight (5% or more change in a month when not dieting). This may also be an increase or decrease in appetite. For children, they may not gain an expected amount of weight.
- **d.** Difficulty falling or staying asleep (insomnia), or sleeping more than usual (hypersomnia).
- **e.** Behavior that is agitated or slowed down. Others should be able to observe this.
- **f.** Feeling fatigued, or diminished energy.
- **g.** Thoughts of worthlessness or extreme guilt.
- **h.** Reduced ability to think, concentrate, or make decisions.
- **i.** Frequent thoughts of death or suicide, or a suicide attempt.

The person's symptoms must result in great distress or difficulty in functioning at home, work, or other important areas. The condition is also not caused or explained by (1) effects of drugs or medication; (2) a medical condition; or (3) bereavement.

Summarized from the Diagnostic and Statistical Manual of Mental Disorders- Fourth Edition, Text Revision.
Table 2

Research Diagnostic Criteria for Insomnia

A. The individual reports one or more of the following sleep related complaints:
   1. difficulty initiating sleep
   2. difficulty maintaining sleep
   3. waking up too early, or
   4. sleep that is chronically nonrestorative or poor quality

B. The above sleep difficulty occurs despite adequate opportunity and circumstances for sleep.

C. At least one of the following forms of daytime impairment related to the nighttime sleep difficulty is reported by the individual:
   1. fatigue/malaise
   2. attention, concentration, or memory impairment
   3. social/vocational dysfunction, poor school performance
   4. mood disturbance/irritability
   5. daytime sleepiness
   6. motivation/energy/initiative reduction
   7. proneness for errors/accidents at work or driving
   8. tension headaches, and/or GI symptoms in response to sleep loss; and
   9. concerns or worries about sleep