Nocturnal Wakefulness Is Associated With Next-Day Suicidal Ideation in Major Depressive Disorder and Bipolar Disorder

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ABSTRACT

Objective: Self-reported sleep disturbances may confer elevated risk for suicidal ideation, suicide attempts, and death. However, limited research has evaluated polysomnographically determined sleep disturbance as an acute physiologic risk factor for suicidal thoughts. This study sought to investigate the relationship between nocturnal wakefulness in association with next-day suicidal ideation using overnight polysomnography assessment from data collected between 2006 and 2013.

Methods: Sixty-five participants with *DSM-IV*–diagnosed major depressive disorder or bipolar depression underwent overnight polysomnography monitoring in a sleep laboratory. The Hamilton Depression Rating Scale (HDRS) was administered the morning after polysomnography recording to assess next-day suicidal ideation, severity of depressive symptoms, and subjective sleep disturbances.

Results: Using a generalized linear mixed model, a significant time-by-ideation interaction was found indicating greater nocturnal wakefulness at 4:00 AM among participants with suicidal ideation ($F_{4,136} = 3.65$, $P = .007$). Increased time awake during the 4:00 AM hour (4:00 to 4:59) was significantly associated with elevated suicidal thoughts the next day (standardized $\beta = 0.31$, $P = .008$). This relationship persisted after controlling for age, gender, diagnosis, and severity of depressive symptoms.

Conclusions: Greater nocturnal wakefulness, particularly in the early morning hours, was significantly associated with next-day suicidal thoughts. Polysomnographically documented sleep disruption at specific times of night may represent an acute risk factor of suicidal ideation that warrants additional research.

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Every year, nearly 900,000 individuals worldwide die by suicide.[1] Recent epidemiologic and clinical research has focused on insomnia, nightmares, and other sleep disturbances as potentially modifiable risk factors for suicide. This association between sleep disturbance and suicidal thoughts, behaviors, and death has been demonstrated in large epidemiologic and national samples[2,3] and in veterans and military service members.[4] In one analysis, the relationship between sleep disturbance and suicidal thoughts persisted when controlling for shared genetic and environmental influences in adolescent monozygotic twins.[5] Both a meta-analysis[6] and a systematic review[7] noted that subjective sleep disturbances, including insomnia and nightmares, are evidence-based risk factors for suicidal thoughts, behaviors, and death, independent of depressed mood. This relationship is further supported by results from the National Violence Death Reporting System demonstrating that suicide deaths are most likely to occur between midnight and 4:59 AM when accounting for the proportion of the population who is awake, with a peak incidence of death in the 2:00–2:59 hour.[8] These promising epidemiologic and clinical results have led to ongoing clinical trials investigating the use of sleep treatments—both pharmacologic and psychotherapeutic—for potential use with suicidal patients (see NCT01770587 and NCT01689909).

Despite findings from self-reported data, relatively few analyses have investigated potential time-related factors over the course of the night that may underlie the relationship between impaired sleep and suicide. Studies of sleep architecture using polysomnography suggest that percentage of increased rapid eye movement (REM) sleep, REM activity, and REM duration are all associated with suicidal thoughts or behaviors in depressed adults, depressed young adults, and patients with psychosis or schizophrenia.[9,10] Polysomnographically assessed decreased sleep efficiency has also been associated with higher number of lifetime suicide attempts.[10] Other investigations have suggested that altered chronobiological activity is related to both suicidal thoughts[11] and suicide deaths.[12] The electroencephalographic sleep literature and systematic investigations evaluating time of day effects on suicide risk are relatively sparse, however, and analyses often do not adjust for depressive symptoms or use current suicidal thoughts as an outcome measure. Further evaluation of the epidemiologically and clinically reported link between "sleep disturbances" and current suicidal ideation, using techniques such as polysomnography that can detect temporal variations in wakefulness over the course of the night, is warranted. Such analyses can evaluate the extent of sleep disruption and its temporal distribution over the course of the night to assess etiology and guide the development of targeted treatments. Analyses can also be used to guide future research into biological

Clinical Points

- Sleep problems have been associated with suicide risk over the long term but may also represent an acute risk factor for suicide.
- Wakefulness over the course of the night, particularly around 4:00 AM, was associated with increased suicidal thoughts the next morning in depressed patients.
- Sleep problems may be an important element of suicide risk assessment.

Table 1. Demographic and Clinical Characteristics of Participant Sample by Suicidal Ideation[a]

Characteristic	Total Sample (n = 65)	Ideators[b] (n = 39)	Non-Ideators[c] (n = 26)	χ²	P
Male, n (%)	30 (46)	22 (56)	8 (31)	4.13	.04
Lifetime history of suicide attempt, n (%)	27 (42)	22 (56)	5 (14)	8.88	.003
Bipolar I or II diagnosis, n (%)	24 (37)	9 (23)	15 (42)	0.20	.75
				t	P
Age, y	43.8 (12.7)	44.0 (13.1)	43.5 (12.3)	−0.13	.89
Illness duration, y	25.5 (11.8)	25.8 (12.3)	25.1 (12.3)	−0.23	.82
Depression/sleep HDRS item					
Early insomnia	1.2 (.9)	1.1 (0.9)	1.2 (0.9)	0.55	.58
Middle insomnia	1.0 (.8)	1.0 (0.8)	1.1 (0.7)	0.53	.60
Late insomnia	0.6 (.8)	.7 (0.8)	0.6 (0.7)	−0.46	.65
Remaining HDRS items	17.6 (3.2)	18.3 (3.2)	16.4 (2.7)	−2.56	.01

[a]Values shown as mean (SD) unless otherwise noted.
[b]HDRS Suicide item > 0.
[c]HDRS Suicide item = 0.
Abbreviation: HDRS = Hamilton Depression Rating Scale.

mechanisms for the relationship between sleep and suicide risk, including changes in cortisol, melatonin, or clock gene expression.

Given the existing literature linking sleep disturbance and suicide, this study explored the extent to which electroencephalographically assessed sleep disturbance may serve as an acute risk factor of suicidal thoughts among a sample with treatment-resistant major depressive disorder (MDD) or bipolar disorder. We hypothesized that whole-night wakefulness after sleep onset, assessed via polysomnography as a physiologic correlate of disturbed sleep, would be associated with suicidal thoughts the next morning. We also investigated variation in wakefulness by hour from midnight to 4:59 AM, due to the potential importance of the midnight to 4:59 AM time period as a high-risk time for suicide death.[8] We further hypothesized that the relationship between sleep disturbance and suicidal thoughts would occur independent of the severity of depressive symptoms, in line with previous meta-analyses[6] and systematic literature reviews.[7] The main strength of this approach is the use of polysomnography to measure wakefulness, which allows us to accurately detect wakefulness as well as its temporal variation over the course of the night.[13] Current suicidal ideation was chosen as the primary outcome because acute suicidal thoughts are a clinical psychiatric emergency and because of its relationship with future suicidal behavior.[14] Given the relationship between REM sleep and suicidal thoughts and behaviors,[9,10] we also performed this analysis using minutes of REM sleep to identify potential differences in sleep architecture between suicidal ideators and non-ideators.

METHODS

Participants

Sixty-five participants (aged 18–65 years) with treatment-resistant depression, evaluated between 2006 and 2013, were included in the study (see Table 1 for demographic information). All participants had been admitted to the National Institute of Mental Health Experimental Therapeutics and Pathophysiology Branch in Bethesda, Maryland, and provided written informed consent. The National Institutes of Health Combined Central Nervous System Institutional Review Board approved this protocol (NCT00024635). Diagnoses of MDD or bipolar disorder were confirmed via Structured Clinical Interview for *DSM-IV-TR* Axis I Disorders, Research Version, Patient Edition (SCID-I/P).[15] Participants were required to meet criteria for a moderately severe depressive episode (defined as score ≥ 18 on the 17-item Hamilton Depression Rating Scale [HDRS][16] or score ≥ 20 on the Montgomery-Asberg Depression Rating Scale [MADRS]).[17] To qualify as treatment-resistant, they must not have responded to at least 2 previous adequate antidepressant trials. The MDD participants were medication-free for at least 2 weeks prior to polysomnography; the bipolar disorder participants received only lithium or valproate at therapeutic levels. No participants met criteria for active substance use disorder for the 3 months prior to screening, but were permitted use of nicotine and caffeine. Participants were not excluded for insomnia symptoms, but all had a primary mood disorder diagnosis. Sleep disorders, such as sleep apnea or restless legs syndrome, were not exclusion criteria for the study unless the participant was not able to withdraw from their treatment (ie, they were not able to stop their medications or use a continuous positive airway pressure machine for the duration of the study). Participants were determined to be in good physical health as assessed by medical history, physical examination, blood laboratory tests, electrocardiogram, chest x-ray, urinalysis, and toxicology. Women were excluded if they were pregnant or nursing.

Most participants gave consent to be in the study and then underwent a medication taper before polysomnography. They were not eligible for initial consent if they had acute suicidal thoughts (a score of 4 or more on MADRS item 10 or as determined by clinical judgement). Thus, acutely suicidal individuals were not allowed into study and then withdrawn from their medications. Individuals who developed suicidal thoughts over the course of the medication taper or study procedures were not systematically excluded from participation.

Electroencephalography Procedure and Analysis

Participants completed whole-night sleep recordings on the night before clinical ratings; they were

adapted on a prior night to the sleep room and equipment. Participants were permitted to sleep any time after 10:00 PM with a final wake-up time of 7:00 AM. Within this window, participants self-selected their bedtime and communicated the time of lights off to an attending staff member. Naps were not permitted on days of electroencephalogram (EEG) recordings. Participants were inpatients on a voluntary psychiatric unit on the days before and after EEG recordings.

A Nihon-Kohden system (Neurofax version 05-50) and Polysmith Acquisition and Review software (version 4.0.25.0) were used to record EEGs (C3/A2 and C4/A1), electrooculograms (EOGs) to monitor eye movements, and submental electromyograms (EMGs) to monitor muscle activity. EEG electrodes were placed according to the EEG 10–20 montage (Central 3, 4 and Frontal 3, 4). EEG readings were scored in 30-second epochs by a reviewer blinded to participant diagnosis, clinical ratings, and study purpose.[18]

For this analysis, 3 variables were used as general measures of disrupted sleep over the entire night, as determined by polysomnography: (1) total sleep time (TST), (2) wake after sleep onset (WASO; minutes of wakefulness after falling asleep), and (3) sleep efficiency (SE; percentage of time asleep of time spent in bed). To examine wakefulness over the course of the night, 30-second epochs were binned by clock hour. For each hour (eg, from 1:00:00 to 1:59:30 AM), a total sum of minutes awake was calculated for each participant. For the purposes of this analysis, this sum is termed *minutes awake* or *nocturnal wakefulness* in order to distinguish it from WASO, which includes the entire night and is not connected to a specific time. Minutes of REM sleep per hour were also calculated using the same method to assess whether REM distribution across the night, or REM fragmentation, was associated with next-day suicidal ideation.

Assessment

Rating instruments to assess suicidal ideation and depressive symptoms were administered on the morning after EEG recordings were completed. Participants were administered the HDRS, which includes 1 item that evaluates suicidal thoughts and actions on a scale from 0 to 4 (item 3).[16] The HDRS also includes several items of subjective sleep quality: early insomnia, middle insomnia, and late insomnia (items 6, 7, and 8). To evaluate correspondence between objective and subjective sleep items, these sleep items were incorporated into analyses for comparison. The remaining HDRS items (with suicide or sleep items removed) were used to measure severity of depressive symptoms to avoid collinearity and to be consistent with past research.[2,19,20]

The MADRS, which includes a suicide item rated from 0 to 6 (item 10),[17] and the Scale for Suicide Ideation (SSI)[21] were also administered and included in analyses for confirmatory purposes. The SSI includes a 5-item screen; a participant must receive a specific score before the remaining 14 items are administered. For the purposes of this analysis, only the first 5 items were included, as they were consistently administered to all participants. The SSI was administered to 61 of the 65 participants.

Statistical Analysis

Univariate analyses were used to compare the baseline characteristics of participants who reported suicidal ideation (a HDRS score of 1 or greater on the suicide item) against those who reported no suicidal ideation. Spearman correlations evaluated the relationship between suicidal ideation, the whole-night polysomnographic sleep variables TST (minutes), WASO (minutes), and SE (%), and subjective HDRS sleep variables (early, middle, and late insomnia) due to the non-normal distribution of sleep variables in the study sample. The HDRS suicide item was considered the primary measure of suicidal ideation because it is commonly used in clinical trials of depression[22] and because it was administered to all participants; the MADRS suicide item and the 5-item SSI were included to confirm significant findings.

Due to the distribution of wakefulness, a negative binomial generalized linear mixed model with a log linking function was used to evaluate minutes awake by hour of night between individuals who did and did not report suicidal ideation the next day. The time for this model was limited to midnight to 4:59 AM due to the focus on wakefulness after sleep onset. Time, suicidal ideation, and the interaction between time and suicidal ideation were included in this model. A first-order autoregressive structure was used in accordance with the Schwarz Bayesian criterion for best fit. A Satterthwaite approximation was used to determine degrees of freedom due to the smaller sample size. Bonferroni post hoc tests were used to follow up significant omnibus effects. To manage violations of model assumptions, robust estimation of fixed effects and coefficients was used. This model was run again, adjusting for effects of key covariates, including age, gender, diagnosis (MDD vs bipolar disorder), and severity of depression (the HDRS with suicide and sleep items removed) in separate models, to account for potential confounders of sleep time and suicidal thoughts. As a post hoc analysis, the model was run with consecutive minutes awake as an outcome to determine if the sleep disturbance was due to multiple brief awakenings as compared to more prolonged episodes of wakefulness. The model was also run with suicide attempts, rather than suicidal ideation, as a factor to determine potential state versus trait markers of sleep disturbance.

As another post hoc analysis, the same model was run for the time period between 11:00 PM and 6:59 AM, which encompasses the majority of the time the participants were asleep, to ensure that findings were not due to the timeframe of interest. This model was then re-run with REM sleep as the outcome variable, given that REM episodes increase in frequency over the course of the night.

In addition, when times differed significantly between ideators and non-ideators, the relationship between sleep at this time point and suicidal ideation ratings the next morning was evaluated. This analysis took into account the range of suicidal thoughts on the next day. Due to the nonlinear distribution of the data, all variables were ranked and linear regression was conducted using these ranked data. This relationship was evaluated using severity of depression (HDRS with suicide and sleep items removed) as a covariate.

Table 2. Spearman Correlations Between Electroencephalographic Sleep Variables, Next-Day Suicidal Ideation, Reported Sleep, and Depression

	Suicidal Ideation			Reported Sleep and Depression			
Sleep Variable	HDRS Suicide Item	MADRS Suicide Item	SSI 5-Item	HDRS Early Insomnia	HDRS Middle Insomnia	HDRS Late Insomnia	Remaining HDRS Items
Total Sleep Time	−0.05	−0.03	−0.08	−0.24	−0.16	−0.14	0.02
Wake After Sleep Onset[a]	0.30*	0.29*	0.28*	0.13	0.30*	0.19	−0.08

[a]Wake After Sleep Onset = minutes of wakefulness after falling asleep.
*$P < .05$, 2-tailed.
Abbreviations: HDRS = Hamilton Depression Rating Scale, MADRS = Montgomery-Asberg Depression Rating Scale, SSI = Scale for Suicide Ideation.

Figure 1. Polysomnographically Documented Minutes Awake per Hour in Patients Who (A) Reported and (B) Did Not Report Suicidal Ideation the Next Day[a]

A. Reported Suicidal Ideation
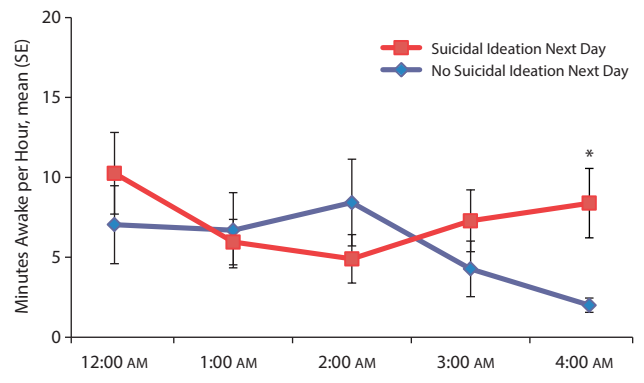
B. Reported No Suicidal Ideation
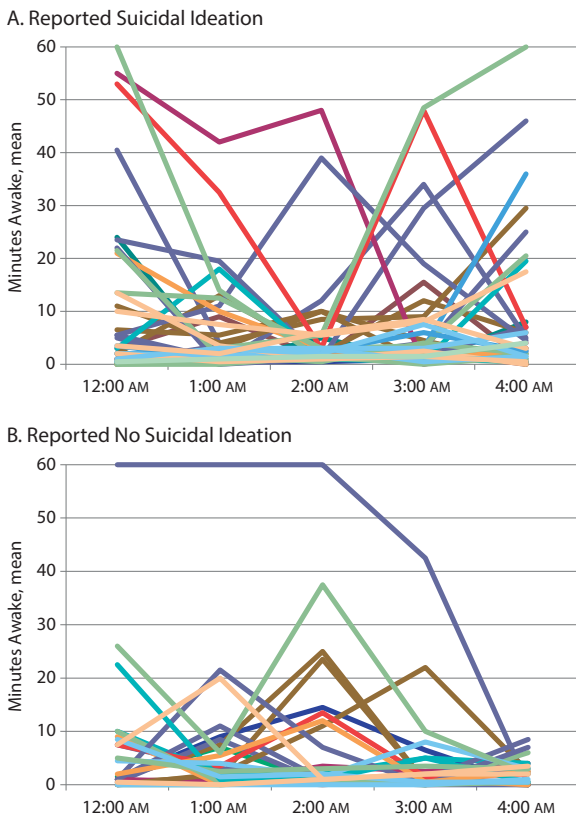
[a]Each line represents the sleep of 1 participant. Time periods represent the entire hour of wakefulness (eg, "12:00 AM" depicts the period from 12:00 AM to 12:59 AM).

Figure 2. Mean (SE) Time Awake From Midnight to 4:00 AM for Patients With and Without Suicidal Ideation the Next Day

*$P < .05$, 2-tailed.

Similar analyses were run using the HDRS sleep items as dependent variables. All statistics were conducted with SPSS version 21 (IBM Corp). Significance was considered at $P < .05$, 2-tailed.

RESULTS

Initial descriptive statistics comparing individuals with and without suicidal ideation (as measured by the HDRS suicide item) are presented in Table 1. Participants reporting suicidal ideation were more likely to be male ($P = .04$), have a lifetime history of suicide attempt ($P = .003$), and report

a higher number of depressive symptoms ($P = .01$). Of the 39 participants who reported suicidal ideation, 6 received a score of 3 on the HDRS suicide item ("suicidal ideas or gestures"). Threshold values for insomnia symptoms were as follows: 51% of the sample (n = 33) reported early insomnia (HDRS item: "complains of nightly difficulty falling sleep"), 29% (n = 19) reported middle insomnia (HDRS item: "waking during the night—any getting out of bed [except to void]"), and 17% (n = 11) reported late insomnia (HDRS item: "unable to fall asleep again if gets out of bed").

Whole Night Analyses

Table 2 displays correlations of measures of suicidal ideation with overall sleep variables over the course of the night, both objective and reported; WASO ($r = 0.28$ to 0.30, $P < .05$) and SE ($r = −0.26$ to $−0.28$, $P \leq .05$) were significantly correlated with suicidal ideation. An additional analysis of the relationship between subjective sleep measures from the HDRS and suicidal ideation found no significance.

Hour-by-Hour Analyses From Midnight to 4:59 AM

Figure 1 displays the minutes awake by hour from midnight to 4:59 AM in participants with and without next-day suicidal ideation. In the negative binomial mixed model of total time awake by hour from midnight to 4:59 AM, the main effect of ideation was not significant ($F_{1,47} = 1.27$, $P = .27$), but a significant time-by-ideation interaction was observed ($F_{4,136} = 3.65$, $P = .007$; Figure 2). Post hoc

analyses revealed significant differences in minutes awake between ideators and non-ideators from 4:00 to 4:59 AM ($F_{1,257} = 4.36$, $P = .004$). Specifically, results revealed that increased nocturnal wakefulness during this clock hour was significantly associated with next-day suicidal ideation. Importantly, this time-by-ideation interaction remained significant in each model when controlling for central covariates: gender ($F_{4,137} = 3.68$, $P = .007$), age ($F_{4,138} = 3.67$, $P = .007$), diagnosis ($F_{4,136} = 3.52$, $P = .009$), and severity of depressive symptoms ($F_{4,112} = 3.48$, $P = .010$).

Post Hoc Analyses of Consecutive Minutes Awake and Suicide Attempts

When the model was run with consecutive minutes awake as the outcome variable, the time-by-ideation interaction was significant ($F_{4,96} = 5.40$, $P = .001$), with a significant difference at the 4:00 to 4:59 AM hour.

When the model for minutes awake (not consecutive minutes awake) was rerun with suicide attempt history as a variable instead of suicidal thoughts, results were not significant for effect of suicide attempt history ($F_{1,65} = 0.31$, $P = .58$) or time-by-attempt interaction ($F_{4,146} = 2.25$, $P = .07$).

Hour-by-Hour Analyses From 11:00 PM to 6:59 AM

When a similar mixed model was run using a timeframe from 11:00 PM to 6:59 AM, the time-by-ideation interaction remained significant ($F_{7,185} = 4.13$, $P < .001$), with a significant difference in minutes awake between ideators and non-ideators from 4:00 to 4:59 AM ($F_{1,167} = 8.33$, $P = .004$). The main effect of ideation on minutes awake was not significant. In a model evaluating minutes spent in REM sleep over the same extended timeframe, neither the main effect of suicidal ideation nor the time-by-ideation interaction was significant ($P > .05$). As a result, no further analyses were pursued using REM sleep.

Linear Regression of Wakefulness in the 4:00 to 4:59 AM Hour

On linear regression of ranked variables, time spent awake in the 4:00 to 4:59 AM hour predicted suicidal ideation the next day using the HDRS suicide item (standardized $\beta = 0.31$, $P = .008$) when controlling for severity of depressive symptoms as measured by the remaining HDRS items. Similar results were found for the suicide item from the MADRS (standardized $\beta = 0.31$, $P = .01$) as well as the 5-item SSI (standardized $\beta = 0.30$, $P = .02$), also controlling for severity of depressive symptoms. Wakefulness from 4:00 to 4:59 AM was not correlated with reported next-day HDRS-assessed subjective sleep disturbances, such as early (standardized $\beta = -0.18$, $P = .16$) or middle (standardized $\beta = 0.19$, $P = .13$) insomnia; however, results for late insomnia symptoms approached significance (standardized $\beta = 0.22$, $P = .08$).

DISCUSSION

In an evaluation of individuals with both MDD and bipolar disorder, participants with next-day suicidal ideation demonstrated a pattern of nocturnal wakefulness different from those without suicidal ideation. Specifically, nocturnal wakefulness during the 4:00 to 4:59 AM hour was associated with suicidal ideation the next day. This relationship persisted across multiple measures of suicidal thoughts and remained even after adjusting for age, gender, diagnosis, and severity of depressive symptoms. The results emphasize the importance of both reported and physiologic approaches when evaluating this relationship; they also underscore the potential use of polysomnographic sleep parameters as pathophysiologic indicators of disturbed sleep and as acute risk factors for suicidal ideation. While the use of polysomnography will not be a feasible or appropriate monitor of acute suicide risk, these results can help clinicians conduct suicide risk assessments with their patients. The results also inform future research investigating possible biological mechanisms (discussed later in this section) underlying the relationship between sleep disturbance and suicide.

Our results indicate that disrupted sleep and time spent awake, particularly in the early morning hours, may be a potential indicator of suicidal ideation. This factor may be associated with fundamental aspects of sleep/wake regulation, which may impact risk for suicidal thoughts and symptoms. Although nocturnal wakefulness is a correlate of insomnia, the time from 4:00 AM to 6:00 AM corresponds to the human core body temperature nadir and the highest degree of circadian propensity for sleep.[23] It is possible that being awake during this time could perpetuate changes in next-day mood regulation, executive function, or risk for suicidal thoughts. Interestingly, REM sleep, which is hypothesized to maintain affective homeostasis in the brain, did not differ overnight in participants with and without suicidal ideation. Further analyses are warranted to replicate this finding and investigate other potential neurobiological factors that may define this subgroup. In particular, biological markers such as cortisol have been linked to suicide risk[24]; it is possible that cortisol changes over the course of the night could be related to the relationship between sleep and suicide. Furthermore, recent analyses of clock genes have found altered circadian patterns of clock gene expression in individuals with MDD compared to healthy controls.[25] Future work is indicated to investigate whether clock gene expression contributes to suicide risk.

Sleep restriction and deprivation studies highlight the confluence of symptoms that may arise when an individual has insufficient sleep. One functional magnetic resonance imaging study[26] of healthy controls found that restricted sleep (4 hours per night over 5 days) was associated with increased anxiety and amygdala activity in response to fearful faces. Sleep loss in healthy controls has also been associated with disinhibition, including altered brain activity in the nucleus accumbens in response to risky decision-making[27] as well as increased negative affect in response to mild stress.[28] Each of these clinical outcomes has been associated with suicidal behavior.[29]

Paradoxically, 36 hours of complete or partial sleep deprivation is a well-known, rapid-acting treatment for

depressive symptoms.[30] Sleep deprivation in conjunction with lithium and light therapy has also been demonstrated to rapidly reduce suicidal thoughts in bipolar disorder patients[31] but, to our knowledge, no systematic studies of the ability of sleep deprivation alone to reduce suicidal thoughts has been conducted.[32] Even with these seemingly contradictory findings, the sleep deprivation literature in both healthy volunteers and depressed patients underscores the importance of sleep in suicide risk and the potential of sleep-focused interventions for the treatment of suicidal patients.

These results are consistent with previous research implicating disrupted sleep in suicide risk, and suicidal thoughts in particular.[2–4] Strengths of our current approach include studying a sample of treatment-resistant depressed participants who were assessed for depressive symptoms and suicidal thoughts using multiple measures the morning after electroencephalographic sleep recording. We were able to assess current suicidal thoughts as well as subjective measures of sleep quality. Polysomnographic recordings were scored by a reviewer blinded to participant diagnosis, clinical ratings, and study purpose, ensuring the objectivity of the recordings. Other strengths include the fact that participants were medication-free (for MDD) or on minimal psychotropic treatment (valproate or lithium) for bipolar disorder, thus minimizing the confounding effects that drugs may have on sleep architecture parameters.

Nevertheless, the study is also associated with some limitations. First, the study excluded individuals at acute risk of suicide; additional analyses are indicated in an acutely suicidal sample. Second, suicidal thoughts can occur outside the context of a depressive episode. Third, the findings may not necessarily apply to patients with non–treatment-resistant depression. Fourth, other components of sleep architecture, such as REM latency and slow-wave sleep, may also influence the relationship between sleep and suicide. Fifth, analyses may have benefited from formal diagnoses of *DSM-5* insomnia disorder or other sleep disorders to evaluate any possible relationships between these diagnoses and the results. Sixth, it is possible that the relationship between sleep disturbance and suicidal thoughts may be mediated by clinical factors, such as melancholic depression, which has been linked to suicide risk,[33] as well as disinhibition; further analyses are indicated to identify potential mediators or mechanisms. Finally, prospective analyses of the relationship between wakefulness over the night and suicidal ideation are warranted to replicate findings and further explore how and why sleep disruptions lead to suicidal thoughts.

In summary, we found that wakefulness in the early morning hours, particularly 4:00 to 4:59 AM, was associated with next-day suicidal thoughts in a treatment-resistant combined sample of participants with MDD or bipolar disorder. This highly specific time-dependent finding emerged even after controlling for severity of depressive symptoms, suggesting that risk may be conferred relatively independent of depressed mood. This is the first known report to evaluate polysomnographic sleep parameters as an acute indicator of risk for next-day suicidal ideation. The findings highlight particular night-time intervals that may enhance risk detection and inform potential intervention targets for the prevention and treatment of suicidal ideation.

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Editor's Note: We encourage authors to submit papers for consideration as a part of our Focus on Suicide section. Please contact Maria A. Oquendo, MD, at moquendo@psychiatrist.com.