It is illegal to post this copyrighted PDF on any website. Objectively Assessed Sleep Variability as an Acute Warning Sign of Suicidal Ideation in a Longitudinal Evaluation of Young Adults at High Suicide Risk

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ABSTRACT

Objective: Young adults attempt suicide at disproportionately high rates relative to other groups and demonstrate high rates of sleep disturbance. No study has yet prospectively evaluated disturbed sleep as an acute indicator of risk using an objective index of sleep. We investigated objective and subjective parameters of disturbed sleep as a warning sign of suicidal ideation among young adults over an acute period.

Methods: A longitudinal study across a 21-day observation period and 3 time points. Fifty of 4,847 participants (aged 18– 23 years) were prescreened from a university undergraduate research pool (February 2007–June 2008) on the basis of suicide attempt history and recent suicidal ideation. Actigraphic and subjective sleep parameters were evaluated as acute predictors of suicidal ideation (Beck Scale for Suicide Ideation), with adjustment for baseline symptoms. Hierarchical regression analyses were employed to predict residual change scores.

Results: Ninety-six percent of participants (n = 48) endorsed a suicide attempt history. Mean actigraphy values revealed objectively disturbed sleep parameters; 78% (n = 39) and 36% (n = 18) endorsed clinically significant insomnia and nightmares, respectively. When results were controlled for baseline suicidal and depressive symptoms, actigraphic and subjective sleep parameters predicted suicidal ideation residual change scores at 7- and 21-day follow-ups (P < .001). Specifically, actigraphy-defined variability in sleep timing, insomnia, and nightmares predicted increases in suicidal ideation (P < .05). In a test of competing risk factors, sleep variability outperformed depressive symptoms in the longitudinal prediction of suicidal ideation across time points (P < .05).

Conclusions: Objectively and subjectively measured sleep disturbances predicted acute suicidal ideation increases in this population, independent of depressed mood. Self-reported insomnia and nightmares and actigraphically assessed sleep variability emerged as acute warning signs of suicidal ideation. These findings highlight the potential utility of sleep as a proposed biomarker of suicide risk and a therapeutic target.

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^bDepartment of Psychology, Florida State University, Tallahassee **Corresponding author*: Rebecca Bernert, PhD, Suicide Prevention Research Laboratory, Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, 401 Quarry Rd, Stanford, CA 94304-5797 (rbernert@stanford.edu). **S** uicide represents a preventable public health problem and global disease burden, accounting for nearly 1 million deaths annually worldwide.¹ The Institute of Medicine furthermore estimates an additional 25 attempts (100–200 for youth) for every suicide death.² Calls to action by the US Surgeon General consistently highlight the need to identify risk factors to enhance surveillance and treatment development to prevent suicide, particularly among youth.³ In general, selective interventions for suicide as an indication remain alarmingly scarce, unacceptable (ie, based on attrition), or inaccessible to those highest in need.

Sleep disturbances are among the top warning signs of suicide according to the Substance Abuse and Mental Health Services Administration,⁴ and preliminary research suggests they may confer risk for suicidal behaviors.⁵ Even so, numerous methodological limitations, often inherent to the study of suicide, constrain the impact of such findings.^{6,7} These include the frequent use of retrospective and cross-sectional study designs, chart review or historical assessment of suicidal symptoms, and reliance on single-item evaluations of suicidal symptoms (eg, from depression inventories) versus validated instruments.⁷ Finally, investigations often fail to control for the confounding influence of existing psychopathology, particularly depression severity.⁷ Because sleep and suicidal symptoms are diagnostic criteria for depression,8 and among the strongest predictors of suicide risk,^{6,9} controlling for depression severity is crucial to delineating independent risk for suicidal behaviors (ie, versus representing a mere correlate of depression).

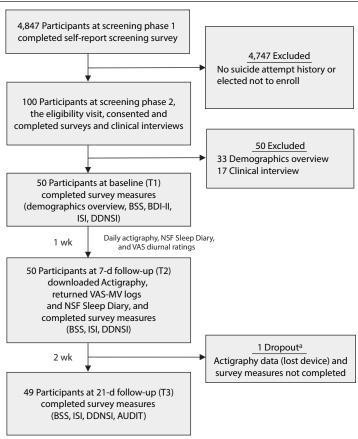
Evaluation among young adults is motivated by the shared prevalence of sleep disturbance and suicide risk during this developmental period. Sleep disturbances are overrepresented among young adults,^{10,11} and suicide is the second leading cause of death among those aged 19–24 years.¹² Relative to other risk factors, sleep appears visible as a warning sign. In a psychological autopsy study¹³ of 140 adolescent suicide decedents and 131 community-matched controls, sleep problems were visible to friends and family in the weeks and months prior to death. Even after adjustment for depression, disturbed sleep predicted up to a 10-fold greater risk for suicide compared to controls. Population-based studies of adolescents also identify poor sleep in association with suicidal behavior,¹⁴ controlling for depressive symptoms.¹⁵

According to a systematic review⁷ of studies addressing the previously mentioned methodological issues, research supports sleep disturbances (eg, insomnia, poor sleep quality, nightmares) as an independent risk factor for suicidal ideation, suicide attempts, and suicide fatalities—with adjustment

Bernert et al It is illegal to post this copyrighted PDF on any website. electroencephalographic (EEG)-assessed sleep in

- Self-reported sleep disturbances confer risk for suicide; however, little is known about objective sleep parameters as a warning sign for suicidal behaviors.
- Assessment and management of suicide risk are indicated among patients with disturbed sleep, particularly variability in sleep timing, insomnia, and nightmares.
- Poor sleep is proposed as a biomarker of risk and a potential therapeutic target for suicide prevention.

Figure 1. CONSORT Diagram of Recruitment, Enrollment, and Study Timeline



^aThis participant completed the 7-day but not the 21-day follow-up. Abbreviations: AUDIT = Alcohol Use Disorders Identification Test, BDI-II = Beck Depression Inventory-II, BSS = Beck Scale for Suicide Ideation, DDNSI = Disturbing Dreams and Nightmare Severity Index, ISI = Insomnia Severity Index, NSF = National Sleep Foundation, T = time point, VAS-MV = Visual Analog Scale mood variability.

for depression—across investigations diverse in design, samples, and assessment techniques. This evidence includes self-reported insomnia and fatigue as correlates and risk factors for suicidal ideation and suicide attempts and poor subjective sleep quality as a risk factor for suicide death in a longitudinal, epidemiologic study.¹⁶ Given the inherent costs and methodological challenges to assessing sleep objectively within large-scale studies of suicide, reports have primarily relied on surveyed sleep complaints versus objective sleep parameters.^{5,7} By comparison, objective assessment of sleep in association with suicidal behaviors has received less attention in suicide research. Indeed, of 10 total studies⁷ conducted evaluating

electroencephalographic (EEG)-assessed sleep in association with suicide risk, only 1 study¹⁷ included depression as a covariate. Nonetheless, this study¹⁸ reported significant relationships between EEG parameters and past suicidal ideation and suicide attempts, with depression severity as a covariate.

To address these gaps in the literature, we sought to confirm that disturbed sleep confers independent risk for suicidal ideation symptoms in young adults (ie, beyond known covariates, depression^{6,9} and alcohol use^{19,20}) using a longitudinal design, validated symptom measures, and an acute time frame (aim 1) and to evaluate whether this relationship emerges using objective and subjective sleep measures (aim 2). Because of the invasiveness of EEG and its time-limited nature in the context of suicidal symptom change (ie, single-night vs ongoing assessments), actigraphy was selected as our primary sleep measure. Last, on the basis of research suggesting that emotion regulation deficits are associated with sleep disruption²¹ and suicidal behaviors,^{22–24} we explored whether intraindividual variation in mood was related to suicidal ideation and sleep parameters (aim 3).

METHODS

Participants and Procedures

Participants aged 18-23 years were recruited from a university undergraduate research pool for high suicide risk through a multiphase screening process (February 2007-June 2008) described in a previous report,²⁵ which is a secondary analysis of the data reported in this prospective primary analysis. Participants were university undergraduates (N = 4,847) screened for high suicide risk for inclusion in the present study (recruitment and enrollment procedures are shown in Figure 1 and Supplementary eTable 1). Inclusion criteria for the current study were (1) age \geq 18 years and (2) endorsement of either ≥ 1 past suicide attempt, verified by clinical interview,²⁶ and recent $(\leq 6 \text{ months})$ suicidal ideation or no suicide attempt history but current (≤ 1 month) and recent (≤ 6 months) suicidal ideation. Suicide attempt history was used as a proxy for current risk based on past research,^{27,28} and study criteria and recruitment procedures were modeled after large-scale suicide prevention trials.²⁹ The National Institutes of Health human subjects and Florida State University institutional review boards approved all study procedures.

Materials

Demographic characteristics. This survey assessed baseline demographic information, personal and family suicide attempt history,

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Table 1. Baseline Sample and Clinical Severity Characteristics

Characteristic	Participants (n = 50)
Demographics	
Age, mean (SD)	19.2 (1.4)
Sex, n (%)	14 (20)
Male Female	14 (28) 36 (72)
Race/ethnicity, n (%) ^a	50 (72)
White	37 (74)
Hispanic	6 (12)
African American	3 (6)
Asian Mixed race	1 (2)
Mixed race Other	2 (4) 1 (2)
Suicidal behavior history	1 (2)
Past suicide attempts, n (%)	
No attempts	2 (4)
Single attempters	33 (66)
Multiple attempters	15 (30)
Time since last suicide attempt, mean (SD), y Age at worst-point suicide attempt, mean (SD), y	4.0 (2.4) 15.0 (2.3)
Suicide attempt method, n (%)	15.0 (2.5)
Overdose/poisoning	29 (58)
Cutting	13 (26)
Asphyxiation Firearm	2 (4) 1 (2)
Other	3 (6)
Pierce SIS intent score, mean (SD)	8.2 (4.4)
Family history of suicide, n (%)	6 (12)
Nonsuicidal self-injury history, n (%)	
No prior history	16 (32)
Prior history Current nonsuicidal self-injury	25 (50) 5 (10)
Psychiatric diagnoses, n (%)	21 (42)
Mood disorder	16 (76)
Anxiety disorder	7 (33)
Attention-deficit/hyperactivity disorder	7 (33)
Eating disorder	1 (5)
Sleep disorder Comorbid disorders	2 (10) 9 (43)
Psychiatric medication use, n (%)	9 (18)
Antidepressants	5 (56)
Selective serotonin reuptake inhibitors (SSRIs)	5 (56)
Other antidepressants	2 (22)
Stimulant/nonstimulant SSRI (SNRI) Anxiolytics	2 (22) 1 (11)
Antipsychotic	1 (11)
Mood stabilizer	1 (11)
Psychiatric symptoms	
BSS, mean (SD)	6.7 (6.2)
Mild symptoms (0–4), n (%)	29 (58)
Moderate symptoms (5–15), n (%) Moderate-severe symptoms (16–23), n (%)	17 (34) 3 (6)
Severe (24–36), n (%)	1 (2)
BDI-II, mean (SD)	19.7 (10.4)
Minimal symptoms (0–13), n (%)	16 (32)
Mild symptoms (14–19), n (%)	9 (18) 17 (24)
Moderate symptoms (20–28), n (%) Severe symptoms (29–63), n (%)	17 (34) 8 (16)
AUDIT, mean (SD)	9.5 (6.9)
Nonclinical symptoms (0–7), n (%)	18 (36)
Clinically significant symptoms (8–29), n (%)	28 (56)
Subjective sleep disturbances	
Insomnia Severity Index, mean (SD)	13.5 (5.6)
Nonclinical symptom range (0–9), n (%) Clinical symptom range (10–28), n (%)	11 (22) 39 (78)
DDNSI, mean (SD)	7.1 (7.0)
Nonclinical symptom range (0–10), n (%)	32 (64)
Clinical symptom range (11–37), n (%)	18 (36)
^a Ethnicity and racial categorization options were crea	ated by the investigators,

^aEthnicity and racial categorization options were created by the investigators, and identification to a given category was based on participant response. Abbreviations: AUDIT = Alcohol Use Disorders Identification Test.

BDI-II=Beck Depression Inventory-II, BSS = Beck Scale for Suicide Ideation, DDNSI = Disturbing Dreams and Nightmare Severity Index, SIS = Suicide Intent Scale, SNRI = serotonin-norepinephrine reuptake inhibitor. medication use, medical history, diagnostic characteristics, shiftwork status, and nonsuicidal self-injury.

Suicide risk measures. Beck Scale for Suicide Ideation (BSS). This 21-item self-report instrument³⁰ assesses suicidal symptom severity. Higher total scores (0–38) indicate greater levels of suicidal ideation. This scale shows strong reliability and validity and has been normed among inpatient and outpatient samples.³⁰

<u>Pierce Suicidal Intent Scale.</u> This 12-item, clinicianadministered interview²⁶ documents the severity and intent of past suicide attempts. Total scores (0–25) reflect summed subscales (circumstances, self-report, medical risk). Research demonstrates good psychometric properties for this measure²⁶ used to verify inclusion criteria.

Objective sleep measures. Actigraphy. Actigraphy (Actiwatch; Respironics) provided an objective measurement of sleep. Actigraphs are small, watch-like devices $(37 \times 29 \times 9)$ mm; 17 g) worn on the nondominant wrist. An electronic accelerometer records movement over preprogrammed 30-second intervals. The actigraph wearer inserts event markers by pressing a button on the actigraph to demarcate, in real time, his or her attempted sleep onsets and offsets, which define a given sleep interval. Data were verified for adherence and correspondence with sleep diaries and analyzed by the first author using commercially available software algorithms (Actiware), which automatically generate sleep-wake statistics. Actigraphy data reliably discriminate sleep-wake patterns,³¹ which show good correspondence with EEG data.³² For each sleep interval, derived variables included *sleep-onset latency* (minutes elapsed between attempting and achieving sleep onset), total sleep time (sleep duration, minus awakenings), wake after sleep onset (minutes awake following sleep onset), sleep efficiency (percentage of time asleep to time in bed), and sleep variability (standard deviations of daily *sleep onsets* [ie, time when sleep was initiated] and *sleep offsets* [ie, time of final wakening]; these indices were summed to provide an overall index of sleep variability, consistent with past reports³³), identified using Actiware algorithms. Additional variables included average bedtime and wake time, time in bed (hours in bed, regardless of time asleep), and nap and sleep interval frequency. For post hoc analyses, standard deviations of sleep-onset latency, total sleep time, wake after sleep onset, and sleep efficiency were also calculated. Actigraphy sleep data were computed based on a 7-day period for each participant.

<u>Daily Sleep Diary</u>. Actigraphy data were verified using the National Sleep Foundation diary (https://sleepfoundation. org/sleep-diary/SleepDiaryv6.pdf), adapted for study use. Diaries provide reliable comparison with actigraphy³² and were inspected for missing event markers, consistent with past studies.^{31,34,35}

Subjective sleep measures. Insomnia Severity Index (ISI). This 7-item self-report measure³⁶ assesses the frequency and severity of insomnia symptoms. Higher total scores indicate greater insomnia severity. This measure is a gold standard insomnia instrument,³⁷ widely used in clinical trials. Scores ≥ 10 appear to provide optimal sensitivity and specificity.³⁷

Bernert et al It is illegal to post this copyrighted PDF on any website Table 2. Sample Subjective and Objective Sleep Parameter Table 2. Sample Subjective and Objective Sleep Parameter

Table 2. Sample Subjective and Objective Sleep Parameter Descriptives Assessed at 7-Day Follow-Up

Parameter	Value	Minimum	Maximum
Subjective sleep parameters			
Insomnia Severity Index, mean (SD)	11.8 (4.8)	1	23
Nonclinical symptom range (0–10), n (%)	14 (28)		
Clinical symptom range (11–28), n (%)	36 (72)		
DDNSI, mean (SD)	5.5 (6.3)	0	24
Nonclinical symptom range (0–10), n (%)	39 (78)		
Clinical symptom range (11–37), n (%)	11 (22)		
Objective sleep parameters, mean (SD) ^a			
Bedtime, hh:mm	02:08 (1:34)	22:06	05:54
Wake time, hh:mm	09:21 (1:37)	04:06	12:12
Total time in bed, h	7.7 (1.1)	5.0	11.0
No. of naps	1.35 (1.78)	0	7
No. of sleep intervals	8.37 (2.02)	6	15
Sleep-onset latency, min	11.6 (7.8)	1.2	44.9
Total sleep time, h	5.9 (1.1)	3.2	7.6
Wake after sleep onset, min	31.2 (14.1)	10.3	73.9
Sleep efficiency, %	84.4 (6.2)	64.4	93.6
Sleep variability, h	6.0 (4.2)	1.24	20.0
Onset, h	3.1 (2.3)	0.4	9.6
Offset, h	2.9 (2.1)	0.3	10.4

^aOne participant lost the Actiwatch device and completed 7-day but not 21-day follow-up.

Abbreviations: DDNSI = Disturbing Dreams and Nightmare Severity Index,

hh:mm=hour:minute.

Table 3. Baseline Values and Intercorrelations Between Measures

	1	2	3	4	5	6
1.BSS	1	0.487*	0.026	0.254	0.343*	0.385**
2. BDI-II		1	0.303*	0.552**	0.503**	-0.087
3. AUDIT			1	0.224	0.104	-0.149
4. Insomnia Severity Index				1	0.344*	-0.062
5. DDNSI 6. Pierce SIS					1	-0.062 1
Mean	6.7	19.7	9.5	13.5	7.1	8.2
SD	6.2	10.4	6.9	5.6	7.0	4.4
Range	1–27	1–41	0-29	0-24	0-21	1–12
α	.83	.90	.86	.84	.74	.76

*P<.05. **P<.01.

Abbreviations: AUDIT = Alcohol Use Disorders Identification Test,

BDI-II = Beck Depression Inventory-II, BSS = Beck Scale for Suicide Ideation, DDNSI = Disturbing Dreams and Nightmare Severity Index, SIS = Suicide Intent Scale.

Disturbing Dreams and Nightmare Severity Index (DDNSI). This 5-item self-report scale³⁸ assesses the intensity, frequency, and severity of disturbing dreams and nightmares. It is a revised version of the Nightmare Frequency Questionnaire³⁹ and is used commonly in nightmare assessment. Scores >10 suggest clinically significant nightmares.

Covariate measures. Beck Depression Inventory-II (BDI-II). This 21-item self-report inventory⁴⁰ assesses depressive symptomatology, with higher scores reflecting greater symptom severity. It yields adequate reliability estimates and psychometrics.⁴⁰ To prevent collinearity, overlapping items (9, 16, 20) were removed, consistent with previous reports.^{15,16}

<u>Alcohol Use Disorders Identification Test (AUDIT)</u>. This 10-item self-report questionnaire⁴¹ screens for hazardous alcohol use. Items address consumption, alcohol-related problems, and dependence symptoms. Total scores ≥ 8 generally signal harmful drinking.⁴¹ *mood ratings.* Self-ratings of depressed mood were administered alongside daily sleep diaries diurnally (ie, once in the morning, once at night). Participants used a vertical line to indicate ratings (anchors: "not at all depressed" to "very depressed"). To index intraindividual mood variation, the standard deviation of VAS (VAS mood variability [VAS-MV]) was calculated as a proxy for mood lability.

Sequence of Investigation

Those invited from screening phase 1 scheduled in-person eligibility visits for screening phase 2 using a secure, fully encrypted online network. Participants provided written informed consent after thorough explanation of study procedures. Visits occurred at 3 study time points: T1 (baseline), T2 (7-day follow-up), and T3 (21-day follow-up).

Statistical Analyses

Descriptive statistics were planned for all key variables, including intercorrelations between measures. Factors significantly associated with baseline BSS score were planned for inclusion as covariates.

Linear hierarchical multiple regression analyses were employed to test hypotheses. To assess causal risk and temporal ordering, symptom relationships were assessed longitudinally, with adjustment for baseline symptoms in each model. BSS residual change scores were created to evaluate actigraphic and subjective sleep parameters in association with suicidal symptom increases at 7- and 21-day follow-ups (T2, T3). To create residual change scores, T1 BSS total scores were entered into block 1 of each regression; planned covariates were entered into block 2. For actigraphy analyses, lower sleep efficiency and higher total sleep time, sleep-onset latency, wake after sleep onset, and sleep variability were hypothesized to predict T2 and T3 BSS increases. This approach was repeated for subjective sleep analyses, wherein higher ISI/ DDNSI scores were hypothesized to predict T2 and T3 BSS increases. For exploratory analyses, higher VAS-MV was expected to predict BSS change and actigraphic and subjective sleep parameters.

Analyses were conducted using SPSS Software, Version 23.00 (IBM Inc).

Power

Based on similarly designed studies, 16,42 proposed analyses had adequate power $(1 - \beta > .85; \alpha < .05)$ to detect a medium effect size (*d* of approximately 0.5) or higher.

RESULTS

Descriptive Statistics

Sample characteristics and descriptive statistics are presented in Tables 1–3.

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Sovariates. Alcohol-related problem as measured by AUDIT were common, and participants reported moderate to severe depressive symptoms as assessed by BDI-II.

Suicidal symptoms. Mean BSS scores indicated moderate suicidal symptoms, with maximum scores in the severe range for suicidal ideation.

Actigraphic sleep parameters. Sleep diaries were complete in 100% of cases, which paralleled actigraphy use compliance (>98%). Event marker adherence was also high (2.67 event markers missing of 14.77 mean total). Independent of shiftwork status (3 participants recorded shiftwork schedules from 1 to 3 days; ie, schedules overlapping with midnight), 3 other participants demonstrated extended wakefulness (ie, 24-hour periods without initiating sleep). Both shiftwork and extended wakefulness appeared associated with greater sleep variability, according to mean actigraphy metrics and their intercorrelations. For example, sleep variability correlated with delayed bedtime (r = 0.46, P = .001), wake time (r=0.45, P=.001), nap frequency (r=0.42, P=.001)P = .003), and sleep interval number (r = 0.27, P = .052).

Subjective sleep parameters. Mean ISI scores were consistent with an insomnia diagnosis³⁷; one-third of participants reported clinically significant nightmares.

Covariate Analyses

Demographic variables were not significantly correlated with BSS (age: r = -0.08, P = .57; sex: r = -0.05, P = .74). Total BDI-II scores correlated with BSS across time points (r = 0.40 to 0.50, P < .01), whereas AUDIT scores did not (r = -0.05 to 0.10,P > .05). The BDI-II was thus retained as a covariate.

Regression Analyses

Model statistics are shown in Table 4.

Actigraphic sleep parameters. For regressions 1 and 2, actigraphy variables, as a set, significantly predicted T2 and T3 BSS residual change scores when controlled for BDI-II score. However, only sleep variability predicted such change relative to other actigraphic parameters (Figure 2).

Subjective sleep parameters. For regressions 1 and 2, higher scores on the ISI and DDNSI were significantly associated with T2 and T3 BSS residual change scores when adjusted for BDI-II score. Each emerged as individual predictors of symptom increases.

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	Table 4. Model Statistics for	Hierarchical Line	ar Regress	ion Analyses

	t	β (95% Cl)	P Value	Model Statistics
Actigraphy sleep measures				
Regression 1: T2 BSS				$R^2 = 0.69$,
Block 1				$F_{7,49} = 13.36$,
T1 BSS	7.43	0.78 (0.47 to 0.83)	<.01**	<i>P</i> ≤.001
BDI-II	-0.41	-0.04 (-0.14 to 0.09)	.67	
Block 2		/		
Sleep efficiency	-0.18	-0.03 (-0.38 to 0.31)	.85	
Wake after sleep onset	-0.56	-0.09 (-0.15 to 0.08)	.57	
Sleep-onset latency	0.85	0.08 (-0.07 to 0.19)	.39 .40	
Total sleep time Sleep variability	0.84 3.18	0.12 (-0.01 to 0.03) 0.28 (0.13 to 0.58)	.40 <.01**	
· · ·	5.10	0.20 (0.15 to 0.50)	1.01	$R^2 = 0.55,$
Regression 2: T3 BSS Block 1:				
T1 BSS	5.28	0.67 (0.37 to 0.84)	<.01**	$F_{7,48} = 16.36,$ $P \le .001$
BDI-II	0.44	0.05 (-0.12 to 0.18)	.66	r ≤.001
Block 2:	0.44	0.03 (-0.12 to 0.18)	.00	
Sleep efficiency	1.27	0.32 (-0.17 to 0.75)	.21	
Wake after sleep onset	0.68	0.13 (-0.10 to 0.21)	.49	
Sleep-onset latency	0.67	0.08 (-0.11 to 0.23)	.50	
Total sleep time	-0.58	-0.10 (-0.03 to 0.02)	.56	
Sleep variability	2.46	0.27 (0.06 to 0.66)	.01 ^a	
Subjective sleep measures				
Regression 1: T2 BSS				$R^2 = 0.69$,
Block 1				$F_{4,49} = 25.22,$
T1 BSS	8.41	0.81 (0.51 to 0.83)	<.01**	P≤.001
BDI-II	-1.46	-0.16 (-0.20 to 0.03)	.15	
Block 2				
T2 Insomnia Severity Index	2.04	0.18 (0.00 to 0.40)	.04*	
T2 DDNSI	2.49	0.22 (0.03 to 0.33)	.01*	
Regression 2: T3 BSS				$R^2 = 0.59,$
Block 1				$F_{4,48} = 16.36$,
T1 BSS	4.62	0.52 (0.26 to 0.67)	<.01**	<i>P</i> ≤.001
BDI-II	-0.38	-0.04 (-0.16 to 0.11)	.70	
Block 2				
T3 Insomnia Severity Index	3.10	0.32 (0.11 to 0.52)	<.01**	
T3 DDNSI	2.19	0.22 (0.01 to 0.37)	.03*	
Exploratory mood measures				
Regression 1: T2 BSS				$R^2 = 0.66$,
Block 1				$F_{3,49} = 30.91,$
T1 BSS	7.48	0.73 (0.44 to 0.77)	<.01**	<i>P</i> ≤.001
BDI-II	-0.73	-0.07 (-0.15 to 0.07)	.46	
Block 2: VAS-MV	2.80	0.26 (0.12 to 0.76)	<.01**	2
Regression 2: T3 BSS				$R^2 = 0.49$,
Block 1	4.00			$F_{3,48} = 14.48,$
T1 BSS	4.90	0.60 (0.31 to 0.76)	<.01**	<i>P</i> ≤.001
BDI-II Block 201/AS MIV	0.26	0.03 (-0.13 to 0.17)	.79	
Block 2: VAS-MV	1.59	0.18 (-0.09 to 0.78)	.11	D ² 0.55
Regression 3: VAS-MV	2.40	0.22 (0.01 + . 0.10)	014	$R^2 = 0.38$,
Block 1: BDI-II	2.48	0.32 (0.01 to 0.18)	.01*	$F_{6,48} = 4.37$,
Block 2	0.46	012 (0 22 + 0 25)	EA	P=.002
Sleep efficiency Wake after sleep onset	0.46	0.13 (-0.22 to 0.35) -0.01 (-0.10 to 0.09)	.64	
Wake after sleep onset Sleep-onset latency	-0.04 2.35	-0.01 (-0.10 to 0.09) 0.33 (0.01 to 0.24)	.96 .02*	
Total sleep time	2.55 -0.19	-0.03 (-0.02 to 0.01)	.02	
Sleep variability	2.79	-0.03 (-0.02 to 0.01) 0.35 (0.07 to 0.44)	.04 <.01**	
	2.19	0.00 (0.07 (0 0.44)	<.UT	$R^2 = 0.21$,
Regression 4: VAS-MV Block 1: BDI-II	2.20	0.32 (0.00 to 0.20)	.03*	
Block 2	2.20	0.52 (0.00 10 0.20)	.03	F _{3,49} =4.24, P=.010
T2 Insomnia Severity Index	1.29	0.18 (-0.06 to 0.30)	.20	, =.010
T2 DDNSI	0.46	0.06 (-0.10 to 0.17)	.20	
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significant for model statistics. However, this was a nonsignificant trend for T3 BSS. For regression 3, whereas actigraphy variables jointly predicted VAS-MV when controlled for BDI-II score, only sleep-onset latency and sleep variability individually contributed to the model variance. For regression 4, neither ISI nor DDNSI individually predicted VAS-MV.

Table 4 (continued). Model Statistics for Hierarchical Linear Regression Analyses

	t	β (95% Cl)	P Value	Model Statistics
Post hoc analyses				
Regression 1: T2 BSS				$R^2 = 0.70,$
Block 1				$F_{4,48} = 25.86$
T1 BSS	8.51	0.81 (0.51 to 0.83)	<.01**	P<.001
BDI-II	-0.28	-0.02 (-0.12 to 0.09)	.77	
Block 2				
Sleep variability onset	2.79	0.41 (0.26 to 1.61)	<.01**	
Sleep variability offset	-0.91	-0.13 (-1.07 to 0.40)	.36	
Regression 2: T3 BSS				$R^2 = 0.53$,
Block 1				$F_{4.48} = 12.73$
T1 BSS	5.52	0.66 (0.37 to 0.80)	<.01**	P<.001
BDI-II	0.45	0.05 (-0.11 to 0.17)	.65	
Block 2				
Sleep variability onset	1.74	0.32 (-0.12 to 1.70)	.08	
Sleep variability offset	-0.30	-0.05 (-1.15 to 0.85)	.76	
Comparison of predictors: T2 BSS				$R^2 = 0.69$,
Block 1: BDI-II	7.91	0.76 (0.47 to 0.79)	<.01**	$F_{4.48} = 25.41$
Block 2		,		P<.001
Sleep variability	2.22	0.20 (0.02 to 0.48)	.03 ^a	
VAS-MV	1.73	0.17 (-0.04 to 0.63)	.09	
BDI-II	-0.88	-0.08 (-0.15 to 0.06)	.38	

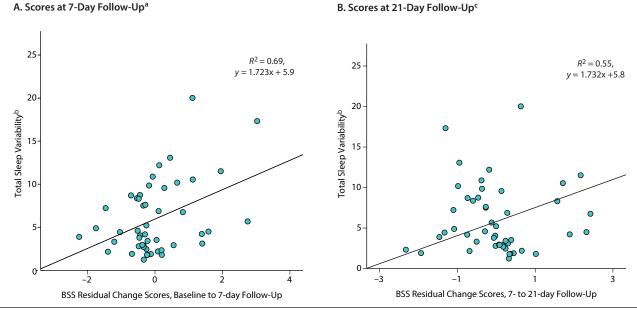
^{*}P<.05. **P<.01

Abbreviations: BDI-II = Beck Depression Inventory-II, BSS = Beck Scale for Suicide Ideation, DDNSI = Disturbing Dreams and Nightmare Severity Index, T1 = baseline, T2 = 7-day follow-up, T3 = 21-day follow-up, VAS-MV = Visual Analog Scale mood variability.

Based on observed findings for sleep variability as a significant predictor of risk, post hoc analyses were conducted to evaluate whether a specific component of the sleep-wake cycle (ie, sleep onsets vs offsets) differentially contributed to risk and, by extension, might serve as a treatment target. Specifically, sleep-wake timing variability (ie, sleep variability onset vs sleep variability offset) was simultaneously compared in the model. Including BDI-II and baseline BSS as covariates, sleep variability onset accounted for a significant portion of the variance in T2 and T3 BSS change scores relative to sleep variability offset. Variability of other sleep parameters (ie, variations in sleep efficiency, wake after sleep onset, sleep-onset latency, and total sleep time) was also examined as predictors of risk within a single model with sleep variability, including BDI-II and baseline BSS as covariates. Only greater sleep variability and less variability in total sleep time were significant ($P \le .02$) predictors of T2 BSS change scores (Supplementary eTable 2).

Correlations were employed to elucidate sleep variability in relationship to other sleep parameters. Beyond delayed bedtime/wake time and nap frequency, sleep variability was not significantly correlated with other





^aScatterplot of actigraphically assessed total sleep variability by BSS suicidal ideation residual change scores (baseline to 7-day follow-up), adjusting for baseline BDI-II.

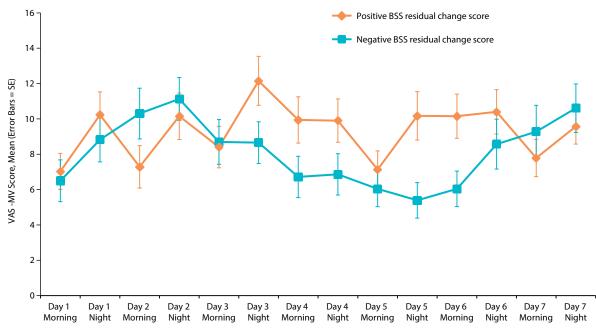
^bSleep variability represents the standard deviation of actigraphically assessed sleep offsets and sleep onsets, summed, as an overall index of sleep timing and irregularity.

^cScatterplot of actigraphically assessed total sleep variability by BSS suicidal ideation residual change scores (7- to 21-day follow-up), adjusting for baseline BDI-II.

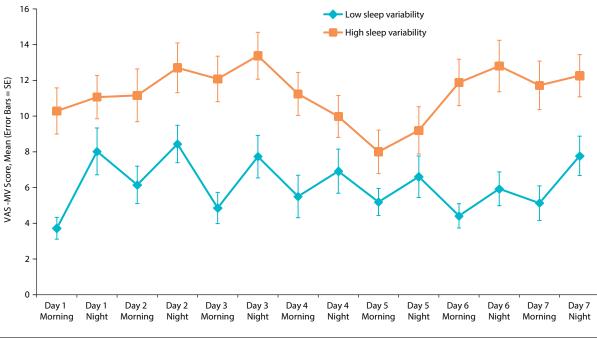
Abbreviations: BSS = Beck Scale for Suicide Ideation, BDI-II = Beck Depression Inventory-II.

Is not in the second se to nost thi convrighted any website DI C n Figure 3. Mean VAS-MV and Suicidal Ideation Residual Change Scores in Young Adults at High Risk for Suicide





B. Individuals With Low and High Sleep Variability^b



^aBSS residual change scores represent suicidal ideation symptom increases from baseline to 7-day follow-up, controlling baseline BSS and BDI-II. ^bSleep variability represents an overall index of sleep timing and sleep irregularity (ie, the summed standard deviation of sleep offsets and sleep onsets). Abbreviations: BSS = Beck Scale for Suicide Ideation, BDI-II = Beck Depression Inventory-II, VAS-MV = Visual Analog Scale mood variability.

actigraphy variables (total sleep time, sleep-onset latency, wake after sleep onset, sleep efficiency; P > .05), although a nonsignificant trend emerged for total sleep time (r = -0.26, P = .07). Significant intercorrelations were, however, observed for sleep variability and both T2 ISI (r=0.35, P = .02) and DDNSI (r = 0.02, P = .04).

Finally, given that sleep variability and VAS-MV significantly predicted T2 BSS symptom change when the results were controlled for BDI-II, a follow-up test was conducted to identify the most robust predictor of risk. All 3 variables were included in a competing model for simultaneous comparison as predictors (regression 3) and

Bernert et al It is illegal to post this copyrighte to replicate past findings,^{16,43} using an objective sleep index.

Surprisingly, sleep variability and VAS-MV accounted for more unique variance in prediction of BSS symptom change compared to BDI-II (Figure 3).

DISCUSSION

Findings revealed that actigraphic and self-reported sleep disturbances (ie, sleep variability, insomnia, and nightmares) predicted acute suicidal ideation symptom changes, an effect that occurred independent of depressive symptoms at 7- and 21-day follow-ups. This study converges with past reports^{7,13,16} demonstrating associations between subjective sleep problems and suicidal behaviors-when data were controlled for depression severity and affective disorderand with studies^{44,45} identifying nocturnal wakefulness as a predictor of suicidal ideation and suicide deaths. Such effects were observed despite clinical levels of covariates and sleep problems commensurate with a diagnosis. Likewise, mean actigraphy indices exceeded cut points distinguishing participants with insomnia from controls,^{34,35} which revealed significant variability in the timing of sleep onsets and offsets (\geq 2.9 hours). Such patterns strongly conflict with an increased developmental need for sleep among this age group.^{10,46}

Although actigraphic parameters together predicted suicidal ideation increases, only sleep variability-in particular, sleep-onset variability-individually predicted such symptom change. Greater variability of other objective sleep parameters (ie, sleep efficiency, wake after sleep onset, sleep-onset latency) did not predict suicidal ideation changes, whereas less variability in total sleep time (ie, consistent lack of sleep) significantly predicted risk, alongside irregularity in the overall timing of sleep. Our findings build upon an emerging literature tying intraindividual variability in sleep timing to an array of adverse outcomes, including stressful life events, negative affect, insomnia, and depression.^{33,47} Similar to studies among youth,⁴⁸ our study found significant correlations between sleep variability and subjective sleep complaints, delayed bedtimes, and nap frequency. This link aligns with conceptual models of insomnia development, underscoring the unpredictability of sleep as a cause and a consequence of insomnia and its maintenance.49,50 Such findings suggest that sleep variability may be an important feature-alongside insomnia, nightmares, and nocturnal wakefulness^{44,45}-to assess in the presence of other wellestablished suicide risk factors. These findings may also guide application to risk assessment, given findings that combination of actigraphy and self-reported sleep may significantly aid prediction of risk and specific mood states.51,52

Our sample reflected a group at heightened risk for suicide based on history of suicidal behaviors²⁸ and nonsuicidal self-injury.^{53,54} The majority of participants endorsed a past suicide attempt, and one-third reported multiple attempts. In most cases, these occurred by 15 years of age. This finding corresponds with a recent epidemiologic study⁵⁵

among adolescents (n = 12,395) in which a newly identified "invisible" risk group (ie, with reduced sleep, high media use, and sedentary behaviors) showed prevalence of suicidal ideation comparable to those classified by more traditional risk factors. Given escalation of suicide risk from adolescence to adulthood among those with past attempts,^{56,57} sleep may warrant investigation as a risk factor and intervention target for repeat suicidal behaviors.

Regarding clinical rationale, sleep disturbances are arguably less stigmatized compared to other risk factors yet modifiable and highly treatable. Gold standard insomnia interventions indicate preliminary efficacy in as few as 1–4 treatment sessions.⁵⁸ Such treatments reduce sleep variability, which otherwise predicts treatment resistance.^{47,59} Insomnia and nightmare treatments furthermore demonstrate improvements in nonsleep outcomes, including depression and suicidal ideation.^{39,60} Additionally, the brevity of this approach appears well matched to the acute nature of a suicidal crisis and treatment engagement difficulties following a suicide attempt (ie, where up to half will refuse treatment⁶¹ and 75% may drop out in ≤ 1 year⁶²). Taken together, sleep treatment may represent a low-risk intervention strategy for suicidal behaviors.

As a proposed exploratory factor, intraindividual mood variation predicted suicidal symptom increases, independent of depressive symptoms. Although main effects were observed for objective and subjective sleep parameters, only sleep variability and sleep-onset latency were individually related to mood fluctuations, which may be unsurprising given the degree of symptom overlap. Finally, in a competing risk model, we compared sleep variability, depressive symptoms, and mood variability as predictors of suicidal ideation. Remarkably, sleep variability-and to a lesser extent, mood variability-outperformed depression severity in the prediction of acute suicidal symptom change. While unexpected, this finding converges with at least 2 reports, including a study⁴³ among military personnel referred for imminent suicide risk and a population-based investigation¹⁶ of late-life suicide. In both cases, poor subjective sleep quality outperformed depressive symptoms and hopelessness in the prediction of incident risk for suicide attempts (ie, ≤ 1 month) and fatalities (ie, ≤ 10 years). To our knowledge, this is the first study yielding similar results utilizing an actigraphic sleep measure and acute time frame.

Sleep disturbances and suicidal behaviors cut across psychiatric and medical illness,^{63,64} suggesting a shared underlying neurobiology. On the basis of the role of sleep in emotion²¹ and its association to suicide risk,²⁴ we evaluated mood variability as an exploratory risk factor. Our findings broadly converge with experimental and nonexperimental studies of sleep deprivation, which show effects on emotional reactivity,⁶⁵ amygdala activation,⁶⁶ a blunting of positive affect,⁶⁵ and depression-like changes in serotonergic function.⁶⁴ Interestingly, a number of biomarkers (eg, inflammatory cytokines, brain-derived neurotrophic factor, serotonin transporter expression, etc) exist at the intersection of sleep and suicidal behaviors,^{48,67,68} suggesting that sleep **It is illegal to post this copyr** loss may induce vulnerability at the molecular level. Given the neurocognitive deficits observed in suicidal behaviors,⁶⁹ and the degree to which poor sleep and suicide cut across psychiatric illness,⁸ we recommend further study of sleep using a systems neuroscience approach, which would be commensurate with initiatives emphasizing the importance

of transdiagnostic risk factors⁷⁰ and development of a biosignature for suicide.^{67,68}

Several limitations should be noted. First, actigraphy served as our objective measure of sleep versus polysomnography. Future studies evaluating correspondence to sleep architecture are needed. Next, although research identifies poor sleep as a risk factor across diagnostically diverse samples, our study was limited to self-reported diagnostic histories. Replication is thus warranted using clinician-administered diagnostic interviews and to evaluate generalizability among those without a suicide attempt history. Finally, suicidal behaviors range in severity from suicidal ideation to suicide attempts to suicide fatalities. while suicidal thoughts are well established as a suicide risk factor,⁷¹ especially in the presence of past attempts,^{28,72} investigation of actigraphically assessed sleep and for suicide attempt risk is strongly recommended.

CONCLUSIONS

Research suggests that less than 1% of studies examining suicide risk reflect the weeks prior to suicidal behaviors,⁶ elevating the need for methodologically rigorous screening and evaluation of warning signs. Study strengths include its highly selective sample, longitudinal design, and acute time frame. To our knowledge, this is the first longitudinal report indicating that objectively and subjectively measured sleep disturbance confers risk for suicidal ideation independent of depression severity. Given the ease of sleep disturbance assessment and treatment, and its unique visibility as a warning sign, we propose poor sleep as a potential biomarker and therapeutic target for suicide prevention.

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Supplementary material: See accompanying pages.

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Supplementary material follows this article.



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Supplementary Material

- Article Title: Objectively Assessed Sleep Variability as an Acute Warning Sign of Suicidal Ideation in a Longitudinal Evaluation of Young Adults With High Suicide Risk
- Authors: Rebecca A. Bernert, PhD; Melanie A. Hom, MS; Naomi G. Iwata, MSc; and Thomas E. Joiner, PhD
- DOI Number: https://doi.org/10.4088/JCP.16m11193

List of Supplementary Material for the article

- 1. <u>eTable 1</u> Additional Baseline Sample and Clinical Severity Characteristics
- 2. <u>eTable 2</u> Variability of Actigraphic Sleep Parameters as Predictors of Suicidal ideation Changes at 7-Day Follow-Up

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SLEEP VARIABILITY AND ACUTE SUICIDE RISK

	No. (%) or Mean (SD)
Suicidal Behavior History	
2 Suicide Attempts, No. (%)	9 (18)
\geq 3 Suicide Attempts, No. (%)	6 (12)
Non-Suicidal Self-Injury History, No. (%)	
Years Since Last NSSI, mean (SD)	2.7 (2.0)
≥ 20 Times Engaged in NSSI, mean (SD)	5 (10)
Psychiatric Diagnoses, No. (%)	
Major Depressive Disorder, No. (%)	12 (57)
Schizoaffective Disorder, No. (%)	1 (5)
Bipolar Disorder, No. (%)	3 (14)
Generalized Anxiety Disorder, No. (%)	5 (24)
Social Anxiety Disorder, No. (%)	1 (14)
Obsessive-Compulsive Disorder, No. (%)	1 (14)
Bulimia Nervosa, No. (%)	1 (5)
Insomnia, No. (%)	2 (10)

Table 1. Additional Baseline Sample and Clinical Severity Characteristics

Abbreviations: NSSI, non-suicidal self-injury

SLEEP VARIABILITY AND ACUTE SUICIDE RISK

	t	β (95% CI)	P Value	Model Statistics
Regression 1: T2 BSS		<u> </u>		
Block 1:				
T1 BSS	7.53	0.76 (0.46 to 0.80)	< 0.01	
BDI-II	0.12	0.01 (-0.10 to 0.12)	0.91	$R^2 = .75$
Block 2:				F(7,41)=17.53
SE, SD	0.27	0.03 (-0.15 to 0.19)	0.79	P<.01
WASO, SD	-0.73	-0.06 (-0.12 to 0.06)	0.47	
SoL, SD	0.92	0.08 (-0.06 to 0.15)	0.36	
TST, SD	-2.38	-0.25 (-3.35 to -0.28)	0.02	
SV, SD	3.89	0.34 (0.20 to 0.64)	< 0.01	
Regression 2: T3 BSS				
Block 1:				
T1 BSS	4.98	0.62 (0.33 to 0.78)	< 0.01	
BDI-II	0.92	0.12 (-0.08 to 0.22)	0.36	$R^2 =55$
Block 2:				11 100
SE, SD	-0.81	-0.10 (-0.32 to 0.14)	0.42	F(7,41)=9.41 P<.01
WASO, SD	-0.55	-0.06 (-0.15 to 0.09)	0.58	<i>I</i> ≤.01
SoL, SD	0.49	0.05 (-0.11 to 0.17)	0.63	
TST, SD	-1.79	-0.23 (-3.89 to 0.23)	0.08	
SV, SD	2.82	0.31 (0.13 to 0.71)	0.01	

Table 2. Variability of Actigraphic Sleep Parameters as Predictors of Suicidal Ideation Changes at 7-Days Follow-Up

<u>Note.</u> BDI-II, Beck Depression Inventory; BSS, Beck Scale for Suicide Ideation; SE, Sleep Efficiency; WASO, Wake After Sleep Onset; SoL, Sleep Onset Latency; TST, Total Sleep Time; SV, Sleep Variability; SD = Standard Deviation