Current Psychiatry Reports (2020) 22: 34
https://doi.org/10.1007/s11920-020-01155-2

MOOD DISORDERS (E BACA-GARCIA, SECTION EDITOR)

Ecological Studies of Sleep Disturbances During Suicidal Crises

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Published online: 14 May 2020

Abstract

Purpose of Review Several reviews and metanalyses have shown that sleep disturbances, such as insomnia and nightmares, can predict suicidal ideations and behaviors. Common physio-pathological pathways may explain this relationship. However, only in recent years, some research groups have tried to apply this knowledge in the quest for a reliable tool of suicide risk prediction. We aim to describe in this paper the results of studies using ecological or quasi-ecological assessment methods that connect sleep disturbances and suicide risk.

Recent Findings Our review confirms the paucity of studies on this topic. The few studies that we could analyze suggest the interest of ecological methods of sleep assessment since sleep disturbances predicted the onset or worsening of suicidal ideations and behaviors.

Summary Ecological assessment of sleep can help to understand how sleep disturbances contribute to the emergence of suicidal ideations and behaviors. Sleep disturbances appear as a promising "real-life" marker of risk, but further studies are needed to determine if sleep monitoring could guide preventive interventions.

Keywords Sleep–suicidality · Ecological momentary assessment · Insomnia · Suicide attempt

Introduction

Suicidal behavior prevention is an international public health priority. Despite a huge death toll that makes suicide a leading global cause of unnatural death [1] and an enormous economic burden estimated in billions of euros per year in developed countries [2], suicide prevention strategies are not achieving the expected results in many countries [3]. Through the last decades, a plethora of relevant factors associated with suicidal ideations and behaviors (SIB), such as sleep disturbances, has emerged. These risk factors shed light in the understanding of the etiopathogenesis of suicide, but they are not accurate predictors of emergent SIB in a given person. Suicide risk prevention may thus need to focus on the detection of warning signs, related to current functioning and near-term risk, in order to design timely interventions [4].

Sleep disturbances, a broad term that includes clinical diagnoses of sleep disorders, difficulties in initiating or maintaining sleep, complaints of poor sleep, and alterations of sleep health [5], are promising warning signs for SIB. Several recent studies have shown a significant association between sleep disturbances and suicide. In a 2012 meta-analysis of 39 studies, Pigeon et al. concluded that sleep disorders, particularly insomnia and nightmares, were associated with an increased risk of suicidal behaviors, including suicidal ideation, suicide attempts, and completed suicide, independently of psychiatric diagnoses. However, the studies included in this meta-analysis show numerous differences in the type of measurements

This article is part of the Topical Collection on *Mood Disorders*

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(subjective or objective), the design of the study (only 10 out of 39 used a longitudinal methodology), and the study population (issued from the community, clinical samples, or university students) limiting the interpretability of the results. Two years later, Malik et al. performed a systematic review focused on the effect of sleep disturbances on suicide risk in psychiatric patients [6]. They confirmed the association between suicidal behaviors and sleep disturbances in a range of mental disorders including schizophrenia, depression, panic disorder, and post-traumatic stress disorder. More precisely, insomnia, parasomnia, and sleep-related breathing disorders, but not hypersomnia, conveyed an increased risk of suicidal behaviors. According to their results, the comorbidity of sleep disorders and mental disorders was associated to a slightly increased risk of completed suicide, a twofold risk of presenting suicidal ideation and a fourfold risk of attempting suicide.

As for the mechanisms underlying this association, Porras-Segovia et al., in their recent systematic review on the topic, pointed to mental disorders, impairment in decision-making, alterations in circadian rhythms, emotional dysregulation, and negative feelings [7]. They also highlighted the role of sleep disturbances in the last phases of the pathway to suicide, acting as proximal factors that immediately precede the suicidal act.

Despite the strong association between sleep disturbances and SIB, several questions remain unanswered and require further studies with appropriate methodologies. For example, the dynamics of the relationship between sleep disturbances and SIB are still unclear. EMA methodology could improve our understanding and the quality of the data collected. Indeed, the "ecological" aspect of EMA refers to a data collection made in a real-world environment while individuals continue their daily lives. The "momentary" aspect of the EMA refers to the assessment of the subject's condition at multiple time points, closer to daily life experiences, and thus reducing memory biases. Data are collected in real time when the variable studied (e.g., affective fluctuations) occurs. The observation periods are chosen according to their relevance (e.g., at awakening for a sleep agenda) or proposed at random. Importantly, the data can be objective, if emerging directly from smartphone sensors, or subjective, when it is based on the answers to push notifications or questionnaires appearing on the phone.

The objective of this review is to synthesize the literature that used ecological assessments to investigate the association between sleep disturbances and SIB. We will focus particularly on studies using ecological momentary assessment (EMA), which allows for the collection of real-time information using different devices, repeatedly, and in a natural environment [8]. Given that the number of EMA studies is still scarce and this is, to our knowledge, the first review of the literature on this topic, we applied broad criteria in the selection of studies and included some that did not use an EMA methodology. Thus, studies based on a longitudinal methodology and using repeated measures, even in non-ecological contexts, were included in the review to explore the association between sleep disturbances and SIB.

Methods

Search Strategy

We performed a review of PubMed and Web of Science databases by using the text words ("ecological momentary assessment" OR "experience sampling" OR "sleep diary" OR "actigraphy "OR "real-time assessment" OR "experience momentary assessment") AND ("suicide") AND ("sleep" OR "insomnia" OR "Hypersomnolence" OR "Hypersomnia" OR "Drowsiness" OR "Sleepiness") in the title, topic, or abstract. No time limits were set for the search, and the only limitation criterion was language: English. The bibliography of the papers issued from this research was explored for relevant articles or communications, and other papers suggested by the authors were included if considered relevant for the purpose of the review.

Characteristics of Studies

Studies that met the following criteria are described in detail: (1) original papers published in a peer-review publication, (2) written in English, and (3) using an ecological or quasi-ecological assessment of sleep disturbances and SIB. The initial search identified fourteen potentially relevant articles. After initial screening of abstracts, full-text revision, and selection process as appropriate, only four articles met the inclusion criteria [9••, 10••, 11••, 12], three of them used EMA methods. Considering the small number of articles, a quantitative analysis of the results could not be made. We performed a descriptive synthesis of all the articles identified as well as other longitudinal studies [13, 14••, 15••] and an ongoing project that are relevant to the purpose of this review.

Results

EMA Studies Connecting Sleep Disturbances and SIB

Littlewood et al. [9••] performed a 7-day longitudinal study to explore the possible bidirectional association. The study intended to verify the following hypotheses: (1) sleep disturbances would predict the severity of next-day suicidal ideation; (2) higher severity of daytime suicidal ideation would predict sleep disturbances the following night; (3) poor sleep may moderate the relationship between pre-sleep feelings of entrapment and levels of suicidal ideation at the moment of

awakening. Data were obtained from a sample of 51 individuals aged 18–65 years, diagnosed with a major depressive episode (DSM-IV criteria) and presenting suicidal ideation in the month prior to inclusion. The EMA study protocol included four phases: (1) screening to verify the eligibility of the participants; (2) pre-EMA assessment, with demographical and clinical measures including mental health problems, suicide ideation and sleep, and briefing about the EMA procedure; (3) 7-day EMA procedure which collected objective data continuously with the PRO-Diary Watch (activity tracker) and subjective data on waking each morning with a sleep diary and at six quasi-random time points per day; and (4) debriefing at the end of the study period. The results, after adjustment for anxiety and depression severity, confirmed a unidirectional association between sleep disturbances and next-day suicidal ideation. Objective and subjective total sleep quality, but not sleep efficiency, predicted next-day suicidal ideation. On the contrary, high levels of daytime suicidal ideation did not predict sleep disturbances the subsequent night. Finally, the subjective quality of sleep moderates the relationship between intensity of entrapment before sleep and levels of suicidal ideation at the moment of awakening. Thus, when sleep quality was rated as good, high pre-sleep feelings of entrapment were not associated with awakening levels of suicidal ideation. These results confirm previous data on the dynamic association between sleep disturbances or short sleep duration and SIB and suggest a unidirectional link. According to the authors, these findings justify the need for guidelines about sleep time and sleep quality assessment during suicidal crises. From a clinical perspective, they underline the importance of subjective evaluations in a risk assessment context.

Bernet et al. [10••] recruited 50 participants with high suicide risk, presenting both a history of suicide attempts and recent suicidal ideation, from a university undergraduate research pool to investigate objectively the role of sleep disturbances as an acute indicator of suicide risk. Using a longitudinal design, across a 21-day observation period and 3 time points (baseline, 7 days and 21 days follow-up), they showed that poor sleep measures (based on 7 days of actigraphy verified with a sleep diary) predicted increases in suicidal ideation (assessed at baseline, 7 and 21 days follow-up), even after adjustment for depression severity. This was the first study using a longitudinal design and both objective and subjective measures of sleep disturbance. The characteristics of the sample, with high suicide risk and issued from university students, may limit the generalizability of the results to other populations.

In a case–control study, Benard et al. [11••] measured sleep and circadian rhythms in currently remitted bipolar disorder (BD) patients with a history of suicide attempts ($n = 57$) or without a history of suicide attempts ($n = 90$) and healthy controls ($n = 89$). Sleep and circadian rhythms were evaluated consecutively for 21 days using daily self-assessment measures and actigraphy measures. The results revealed differences between the three groups regarding sleep and circadian rhythms. Attempters with BD, contrary to non-attempters, showed worse scores in a self-reported questionnaire assessing sleep quality, the Pittsburg Sleep Quality Index [16], compared to the control group. On the other hand, objective data from actigraphy showed that non-attempters with BD spent more time in bed but with more awake times during sleep than controls. Finally, the results highlighted a significant difference in the onset of the M10 marker, suggesting that attempters started their day earlier than non-attempters. This study is strengthened by the use of objective and subjective validated assessments, a large sample size, a long-term follow-up (21 days), and the precise inclusion criteria.

Other Longitudinal Studies Connecting Sleep Disturbances and SIB

Using data archived from a previous epidemiological study of sleep, Woosley et al. [12] explored the aspects of insomnia that predicted suicidal ideation in a community sample of 768 participants. The insomnia complaint was identified by the answer to the question "Do you have sleep problems?". They studied the sleep profile obtained from a 2-week follow-up using a sleep diary including bedtime, sleep onset latency, number of awakenings during the night, wake time after sleep onset, time of final wake up, rising time, bedtime medication/alcohol, and nap duration for the previous day. These results reveal that qualitative complaints about insomnia are a better predictor of suicidal ideation than quantitative indexes of sleep. In other words, poor subjective sleep quality is a good marker of risk for SIB. These results are in line with prior findings indicating that poor subjective sleep quality are associated with an increased risk of suicide death [17]. However, some methodological limitations must be considered: only subjective measures were used; suicidal ideation and sleep complaints were assessed using a single non-validated item; and, finally, except for the sleep diary, the other measures were obtained retrospectively.

Hom et al. [13] investigated psychological factors that could mediate the relationship between insomnia and suicidal ideation among young adults ($N = 226$) during a 2-month follow-up at three time points. Interestingly, disgust with others and the world measured at 1 month, but not any other psychological factor, showed a mediating effect between insomnia symptoms at baseline and the severity of suicidal ideation at the end of follow-up. The psychological variable of disgust has a major role in the development and maintenance of many mental health disorders [18], and alterations in the explicit recognition of disgust might increase suicidal vulnerability [19]. As noted by the authors, failure to correctly perceive emotions such as disgust may diminish the ability to interact with others, increasing the risk of interpersonal

conflict, negative emotions, and SIB. Although it did not follow an ecological design, the interest of this study lies in the identification of a possible therapeutic target. A psychotherapeutic treatment addressing this emotion may reduce the development of suicidal ideation in patients with sleep disturbances. However, the results need to be replicated in samples of acutely suicidal patients.

Mirsu-Paun et al. [14••] completed a pilot study to explore prospectively the association between insomnia severity and wish to die in a sample of 64 patients that had just experienced a suicidal crisis. Inclusions were made during hospitalization in a specialist unit of emergency psychiatry. Data were collected during a 1-month follow-up at four time points using self-rated and physician-rated scores of sleep quality and SIB. Wish to die after 1 month was associated with insomnia severity, low satisfaction with sleep, and low sleep duration at the end of the follow-up. These results suggest that subjective sleep quality could be used as an indicator of suicide risk during the month following a suicidal crisis. Accordingly, the authors proposed the use of self-questionnaires of sleep using smartphones to identify high-risk patients and the implementation of cognitive and behavioral therapies for sleep disturbances during hospitalization or follow-up care to reduce suicide risk.

Ballard et al. studied the association between nocturnal wakefulness and next-day suicidal ideation using a polysomnography procedure in a sample of 65 mood-disordered participants, with either major depressive disorder or bipolar disorder [15••]. At the time of the assessment, all participants were moderately or severely depressed and responded to the criteria for treatment-resistant depression. Data collection occurred during a whole-night sleep recording with electroencephalography to determine total sleep time, wake after sleep onset, and sleep efficiency, as well as electrooculograms and electromyograms to capture eye movements and muscle activity. After the polysomnography, participants were questioned about suicidal ideation, depressive symptoms, and sleep using validated instruments. Next-day suicidal ideation was associated with early morning wakefulness, particularly from 4:00 to 4:59 am. Since this timing corresponds to the lowest core body temperature and the highest propensity to sleep according to circadian rhythms [20], the authors suggest that wakefulness at this moment impacts next-day capacity for emotional regulation and executive functioning, facilitating the emergence of suicidal ideation. Polysomnography is too costly to be used in usual assessments of suicidal risk, but this study provides further support to the association of early morning awakening with suicidal ideation [11••, 21] and suggests that the timing of sleep disturbances needs to be taking into account.

The Smart-Crisis study (clinical trial number: NCT03720730) is investigating the utility of EMA, actigraphy, and smartphone utilization to predict the emergence of suicidal ideation after a suicidal crisis during a 6-month follow-up in a Franco-Spanish clinical cohort. To date, there is no instrument capable of predicting the risk of SIB in a sufficiently precise manner to undertake preventive actions [22]. The Smart-Crisis project aims at creating a precision tool that can keep track of the evolution of suicidal risk in everyday life using indirect markers well accepted by the participants (including sleep, alimentation, or smartphone use). Preliminary data from the study confirms that the use of smartphones applications and sensors makes participation in the study easier for participants and allows a closer look to their day-to-day functioning (ecological assessment) even over a relatively long period of time. Of note, the participants did not receive any economical incentive but so far, (189 participants) the feasibility is fairly good. Eighty percent of screened patients agree to participate, although 20% drop out in the first few days, and after 2 months, the rate of patients continuing the study is still around 70% (unpublished data, see [23] for details on the protocol).

Discussion

This is the first review to summarize the evidence about the association between sleep disturbances and SIB in ecological studies. Despite the robust association between both conditions, only a few studies have investigated this association in real life using EMA or other methods. This is surprising since data collection needs to take into account that sleep disturbances [24] and suicidal ideation are fluctuating over time [25, 26]. As reported by Kleiman and Nock [27] based on a meta-analysis by Franklin et al. [28], over the last 50 years, the association between sleep disturbances and SIB was explored using retrospective and subjective data reports with a long-time interval (e.g., past month, year, or lifetime), which represents an important limit because it does not take into account the dynamic characteristics of sleep and SIB. Indeed, most studies assess sleep through questionnaires in a cross-sectional or retrospective manner [29]. This kind of studies does not allow to establish causality and is subject to biases, particularly concerning the recall of sleep disturbances. Self-report measures, which are frequently used, produce another limitation due to their subjectivity. For instance, a recent study comparing patients with bipolar disorder and healthy controls showed that self-reported sleep disturbances were subject to recall biases depending upon current mood/affect states, level of education, or level of functioning. Low-functioning bipolar patients tended to overestimate sleep duration [30]. However, subjective sleep problems may reflect an underlying emotional distress that could be more closely linked to suicidal risk than other psychiatric symptoms or diagnoses.

The few studies that we summarize in this review confirm the interest of ecological assessments of sleep in SIB.

However, these studies show numerous differences that limit the interpretability of the results. The most important is the large difference in the length of observation periods and whether the data collection was continuous or not, ranging from one continuous night to 6-month follow-up at several time points. In addition, the terminology used by the authors relating to sleep was heterogeneous and sometimes imprecise. For instance, some authors applied the term "sleep disturbances" while others preferred "sleep disorders." The second term is more specific and refers to clinical diagnoses, but a strict definition was missing in some of the reviewed papers.

Despite these limits, sleep disturbances appear as a promising biomarker for suicidal behavior, with potential implications for clinical practice. As shown by Littlewood et al., poor sleep quality and short sleep duration, both objectively and subjectively measured, are valid predictors of next day suicidal ideation [9••]. Suicidal ideation or the distress that comes with, on the contrary, did not predict the occurrence of sleep disturbances. Thus, acute onset sleep disturbances could be used as a warning sign that alerts us of an emergent suicide risk, especially if used in addition to other well-known risk factors for suicide, such as the existence of previous suicide attempts. Monitoring of sleep in at-risk populations could become a cost-effective approach to suicide prevention.

Increasing sleep quality may prevent the transition between negative emotional states and suicidal ideation. Some interesting preliminary studies suggest the involvement of emotions, such as the feelings of entrapment or disgust, as mediating factors in the association of sleep disturbances and SIB. The subjective perception of a good quality sleep represents a protective factor between the presence of a negative emotional state before bedtime and awakening levels of suicidal ideation, while disgust has a mediating effect between insomnia and the severity of suicidal ideation. Indeed, a growing body of research suggest a close association between sleep and emotions [31]. Sleep restriction is associated with impaired emotional processing and emotional regulation by inhibiting top–down control from the prefrontal cortex to the amygdala [32]. Several studies, notably using functional MRI, confirm the regulatory role of sleep on emotional distress [33]. In a recent MRI study, Wassing et al. [34] compared brain activity during an emotional memory retrieval task in people with (n = 27) and without sleep disorders (n = 30) according to international classifications. The results revealed differences in the activation of limbic areas. Sleep-disordered participants showed a limbic response, particularly in the dorsal anterior cingulate cortex, when recalling either recent or more distant shameful experiences. In the absence of sleep disorders, only novel experiences produced a similar activation. In other words, sleep-disordered individuals will find more difficult to avoid the neurophysiological activation of their limbic circuitry and the subsequent emotional distress, when recalling past emotional experiences.

One potential reason is the frequent presence of rumination, or repetitive negative thinking about the past, in association with sleep disturbances. Rumination, a common correlate to SIB, is often responsible for the activation of the limbic system and the emergence of emotional distress [35–37]. According to the integrated motivational–volitional model [38, 39], one of the predominant models explaining the suicidal process, it is possible to hypothesize that rumination, triggered by defeat or humiliating experiences with no possibility to escape, primes the feelings of entrapment. Entrapment is a major driver connecting adverse emotional experiences to suicidal ideation. In a sample of adult outpatients receiving psychotherapy, Teismann and Forkmann confirmed that the perception of entrapment fully mediated the association between rumination and suicidal ideation [40]. In a qualitative study interviewing adults with major mood disorders and SIB, Littlewood et al. found that sleep time was often used to escape the perception of entrapment [41••]. This study was the first to employ a qualitative methodology to explore narrative accounts about the role of sleep in relation to SIB. According to the authors, individuals that tend to sleep during the day disrupt nocturnal sleep and in turn aggravate emotional dysregulation, rumination and suicidal ideas. Individuals enduring nightmares may try to avoid sleep increasing the perception of entrapment and hopelessness [42].

The interest of EMA in this context, particularly the implicit methods of data collection not requiring an input from the patients (e.g., automatic recording of sleep activity with an actimeter), is supported by the fact that it is a minimally invasive method that eliminates many of the biases associated with traditional assessment. Real-time data collection, close to the experience, makes it possible to improve the quality of the data which are naturalistic (in usual environment and daily life) and valid (no recall bias, objective input of activity). EMA also allows to verify the direction of causality. The automatization of data recording in EMA opens the possibility to obtain data during crises, a period when subjective data collection is not only far more difficult but also over relatively long periods. Continuous assessment, up to 21 days in two studies presented in this review, may help to understand the suicidal process. Implicit EMA facilitates data collection in larger samples which is important in studies with suicidal patients since outcome behaviors, such as suicide attempts, have a low probability of occurrence. Note also that as pointed out by Kleiman and Nock [27], the EMA use fits well in the perspective of Rudd's Theory known as Fluid Vulnerability Theory, which postulates a fluctuation of suicidal ideation close to a baseline with episodic peaks representing suicidal crises [4]. Finally, the acceptability and feasibility of EMA studies is also important considering the low compliance to health care of suicidal patients [43]. Wearable devices, extensively used by the general population, are an efficient method (low-cost and high-quality data) for research on this topic but

raise ethical questions about the management of situations detected as high risk.

In addition to its potential as a risk marker, sleep is also an important therapeutic target. In this regard, some evidence-based treatments for insomnia, such as cognitive behavioral therapy (CBT), have shown anti-suicidal effects [44, 45]. Also, the anti-suicidal properties of ketamine could be mediated by its effects on sleep architecture, as suggested by some studies [46, 47]. Overall, these studies suggest that targeted insomnia assessment and treatment (for example with CBT) should become part of usual care for suicidal patients.

Conclusion and Future Directions

Ecological assessments, and EMA in particular, present an undeniable strength to improve our understanding of the suicide/sleep relationship and can also become a valuable preventive tool allowing for a continuous monitoring of patients at risk. Unlike most risk factors for suicidal behavior, insomnia and sleep disturbances can be modified, increasing the interest of such monitoring. However, very little research has been yet done using ecological approaches in this domain. This is probably due to the relatively recent development of this field of knowledge, which follows technological advances, and the ethical concerns about the detection of suicidal risk in real life, which entails important consequences on how usual care needs to be designed and implemented.

A promising preventive strategy is the use of mobile phone applications that monitor sleep in high-risk patients, such as those with a history of suicide attempt. The development of algorithms to analyze the increasingly big and time-lagged sets of data, resulting from wearable devices, is one of the main challenges. But arguably, the most crucial next step is to explore the use of EMA for clinical interventions, known as ecological momentary intervention (EMI) [48]. The development of EMI, based on the appropriate use of accurate data processing algorithms, raises deontology and ethical issues and requires skills and resources that are rarely available in clinical practice.

Acknowledgments The editors would like to thank Dr. Jean Arthur Micoulaud-Franchi for taking the time to review this manuscript.

Compliance with Ethical Standards

Conflict of Interest Laurent Chaïb and Alejandro Porras Segovia each declare no potential conflicts of interest.

Enrique Baca-Garcia reports personal fees from JANSSEN and Otsuka.

Jorge Lopez-Castroman reports personal fees from JANSSEN and LUNDBECK.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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