

University of Groningen

On edge: night and day. Understanding the association between poor sleep and aggression van Veen, Maaïke

DOI:
[10.33612/diss.248586077](https://doi.org/10.33612/diss.248586077)

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2022

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

van Veen, M. (2022). *On edge: night and day. Understanding the association between poor sleep and aggression*. [Thesis fully internal (DIV), University of Groningen]. University of Groningen.
<https://doi.org/10.33612/diss.248586077>

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CHAPTER 1

Sleep and mental well-being are closely associated. A bad night's sleep, let alone consecutive nights of disrupted sleep, often result in fatigue, problems concentrating and attenuated mood. The pivotal role of disturbed sleep in psychopathological processes and psychiatric disorders has gained considerable research attention over the last decades. One particular area of interest is the association between sleep and aggression, which is the topic of this thesis. In this first chapter, I will shortly introduce the constructs under investigation, providing some theoretical underpinnings for their association, describe current research gaps and present the aim and outline of the thesis.

SLEEP AND MENTAL HEALTH

Sleep is an indispensable part of human life; providing a period of restoration for both body and brain. See Box 1 for a description of sleep and overview of commonly used terms in sleep research and throughout this thesis.

Healthy sleep is paramount for optimal psychological functioning (1). We know from previous research that disturbed sleep impairs the adequate regulation of emotions (2), self-control (3), cognitive performance (4) and memory processing (5). These effects are likely to contribute to various forms of psychopathology, such as amplified negative and reduced positive affect, increased impulsive behavior and negative appraisal of otherwise emotionally neutral stimuli (2,3). Sleep can be disrupted in multiple ways, ranging from transient and mild complaints of sleep problems to sleep disorders such as insomnia, sleep apnea or restless legs syndrome. These all compromise psychological functioning in distinct ways and variable degrees of severity.

The neurobiological systems involved in the regulation of sleep have important overlap with those implicated in the pathophysiology of psychiatric disorders (6). It is therefore not surprising that sleep disturbances and psychiatric disorders are closely intertwined (1). For several decades, disturbed sleep was predominantly conceptualized as either symptom or consequence of psychiatric disorders, which would dissolve during treatment of the disorder. Most research on the prevalence of disturbed sleep in psychiatry has been conducted in patients with depression, with a large majority of patients reporting difficulties in getting to sleep or maintaining sleep, frequent awakenings and overall poor sleep quality (7). Additional research increasingly shows high numbers of reported sleep problems over the entire spectrum of psychiatry, for example in patients with psychotic (8), developmental (9) and substance use disorders (10). These subjective experiences of disturbed sleep have been confirmed in polysomnographic studies, showing alterations in sleep architecture and sleep continuity in almost all psychiatric disorders (11).

The fact that disturbed sleep is so common in patients with psychiatric vulnerabilities may have contributed to sleep being regarded as a non-specific factor in psychopathology, thus renouncing its possible significance. However, we now know that disturbed sleep is a risk factor for the development of psychiatric disorders, and holds importance for treatment prognosis and relapse risk (1,12). The association of sleep and mental health is thus bidirectional and warrants specific assessment and treatment of sleep disturbances, especially in patients with psychiatric vulnerabilities.

BOX 1. SLEEP IN A NUTSHELL

- Sleep is often described by the typical features of closed eyes, muscle relaxation and poor responsiveness to external stimuli. It has long been regarded as a relatively inactive state of body and brain, recurring for several hours every night and occupying a third of the human life span. However, under this restful external appearance, a myriad of processes involving regulation, repair and growth are taking place. Sleep thus plays an essential and central role in both our physical and psychological health.
- Sleep depends on the complex interplay between the wake-dependent homeostatic sleep drive (sleep pressure) and the body's internal biological clock (circadian rhythm). It consists of several stages with different functions, such as rapid eye movement (REM) and non-REM sleep, which occur in alternating cycles of approximately 90 minutes (See Figure 1).
- Sleep can be defined in terms of duration, quality and timing. Descriptions of varying sleep duration are relatively straightforward, as either being short long or expressed in hours or minutes. Sleep deprivation or sleep restriction, usually regarded as not receiving the preferred or needed amount of sleep, can be either habitual or part of an experimental protocol. Attenuated sleep quality is expressed far more variable and often labelled as poor sleep or disturbed sleep. This can refer, for example, to frequent nocturnal awakenings or non-restorative sleep. Disrupted sleep is an umbrella term covering elements of both disturbances in sleep duration and quality. Alterations in the timing of sleep in relation to the internal circadian rhythm can lead to suboptimal duration and quality of sleep.
- Assessment of sleep duration and quality can be performed by questionnaires and sleep diaries, often labelled subjective measurements. Research employing such subjective measures may describe attenuated sleep as sleep problems or perception of poor sleep. Wrist actigraphy and polysomnography are regarded as more objective measurements of sleep, yielding additional information on i.e. sleep efficiency and frequency of arousals.
- Specific sleep disorders, such as insomnia disorder, sleep apnea or restless legs syndrome, are defined by several international classification systems and need to be distinguished from more general terms describing poor sleep.
- While designing and interpreting research on disrupted sleep, it is important to realize that sleep can be compromised in various dimensions: acute versus chronic, intrinsic versus extrinsic and subjective versus objective.

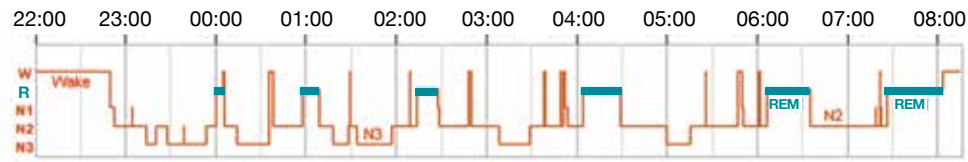


Figure 1. Hypnogram indicating sleep stages of a normal sleeper during one night (female, 35 years old). W = wake; R = REM sleep; N1 / N2 = lighter non-REM sleep; N3 = deep sleep.

Aggression

Aggression is considered a normal feature of human behavior that includes an extensive array of emotional, cognitive and behavioral aspects (13). Box 2 provides some additional information on aggression and aggression subtypes that is relevant to this thesis.

There are numerous factors described to be important to aggressive tendencies and actual aggressive behavior. On the one hand, these encompass dynamic aspects, defining internal state (i.e. arousal level and mood) and modifying appraisal and decision making (i.e. hostile attribution bias and impulsivity). On the other hand, aspects that are more static are of importance, such as personality traits, earlier victimization, and societal attitudes towards aggression. The interplay between these aspects can eventually result in a wide range of symptoms, varying from anger, irritability and hostility to externalizing and physical or verbal aggressive behavior, displaying the complexity of the aggression construct.

In attempts to provide some coherence in the considerable number of established risk factors for aggression, several theoretical frameworks have been developed. The General Aggression Model or GAM is the most widely used framework, offering an integrative overview of social, cognitive, personality, developmental, and biological factors in aggression (14). It distinguishes between proximate processes, in which personal and situational factors directly affect aggressive or nonaggressive behavioral outcomes, and distal processes in the background, in which biological and environmental factors interact to influence personality and thus the proximate processes. An important concept within the GAM is the development of knowledge structures, affecting perception, interpretation, decision-making and subsequent behavior. These knowledge structures include, for example, attitudes towards aggression and perception or expectation schemata. They evolve by repetitive experiences related to aggression and may even turn into partially automatized processes. Another example of a theoretical framework is the I³ model (15). This model presents an easily comprehensible structure of three distinct processes: instigation, impellance and inhibition, whose interplay affects both the occurrence and intensity of aggressive behavior. Instigating triggers are acute environmental stimuli that might evoke a normative aggressive response. Impelling forces are situational factors, social norms or personality traits (e.g. hostility) that influence how a certain trigger influences the propensity to experience and act on an aggressive response. Factors affecting inhibition can also be situational (e.g. alcohol intoxication) or personal and determine the ability to override the impulse to respond aggressively to instigating triggers and impelling forces.

BOX 2. AGGRESSION IN A NUTSHELL

- Human aggression is usually defined as any social interaction with the objective to harm or injure another, either physically or psychologically, who does not wish to be harmed or injured. Overt aggression is characterized by directly visible physical or verbal behavior, such as arguing, making fun of someone or fighting. Covert aggression is more concealed behavior, such as stealing and lying, but also including exerting a negative influence on social relations, such as spreading rumors about someone.
- In its adaptive form, aggressive features can serve many purposes, such as protective or competitive goals in social contexts. However, if aggression occurs out of context or is too easily provoked, it can be regarded as non-adaptive or pathological. Such non-adaptive aggressive behavior has major consequences for individual development and interpersonal functioning for both aggressive individuals and victims. Moreover, it poses a large emotional and financial burden on society, urging research to untangle the many factors involved in the manifestation of aggression.
- As aggression encompasses a wide range of behaviors throughout the population, several attempts have been made to identify different subtypes of aggression. A widely accepted approach to differentiate subtypes within aggressive behavior distinguishes two main types: reactive and proactive aggression. Reactive aggression, sometimes referred to as “hot” aggression, is mainly driven by frustration, anger and impulsivity and elicited by provocation or threat. Proactive aggression is more planned or premeditated and marked by low emotional arousal, lack of remorse and callousness, hence the attribution “cold”. It is associated with psychopathy and delinquent behavior, as well as instrumental in nature i.e. directly motivated to achieve a personal goal. Although these aggression subtypes have distinct genetic and neurobiological correlates, they should not be regarded as mutually exclusive categories. Features of proactive and reactive aggression are also interrelated and often co-occur in persons displaying aggressive behavior.
- Assessment of aggressive features and behavior is as wide-ranging as the construct itself, varying from self-report questionnaires and observer-rated symptoms to physiological measurements and neuropsychological tests.
- Aggressive behavior may occur within the context of many different psychiatric disorders. In the Diagnostic and Statistical Manual of Mental Disorders (DSM-5, American Psychiatric Association, 2013), aggression is mentioned as criterion for several classifications, of which conduct disorder, oppositional defiant disorder, intermittent explosive disorder and antisocial personality disorder are most well-known.

Eventually, the actual occurrence of aggressive behavior in a given situation is more likely when instigation and impellance are strong and inhibition is weak.

Many of these known risk factors for aggression cluster transdiagnostically in patients with psychiatric disorders, contributing to increased occurrence of aggressive tendencies and actual aggressive behavior. Indeed, impulsivity, anger and hostility are all common in psychiatric patients (16), as well as verbal and physical aggression (17), calling for effective management strategies that specifically address aggression in this group.

THE ASSOCIATION BETWEEN SLEEP AND AGGRESSION

Despite disrupted sleep being recognized in the regulation of emotions and behavior, the association between sleep and aggression received only modest research attention to date. In 2012, Jeanine Kamphuis and colleagues wrote a narrative review on sleep and aggression, which has been frequently cited in subsequent research in this field (18). It provides an overview of experimental and epidemiological studies in both children and adults, which show disturbed sleep to be associated with multiple aspects of aggression, such as increased anger and hostility, higher tendencies to blame others and the increased occurrence of verbally or physically aggressive behavior.

Since then, research attention has grown significantly, establishing the association between sleep and aggression in both general (19-21) and psychologically vulnerable populations, such as prisoners and forensic psychiatric patients (22-24). Moreover, some small-scale experimental studies show that improving sleep reduces behavioral problems and aggression (25,26), which supports a causal effect.

When conceptualizing the possible ways in which sleep disruption may influence the propensity for aggression, the review presented by Krizan and Herlache provides useful insights (27). The pathways they propose involve attenuated regulation of emotions, leading to amplification of negative emotions like anger, and increased perception of possible threat, creating a more hostile cognitive state. Furthermore, self-control, the effortful inhibition of aggressive inclinations that is considered a crucial preventative for aggression, is strongly affected by sleep disruption (Figure 2). Of course, we must also consider the possible reverse association, namely negative influence of aggression on sleep (27). Anger, hostile thoughts or aggressive incidents during the day will augment arousal and stress and may thus compromise sleep at night. The association between sleep and aggression is therefore hypothesized to be bidirectional. Although the evidence for aggression affecting sleep is still less pronounced than vice versa (28,29), it seems clear that both associations will contribute to a continuously reinforcing cycle with major impact on well-being and behavior.

Several underlying neurobiological mechanisms have been proposed to be involved in the pathways that connect sleep and aggression. For example, dysfunctions of the serotonergic system are thought to play either a causal or a modulatory role in the generation and expression of impulsive and aggressive behavior and disrupted sleep may augment such effects (18). Another theory, though still in need of exploration, involves the

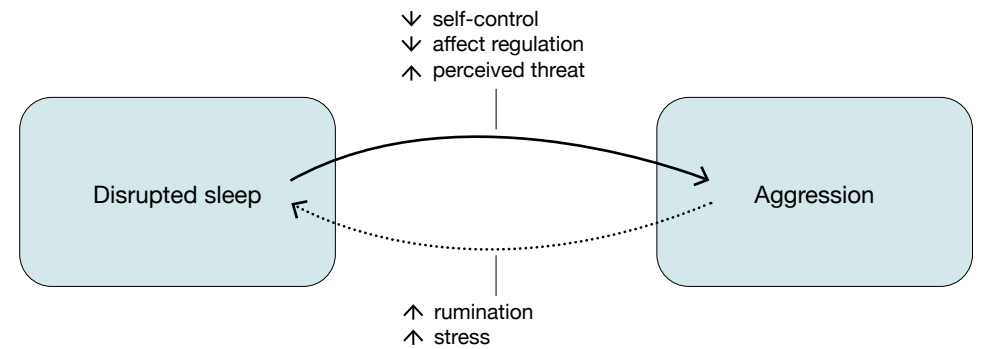


Figure 2. Conceptual model of possible pathways between sleep and aggression (based on Krizan & Herlache 2016)

hypothalamic-pituitary-adrenal (HPA) axis in a bidirectional way. Normal, healthy sleep has a calming and inhibitory effect on the HPA system, whereas HPA axis activation leads to arousal, stress and sleeplessness (18). Finally, a crucial role is attributed to the interplay between the prefrontal cortex (PFC) and limbic system, in which disrupted sleep strongly attenuates the monitoring and control of emotional responses leading to increased negative affect and disinhibition of behavior (2). It has been suggested that individuals with existing dysfunctions in the aforementioned mechanisms may be even more susceptible to the effects of sleep disturbances (18), but this has not yet been thoroughly investigated in humans.

SLEEP AND AGGRESSION - RESEARCH GAPS

Poor sleep may be a likely risk factor for aggressive behavior, and targeting sleep could be a promising additional approach in the management of aggression, both from an individual and societal perspective. This may be of particular importance in psychiatric populations, with high occurrence rates of sleep problems, impulsivity, anger and aggressive behavior. However, to date, a systematically performed overview of observational or experimental research on sleep and aggression to assess the consistency and magnitude of the association is still lacking. Furthermore, it is not known whether this association is different for general or psychologically vulnerable populations. In addition, many observational studies on the association between sleep and aggression in vulnerable populations do not differentiate between possible pathways linking sleep to aggression nor thoroughly account for comorbid psychopathology, which could partly explain the association. Another aspect still to be explored is how poor sleep influences aggression over time in a psychologically vulnerable population, to shed more light on cause and effect in this specific group. Lastly, no randomized controlled trials have been conducted assessing the effects of treatment of disturbed sleep on aggression in a population where both sleep problems and aggression are very prevalent, leaving the possible impact of poor sleep as a dynamic risk factor for aggressive behavior underexplored.

OBJECTIVES OF THIS THESIS

The general objective of this thesis is to expand knowledge on the association between sleep and aggression in both general and psychologically vulnerable populations. To do so, I use several different methodological approaches in order to address the abovementioned research gaps.

The aim of the first part of the thesis is to synthesize all available research on the association of sleep with aggression by performing a systematic review and meta-analysis. We intend to gain further insight in factors influencing this association by multiple sensitivity analyses, with special interest in identifying possible vulnerable populations or age groups.

In the second part of the thesis, my focus lies on replicating and expanding previous observational work on poor sleep in association with impulsivity and aggression in a specific vulnerable population: forensic psychiatric patients. Forensic patients have committed a crime or are at risk of committing a crime in conjunction with having a psychiatric disorder. We know from previous work by Kamphuis and colleagues that sleep problems, varying from reporting poor sleep quality to having insomnia disorder, are common in forensic psychiatric patients (30). Moreover, these sleep problems are associated with higher impulsivity and aggression (24). The aim of the second part is to explore several subcomponents of the impulsivity and aggression constructs and to assess the role of psychopathology in the association between sleep and aggression. Furthermore, I want to investigate the association between sleep, impulsivity and aggression over time by performing an auto-regressive analysis.

OUTLINE OF THE THESIS

The work I present in this thesis comprises two major parts, each based on different methodological approaches and populations.

Part I “Syntheses of available research on sleep and aggression” two systematic reviews and meta-analyses are presented. Each represents a synthesis of all available research work on the association of sleep with aggression. Because of conceptual differences between sleep quality and sleep duration in their association to aggression, as well as the large amount of eligible papers to be included, the results of the initial systematic search are split in two, thus yielding two systematic reviews and meta-analyses.

Chapter 2 “*Systematic review and meta-analysis on sleep quality and aggression*” includes a synthesis of observational studies on the association of sleep quality with aggression, exploring factors influencing this association such as different measurement instruments and type of population.

Chapter 3 “*Systematic review and meta-analysis on sleep duration and aggression*” includes a synthesis of both observational and experimental studies on the association of sleep duration with aggression. Again, several factors influencing this association are investigated.

Part II “Empirical studies on sleep, impulsivity and aggression in forensic psychiatry” presents three studies based on analyses of routine outcome measurements in a forensic psychiatric facility in the Netherlands.

Chapter 4 “*Sleep quality and impulsivity*” describes the cross-sectional association between poor sleep and self-reported impulsivity in forensic patients with inherent high impulsivity, namely those with antisocial or borderline personality disorder (or traits thereof). The influence of having a comorbid psychiatric diagnosis is examined, as well as the association of poor sleep with subcomponents of impulsivity.

Chapter 5 “*Sleep quality and aggression*” contains a study on the cross-sectional association of poor sleep quality and both self-reported aggression and clinician-rated hostility in forensic psychiatric patients. Several components of self-reported aggression are explored, as well as the influence of general psychopathology.

Chapter 6 “*Sleep quality and changes in impulsivity and aggression*” describes the association of poor sleep quality and changes in self-reported and clinician-rated impulsivity and aggression over the course of one year in forensic psychiatric patients, exploring the influence of general psychopathology.

Finally, in **Chapter 7** “*Summary and general discussion*”, the main findings presented in this thesis are summarized including methodological considerations and further discussed by addressing several theoretical and methodological dilemmas, concluding with implications for clinical practice and future research.

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