On edge: night and day. Understanding the association between poor sleep and aggression

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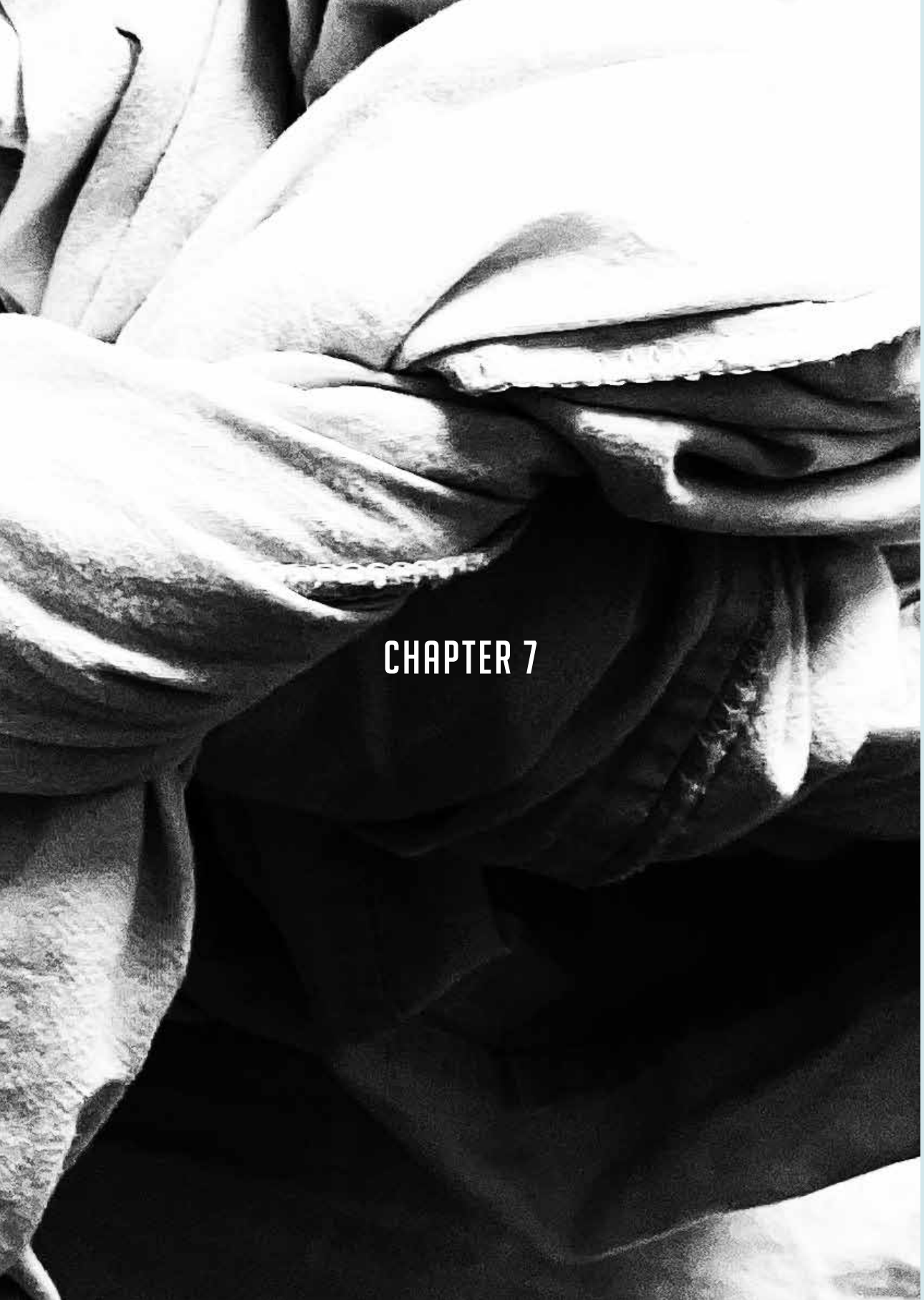

CHAPTER 7

PREFACE

The aim of this thesis was twofold: (1) to synthesize all available research on the association of sleep with aggression and (2) to explore several subcomponents of the impulsivity and aggression constructs and assess the role of psychopathology in the association between sleep and aggression in forensic psychiatric patients. In this final chapter, I will summarize the main findings originating from Chapter 2 through 6, including methodological considerations, followed by discussion of several theoretical and methodological dilemmas. In addition, I will describe the implications of my results for clinical practice, offer some recommendations for future research and end with a final overall conclusion.

SYNTHESES OF RESEARCH ON SLEEP AND AGGRESSION:

Summary and methodological considerations

In the first part of the thesis, two systematic reviews and meta-analyses of available research to that date on sleep and aggression were described. The results of the initial systematic search were split in two, because of the large number of papers and conceptual differences between sleep quality and sleep duration and the associations to aggression.

Chapter 2 presented a systematic review and meta-analysis of observational studies on the overall association between sleep quality and measures of aggression. Both the quantitative as well as the qualitative synthesis consistently confirmed the association of poor sleep quality with increased aggression across different populations, substantiating previous non-systematic and qualitative reviews. The quantitative results were highly heterogeneous, which was a direct consequence of the broad range of available studies. Sensitivity analyses revealed that the association between sleep quality and aggression was more pronounced and less heterogeneous in participants with psychological vulnerabilities or medical conditions. Also, self-reported measures of sleep quality showed stronger and less heterogeneous associations with aggression than objective measures. We observed no considerable effects for methodological quality or different age groups on effect estimates or heterogeneity. Though no causal inferences about the association between sleep quality and aggression can be made, as most work was cross-sectional, our findings emphasize the possible impact of diagnosing and targeting disturbed sleep in the prevention and treatment of aggression, specifically in populations with psychological or medical comorbidities.

In **Chapter 3**, my second systematic review and meta-analysis was presented, this time of observational and experimental studies on sleep duration and aggression. Meta-analysis of observational studies supported an association of shorter sleep duration with higher levels of aggression. Again, heterogeneity was high, a result of the wide range of available studies. In this review we included experimental studies as well which generally pointed into one direction, namely that restriction of sleep duration was associated with higher aggression and extension of sleep duration was associated to lower aggression. In sensitivity analyses of the observational studies, the associations we found were stronger in individuals with psychological vulnerabilities and younger persons. In addition, self-reported measures of sleep duration showed stronger and less heterogeneous associations with aggression than actigraphic measures. We concluded sleep duration to be associated with aggression, especially in individuals with psychological vulnerabilities and that, though more well-designed studies are required, accumulating experimental evidence supports causality.

In the rigorous effort of performing a systematic synthesis of evidence, numerous choices are made regarding the level of specificity of the research question, search terms, criteria for inclusion of papers and analyses. We chose quite an unusual approach by keeping a wide-ranging scope in our search for papers on the association between sleep and aggression, not applying extensive selection criteria regarding the type of studies, definition of the constructs or study population. Whether this is a strength or weakness of these two reviews is debatable. The fact that we included studies with varying populations, age groups and assessments of sleep and aggression unavoidably leads to heterogeneous results, which can be considered an important disadvantage. Especially in observational research, the overall risk of bias, such as selection or information bias, far exceeds the usually examined publication bias. This warrants thorough investigation of possible sources of heterogeneity rather than solely focusing on the calculated overall effects. Indeed, the results from these meta-analyses require careful interpretation as the effect estimates were not meant to be precise representations, but rather general impressions of the order of magnitude and direction of the association between measures of sleep and aggression. The rigorous search and assessment methods and large sample size are strong features of these reviews, and the broad inclusion of different studies offered an opportunity to examine possible sources of heterogeneity, such as specific subgroups and use of various measurement instruments. With those strengths and limitations in mind, these reviews are the first systematic evaluations of this topic and the results endorse previous non-systematic and qualitative reviews on sleep and aggression (1,2).

STUDIES ON SLEEP, IMPULSIVITY AND AGGRESSION IN FORENSIC PSYCHIATRY:

Summary and methodological considerations

In the second part of this thesis, I described three empirical studies on the associations between sleep, impulsivity and aggression in a cohort of forensic psychiatric patients. By investigating these associations in more detail in a specific subgroup with known high levels of both disturbed sleep and impulsive and aggressive behavior, we intended to replicate and refine previous work in this area.

In **Chapter 4,** we investigated the prevalence of sleep disturbances in forensic psychiatric patients with antisocial or borderline personality disorder or traits thereof and the associations between sleep quality, chronic insomnia and self-reported impulsivity. We found that more than half of these patients reported poor sleep quality, and almost a quarter met criteria for chronic insomnia. Lower sleep quality and higher insomnia scores were associated with more impulsivity, especially with attentional impulsiveness, i.e. difficulties with focusing and controlling thoughts. Comorbid psychiatric diagnoses, such as substance abuse disorders or mood disorders did not influence the association of poor sleep with impulsivity. This study confirms the high prevalence of sleep problems in

a clinical sample with high intrinsic impulsivity as well as the independent cross-sectional association between sleep and self-reported impulsivity in this group.

To further explore the possible confounding role of comorbid psychopathology, we assessed the association between sleep quality and measures of aggression in forensic psychiatric patients in **Chapter 5**. We included patients with any type of psychiatric diagnosis, aiming to control for a general, continuous measure of psychopathology. Again, almost half of the patients reported to be poor sleepers. Poor sleep quality was associated to higher self-reported aggression and clinician-rated hostility, though the latter association was less robust. Importantly, the association between sleep quality and self-reported aggression was maintained when controlling for general psychopathology. This was observed for all subcomponents of self-reported aggression: physical aggression, verbal aggression, anger and hostility. We concluded that the associations of poor sleep quality with (subcomponents of) self-reported aggression are not better accounted for by the general level of psychopathology.

Chapter 6 builds on the cross-sectional associations between sleep quality, impulsivity and aggression confirmed in this thesis by investigating longitudinal associations. We performed an auto-regressive analysis to investigate the association between sleep quality, impulsivity and aggression over one year time in forensic psychiatric patients, using impulsivity and aggression as outcome measures and correcting the analyses for their baseline value as well as general psychopathology. Poor sleep quality was associated with increased self-reported aggression over one year. This association was unaltered by correction for general psychopathology, which indicates an independent association. However, poor sleep quality was not associated with changes in self-reported impulsivity, clinician-rated impulsivity or clinician-rated hostility in this population. We concluded that sleep quality could be an important and tangible factor to target in reducing aspects of aggression in (forensic) psychiatric patients.

By investigating the association between sleep quality, impulsivity and aggression in a cohort of forensic psychiatric patients, we were able to explore the association in a specific subgroup with known high levels of both disturbed sleep and impulsive and aggressive behavior. The fact that the data were derived from ongoing routine outcome assessments does entail both selection and information bias. Not all patients were willing or able to take part in the measurements, and we had incomplete information on these non-participants to investigate the possible impact thereof. In addition, the measurement instruments used in this cohort were not priorly intended for the research questions addressed in this thesis. Psychometric properties, including content validity and responsiveness, restricted the interpretation of some of our results. For example, in the use of observational instruments that have limited accordance with self-reports or show little sensitivity to change. In addition, we did not explore the association of sleep duration with aggression in this population. Furthermore, sufficient data were available for two time points only, baseline and one-year follow-up. The results therefore do not yield specific information about causal direction or possible mechanisms connecting poor sleep and aggression. On the other hand, strengths of these studies are the proper correction for important confounders and longitudinal analysis, as well as the relatively large and well-described sample of patients known for their complex psychopathology. Together, they confirm the association between poor sleep and aggression in a psychiatric population and substantiate the vulnerability hypothesis.

INTEGRATION: DILEMMA'S AROUND SLEEP, AGGRESSION AND ETIOLOGY

In the following section, I will further discuss the findings presented in this thesis, integrating them with other research on sleep and aggression. I will do so by exploring three specific theoretical and methodological dilemmas around sleep, aggression and etiology.

Quality over quantity? Aspects of sleep

Our meta-analyses showed that the association of sleep quality with aggression was more pronounced than that of sleep duration with aggression (**Chapter 2 and 3**). This finding has arisen as well from numerous individual studies directly comparing sleep quality and duration (for example (3,4)), leading scientist to believe that quantity of sleep is less important than quality in its association to measures of aggression. The question is: does this observation reflect a true dissimilarity in association or is it strongly distorted by methodological issues? In my opinion, there are several arguments to support the latter.

The main argument here is that sleep duration is known to follow a curvilinear shape when related to important health outcomes, including aggression (5,6). The majority of studies on sleep and aggression in which both sleep duration and sleep quality are assessed, use the same (linear) regression analysis techniques for both associations. Fitting a linear model to a U- or J- shaped association can result in a very weak or even absent association of sleep duration with aggression, thus leading to the incorrect assumption that sleep duration does not play an important role in aggression as opposed to sleep quality. This problem may be resolved by more closely following the actually observed relationship, for example by fitting quadratic models or analyzing multiple categories of sleep duration. Studies adopting such approaches do show relevant associations between sleep duration and measures of aggression (5-7). Moreover, experimental studies that highlight the negative effect of restricted sleep duration on aggression (8,9), and especially those that show a decrease in aggressive behavior following sleep extension (10), support the role of sleep duration in aggression.

A second argument is that sleep duration cannot be seen separately from sleep quality. Short sleep duration caused by external factors (e.g. family or work obligations) or by simply providing oneself little opportunity to sleep can still be of sufficient quality, which greatly differs from insufficient amount of sleep due to insomnia. Central features of insomnia disorder, such as cognitive, emotional and physical hyperarousal (11), will negatively influence both actual sleep duration and quality, but moreover, the subjective experience of sleep duration and quality. The interaction between sleep duration, sleep quality and how they are perceived may partly explain apparent differences in their associations with aggression (12) and should be taken into consideration when interpreting results.

Closely related to the former argument is the fact that the element of perception will inevitably lead to differences between subjective or self-report instruments and more objective measures for the evaluation of sleep duration and quality (13). Although we did not explore the influence of type of sleep measurements in depth, both our meta-analyses (**Chapter 2 and 3**) showed that the association of sleep parameters assessed by actigraphy with measures of aggression was less pronounced compared to sleep parameters assessed by self-report. Indeed, several previous studies using both types of measures have indicated that subjective evaluations of sleep are more prominently related to aggression, than objective measurements (4,14). This discrepancy has not been specifically addressed in forensic psychiatric or prison populations to date. As the measures of sleep quality we used in the studies in forensic patients were all self-reported (**Chapter 4, 5 and 6**), a further exploration of more objective measures of sleep is warranted in this population. The fact that objective measures, that were long regarded the norm in evaluating sleep, often do not sufficiently explain the subjective perception of sleep presents an important challenge to sleep research in general (15). Especially in association to psychopathology, it is important to realize that the perception of sleep represents a much broader concept of inner experiences, including emotions and cognitive attributions, than can be captured by current objective assessments of sleep.

A central feature related to sleep that is noticeably not addressed in this thesis is the timing of sleep in association to aggression. Most research on this subject focusses on chronotype, which refers to a person's preferred sleep-wake timing. It is a relatively stable trait that is normally distributed among individuals, varying between having a morning, intermediate or evening preference. Having an evening chronotype has been increasingly recognized as an important transdiagnostic correlate of mental health problems (16), and more specifically of impulsivity and aggression (17). This association could be the result of a mismatch between the sleep-wake cycle and the internally dictated preference, referred to as circadian misalignment, which negatively influences both sleep duration and quality. Furthermore, evening chronotype is directly associated with certain personality traits and altered function of neurotransmitter systems, both predisposing for aggression. A recent comprehensive review on this topic also states that chronotype and aggression are influenced by the expression of the same genes (18). Despite these possible explanations, the association between chronotype and aggression is still largely unexplored in humans, particularly in individuals with high propensity for impulsive and aggressive behavior such as forensic populations (18).

Taken together, the issues addressed above warrant a more integrated approach to investigating quantitative, qualitative and timing aspects of sleep that are crucial to mental health, including aspects of aggression.

Hot or cold? Aspects of aggression

The conceptualization as well as the measurement of aggression requires some further explanation for a better understanding of the association with disturbed sleep that is confirmed in this thesis.

Aggression is a multi-faceted construct, encompassing a highly heterogeneous range of behaviors throughout the population. As described in Chapter 1 (Box 2), a widely accepted differentiation of subtypes of aggression distinguishes two main subtypes: reactive or "hot" aggression and proactive or "cold" aggression. The focus of this thesis predominantly lies on reactive forms of aggression. In our meta-analyses, which show clear associations of poor sleep quality and shorter sleep duration with higher aggression (**Chapter 2 and 3**), we selected studies by using search terms related to reactive aggression and externalizing behavior, including irritability, hostility and anger. Externalizing behavior usually incorporates aspects of both reactive and proactive aggression, such as conduct problems and rule-breaking. Studies exclusively focusing on rule-breaking, delinquency, conduct problems or antisocial behavior were excluded because of the conceptual and neurobiological differences with reactive aggression. As our meta-analyses were not specifically aimed at disentangling the association of disturbed sleep with various components of reactive aggression, I am hesitant to draw firm conclusions based on the results from sensitivity analyses. These results were rather divergent, showing that sleep quality was slightly more prominently associated to externalizing behavior, for example as measured by the Child Behavior Checklist, compared to other aspects of aggression (**Chapter 2**). This could imply that the association between sleep quality and aggression is more defined by behavioral aspects, but could also represent an age effect, as these instruments are mostly used in children. Sleep duration however, was most clearly associated to anger and composite measures of aggression including anger, such as the Aggression Questionnaire (**Chapter 3**), suggesting that affect regulation indeed plays an important part in the association of sleep duration with aggression.

The studies in forensic psychiatric patients used self-report and clinician-rated outcome measures for impulsivity and aggression (**Chapter 4,5 and 6**), which assess mixed aspects of aggression but with emphasis on reactive aggression. As for self-reported outcomes, we found that poor sleep was associated to higher self-reported impulsivity (**Chapter 4**), an association observed previously in comparable study samples (19-21). As impulsivity, or its counterpart self-control, is regarded as one of the key components determining the risk for reactive aggression in theoretical frameworks, this association highlights the possible importance of poor sleep as contributing factor in the propensity for aggressive behavior. A study assessing mediating factors indeed highlights impulsivity to explain part of the association between sleep and marital aggression (22). In **Chapter 5**, we found that poor sleep quality was associated to higher self-reported aggression. This was observed equally for all subcomponents of self-reported aggression measured by the Aggression Questionnaire: physical aggression, verbal aggression, anger, and hostility, covering features of both reactive and proactive aggression. However, **Chapter 6** showed that poor sleep quality was associated to an increase in self-reported aggression over one year, but not to self-reported impulsivity. We speculated that the absence of an association of poor sleep with impulsivity over time might be explained by the fact that the Barratt Impulsiveness Scale is mostly regarded as a measurement of trait rather than state impulsivity, and thus may be less responsive to change (23).

For clinician-rated outcomes, the associations of poor sleep with impulsivity and hostility were less straightforward. We found weak cross-sectional associations, and no longitudinal

associations. These findings are open to several interpretations. First, there could be hardly any "true" association between poor sleep and actually observable measures of aggression in forensic patients. Maybe, the internally experienced aspects of aggression (such as self- reported anger and hostility) relate most clearly to poor sleep quality. In other words, the perception of poor sleep encompasses a large array of experiences that extends beyond the traditional definition of sleep and could thus go hand-and-hand with the perception of higher aggression, as stated previously in this thesis and supported by several previous studies (3,20,24). Second, the measures we employed could be less appropriate for sufficient detection of variations in observed aspects of aggression, possibly leading to an underestimation of the association under study. We used two items from a risk taxation instrument (25), scored on a 5 point-Likert scale, which were not developed nor psychometrically tested for single use. Furthermore, changes in outwardly visible aggressive behavior can be far more subtle than internal experience and could easily go unnoticed when using observer ratings. Taken together, the methodological considerations regarding our results underline the need for more homogeneous and appropriate measurements of both subjective and objective aggression especially in contexts with highly impulsive and aggressive individuals, as recognized by a recent systematic review of studies the association between insomnia and aggression in forensic populations (26).

As the type of aggression mainly studied in this thesis was reactive "hot" aggression, I want to address the association of poor sleep with proactive, instrumental or "cold" aggression to provide a more complete understanding. Research findings on this topic reflect both the distinctions between these subtypes of aggression as well as overlapping aspects. Considering the differences in neurobiological systems involved, it seems likely that poor sleep is otherwise associated to aggression that is characterized by psychopathic features, callousness and low arousal, than to reactive, impulsive aggression. Indeed, a study in prisoners showed that sleep problems were not associated to psychopathic personality traits, such as egocentrism and a lack of empathy (21). Two studies by Denis and colleagues support this observation (27), demonstrating that higher levels of callous-unemotional personality traits were associated with better subjective sleep quality and, even more remarkable, with better objective sleep quality as well. Moreover, higher levels of callousness showed a weaker association of externalizing behavior with poor sleep quality than lower levels. One theory is that the lack of emotional reactivity and guilt, which accompany psychopathic personality traits could protect against sleep disturbances, considering the fact that cognitive and emotional hyperarousal are central to the development and maintenance of insomnia. Evidence from a large twin study confirms that rule-breaking behavior, such as lying or theft, has weak genetic correlations with sleep disturbances, as opposed to more overt aggressive features (28). These studies suggest a differential association of poor sleep with proactive aggression, psychopathic traits and delinquent behavior, compared with reactive, impulsive aggression.

However, as mentioned in Chapter 1 (Box 2), proactive and reactive aggression do have overlapping aspects and can occur at the same time in aggressive individuals (29). Further exploration of mixed features of aggression and their association with poor sleep indeed provides a more nuanced view. A study in male prisoners has shown that poor sleep quality is associated to both emotionally driven (reactive, hot) and planned (proactive, cold)

aggression (3). When looking at associations of sleep problems or short sleep duration with delinquency and criminal behavior, which can include both proactive and reactive aspects, studies show clear associations as well, for example with antisocial behavior, handgun carrying and the likelihood for arrest (30-32). A strictly dichotomous approach to subtypes of aggression in relation to sleep is thus not recommended. This resonates with our research in forensic patients, who often exhibit mixed types of aggression and criminal offences, and frequently experience sleep disturbances, regardless of their specific psychopathology (19,33-35).

In conclusion, sleep relates to several aspects of the highly heterogeneous aggression construct and is therefore a relevant factor to incorporate in theoretical frameworks, clinical management and further research of aggressive behavior. Exploration of aggression in relation to disturbed sleep requires thorough consideration with regard to a dimensional instead of a dichotomous approach of aggressive features and to the use of measures detecting internally experienced or outwardly visible aggression, to optimally address the specific questions under study

Poor sleep and aggression: cause, consequence or common basis? Aspects of etiology

In this section, I would like to elaborate on etiologic aspects, tapping into questions concerning causality and direction of the association between sleep and aggression and address emerging evidence on shared genetic or environmental vulnerabilities.

A key finding from our two meta-analyses is that the association of sleep quality and duration with aggression was more pronounced in populations with psychological vulnerabilities (**Chapter 2 and 3**). This is in accordance with the hypothesis posed by Kamphuis and colleagues that especially individuals with existing dysfunctions in systems involving stress, arousal and inhibition may be more susceptible to the negative effects of sleep disturbances (2). A very recent systematic review on insomnia and aggression, specifically directed at prison and forensic populations, also concludes that the association between sleep and aggressive tendencies is not specific to, but more pronounced in high-risk populations (26). The studies we performed in a sample of forensic psychiatric patients enabled us to explore the association between sleep quality and aggression in more detail in a specific subgroup with known high levels of both disturbed sleep and impulsive and aggressive behavior. The combined results indeed support the vulnerability hypothesis by showing associations between sleep and impulsivity or aggression, which were of equivalent strength as those found in our meta-analyses of populations with psychological vulnerabilities.

Much discussion in this field of research has been focused on the direction of the association between sleep and aggression. Studies directly comparing associations in both directions are scarce, but tend to favor poor sleep to aggravate aggression. For example, two longitudinal studies in children from community samples show that the association of poor sleep with aggressive or externalizing behavior is more pronounced than vice versa (14,36). Meta-analyses on sleep in relation to other forms of psychopathology provide

similar evidence, mostly supporting the hypothesis that poor sleep precedes the onset of several mental health outcomes such as depression, psychosis, alcohol abuse, anxiety disorder, bipolar disorder and suicide (37,38). In addition, experimental work investigating the effects of manipulating the quantity of sleep in both directions, i.e. sleep restriction (8,9) or sleep extension (10), clearly supports causal inference with regard to poor sleep relating to increased aggression. Though aggression, whether in the form of emotional, cognitive are behavioral dysregulation, is very likely to attenuate sleep on a day-to-day basis, this association has received limited research attention thus far (39).

As the exact mechanisms or pathways that link sleep and aggression together are not specifically addressed by the studies in this thesis, I feel somewhat reluctant to speculate much further than what is already outlined in **Chapter 1**. Both possible pathways as well as examples of neurobiological systems involved have been accurately described in previous reviews (1,2). I do, however, want to highlight some emerging evidence on the reciprocal connections of poor sleep with stress and arousal, because of their close association with reactive aggression. For example, Wassing and colleagues demonstrated that the effects of chronic insomnia are not just a matter of lacking healthy sleep's restorative capacities. Insomnia, which is characterized by fragmented and light sleep (See Figure 3), actually worsens the perception of physical distress overnight (40). We know that individuals respond very differently to stressors, whether physical or psychological, and these differences in stress reactivity are considered trait characteristics because of their stability over time and situations (41).

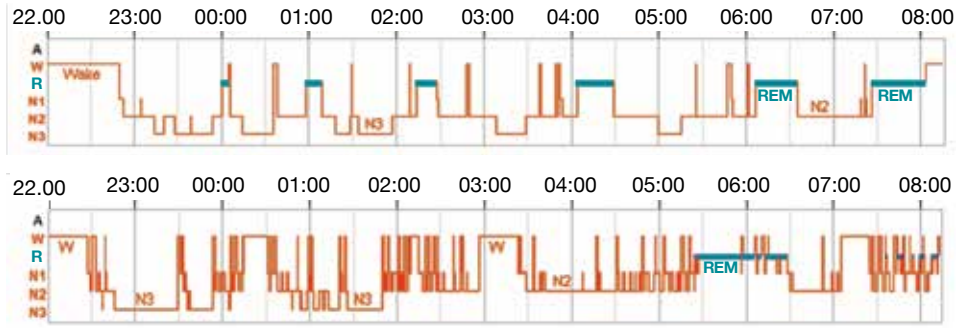

Figure 1. Upper hypnogram indicating sleep stages of a normal sleeper (female, 35 years old). Lower hypnogram indicating sleep stages of a patient with insomnia disorder (female, 39 years old). W = wake; R = REM sleep; N1 / N2 = lighter non-REM sleep; N3 = deep sleep.

The individual responses to stressors take effect on sleep as well as on emotions and cognitions, continuously interacting and contributing to the risk for developing insomnia. High trait responsivity to stress can thus negatively interfere with sleep (known as "sleep reactivity"), with strong cognitive-emotional reactions (like worrying or rumination) further

enhancing the detrimental effects on sleep, which in turn aggravates responses to stress. When combining these research examples, a vicious circle emerges, in which poor sleep and physical, emotional and cognitive arousal can maintain one another in susceptible individuals. Considering the role of stress and arousal in aggression, this theory indeed provides support for the association of poor sleep and aggression in both directions, but still warrants further investigation. This could be of special interest to the forensic psychiatric population, with their high levels of sleep problems (**Chapter 4 and 5**), anger, impulsivity and hostility (42), including high levels of stress (43). Though studies in forensic patients have primarily considered the causal pathway of poor sleep aggravating aggression, it is likely that the reciprocal interactions between poor sleep, stress reactivity and aggressive features described above, play a central role in the psychopathology of forensic patients.

Apart from supporting bidirectional associations between sleep and aggression, the connections addressed in the previous paragraph could also imply the possibility of shared vulnerability or trait characteristics. Several authors in this field have even suggested that the perception of poor sleep, anger and hostility may be regarded expressions of shared genetic bases, as individual differences in these features have shown to be heritable (20,39). This notion has initiated an important shift in research perspective on the association between sleep and aggression over the last decade. Indeed, recent large twin studies have demonstrated a shared genetic basis, with identification of genetic correlations between sleep problems and aggression (28,44). Recent evidence from a genome-wide gene-based association study shows high genetic correlation of insomnia with several psychiatric outcomes (45), though features of aggression or externalizing behavior were not among the available outcomes tested. The strongest correlations were found for anxiety and depression, disorders that are predominantly characterized as internalizing psychopathology in the traditional dichotomy, whereas aggression is usually placed at the other, externalizing, side. However, both anxiety and depressive symptoms are considered important risk markers for aggressive behavior (46,47), and are frequently overlooked in research on aggression. This example shows the need for careful use of dichotomous constructs and illustrates the complexity of interpreting research on underlying mechanisms linking sleep and aggression.

Closely connected to the question whether sleep and aggression are mutually influencing or perhaps both associated to the same vulnerable traits, is our finding that the association of sleep with aggression proved to be largely independent of the general level of psychopathology. In other words: in this forensic population poor sleep and aggression were clearly related, irrespective of co-morbid psychiatric symptoms such as depression, anxiety, distrust or interpersonal sensitivity. We know from previous research that the perception of having slept poorly, even when unjustified, attenuates emotional and cognitive functioning throughout the subsequent day (48). This is likely to lead to a further negative bias of inner experiences, and thus to a general over-reporting of symptoms including features of aggression. This may even be more applicable in this forensic patient group with highly prevalent sleep problems, general psychiatric symptoms and aggression. By adjusting our analyses for general psychopathology, we aimed to correct for an important confounder of the association between sleep and aggression, but at the same time dealt

with the element of perception and possible tendency to inflate symptoms. It is therefore striking that the association of poor sleep with increased aggression was independent of other reported psychopathological symptoms, underlining their unique relation either by a shared underlying vulnerability or through (bidirectional) causal mechanisms still to be explored.

An important aspect which is not addressed by the studies in this thesis, but appears time after time when studying poor sleep, stress reactivity, hyperarousal and aggression, are traumatic experiences. Trauma is increasingly recognized as a transdiagnostic factor that is highly important in development and prognosis of mental health problems (49). Adverse events in childhood as well as continuing victimization contribute to sleep problems (50) and to aggression (49), for example by influencing stress reactivity (51). Trauma must therefore be considered as one of the underlying environmental mechanisms leading to both sleep disturbances and aggression.

To conclude, though disturbed sleep is a contributory causal factor in the occurrence of most mental health conditions, there seems to be a distinct and unique connection between disturbed sleep and features of aggression. This is likely to be the reflection of the complex interplay of a common genetic basis, early environmental factors including adverse childhood experiences, and mutually reinforcing negative effects persisting throughout life, illustrated in Figure 4. Combining these multiple perspectives in clinical practice and future research will hopefully bring this field further forward.

IMPLICATIONS FOR CLINICAL PRACTICE

In this section, I will discuss the broader implications for clinical practice emerging from this thesis, providing several recommendations which may be implemented quite easily in (forensic) psychiatry.

Considering the high prevalence of sleep problems in forensic psychiatric patients and the possible consequences for mental health and especially aggression outlined in the previous paragraphs, it seems almost redundant to stress the importance of screening for sleep disturbances in this particular population. Early detection is crucial to prevent a gradual worsening of both poor sleep and aggressive features. However, we know that sleeping difficulties in forensic patients have often been present for many years, but have neither been noted nor properly addressed despite intensive psychiatric treatment (35). The prolonged admission to a highly regulated environment, such as a closed forensic psychiatric ward usually does not resolve sleep problems. On the contrary, many patients experience an increase in sleep problems due to stress, noise, lack of daytime activity and inability to pursue their own sleep-wake timing preferences.

The use of concise sleep questionnaires combined with simple sleep diaries provides an excellent and easily accessible source of information, quickly discerning good from poor sleepers. The second step is to take sleep complaints seriously, further explore them and consider the need for additional diagnostics. To guarantee this process, staff members should receive proper training on healthy as well as disturbed sleep, including detection of symptoms of specific sleep disorders. Depending on severity and type of sleep problems,

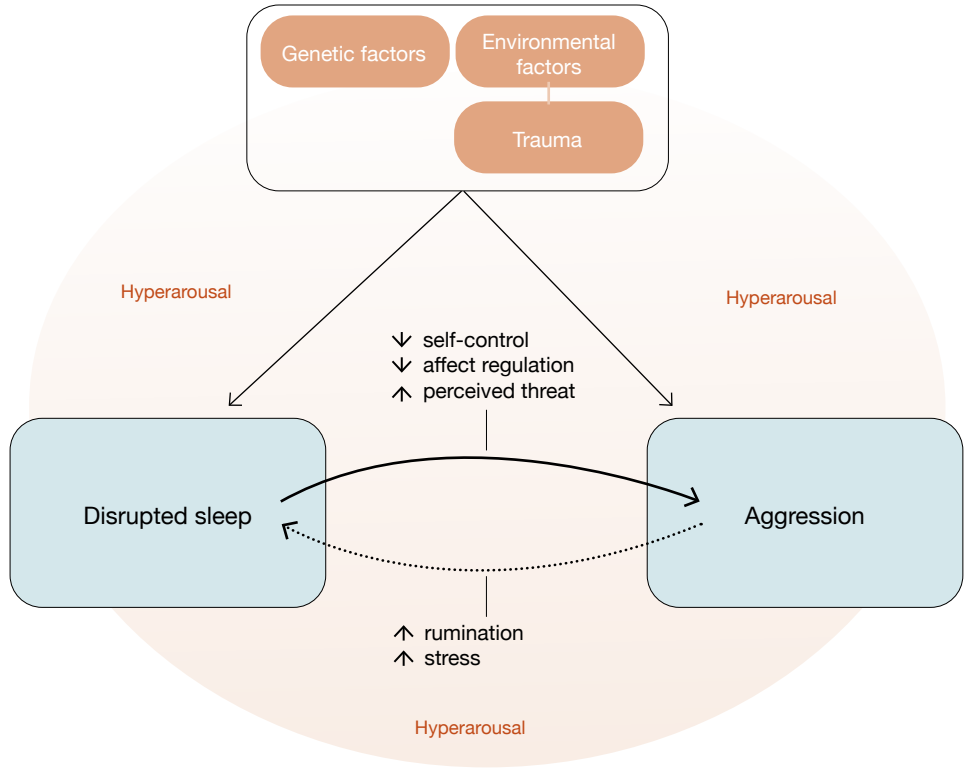

Figure 2. Conceptual model of possible pathways connecting sleep and aggression, including shared etiological factors.

adjustments can be made to treatment goals and referral to a sleep center may be considered. Sleep should thus become part of the standard patient evaluation protocol.

In addition, the relative neglect for sleep problems specifically in forensic patients is striking considering the main priority of forensic psychiatric treatment, which is to reduce the risk of repeated aggression and criminal offenses. Identification of static and dynamic risk factors to predict and prevent recidivism has been the focus of research in forensic psychiatry for many years, but poor sleep has been largely overlooked within this field. This is illustrated by the fact that sleep is not incorporated in standardized risk assessment instruments in forensic psychiatry. A valuable study by Langsrud and colleagues has shown the additional value of adding a sleep variable to the assessment of aggressive behavior, improving the prediction of aggressive incidents in a general psychiatric intensive care unit (52). These results underline the potential of disturbed sleep to serve as an indicator for an elevated risk of aggression and we strongly recommend integrating sleep in revisions of specific forensic risk assessment instruments as well.

Apart from the individual assessment of sleep, careful attention should be directed at the environmental aspects and ward regime of a high security level psychiatric hospital. Much can be gained by ensuring structured sleep-wake cycles, with sufficient exposure to daylight and (outside) activities as well as discouraging bed rest during the day. Other aspects may comprise the reduction of noise, tailored timing of medication administration and optimization of facilities within patients' individual rooms (35). These examples may all contribute to healthier sleep circumstances, directly preventing development or worsening of sleep problems and perhaps indirectly reducing aggressive behaviors.

Treatment of disturbed sleep seems a promising target to reduce aggression, but can also improve general treatment engagement and mental health outcomes (53). Although the actual reduction of aggression via improvement of sleep has not been extensively studied in psychiatric populations, let alone in forensic patients, there are multiple reasons to assume beneficial effects. Several case reports and small sample studies report important decreases in aggressive behavior following treatment of sleep problems or sleep apnea, as previously reviewed (2,54). For example, a group-based cognitive-behavioral sleep intervention improved aggressive behavior in adolescents with high levels of sleep problems and anxiety via improvement of sleep quality (55). Furthermore, habitual short-sleepers have been shown to benefit from extending their sleep duration by approximately one hour, reducing feelings of anger (10). Dewa and colleagues have devoted their research in recent years to assessment and treatment of the high prevalence of disrupted sleep in prisoners, a population to a certain extent comparable to forensic psychiatric patients. They designed a treatment pathway for insomnia in prison, aimed not only to ameliorate sleep but also the likelihood of reoffending and safety of the prison environment (56).

For forensic patients, treatment choices must be made depending on the type and severity of sleep problems. Basic education on sleep-wake regulation and healthy sleep habits could be beneficial for all, but specific sleep disorders require further evaluation and treatment. Because of the high prevalence in forensic psychiatry, we will discuss some aspects of the management of insomnia disorder here, but again, no research to date has been conducted on insomnia treatment in forensic patients. General guidelines for treating chronic insomnia primarily emphasize the use of non-pharmacological interventions, whilst support for pharmacological treatment is only limited to the very short term (3-4 weeks) (57,58). The most widely studied and applied intervention is cognitive behavioral therapy for insomnia or CBT-I (59), a protocol proven feasible and effective in psychiatric populations (60,61). Furthermore, promising research on CBT-I specifically directed at psychiatric inpatients has generated several adaptions to successfully engage patients and integrate sleep in acute psychiatric treatment (62). A pilot study shows encouraging effects on sleep and duration of stay, as well as feasibility (63). Sleep treatment protocols, such as this CBT-I adapted to the inpatient setting, combined with staff involvement and environmental adjustments, could and should be easily translated to forensic psychiatry.

To conclude, I strongly recommend active and systematic screening, diagnosing and targeted treatment of sleep disturbances in the (forensic) psychiatric population, summarized in BOX 3. Though the single contribution of sleep within the context of the many factors involved in aggression may be modest, poor sleep plays a central role in the perpetual circle of emotional reactivity and arousal tying sleep and aggression together. Sleep could be an important modifiable factor for reducing aggression, prevention of recidivism and general treatment outcomes in forensic psychiatry and should therefore be integrated in standard care. This must involve education of professionals in forensic psychiatry about disrupted sleep and the vital role of treatment, to ensure commitment both in individual treatment and environmental adaptations.

BOX 3. RECOMMENDATIONS FOR CLINICAL PRACTICE - IN BRIEF

- Active screening and diagnostic assessment of sleep problems in (forensic) psychiatric patients, striving for early detection
- Integration of sleep in (forensic) risk assessment instruments to predict aggression
- Education of mental health care professionals on assessment and t reatment of sleep disorders
- Optimize psychiatric hospital environments to promote healthy sleep-wake cycles
- Tailored treatment of disrupted sleep, depending on type of sleep disorder, to improve aggression as well as mental health outcomes and treatment engagement

FUTURE RESEARCH AGENDA

It is tempting to complete this thesis with an extensive overview of issues concerning the association of sleep and aggression that are in need of follow-up studies. However, many of the topics that require further exploration have already been addressed in the previous paragraphs, so I will try to summarize these and highlight a few topics that, in my opinion, deserve specific attention. Some of these topics are theoretical, comprising etiologic and methodologic challenges, others are directly addressing clinical practice.

First, when it comes to investigating sleep and aggression, several examples in this thesis stress the need for consensus on the use of instrument types and on proper adjustment for important confounders, especially psychopathology, in statistical analyses. Further examination of the way that distinct features of sleep, including specific sleep disorders, affect different aspects of aggression using prospective designs is warranted, aiming to discern various possible pathways of influence. Other areas that are in certain need of exploration are age and gender differences in the association between sleep and aspects of aggression.

Second, the evaluation of sleep should ideally integrate aspects of quality, duration and timing of sleep. For sleep duration specifically, studies should account for non-linearity of associations with aggression and investigate dose-response effects. A major challenge for sleep research is presented by evolving insights on subjective and objective measurements of sleep quality and their mutual association. Polysomnography (PSG), which has long been the gold standard for evaluating sleep, undoubtedly has worth for diagnosing sleep disorders, such as sleep apnea, but the usually derived sleep parameters show quite some limitations in predicting the subjective perception of sleep (15). Emerging work from several sleep research groups comprises the development of new PSG indicators, which relate more closely to the subjective experience of sleep quality and provide insight in pathophysiology. These comprise, for example, restless REM sleep contributing to hyperarousal (64) and duration of undisturbed sleep at the beginning of the night dictating the perception of sleep onset (65). Such approaches could open up a completely new understanding of aspects of sleep and their relation to psychopathology, including aspects of aggression.

The third topic considers the fact that a more dimensional view on characteristics of those suffering from poor sleep could support a better understanding of the complex association with aggressive features. Here, I want to highlight the work by Blanken and colleagues, displaying various subtypes of insomnia based on a set of variables related to sleep, personality traits and life events (66). Interestingly, several aspects that are known contributors to the risk of aggression, such as emotional reactivity, arousal, rumination and childhood trauma, are among the most discriminating characteristics for insomnia subtype classification. Identification of such phenotypes might not only benefit insight in underlying mechanisms but also guide optimal personalization of treatment, as already explored by this research group. An example indicative of its clinical relevance is that CBT-I was ineffective in a subtype with generally low distress but highly reactive features. Although effective in several populations and settings, a subgroup of patients indeed does not profit sufficiently of standard CBT-I. Subtyping of insomnia could support identification of the need for individual adaptations and precision intervention. Subtyping of aggression may follow a similar approach, being based on larger sets of variables rather than dichotomous categories of reactive and proactive aggression. These should definitely incorporate features of sleep, considering the central role of disturbed sleep in various forms of aggression and externalizing behavior presented in this thesis, as well as indicators of anxiety, depression, hyperarousal and traumatic experiences.

Apart from subtyping, which still withholds some extent of generalization, a fourth topic of future studies is the assessment of daily within-person associations between sleep and aggression. This may help to identify specific aspects connecting both variables and identify underlying mechanisms on a more individual level. Some studies have found that the association between sleep and aggression is mainly dictated by individual night-to-night variations in sleep (67,68). However, structured diary techniques, for example the experience sampling method (ESM), have hardly been applied in forensic psychiatric patients, despite their increasing use in research in general psychiatry (69). By using similar methods, especially when combined with objective information from wearables, variations in experiences can be monitored throughout day and night in a variety of contexts. For forensic psychiatry, this may benefit the previously mentioned individual risk assessments and contribute to more personalized and targeted interventions.

Fifth, treatment of sleep problems as a means to decrease aggression in forensic psychiatric patients has not been explored to date. Considering the notable prevalence of chronic insomnia, high quality controlled trials on the feasibility and possible benefits of CBT-I on sleep and multiple aspects of aggression are warranted in this complex population. We are currently conducting a randomized controlled trial evaluating the effects standard CBT-I on sleep, impulsivity and aggression in forensic psychiatric patients. A specifically strong feature is the use of both subjective and objective measurements of sleep and of impulsivity and aggression. As this trial is still ongoing at the completion of this thesis, we are not able to provide preliminary results. The encouraging results of adapted CBT-I in psychiatric inpatients (63) support further development of this intervention in forensic context. Especially the integration of targeted light/dark exposure to stabilize circadian rhythms seems of interest, considering the link with aggressive and externalizing behavior. This concerns not only an individual adaptation but adjustments in the hospital environment as well. An example of a very practical innovation making use of the environment in psychiatric hospitals is the installation of dynamic light sources. Blue-depleted lighting in the evening is expected to reduce the disruptive effects of artificial light on the circadian system (70). First results are promising, showing clear beneficial effects on sleep and arousal levels. More follow-up studies are expected from this Norwegian research group, on general mental health outcomes as well as the possibility of reducing aggression, which makes it of special interest for application in forensic psychiatric hospitals.

A final and overarching topic is that the potential positive effects of integrated sleep treatment extend beyond aggression and forensic psychiatry to mental health in general. Treatment of sleep disturbances improves mental health difficulties, as shown by multiple studies (71) including a recent meta-analysis (53), underlining the causal role of disrupted sleep in psychiatric symptomatology. This stresses the need for a wide-ranging and transdiagnostic integration of sleep in future mechanistic and intervention research in psychiatry, as advocated by the inclusion of sleep-wake and arousal among the key research domain criteria formulated by the National Institute of Mental Health (72).

CONCLUSION

This thesis aimed to substantiate and refine the association of poor sleep with higher aggression. The results from various study designs confirm this association, with key findings being that the association is stronger in individuals with psychological vulnerabilities and largely independent of general symptoms of psychopathology in forensic psychiatric patients. Several methodological pitfalls have been identified, considering the use of varying measurements of sleep and aggression and the interpretation of statistical analyses. Important topics of discussion are the mechanisms through which sleep and aggression are connected, which has been predominantly focused on the causal direction of poor sleep affecting aggression. However, combining insights from a broad range of research in this field indicates that sleep and aggression are interrelated through a

myriad of factors including genetics, environmental influences and subsequent reciprocal aggravation. Future research could shed more light on such mechanisms, especially when embracing a more dimensional approach to the association between sleep and psychopathology, including aggression.

Although the scientific worth of further disentangling the connection between sleep and aggression is undoubtedly high, the current knowledge as described in this thesis shows already that it is pressingly recommendable to identify and treat sleep problems in psychiatrically vulnerable patients, especially in forensic populations. That involves the structured use of suitable screening instruments, ongoing education of mental health professionals and adjustments to treatment environment. Though experimental work still needs to refine interventions and predictors for effect, restoring sleep seems an important potential strategy to reduce anger, hostility and aggressive behavior.

REFERENCES

(1) Krizan Z, Herlache AD. Sleep disruption and aggression: Implications for violence and its prevention. Psychol Violence 2016 10;6(4):542-552.
(2) Kamphuis J, Meerlo P, Koolhaas JM, Lancel M. Poor sleep as a potential causal factor in aggression and violence. Sleep Med 2012 Apr;13(4):327-334.
(3) Barker LF, Ireland JL, Chu S, Ireland CA. Sleep and its association with aggression among prisoners: Quantity or quality? Int J Law Psychiatry 2016 Jul-Aug;47:115-121.
(4) Tsuchiyama K, Terao T, Wang Y, Hoaki N, Goto S. Relationship between hostility and subjective sleep quality. Psychiatry Res 2013 Oct 30;209(3):545-548.
(5) James S, Hale L. Sleep duration and child well-being: a nonlinear association. Journal of Clinical Child & Adolescent Psychology 2017;46(2):258-268.
(6) Fuligni AJ, Arruda EH, Krull JL, Gonzales NA. Adolescent sleep duration, variability, and peak levels of achievement and mental health. Child Dev 2018;89(2):e18-e28.
(7) Vaughn MG, Salas-Wright CP, White NA, Kremer KP. Poor sleep and reactive aggression: Results from a national sample of African American adults. J Psychiatr Res 2015 Jul-Aug;66-67:54-59.
(8) Krizan Z, Hisler G. Sleepy anger: Restricted sleep amplifies angry feelings. J Exp Psychol Gen 2018 Oct 25.
(9) Baum KT, Desai A, Field J, Miller LE, Rausch J, Beebe DW. Sleep restriction worsens mood and emotion regulation in adolescents. Journal of Child Psychology and Psychiatry 2014;55(2):180-190.
(10) Van Dyk TR, Zhang N, Catlin PA, Cornist K, McAlister S, Whitacre C, et al. Feasibility and emotional impact of experimentally extending sleep in short-sleeping adolescents. Sleep 2017;40(9).
(11) Riemann D, Spiegelhalder K, Feige B, Voderholzer U, Berger M, Perlis M, et al. The hyperarousal model of insomnia: a review of the concept and its evidence. Sleep medicine reviews 2010;14(1):19-31.
(12) El-Sheikh M, Saini EK, Gillis BT, Kelly RJ. Interactions between sleep duration and quality as predictors of adolescents' adjustment. Sleep Health 2019;5(2):180-186.
(13) Hsiao F, Tsai P, Wu CW, Yang C, Lane TJ, Lee H, et al. The neurophysiological basis of the discrepancy between objective and subjective sleep during the sleep onset period: an EEG-fMRI study. Sleep 2018;41(6):zsy056.
(14) Kelly RJ, El-Sheikh M. Reciprocal relations between children's sleep and their adjustment over time. Dev Psychol 2014;50(4):1137-1147.
(15) Kaplan KA, Hirshman J, Hernandez B, Stefanick ML, Hoffman AR, Redline S, et al. When a gold standard isn't so golden: Lack of prediction of subjective sleep quality from sleep polysomnography. Biol Psychol 2017 Feb;123:37-46.
(16) Taylor BJ, Hasler BP. Chronotype and mental health: recent advances. Curr Psychiatry Rep 2018;20(8):1-10.
(17) Schlarb AA, Sopp R, Ambiel D, Grünwald J. Chronotype-related differences in childhood and adolescent aggression and antisocial behavior–A review of the literature. Chronobiol Int 2014;31(1):1-16.
(18) Deibel SH, McDonald RJ, Kolla NJ. Are owls and larks different when it comes to aggression? Genetics, neurobiology, and behavior. Frontiers in behavioral neuroscience 2020;14:39.
(19) Kamphuis J, Dijk DJ, Spreen M, Lancel M. The relation between poor sleep, impulsivity and aggression in forensic psychiatric patients. Physiol Behav 2014 Jan 17;123:168-173.
(20) Ireland JL, Culpin V. The relationship between sleeping problems and aggression, anger, and impulsivity in a population of juvenile and young offenders. Journal of Adolescent Health 2006 6;38(6):649-655.
(21) Harty L, Duckworth R, Thompson A, Stuewig J, Tangney JP. Are inmates' subjective sleep problems associated with borderline personality, psychopathy, and antisocial personality independent of depression and substance dependence? J Forens Psychiatry Psychol 2010 Feb 1;21(1):23-39.
(22) Keller PS, Haak EA, DeWall CN, Renzetti C. Poor Sleep Is Associated With Greater Marital Aggression: The Role of Self Control. Behav Sleep Med 2017 Apr 18:1-8.
(23) Stanford MS, Mathias CW, Dougherty DM, Lake SL, Anderson NE, Patton JH. Fifty years of the Barratt Impulsiveness Scale: An update and review. Personality and Individual Differences 2009;47:385-395.
(24) Taylor ND, Fireman GD, Levin R. Trait hostility, perceived stress, and sleep quality in a sample of normal sleepers. Sleep Disord 2013;2013:735812.
(25) Canton WJ, Van Der Veer TS, Van Panhuis PJA, Verheul R, Van Den Brink W. The predictive validity of risk assessment in 'pro justitia' reports. A study of the hkt-30 and clinical assessment. Tijdschrift voor Psychiatrie (Dutch) 2004;46:537-542.
(26) Sarzetto A, Bosia M, Pasqualoni E, Travaini G. Eyes wide open: A systematic review of the association between insomnia and aggression in forensic contexts. Int J Law Psychiatry 2021;78:101734.
(27) Denis D, Akhtar R, Holding BC, Murray C, Panatti J, Claridge G, et al. Externalizing Behaviors and Callous-Unemotional Traits: Different Associations With Sleep Quality. Sleep 2017 Aug 1;40(8):10.1093/sleep/zsx070.
(28) Madrid-Valero JJ, Ordoñana JR, Klump KL, Burt SA. Children sleep and antisocial behavior: Differential association of sleep with aggression and rule-breaking. J Abnorm Child Psychol 2019;47(5):791-799.
(29) Waltes R, Chiocchetti AG, Freitag CM. The neurobiological basis of human aggression: a review on genetic and epigenetic mechanisms. American Journal of Medical Genetics Part B: Neuropsychiatric Genetics 2016;171(5):650-675.
(30) Chang L, Wu W, Wu C, Lin LN, Yen L, Chang H. The role of sleep problems in the relationship between peer victimization and antisocial behavior: A five-year longitudinal study. Soc Sci Med 2017;173:126-133.
(31) Meldrum RC, Jackson DB, Zgoba K, Testa A. Sleep duration, handgun carrying, and taking a handgun to school: An analysis of a statewide sample of Florida youth. Sleep health 2020;6(2):153-158.
(32) Partin RD, Lehmann PS. The Association Between Sleep Duration and Arrest Among Adolescents. Crime & Delinquency 2021:00111287211047532.
(33) Van Veen MM, Karsten J, Lancel M. Poor Sleep and Its Relation to Impulsivity in Patients with Antisocial or Borderline Personality Disorders. Behav Med 2017 Jul-Sep;43(3):218-226.

(34) Van Veen MM, Karsten J, Verkes R, Lancel M. Sleep quality is associated with aggression in forensic psychiatric patients, independent of general psychopathology. The Journal of Forensic Psychiatry & Psychology 2020;31(5):699-713.
(35) Mijnster T, Boersma G, Engberts J, Vreugdenhil-Becherer L, Keulen-de Vos M, de Vogel V, et al. Lying awake in forensic hospitals: a multicenter, cross-sectional study on the prevalence of insomnia and contributing factors in forensic psychiatric patients. The Journal of Forensic Psychiatry & Psychology 2022:1-19.
(36) Gregory AM, O'Connor TG. Sleep problems in childhood: a longitudinal study of developmental change and association with behavioral problems. J Am Acad Child Adolesc Psychiatry 2002 Aug;41(8):964-971.
(37) Hertenstein E, Feige B, Gmeiner T, Kienzler C, Spiegelhalder K, Johann A, et al. Insomnia as a predictor of mental disorders: A systematic review and meta-analysis. Sleep Med Rev 2018 Nov 16;43:96-105.
(38) Pigeon WR, Bishop TM, Krueger KM. Insomnia as a precipitating factor in new onset mental illness: a systematic review of recent findings. Curr Psychiatry Rep 2017;19(8):1-11.
(39) Hisler G, Krizan Z. Anger tendencies and sleep: Poor anger control is associated with objectively measured sleep disruption. Journal of Research in Personality 2017;71:17-26.
(40) Wassing R, Benjamins JS, Talamini LM, Schalkwijk F, Van Someren EJ. Overnight worsening of emotional distress indicates maladaptive sleep in insomnia. Sleep 2019;42(4):zsy268.
(41) Kalmbach DA, Cuamatzi-Castelan AS, Tonnu CV, Tran KM, Anderson JR, Roth T, et al. Hyperarousal and sleep reactivity in insomnia: current insights. Nature and science of sleep 2018;10:193.
(42) Tuente SK, Bogaerts S, Veling W. Mapping aggressive behavior of forensic psychiatric inpatients with self-report and structured staff-monitoring. Psychiatry Res 2021;301:113983.
(43) Nigel SM, Streb J, Leichauer K, Hennig B, Otte S, Franke I, et al. The role of psychopathic personality traits in current psychological and physiological subclinical stress levels of forensic inpatients: a path analysis. International Journal of Forensic Mental Health 2019;18(2):164-177.
(44) Krizan Z, Hisler G, Krueger RF, McGue M. Why is personality tied to sleep quality? A biometric analysis of twins. Journal of Research in Personality 2021;90:104048.
(45) Hammerschlag AR, Stringer S, De Leeuw CA, Sniekers S, Taskesen E, Watanabe K, et al. Genome-wide association analysis of insomnia complaints identifies risk genes and genetic overlap with psychiatric and metabolic traits. Nat Genet 2017;49(11):1584-1592.
(46) Dutton DG, Karakanta C. Depression as a risk marker for aggression: A critical review. Aggression and Violent Behavior 2013;18(2):310-319.
(47) Granic I. The role of anxiety in the development, maintenance, and treatment of childhood aggression. Dev Psychopathol 2014;26(4pt2):1515-1530.
(48) Draganich C, Erdal K. Placebo sleep affects cognitive functioning. Journal of Experimental Psychology: Learning, Memory, and Cognition 2014;40(3):857.

(49) Hughes K, Bellis MA, Hardcastle KA, Sethi D, Butchart A, Mikton C, et al. The effect of multiple adverse childhood experiences on health: a systematic review and meta-analysis. The Lancet Public Health 2017;2(8):e356-e366.
(50) Testa A, Semenza DC, Jackson DB. Violent victimisation trajectories from adolescence through adulthood: consequences for sleep problems. J Epidemiol Community Health 2022;76(2):140-145.
(51) Ivanov I, Yehuda R, Greenblatt E, Davidow J, Makotkine I, Alfi L, et al. The effect of trauma on stress reactivity in aggressive youth. Psychiatry Res 2011;189(3):396-402.
(52) Langsrud K, Vaaler A, Morken G, Kallestad H, Almvik R, Palmstierna T, et al. The predictive properties of violence risk instruments may increase by adding items assessing sleep. Frontiers in psychiatry 2019;10:323.
(53) Scott AJ, Webb TL, Martyn-St James M, Rowse G, Weich S. Improving sleep quality leads to better mental health: A meta-analysis of randomised controlled trials. Sleep medicine reviews 2021;60:101556.
(54) Lee EK, Douglass AB. Sleep in psychiatric disorders: where are we now? The Canadian Journal of Psychiatry 2010;55(7):403-412.
(55) Blake MJ, Snoep L, Raniti M, Schwartz O, Waloszek JM, Simmons JG, et al. A cognitive-behavioral and mindfulness-based group sleep intervention improves behavior problems in at-risk adolescents by improving perceived sleep quality. Behav Res Ther 2017;99:147-156.
(56) Dewa LH, Hassan L, Shaw J, Senior J. Design of a treatment pathway for insomnia in prison settings in England: a modified Delphi study. BMJ open 2018;8(8):e022406.
(57) Qaseem A, Kansagara D, Forciea MA, Cooke M, Denberg TD, Clinical Guidelines Committee of the American College of Physicians. Management of Chronic Insomnia Disorder in Adults: A Clinical Practice Guideline From the American College of Physicians. Ann Intern Med 2016 Jul 19;165(2):125-133.
(58) Riemann D, Baglioni C, Bassetti C, Bjorvatn B, Dolenc Groselj L, Ellis JG, et al. European guideline for the diagnosis and treatment of insomnia. J Sleep Res 2017;26(6):675-700.
(59) Perlis ML. Cognitive Behavioral Treatment of Insomnia – a session-by-session guide. 2005;New York.
(60) Wu JQ, Appleman ER, Salazar RD, Ong JC. Cognitive Behavioral Therapy for Insomnia Comorbid With Psychiatric and Medical Conditions: A Meta-analysis. JAMA Intern Med 2015 Sep;175(9):1461-1472.
(61) Taylor DJ, Pruiksma KE. Cognitive and behavioural therapy for insomnia (CBT-I) in psychiatric populations: a systematic review. Int Rev Psychiatry 2014 Apr;26(2):205-213.
(62) Sheaves B, Isham L, Bradley J, Espie C, Barrera A, Waite F, et al. Adapted CBT to Stabilize Sleep on Psychiatric Wards: a Transdiagnostic Treatment Approach. Behav Cogn Psychother 2018 Nov;46(6):661-675.
(63) Sheaves B, Freeman D, Isham L, McInerney J, Nickless A, Yu LM, et al. Stabilising sleep for patients admitted at acute crisis to a psychiatric hospital (OWLS): an assessor-blind pilot randomised controlled trial. Psychol Med 2018 Jul;48(10):1694-1704.

(64) Riemann D, Spiegelhalder K, Nissen C, Hirscher V, Baglioni C, Feige B. REM sleep instability–a new pathway for insomnia? Pharmacopsychiatry 2012;45(05):167-176.
(65) Hermans LW, Leufkens TR, van Gilst MM, Weysen T, Ross M, Anderer P, et al. Sleep EEG characteristics associated with sleep onset misperception. Sleep Med 2019;57:70-79.
(66) Blanken TF, Benjamins JS, Borsboom D, Vermunt JK, Paquola C, Ramautar J, et al. Insomnia disorder subtypes derived from life history and traits of affect and personality. The Lancet Psychiatry 2019;6(2):151-163.
(67) Lemola S, Schwarz B, Siffert A. Interparental conflict and early adolescents' aggression: Is irregular sleep a vulnerability factor? J Adolesc 2012;35(1):97-105.
(68) Langsrud K, Kallestad H, Vaaler A, Almvik R, Palmstierna T, Morken G. Sleep at night and association to aggressive behaviour; Patients in a Psychiatric Intensive Care Unit. Psychiatry Res 2018 Mar 6.
(69) Habets P, Delespaul P, Jeandarme I. The Importance of Context: An ESM Study in Forensic Psychiatry. Int J Offender Ther Comp Criminol 2022;66(1):84-97.
(70) Vethe D, Scott J, Engstrøm M, Salvesen Ø, Sand T, Olsen A, et al. The evening light environment in hospitals can be designed to produce less disruptive effects on the circadian system and improve sleep. Sleep 2021;44(3):zsaa194.
(71) Freeman D, Sheaves B, Waite F, Harvey AG, Harrison PJ. Sleep disturbance and psychiatric disorders. The Lancet Psychiatry 2020;7(7):628-637.
(72) Kozak MJ, Cuthbert BN. The NIMH research domain criteria initiative: background, issues, and pragmatics. Psychophysiology 2016;53(3):286-297.

ACHTERGROND

Goed slapen is belangrijk voor onze geestelijke gezondheid. We weten uit eerder onderzoek dat slaapverstoring een negatieve invloed heeft op de wijze waarop emoties worden gereguleerd, op het cognitief functioneren en op zelfcontrole. Er zijn vele manieren waarop slaap in het gedrang kan komen, variërend van te kort slapen of voorbijgaande klachten van slecht slapen tot aan slaapstoornissen zoals chronische insomnie, slaap apneu of rusteloze benen syndroom. Allen hebben op specifieke wijze en in meer of mindere mate invloed op het psychisch functioneren.

Er bestaat een grote overlap in de neurobiologische systemen en processen die betrokken zijn bij slaapregulatie en bij het ontstaan van psychopathologie. Het is dan ook niet verrassend dat verstoorde slaap en psychiatrische aandoeningen vaak samen voorkomen. Er is lang gedacht dat slaapproblemen enkel een symptoom of gevolg waren van psychiatrische aandoeningen. Inmiddels is echter duidelijk dat slecht slapen ook een risicofactor is voor het ontstaan en beloop van psychiatrische aandoeningen. Dit pleit voor gerichte aandacht voor de behandeling van slaapstoornissen, in het bijzonder in de psychiatrie.

Omdat steeds duidelijker is geworden hoe belangrijk de rol van slaap is in het reguleren van emoties en gedrag, is er ook meer aandacht ontstaan voor slaap als mogelijke risicofactor voor agressie. Agressie is een complex en breed begrip dat vele aspecten kan omvatten; van boosheid, vijandigheid en opvliegend gedrag tot aan fysieke agressie. Tot op zekere hoogte is agressie een normaal facet van menselijk gedrag, maar het wordt een probleem als het te vaak, te snel of in niet-passende situaties optreedt. Er zijn vele factoren die een rol spelen in problematische agressie, zowel dynamische factoren zoals stemming en impulsiviteit, evenals meer statische factoren zoals persoonlijkheid en ingrijpende (jeugd) ervaringen. Risicofactoren voor agressie, zoals boosheid of verminderde zelfcontrole, komen vaak voor bij mensen met psychiatrische aandoeningen en dragen bij aan het vaker optreden van agressief gedrag in deze groep. Gezien de grote impact van agressie is het van belang om risicofactoren tijdig te onderkennen en, zo mogelijk, te beïnvloeden. Slecht slapen zou hiervoor een concreet aanknopingspunt kunnen bieden.

Zowel in de algemene bevolking als bij mensen met psychische klachten, waaronder forensisch psychiatrisch patiënten, is het verband tussen slecht slapen en agressie eerder onderzocht en vastgesteld. Daarbij laten meerdere kleine onderzoeken zien dat het behandelen van slaapproblemen agressief gedrag kan verminderen. Hoewel het verband tussen slaap en agressie waarschijnlijk beide richtingen opgaat, lijkt onderzoek tot nu toe erop te wijzen dat slecht slapen sterker leidt tot agressie dan dat dit andersom het geval is. Er zijn meerdere theorieën over de mogelijke manieren waarop verstoorde slaap kan leiden tot meer agressie. Als het gaat om mechanismen wordt gedacht aan het versterken van negatieve emotionele reacties, een toegenomen ervaring van vermeende dreiging en het verlies van zelfcontrole. Als het gaat om onderliggende neurobiologische processen zijn er aanwijzingen dat het serotonerge systeem en de hypofyse-bijnier-as betrokken zijn bij het negatieve effect van verstoorde slaap op agressie. Verder is veel onderzoek gedaan naar de prefrontale cortex, een hersengebied dat erg gevoelig is voor slaapverstoring en als gevolg daarvan zijn regulerende werking verliest over emoties en gedrag. Personen

met al bestaande afwijkingen of gevoeligheden in de genoemde processen zouden wel eens extra gevoelig kunnen zijn voor de gevolgen van slecht slapen, de zogenaamde kwetsbaarheidshypothese, maar dat is bij mensen nog niet goed onderzocht. Al met al lijkt het beschikbare bewijs erop te wijzen dat slaap een belangrijke aanvullende factor zou kunnen zijn in het behandelen van agressie. Dat geldt misschien nog wel in het bijzonder voor de (forensische) psychiatrische populatie, waar al frequent sprake is van slaapproblemen, impulsief gedrag en agressie.

In dit proefschrift heb ik geprobeerd de kennis over het verband tussen slaap en agressie verder te verdiepen en uit te breiden. Het doel van het eerste deel van mijn proefschrift was om een systematisch overzicht te geven van al het beschikbare observationele en experimentele onderzoek naar het verband tussen slaap en agressie, waar mogelijk aangevuld met een samengevoegde analyse van de resultaten. Daarbij werd onderzocht welke factoren mogelijk van invloed zijn op dit verband, zoals verschillen in leeftijd of populatie. In het tweede gedeelte van mijn proefschrift werd het verband tussen slaap en agressie verder bestudeerd in een kwetsbare doelgroep, namelijk patiënten in de forensische psychiatrie. Het doel was om verschillende componenten van impulsiviteit en agressie te onderzoeken en de rol van het algemeen niveau van psychische klachten in het verband tussen slaap en agressie vast te stellen. Tot slot onderzochten we in deze groep ook het longitudinale verband tussen slaap, impulsiviteit en agressie.

BELANGRIJKSTE BEVINDINGEN

In het eerste deel van dit proefschrift werden twee systematische reviews en meta-analyses beschreven. De review in Hoofdstuk 2 richtte zich op het observationeel onderzoek naar het verband tussen slaapkwaliteit en agressie. Gezamenlijk bevestigden de gevonden onderzoeken consistent het verband tussen slaapkwaliteit en agressie. De resultaten waren erg heterogeen, wat een gevolg is van het includeren van studies met een breed scala aan soorten definities en metingen van slaap en agressie, als ook verschillende populaties. Aanvullende analyses lieten zien dat het verband tussen slechte slaapkwaliteit en agressie sterker is bij mensen met een psychologische kwetsbaarheid of comorbide somatische aandoening. Ook vonden we dat zelfrapportage van slaapkwaliteit een sterker verband had met agressie dan objectieve metingen door middel van activiteitenmeters. Kwaliteit van de studie of leeftijdsgroep hadden geen effect op het verband. In Hoofdstuk 3 werden de resultaten van het systematisch overzicht van observationeel en experimenteel onderzoek naar het verband tussen slaapduur en agressie weergegeven. De analyse van observationele studies liet een duidelijk, maar bescheiden, verband zien tussen kortere slaapduur met meer agressie. De resultaten lieten een hoge mate van heterogeniteit zien, samenhangend met het meenemen van veel verschillende soorten onderzoeken. De experimentele studies wisselden enigszins in hun resultaten, maar lieten ook overwegend zien dat een kortere slaapduur geassocieerd was met meer agressie. Uit aanvullende analyses van de samengevoegde observationele studies kwam naar voren dat het verband sterker was bij mensen met een psychologische kwetsbaarheid en bij jongere leeftijdsgroepen. Ook hier werd gezien dat zelfrapportage van slaapduur een sterker verband had met agressie dan objectieve metingen door middel van bewegingsmeters.

Deze beide hoofdstukken samen vormen een duidelijke wetenschappelijke basis voor het verband tussen slaap en agressie. Belangrijk is dat, vanwege de grote heterogeniteit van de resultaten, de uiteindelijke gevonden effecten niet als een absolute maat gezien moeten worden, maar als indicatie voor de sterkte van het verband. Een voordeel van de heterogeniteit is dat met aanvullende analyses, juist in zo'n breed scala aan studies, goed onderzocht kan worden welke factoren van invloed zijn op het verband tussen slaap en agressie. Daarmee betreft het twee methodologisch goed uitgevoerde en omvangrijke reviews die waardevolle informatie opleveren. Er is een duidelijk verband tussen slaapkwaliteit en slaapduur enerzijds en agressie anderzijds, en het nog beperkte experimentele onderzoek ondersteunt de mogelijke impact van het gericht aanpakken van slecht of kort slapen in het voorkomen en behandelen van agressie, met name in psychisch kwetsbare doelgroepen.

Het tweede deel van het proefschrift beschreef de resultaten van drie studies naar het verband tussen slaap, impulsiviteit en agressie bij patiënten in de forensische psychiatrie. Hoofdstuk 4 liet zien dat slaapproblemen veel voorkomen bij forensische patiënten met antisociale of borderline persoonlijkheidsstoornissen of trekken daarvan. We vonden dat deze slaapproblemen een verband hadden met de mate van impulsiviteit. Dat verband was niet afhankelijk van andere psychiatrische diagnosen zoals een stoornis in het gebruik van middelen of een stemmingsstoornis. Dit aspect werd verder onderzocht in hoofdstuk 5, waarin het verband tussen slaapkwaliteit en agressie werd onderzocht. In dit hoofdstuk werd gekeken naar patiënten met allerlei verschillende diagnoses en hebben we de analyses gecorrigeerd voor een continue maat van algemene psychopathologie. Slechte slaapkwaliteit was geassocieerd met een hogere mate van zowel zelf gerapporteerde als geobserveerde agressie. Opvallend was, dat het verband ook statistisch aantoonbaar bleef na aanpassing voor de mate van psychopathologie. Voortbouwend op deze cross-sectionele bevindingen wilden we ook het longitudinale verband tussen slaap, impulsiviteit en agressie bekijken door middel van een auto-regressieve analyse, hetgeen wordt beschreven in hoofdstuk 6. Slechte slaapkwaliteit was geassocieerd met een toename van agressie over een jaar tijd, en opnieuw zagen we dat algemene psychopathologie geen invloed had op dit verband. Veranderingen in impulsiviteit of in geobserveerde agressie werden niet voorspeld door slechte slaapkwaliteit, een bevinding die mogelijk gekleurd is door eigenschappen van de gebruikte meetinstrumenten.

Door het onderzoeken van een cohort van forensisch psychiatrische patiënten, konden we het verband tussen slaap, impulsiviteit en agressie bekijken in een specifieke doelgroep die bekend is door een aanzienlijke mate van problemen rond slaap en rond impulsief en agressief gedrag. Gebruik maken van gegevens uit bestaande metingen naar behandeleffect heeft als nadeel dat er altijd enige selectie optreedt, in dit geval van patiënten die niet mee konden of wilden deelnemen aan het onderzoek. Daarnaast waren sommige eigenschappen, zoals content validiteit en gevoeligheid voor verandering, van de meetinstrumenten die gebruik werden in dit cohort niet allen even optimaal voor het kunnen beantwoorden van onze onderzoeksvragen. We kunnen daarnaast geen harde uitspraken doen over causaliteit door de beperkte beschikbaarheid van longitudinale gegevens. Sterke punten van deze studies zijn de correctie voor belangrijke factoren van invloed en de longitudinale analyse, naast de uitvoering in een goed omschreven cohort van patiënten met complexe psychopathologie. Samen bevestigen zij het verband tussen slecht slapen en agressie in een psychiatrische populatie. Deze studies ondersteunen de kwetsbaarheidshypothese en geven daarnaast aanwijzingen voor het mogelijke belang van het behandelen van slaapproblemen in het verminderen van agressie bij (forensisch) psychiatrische patiënten.

SAMENVATTING EN CONCLUSIE

Met dit proefschrift beoogden we om het verband tussen slecht slapen en agressie te onderbouwen en verder te verfijnen. De resultaten van de verschillende onderzoeken bevestigen dit verband, met als belangrijkste bevindingen dat het verband meer uitgesproken is bij mensen met een psychologische kwetsbaarheid en dat het, bij patiënten in de forensische psychiatrie, grotendeels onafhankelijk is van algemene symptomen van psychopathologie. We kwamen meerdere methodologische valkuilen tegen, met betrekking tot de instrumenten om slaap en agressie te meten en de interpretatie van statistische analyses. De mechanismen die slaap verbinden met agressie blijven een belangrijk punt van discussie, met name omdat veel onderzoek tot nu toe er van uit ging dat slecht slapen een toename van agressie veroorzaakt. Nieuwe inzichten uit dit onderzoeksveld wijzen er echter op dat slaap en agressie op meerdere manieren met elkaar verbonden zijn, waaronder door een gedeelde genetische aanleg, omgevingsfactoren en vervolgens een aanhoudende wederzijdse negatieve invloed.

Hoewel het verder in kaart brengen van het verband tussen slaap en agressie zeker van wetenschappelijke waarde is, laat de kennis die uit dit proefschrift naar voren komt al zien dat het dringend aan te bevelen is om slaapproblemen actief op te sporen en gericht te behandelen bij mensen met psychische klachten, in het bijzonder bij patiënten in de forensische psychiatrie. Dat betekent het implementeren van gestructureerde screening, doorlopende scholing van professionals in de geestelijke gezondheidszorg en aanpassing van (klinische) behandelingen. Hoewel experimenteel onderzoek de mogelijke behandelingen en voorspellers voor het effect daarvan nog verder moet verfijnen, wijst veel er op dat herstel van slaap een belangrijk behandeldoel zou kunnen zijn bij het verminderen van woede, vijandigheid en agressief gedrag.

Het heeft vele jaren geduurd voordat ik mijn lang sluimerende belangstelling voor wetenschap om kon zetten in een besluit te willen promoveren. Daar moesten aardig wat persoonlijke en praktische drempels voor worden overwonnen. Ik wil dan ook beginnen met het bedanken van mensen die in verschillende voorgaande perioden mij hebben gestimuleerd om dit traject aan te gaan.

Om te beginnen Wijbrand Hoek, mijn opleider in de psychiatrie vanaf 2003. Je hebt de gave om de talenten van velen om je heen tot bloei te laten komen, zo bleek te meer op jouw afscheidssymposium in juni 2022. Jij moedigde ook mij al vroeg aan te gaan promoveren, ik had echter zelf wat meer tijd nodig om uiteindelijk die weg te vinden.

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En dan begint het…

Marike, ik weet nog precies waar we waren toen je voor het eerst polste of ik belangstelling had voor een promotietraject. De timing had niet beter kunnen zijn. Ook op de inhoud klikte het direct, want slaaponderzoek had al lange tijd mijn belangstelling. Ik wil je bedanken voor jouw begeleiding: je brede kennis van het veld, de ruimte die je me geboden hebt om dit traject zelf vorm te geven, je geduld met al mijn omwegen, je ondersteuning op lastige momenten en, tot slot, de ongekende snelheid waarmee je altijd reageert als er weer iets nagelezen moest worden.

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Femke, wat een mooie weg hebben we al bewandeld! Je was mijn stage begeleider in de Master Epidemiologie en je hebt volgens mij niet geaarzeld toen ik je vroeg mijn copromotor te worden. Ik heb ontzettend veel van je geleerd, zowel inhoudelijk als over diverse processen in de wetenschap. Je hebt me gesteund op moeilijke momenten, vooral door zaken direct te normaliseren en kaderen. Hoe fijn is het, om inspiratie, drive en kennis te delen, en elkaar daarin te versterken. Synergie in optima forma, en wat mij betreft nog lange tijd.

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Maaike van Veen was born on June 2, 1976, in The Hague, The Netherlands. After finishing her secondary education in 1994, she started studying medicine at Leiden University. She completed her medical internships in 2001 and obtained her medical degree *cum laude*. After that, she started working in different medical disciplines, including internal and emergency medicine, and finally, in psychiatry. She entered the psychiatry residency program of the Haags Leids Opleidings Consortium (HLOCP) in 2003, under the primary supervision of prof. dr. H. Wijbrand Hoek. During her residency training she developed an interest for scientific work, specifically on the role of sleep and circadian rhythm in psychiatric disorders. After finishing her psychiatric training in 2009, Maaike worked as a psychiatrist at several in- and outpatient departments, first at PsyQ The Hague and later on at GGZ Drenthe Mental Health Institute. In 2016 she started her PhD project under supervision of prof. dr. Marike Lancel. At the same time she started a Master study in Epidemiology at VU University Medical Centre in Amsterdam, under supervision of prof. dr. Jos W. R. Twisk. In 2019, she obtained the Master of Science degree in Epidemiology *cum laude*. She currently works as a psychiatrist and researcher at the Centre of Expertise on Sleep and Psychiatry, at GGZ Drenthe Mental Health Institute in Assen, The Netherlands.

IN ENGLISH:

Van Veen MM, Lancel M, Sener O, Verkes RJ, Bouman E, Rutters F. Observational and experimental studies on sleep duration and aggression: a systematic review and meta-analysis. Sleep Medicine Reviews 64 (2022) 101661.

Lancel M, van Marle HJ, Van Veen MM, van Schagen AM. Disturbed sleep in PTSD: thinking beyond nightmares. Front. Psychiatry 12:767760.

Schipper SB, Van Veen MM, Elders PJ, van Straten A, Van Der Werf YD, Knutson KL, Rutters F. Sleep disorders in people with type 2 diabetes and associated health outcomes: a review of the literature. Diabetologia 2021, 1-11.

Van Veen MM, Lancel M, Beijer E, Remmelzwaal S, Rutters F. The association of sleep quality and aggression: a systematic review and meta-analysis of observational studies. Sleep Medicine Reviews 59 (2021) 101500.

Ter Heege FM, Mijnster T, van Veen MM, Pijnenborg GHM, de Jong PJ, Boersma GJ, Lancel M. The clinical relevance of early identification and treatment of sleep disorders in mental health care: protocol of a randomized control trial. BMC Psychiatry 2020, 20(1):331.

Van Veen MM, Rutters F, Spreen M, Lancel M. Poor sleep quality at baseline is associated with increased aggression over one year in forensic psychiatric patients. Sleep Med 2020, 67: 1-6.

Van Veen MM, Karsten J, Verkes RJ, Lancel M. Sleep quality is associated with aggression in forensic psychiatric patients, independent of general psychopathology. The Journal of Forensic Psychiatry & Psychology 2020, 31:5: 699-713.

Van Veen MM, Karsten J, Lancel M. Poor sleep and its relation to impulsivity in patients with antisocial or borderline personality disorders. Behav Med 2017, 43(3):218-226.

Van Veen MM, Kooij JJS, Boonstra AM, Gordijn MCM, Van Someren EJW (2010). Delayed circadian rhythm in adults with ADHD and chronic sleep onset insomnia. Biological Psychiatry 2010:1;67(11): 1091-6.

IN DUTCH:

Lancel M, Ensing I, van Veen M. “Slaap” in Leefstijlpsychiatrie, eds. Cahn W, Deenik J, Vermeulen J. Bohn Stafleu van Loghum, Houten 2022.

Lancel M, van Veen M & Kamphuis J. Slaapstoornissen in de psychiatrie: Diagnose en behandeling, Bohn Stafleu van Loghum, Houten 2020.

De Weerd A, van Veen M. “Hypersomnie” in Slaapstoornissen in de psychiatrie: Diagnose en behandeling, eds. M. Lancel, M. van Veen & J. Kamphuis, Bohn Stafleu van Loghum, Houten 2020, 85-104.

Van Veen M, Risselada R. “Middelgerelateerde en verslavingsstoornissen” in Slaapstoornissen in de psychiatrie: Diagnose en behandeling, eds. M. Lancel, M. van Veen & J. Kamphuis, Bohn Stafleu van Loghum, Houten 2020, 331-362.

Van Veen M, Kamphuis J, Riemersma-van der Lek R. “Psychofarmaca en de behandeling van slaapstoornissen” in Slaapstoornissen in de psychiatrie: Diagnose en behandeling, eds. M. Lancel, M. van Veen & J. Kamphuis, Bohn Stafleu van Loghum, Houten 2020, 403-468.

Lancel M, van Veen MM, Verbeek IHMJC. “Slaap: de basis voor een gezonde leefstijl”, Tijdschrift voor Psychiatrie 2020:62;11,949-954

Jong Baw PG, Van Veen MM, Hoek HW. Thiaminedeficiëntie veroorzaakt door malnutritie; een zeldzame oorzaak? Tijdschrift voor Psychiatrie 2008:50;9,611-615.

Van Veen MM, Wauben PC, Hoffman TO, Blom JD. Het ‘beginning psychiatric training syndrome’ anno 2007. Mythe of realiteit? Tijdschrift voor Psychiatrie 2008:50;3,173-177.