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The relation between sleep and violent aggression

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Chapter 1

General introduction

Matthew, a 31-year-old man, recently became a father for the first time. The new-born currently keeps him and his wife awake most nights, resulting in too short and disrupted sleep for quite a while now. At his work, a colleague makes a joke during the coffee-break. Although normally a cheerful person and in for a joke, Matthew immediately snaps that the colleague should quit. His colleague looks at him and asks: 'Matthew, did you wake up at the wrong side of the bed?'

Although this is a fictional example, it is probably rather realistic. Many people have the experience that a night of disturbed sleep can have a negative effect on emotional reactivity the next day. The saying 'waking up at the wrong side of the bed' shows that even in normal daily conversation we connect grumpiness and short-temperedness to a poor sleep quality in the preceding night(s). The potential effect of aggressive daytime interactions on nocturnal sleep may also be recognized by some of us (lying awake at night, still feeling tensed after an intense argument). While most people do not burst into physical violence, but manage to cope with the consequences of poor sleep in a more or less socially acceptable way, disturbed sleep may have detrimental effects in more vulnerable individuals. Especially groups with an already low impulse control may be at risk, such as psychiatric patients or prisoners. It may be that poor sleep is partially responsible for the well-documented higher incidence of anger and aggressive acts in mentally disturbed individuals (Eronen et al., 1998; Foster et al., 2007; Nijman et al., 1997; Posternak and Zimmerman, 2002). In such populations sleep problems may contribute to loss of aggression control, potentially leading to violent behavior. Working in a forensic psychiatric hospital, where patients are treated who committed a (violent) crime or are at risk of committing a crime under the influence of mental disorders, one gets the impression that this is the case and that poor sleep may contribute to violent crimes. For example:

James, a 28-year-old man, lived alone above a bakery. Although he favoured going to sleep rather late in the night and sleep long in the morning (evening person), he woke up every morning at four o'clock because the baker started working. After this, he tried to fall asleep again, but only succeeded after several hours because of the noise. He had only some superficial friends and no real support from his family. He tried to continue his job at a nearby gas station, but was often on sick leave. One day, sleep deprived as he was, he got into a fight in a local bar one day, because he was convinced that an unknown man looked at him in a hostile way and felt threatened by him. He attacked and kept on kicking his opponent against his head while he was already laying on the ground. The victim needed to be hospitalized. (anonymized and changed)

Violent aggression has immense consequences for individual victims, comes with financial costs for society and poses a burden for health services (Krug et al., 2002; Foster and Jones, 2005). Therefore, it is relevant to investigate factors, especially dynamic ones that may be (positively) influenced, that contribute to loss of aggression control. Despite this, the relation between sleep and aggression/violence is not a field that received a lot of scientific attention.

Aim and outline of the thesis

The aim of this thesis was 1) to investigate the clinical relevance of sleep problems in a population at risk, namely forensic psychiatric inpatients (*chapter 3 and 4*) and 2) to explore the causal direction of the relation between sleep and violent aggression in several animal studies (*chapters 5 to 8*).

Chapter 2 presents a review of the scientific literature on the relationship between sleep, aggression and violent behavior. Cross-sectional studies in children, adults and aggressive populations are summarized, as well as the few studies on the influence of treatment of sleep difficulties on problematic daytime behavior. To explore the causal relation, sleep deprivation studies in humans and animals are also described. In general, the latter studies are rather inconclusive due to several points of methodological concern. This chapter concludes with a few hypotheses on mechanisms underlying the link between sleep debt and disinhibition of aggression control. The likely importance of individual vulnerability to aggression-promoting consequences of sleep problems is highlighted. The following two chapters present data collected in a clinical forensic psychiatric population.

Chapter 3 presents a study on the prevalence and nature of sleep problems in a group of forensic psychiatric inpatients. At the start of this study, no data were available on the sleep quality and sleep disorders present in forensic psychiatric patients. By means of questionnaires, interviews and file information data on subjective sleep quality, sleep disorders, medication use and psychiatric diagnoses were collected. Probable causes for poor sleep quality are discussed, as well as the relation between sleep quality and the psychiatric disorders in the study group.

In *chapter 4* a study is presented in which we investigated the relation between sleep problems, impulsivity and aggression in a group of clinical forensic psychiatric patients. In more detail, by means of regression analyses we examined the association between

sleep quality scores on the Pittsburgh Sleep Quality Index (Buysse et al., 1989) and scores on the chronic insomnia scale of the Sleep Diagnosis List (Sweere et al., 1998), with scores on self-rated aggression and impulsivity questionnaires (based on the Aggression Questionnaire (Buss and Perry, 1992) and Barrat Impulsiveness Scale (Patton et al., 1995)), hostility and impulsivity as rated by the treating clinicians, and whether or not a patient had caused one or more aggressive incidents within the clinic.

The next chapters are aimed at the causal relationship between sleep quality and violence, using the Wild-type Groningen (WTG) rats. These rats seem a suitable animal model to investigate aggression and violence: the broad individual variation in aggressive behavior and the identification of an escalated aggressive phenotype in a relatively small proportion of these feral rats has a considerable degree of face validity to human violence and uncontrolled aggression (Miczek et al., 2013).

In chapter 5 and 6 we aimed to elucidate the causal direction of sleep contributing to the development of abnormal aggression and impulsivity. In the studies, male WTG rats were subjected to a repeated sleep restriction schedule (Roman et al., 2005; Novati et al., 2008), by placing them in slowly rotating drums that were on for 20h per day, for approximately a week at a stretch. This schedule has been shown to lead to a significant loss of non-rapid-eye-movement (NREM) and rapid-eye-movement (REM) sleep (Barf et al., 2012). Rats showed occasional micro sleeps (< 20 seconds) while in the rotating drums, adding up to one hour of sleep during a 20h sleep deprivation period (Barf et al., 2012). In each experiment, we added a forced activity control group to control for the mild physical activity sleep restricted rats performed. The rats in the forced activity control group were placed in rotating drums similar to the ones of the sleep restriction group, but only for 10h per day, rotating at double speed. Thus, these animals walked the same distance as animals in the sleep restriction condition, but had sufficient time to sleep. Previous experiments employing such a repeated sleep restriction protocol with a forced activity control group showed consequences of repeated sleep restriction on stress and neurotransmitter systems (e.g. Roman et al., 2005; Novati et al., 2008). We considered effects found after the first day of sleep restriction as acute and effects observed later in the sleep restriction week as chronic effects. Since in human society particularly chronic poor sleep is generally thought problematic, this sleep restriction protocol offers the possibility to examine this in animal models.

In *chapter 5* the effect of repeated sleep restriction on the expression of abnormal, pathological aggression in male WTG rats was examined. Rats were subjected to a series of tests for violent behavior: we evaluated several aspects of their aggressive behavior

against a male conspecific on day 1 and day 7 of the protocol and confronted them with opponents that normally do not evoke aggressive behavior, such as an unfamiliar female and an anesthetized intruder. We expected that sleep restricted rats would display violent aggressive behavior, with larger effects after chronic than acute sleep restriction.

In chapter 2 we hypothesize a critical role for the prefrontal cortex (PFC) as a brain area susceptible for the consequences of sleep deprivation. We speculate that sleep loss negatively affects PFC function, contributing to a diminished impulse and aggression control. Therefore, in the study presented in *chapter 6* we investigated the effect of chronic sleep restriction on a PFC-dependent operant conditioning task in WTG rats. Optimal performance on this task requires an intact working memory, timing ability, attention control and behavioral inhibition. We were particularly interested whether we would find signs of increased impulsivity, as reflected in an increased behavioral disinhibition.

In *chapter 7* we aimed to investigate the other direction of the potential causal relation between sleep and aggression, by studying the effect of a social conflict on recovery sleep in WTG rats. Unlike earlier studies on this topic (Lancel et al., 2003; Meerlo et al., 1996a; Meerlo et al., 1996b; Meerlo et al., 1997; Meerlo et al., 2001), we were not only interested in the sleep of the animal that experienced the social defeat, but in that of both the winners and losers of the conflict. WTG rats matched on aggression level were confronted with each other in a neutral cage, after which a social conflict occurred. Winners and losers of the conflict were identified. After that, sleep EEG was recorded and sleep-wake patterns were assessed for 18 hours.

In chapter 3 we found that forensic inpatients with an antisocial personality disorder or antisocial traits were particularly dissatisfied with their sleep. Some studies in the literature suggest that sleep as measured by polysomnography is different in antisocial individuals compared to healthy controls (e.g. Lindberg et al., 2003). To investigate whether this is also true in our animal model, we performed a study comparing sleep EEG and sleep-wake patterns in violent and non-violent male WTG rats, which is presented in *chapter 8*. We made sure that both groups were equally aggressive, but that the violent animals only differed in that they expressed abnormal, pathological forms of aggression. Not only did we perform baseline comparisons, but we also subjected both groups to 6h of sleep deprivation in order to examine the sleep homeostatic response and studied the effect of 1h of restraint stress on recovery sleep.

Finally, in *chapter 9* general conclusions are summarized and discussed. Potential future directions of research are proposed.

REFERENCES

- Barf RP, Van Dijk G, Scheurink AJ, Hoffmann K, Novati A, Hulshof HJ, Fuchs E, Meerlo P. Metabolic consequences of chronic sleep restriction in rats: changes in body weight regulation and energy expenditure. *Physiol Behav* 2012;107(3):322-8.
- Buss AH, Perry M. The aggression questionnaire. *J Pers Soc Psychol* 1992;63:452-9.
- Buysse DJ, Reynolds CF 3rd, Monk TH, Berman SR, Kupfer DJ. The pittsburgh sleep quality index: A new instrument for psychiatric practice and research. *Psychiatry Res* 1989;28:193-213.
- Eronen M, Angermeyer MC, Schulze B. The psychiatric epidemiology of violent behavior. *Social Psychiatry and Psychiatric Epidemiology* 1998;33:13-23.
- Foster C, Bowers L, Nijman H. Aggressive behavior on acute psychiatric wards: Prevalence, severity and management. *Journal of Advanced Nursing* 2007;58:140-9.
- Foster EM, Jones DE. The high costs of aggression: Public expenditures resulting from conduct disorder. *American Journal of Public Health* 2005;95:1767-72.
- Krug EG, Mercy JA, Dahlberg LL, Zwi AB. The world report on violence and health. *Lancet* 2002;360(9339):1083-8.
- Lancel M, Droste SK, Sommer S, Reul JM. Influence of regular voluntary exercise on spontaneous and social stress-affected sleep in mice. *European Journal of Neuroscience* 2003;17:2171-2179.
- Lindberg N, Tani P, Appelberg B, Naukkarinen H, Stenberg D, Rimon R, et al. Sleep among habitually violent offenders with antisocial personality disorder. *Neuropsychobiology* 2003;47:198-205.
- Meerlo P, De Boer SF, Koolhaas JM, Daan S, Van den Hoofdakker RH. Changes in daily rhythms of body temperature and activity after a single social defeat in rats. *Physiol Behav* 1996;59:735-9. (a)
- Meerlo P, Overkamp GJF, Benning MA, Koolhaas JM, Van den Hoofdakker RH. Long term changes in open field behavior following a single social defeat in rats can be reversed by sleep deprivation. *Physiol Behav* 1996;60:115-9. (b)
- Meerlo P, Pragt B, Daan S. Social stress induces high intensity sleep in rats. *Neurosci Lett* 1997;225:41-44.
- Meerlo P, Turek FW. Effects of social stimuli on sleep in mice: non-rapid-eye-movement (NREM) sleep is promoted by aggressive interaction but not by sexual interaction. *Brain Res.* 2001;907:84-92.
- Miczek KA, de Boer SF, Haller J. Excessive aggression as model of violence: a critical evaluation of current preclinical methods. *Psychopharmacology (Berl)* 2013;226:445-458.

- Nijman HL, Merckelbach HL, Allertz WF, a Campo JM. Prevention of aggressive incidents on a closed psychiatric ward. *Psychiatric Services (Washington D.C.)* 1997;48(5):694-8.
- Novati A, Roman V, Cetin T, et al. Chronically restricted sleep leads to depression-like changes in neurotransmitter receptor sensitivity and neuroendocrine stress reactivity in rats. *Sleep* 2008;31:1579–1585.
- Roman V, Van der Borgh K, Leemburg SA, Van der Zee EA, Meerlo P. Sleep restriction by forced activity reduces hippocampal cell proliferation. *Brain Res* 2005;1065:53–59.
- Patton JH, Stanford MS, Barratt ES. Factor structure of the barratt impulsiveness scale. *J Clin Psychol* 1995;51:768-774.
- Posternak MA, Zimmerman M. Anger and aggression in psychiatric outpatients. *J Clin Psychiatry* 2002;63(8):665-72.
- Sweere Y, Kerkhof GA, De Weerd AW, Kamphuisen HA, Kemp B, Schimsheimer RJ. The validity of the dutch sleep disorders questionnaire (SDQ). *J Psychosom Res* 1998;45:549-55.

