CONCLUDING REMARKS & GENERAL DISCUSSION

The work described in this thesis starts to address the question how a lack of sleep may induce cognitive impairments. This discussion will start with a brief summary of the work presented before. It will continue with a reflection on methodology, including data not presented elsewhere. The last section is dedicated to a brief discussion of the findings and their interpretation in light of related previous literature on sleep and cognition. This section includes suggestions for future research.

7.1. Summary of the preceding chapters

The introduction starts with a resume of the general knowledge and hypotheses on sleep, and its role in cognitive functioning. It includes a description of the behavioural and electroencephalographic characteristics that we can observe during sleep, which are used to define sleep and distinguish it from wake behaviour. This is followed by the general hypotheses on why we sleep, including sleep's contribution to cognitive functioning, and the specific cognitive domains mostly affected by sleep loss. It provides an overview of common human sleep disorders, which can result in cognitive impairment, and finishes with a description of rodent models for both sleep deprivation and cognitive performance.

Chapter 2 introduces a new method for inducing sleep deprivation in rats, based on variable forced locomotion. Contrary to some other methods of forced locomotion (e.g. Roman et al., 2006), this method does not induce significant stress, as indicated by the observation that corticosterone levels did not exceed the levels normally seen during the 24-hour day. Moreover, the method did not have the drawback of potential confounding of experimental results by an increase in locomotor activity, as may be the case in some other methods. When our method was applied for 12h of sleep deprivation during the light phase, activity levels did not exceed those normally seen during undisturbed conditions.

When testing behaviour in a sleep-deprived state, other possible confounders have to be addressed as well. Notably, the effects of sleep deprivation on a specific cognitive domain may depend on nonspecific cognitive effects that affect performance on the task of interest. For example, the motivation to “work” for a reward may be decreased, and fatigue may slow motor functioning. These potential problems were investigated using a task on which rats show vast levels of lever pressing to receive food rewards, which makes this task highly sensitive to decreases in motivation and motor impairment. Potential decreases in motivation were limited by imposing a food restriction to 12g/rat/day.

Chapter 3 describes the modelling of one sleepless night and one night of disturbed sleep in humans, with 12h of inactive-phase sleep deprivation or sleep disruption in rats. It tests the effect of this sleep disruption on cognitive flexibility and introduces a new switch-task. While 12h of total sleep deprivation during the light (inactive) phase decreases accuracy on
switch-task performance, 12h of repetitive sleep disturbance during the inactive phase does not alter task-switching.

Chapter 4 described the impairment in instrumental learning; the simple association between lever pressing and food reward, after 3h of active phase nap-prevention. EEG was measured before and between task performance. Learning is accompanied by an increase in REM sleep. Baseline sleep parameters do not predict subsequent individual differences in learning abilities.

In chapter 5, both 12h of inactive-phase sleep deprivation (as a model for one sleepless night) and 3h of active-phase nap prevention did not disturb performance on a different cognitive task: spatial reversal learning. Total sleep deprivation for 12h during the inactive phase does not impair the acquisition of a spatial reversal, and 3h of nap-prevention during the active phase does not impair the consolidation of reversal learning. This indicates that also in rats, sleep-related cognitive deficits are not generalized but limited to certain cognitive domains.

In chapter 6, rats were exposed to 5 weeks of non-rotating shiftwork. They showed no learning deficits on an instrumental learning task (the same task as used in chapter 4) in their 5th week on this protocol, which shows that rats may somehow habituate to regular sleep deprivation for 8h per day on 5 days per week (both in the active and in the inactive phase). Furthermore, the undisturbed control groups in this study demonstrate that instrumental learning is similar during the active and the inactive phase.

### 7.2. Reflection on methodology

When investigating the effect of sleep deprivation on cognition in rats, many factors besides sleep deprivation itself can influence the results. The relevant literature has been summarised in chapter 1, while chapter 2 describes the studies which address potential confounding factors with our novel method for sleep deprivation implementing variable forced locomotion. This section will start with a further discussion of the results from chapter 2, and additional results on recovery-sleep after short-term active-phase sleep deprivation, as implemented in chapters 4 and 5.

Combining data from different experiments performed during this project can shed some light on the relative effect of two of the potential confounding factors that can influence the results besides sleep deprivation: inversion of the light-dark cycle and behavioural task structure.

Inversion of the light-dark cycle; keeping rats in the laboratory with the lights on during our night and with the lights off during our day, is often implemented to allow experimenters to work during normal office hours while performing tests during the dark phase of the animals. As the rats are normally raised under a normal light schedule, this procedure involves a phase-shift of 12 hours, which may induce something like a jet-lag, that could affect subsequent experimental results.