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Instrumental learning: An animal model for sleep dependent memory enhancement

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HIGHLIGHTS

- The classic instrumental leaning paradigm can serve as a model to study sleep-dependent memory enhancement.
- Baseline sleep parameters are similar for fast and slow learning rats.
- Task-exposure increased REMS-duration.
- Increasing REMS-duration is related to learning.
- Sleep deprivation interferes with instrumental learning performance enhancement in most rats.

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ABSTRACT

The relationship between learning and sleep is multifaceted; learning influences subsequent sleep characteristics, which may in turn influence subsequent memory. Studies in humans indicate that sleep may not only prevent degradation of acquired memories, but even enhance performance without further practice.

In a rodent instrumental learning task, individual differences occur in how fast rats learn to associate lever pressing with food reward. Rats habitually sleep between learning sessions, and may differ in this respect.

The current study assessed if the instrumental leaning paradigm could serve as a model to study sleep-dependent memory enhancement. Male Wistar rats performed 2 sessions of instrumental learning per day for 1–3 days. Electroencephalography was recorded both before and after the sessions. Sleep deprivation (3 h) was applied between the first and second session in a subgroup of rats. Measurements comprised the number of lever presses in each session, slow wave sleep (SWS) duration, Rapid Eye Movement Sleep (REMS) duration and sleep spindles.

Abbreviations: ANOVA, analysis of variance; EEG, electroencephalogram; EMG, electromyogram; IL, instrumental learning; REMS, rapid eye movement sleep; SEM, standard error of the mean; SWS, slow wave sleep; UK, United Kingdom; USA, United States of America.

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Baseline sleep parameters were similar for fast and slow learning rats. Task-exposure increased REMS-duration. The increase in REMS-duration was observed specifically after sessions in which learning occurred, but not after a later session. Sleep deprivation during the 3 h period between the initial two sessions interfered with performance enhancement, but did not prevent this in all rats. Our considered movement control protocol induced partial sleep deprivation and also interfered with performance enhancement.

The classic instrumental learning task provides a practical model for animal studies on sleep-dependent memory enhancement.

1. Introduction

The relationship between learning and sleep is multifaceted. First, individual differences in specific sleep parameters, including the distribution of sleep stages and phasic events, have been associated with initial performance and learning abilities (Ambrosini et al., 1993; Schabus et al., 2007). Second, exposure to novel learning can change subsequent sleep parameters, e.g. the prevalence of certain sleep stages (Langella et al., 1992; Nishida and Walker, 2007; Gais et al., 2002; Smith, 1985; Wetzel et al., 2003). It is likely that these changes are important to learning, because a large number of studies demonstrate that sleep deprivation can impair learning, as reviewed previously (e.g. Walker and Stickgold, 2004).

1.1. Sleep after learning and performance enhancement

Learning benefits from sleep after task exposure (Stickgold et al., 2002), even from a very brief nap (Lahl et al., 2008; Mednick et al., 2002). It has been argued that a better preservation of newly learned information or skills may just be a confound of the lack of interference by subsequent information. Interference is indeed prevented by being asleep rather than awake. However, this argument cannot easily explain that sleep may even enhance performance, without additional practice (as reviewed by Walker and Stickgold, 2004). This makes sleep-dependent memory enhancement perhaps the most convincing class of observations in the association of sleep with learning and memory, and a primary target for further studies on the brain mechanisms involved.

1.2. Instrumental learning

Several types of learning can be discriminated (refer to e.g. Walker and Stickgold, 2004 for an overview from a sleep research perspective). One elementary type is instrumental learning. A classical paradigm to study instrumental learning in rats is to expose them to a simple action-outcome association; for example that lever pressing is rewarded with a highly desirable food reward.

In our application of the instrumental learning paradigm, we previously observed marked individual differences in how fast individual rats learn to associate lever pressing with food reward, which were associated with differences in neurochemistry (Cheng and Feenstra, 2006).

Casual observations showed that rats habitually sleep between sessions. Because rats may differ with respect to their sleep between sessions, we evaluated if individual differences in post-learning sleep could be involved in the improvement seen from one session to the next. If so, the classical instrumental learning paradigm may serve as an animal model to study brain mechanisms involved in sleep-dependent memory enhancement.

1.3. The current studies

In the first of three experiments, we measured both baseline and post-task electroencephalogram (EEG) & electromyography (EMG) to test the following specific hypotheses: (1) individual differences in baseline sleep recorded prior to learning relate to individual differences in the speed of task acquisition (experiment 1A); (2) learning alters subsequent sleep characteristics (experiment 1B), and (3) the speed of task acquisition is sensitive to 3 h of total sleep deprivation during the active phase (nap prevention) following the first session of instrumental learning (experiment 1C).

Because we applied variable forced locomotion to accomplish sleep deprivation, we performed a second and third experiment to investigate the effects of forced locomotion on sleep parameters (experiment 2) and learning (experiment 3).

2. Materials and methods

2.1. General procedures

All experiments were performed in male Wistar rats (Harlan, Horst, the Netherlands), housed in groups of 4 (unless mentioned otherwise) in type-IV macrolon cages (60 cm × 38 cm × 20 cm), in a room with controlled temperature (20 ± 2 °C) and humidity (60 ± 20%). Rats were kept under a fixed reversed light–dark cycle (lights ON at 19:00 h; lights OFF (red light) at 07:00 h), to facilitate experiments taking place during office hours and yet in the rats' active, dark period. At the onset of EEG experiments, rats had been exposed to the reversed light–dark cycle for at least 4 weeks.

After surgery (described below), rats were housed individually in high type-III macrolon cages (38 cm × 21 cm × 24 cm) to prevent damage to the EEG-connectors.

For the behavioural experiments, food restriction to 16 g per day was started 3 days before the first behavioural session to facilitate learning by increasing the value of food reward (e.g. Leenaars et al., 2012). Before, food was available ad libitum. Water was unrestricted for all rats. All experiments were approved by the experimental animal committee of the Royal Netherlands Academy of Arts and Sciences and performed in accordance with Dutch legislation (wet op de dierproeven, 1996) and European guidelines.

2.2. Experiment 1: sleep and instrumental learning

In this experiment, EEG & EMG were recorded ($n = 38$) for 24 h before the first learning session, in between all the learning sessions, and following the last learning session. In a previous study, 57% of rats were fast learners (Cheng and Feenstra, 2006). The number of rats tested was intended to be sufficient for comparisons between slow and fast learning rats (refer to Section 2.2.2 for the definitions of slow and fast learning), both in the control (undisturbed sleep, $n = 19$) and in the sleep deprived ($n = 19$) group.

2.2.1. EEG and EMG

Following a minimum of one week of habituation to the laboratory, and an additional week of habituation to daily handling, rats were prepared for EEG–EMG recordings. Surgery, recordings and sleep stage scoring were performed as previously described (Leenaars et al., 2012). In short, five home-made EEG electrodes were placed on the dura (AP + 2.0 mm; $L \pm 2.0$ relative to bregma; AP + 2.0; $L \pm 2.0$ relative to lambda; and AP −2.0 on midline relative