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Research Report

Rapid eye movement (REM) sleep homeostatic regulatory processes in the rat: Changes in the sleep–wake stages and electroencephalographic power spectra

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ABSTRACT

The aim of this study was to elucidate physiological processes that are involved in the homeostatic regulation of REM sleep. Adult rats were chronically instrumented with sleep–wake recording electrodes. Following post-surgical recovery, rats were habituated extensively for freely moving polygraphic recording conditions. On the first experimental recording day (baseline day, BLD), polygraphic signs of undisturbed sleep–wake activities were recorded for 4 h (between 11:00 AM and 3:00 PM). During the second experimental recording day (REM sleep deprivation day, RDD), rats were selectively deprived of REM sleep for the first 2 h and then allowed to have normal sleep–wake for the following 2 h. The results demonstrated that during the first 2 h, compared to BLD, RDD recordings exhibited 87.80% less time in REM sleep and 16% more time in non-REM (NREM) sleep. The total percentages of wakefulness remained comparable between the BLD and RDD. During the RDD, the mean number of REM sleep episodes was much higher than in the BLD, indicating increased REM sleep drive. Electroencephalographic (EEG) power spectral analysis revealed that selective REM sleep deprivation increased delta power but decreased theta power during the residual REM sleep. During the last 2 h, after REM sleep deprivation, rats spent 51% more time in REM sleep compared to the BLD. Also during this period, the number of REM sleep episodes with the shortest (5–30 s) and longest (>120 s) duration increased during the RDD. These findings suggest that the REM sleep homeostatic process involves increased delta- and decreased theta-frequency wave activities in the cortical EEG.

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Abbreviations: BLD, baseline/control REM sleep recording day; RDD, REM sleep deprivation recording day; SWA, slow-wave activity; T-1, first two-hour time period (11:00 AM to 1:00 PM); T-2, last two-hour time period (1:00 PM to 3:00 PM)

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1. Introduction

A wide range of behavioral studies have provided considerable evidence supporting the idea that the regulation of the total amount of sleep is a homeostatic process (reviewed in Datta and MacLean, 2007). Homeostatic control mechanisms are activated to compensate for insufficient or excess sleep. In mammals, sleep consists of two major stages: 1) REM sleep and 2) non-REM (NREM) sleep. REM sleep is a distinctive sleep stage that alternates with episodes of NREM sleep. During the sleep-predominant light-on phase, the spontaneous NREM–REM sleep cycle in the rat takes about 12 to 20 min (Trachsel et al., 1991; Vivaldi et al., 1994a,b; Gottesmann, 1996; Datta and Hobson, 2000). Over the last four decades most of the sleep research has focused on identifying relevant brain structures, neuronal networks, and their transmitters that are involved in the generation and regulation of NREM and REM sleep (Alam et al., 1995; Thakkar et al., 1998; Pace-Schott and Hobson, 2002; Blanco-Centurion et al., 2006; Datta and MacLean, 2007). On the contrary, few studies have focused on understanding the possible mechanisms for the ultradian periodic occurrence of NREM–REM sleep.

Some investigators have suggested that there may be a sleep-dependent oscillator that regulates the NREM–REM sleep cycle (Whitehead et al., 1969; Gaillard and Tuglular, 1976; Miyasita et al., 1989; Benington and Heller, 1994a; Vivaldi et al., 1994a,b; Barbato and Wehr, 1998). The results of those studies have also suggested that the appearance of REM sleep in the NREM–REM sleep cycle is a functional need for reversing some consequences of the synchronized bursting activity that occurs during NREM sleep (Benington and Heller, 1994a,b; Bennington et al., 1994). Therefore, the daily amount and frequency of REM sleep is proposed to be regulated by the homeostatic regulation of NREM sleep (Benington and Heller, 1994a,b). Contrary to the idea that the ultradian periodic occurrence of REM sleep is an epiphenomenon and its appearances depend on the homeostatic regulation of NREM sleep (Benington and Heller, 1994a,b), there is experimental evidence which suggests that the homeostatic regulatory process of REM sleep is independent of the NREM sleep homeostatic regulatory process (Vivaldi et al., 1994a,b; Ocampo-Garces et al., 2000; Franken, 2002). Indeed, the occurrence of REM sleep rebound following total sleep deprivation or selective REM sleep deprivation is one of the most common phenomena (Dement, 1960; Vimont-Vicary et al., 1966; Morden et al., 1967; Beersma et al., 1990; Brunner et al., 1990; Endo et al., 1997, 1998; Datta et al., 2004). More specifically, some studies have shown that the increase in REM sleep during recovery was proportional to the amount of REM sleep lost in deprivation (Dement et al., 1966; Kitahama and Valatx, 1980; Parmeggiani et al., 1980; Perez et al., 1992; Amici et al., 1994). Finally, some selective REM sleep deprivation studies have shown that during deprivation there are progressively more frequent attempts at transitions into REM sleep, an indication of a strong homeostatic drive for REM sleep (Endo et al., 1997, 1998; Ocampo-Garces et al., 2000; Werth et al., 2002; Datta et al., 2004). Again, these findings are consistent with the suggestion that some homeostatic regulatory processes accurately regulate the daily amount of REM sleep.

A number of studies have suggested that the intensity of slow-wave activity (SWA; spectral power in the 0.75 to 4.5 Hz range, also called delta frequency range) in the cortical EEG is the single most important process for the homeostatic regulation of NREM sleep (Borbely et al., 1981, 1984; Borbely, 1982; Tobler and Borbely, 1986; Dijk et al., 1987, 1990; Achermann et al., 1993; Dijk and Czeisler, 1995; Franken et al., 2001). In support of this suggestion, studies have shown that the SWA in NREM sleep typically declines in the course of the daily sleep period and increases in recovery sleep after a period of prolonged waking (Tobler and Borbely, 1986; Dijk et al., 1987, 1990; Franken et al., 2001). Furthermore, it has also been reported that the SWA is reduced in the subsequent NREM sleep after a nap and/or excess sleep (Feinberg et al., 1992; Werth et al., 1996). However, the EEG marker(s) of REM sleep homeostasis remains poorly understood.

In the present study, in order to further expand our understanding of the homeostatic regulatory mechanisms of REM sleep, spontaneously sleeping rats were partially deprived of REM sleep, using a selective REM sleep deprivation method (Datta et al., 2004). This was done for a short period of time without disturbing spontaneous NREM sleep and wakefulness. Polygraphic and behavioral states of baseline and experimental recording sessions were analyzed both during and after selective REM sleep deprivation to determine any specific changes in sleep–wake states and behavioral state-dependent delta, theta, alpha, beta, and gamma activity caused by the selective REM sleep deprivation.

2. Results

Following post-surgical recovery, eight rats were habituated extensively (about 15 days) for the freely moving polygraphic recording conditions. During this habituation recording sessions (between 9:00 AM and 3:00 PM), baseline sleep–wake percentages were carefully monitored to determine the day-to-day variations in the total percentages of sleep–wake and REM sleep latency. In these rats, recording sessions for the habituation continued until the total percentages of sleep–wake stages and REM sleep latencies were almost identical for three consecutive recording sessions. During this habituation recording sessions, polygraphic signs were also carefully monitored to select rats that exhibited minimal to no electrical artifacts in their cortical EEG. Based on this qualitative criterion, we have selected six of those eight rats for this study. The final results presented below are obtained from these six selected rats.

2.1. *Effects of selective REM sleep deprivation on wake–sleep states*

Fig. 1 illustrates the experimental design (1A) and changes in the amount of time spent in W, NREM sleep, and REM sleep during (1B; 11:00 A.M to 1:00 PM; T-1 period) and after (1C; 1:00 PM to 3:00 PM; T-2 period) selective REM sleep deprivation. During the T-1 period of the baseline recording session (BLD), these rats spent 78.93% (mean) of time in sleep and remained awake for about 21.1% of total time. Of the 78.93% sleep time, 15.2% of that time was spent in REM sleep (1B). On the next day, during the identical circadian periods of recording session