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Differential effects of two types of environmental novelty on activity and sleep in BALB/cJ and C57BL/6J mice

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Abstract

Change in the sleeping environment can produce significant alterations in sleep. To determine how these alterations may vary with the amount of change and the relative reactivity of the sleeper, we examined the influences of environmental novelty on sleep in two mouse strains that differ in behavioral anxiety. Mice [BALB/cJ ($n=7$) and C57BL/6J ($n=8$)] were implanted for recording EEG and activity via telemetry. Following baseline data collection, activity and sleep were examined over 46 h after routine cage change, after placing a simple novel object (PVC Tee) in the home cage, and after handling controls. Mice of both strains showed immediate increases in activity and decreases in rapid eye movement sleep (REM) and non-REM (NREM) after cage change and novel object. Within strain, changes in activity and sleep were greater after cage change than after novel object. Changes in activity and sleep time were significantly correlated in each strain. Compared to C57BL/6J mice, BALB/cJ mice exhibited greater and longer duration initial reductions in sleep time, and greater increases in EEG slow wave activity power after cage change and novel object, but these changes were not followed with subsequent increases in sleep time. In contrast, C57BL/6J mice showed significantly greater subsequent increases in sleep time following the initial reductions induced by both manipulations. The results suggest that initial decreases and subsequent increases in sleep time are related to putative differences in the intensity of environmental novelty (cage change > novel object) and to previously described strain differences in anxiety (BALB/cJ > C57BL/6J).

Keywords: Cage change; EEG; Environmental enrichment; Sleep; Activity; Novelty; Slow wave activity

1. Introduction

Changes in the sleeping environment may impose novel physical and psychological stimuli that can significantly impact sleep amount and quality. In humans, the best experimental example to illustrate the influences that environmental novelty can have on sleep may be seen in the first night of recording in the laboratory. This first night effect is characterized by prolonged sleep latency and reduced total sleep time compared to later nights [1]. Putatively, patients with anxiety disorders should be more sensitive to changes in sleeping environments and, indeed, the first night effect has been associated with higher state anxiety [2,3]. Subjects with generalized anxiety disorder exhibit a first night effect [4], though changes in sleep from the first to second night may be less than in normal subjects, possibly due to a ceiling effect [5]. First night effects are also seen in patients with depression [6–8] and insomnia [6].

In animal studies, forced confrontation with novelty is a major feature of behavioral tests designed to assess anxiety [9]. Mice and rats display greater changes in rapid eye movement sleep (REM) than in non-REM (NREM) after exposure to novelty [10–12] and after experiencing stressors such as fearful stimuli [13–17] and restraint [17–19]. The relative magnitude and duration of the changes in sleep has been found to vary with strain. For example, compared to C57BL/6J mice, BALB/cJ mice

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have been overwhelmingly reported to have greater anxiety-like behaviors in response to novel environments [20–23], and have been suggested to have pathological trait anxiety [21,23]. BALB/cJ mice also display greater initial post-exposure reductions in REM following a variety of stressors [13,15,16,19]. In addition, exposure to an open field induced greater initial reductions with less subsequent increases in REM in BALB/cJ mice whereas C57BL/6J mice exhibited relatively less initial reductions but a greater subsequent increases [12]. Based on these results, we have suggested that the putative trait anxiety in BALB/cJ mice might play a critical role in the relatively greater effects on REM induced by stressors [12,13,15–17,24].

Experimental rodents routinely experience cage change as part of normal husbandry that produces significant alterations in their sleeping and living environments. Cage change may induce stress in rodents that is related to fear and novelty [23,25]. This view is supported by behavioral and physiological observations including increased rearing and grooming, increased exploratory behavior and increased heart rate and blood pressure after cage change [25]. These responses are consistent with recurring cage changes in animals on weekly change schedules suggesting that the animals do not habituate over time [25]. Cage change also produces arousal indicated by increased activity [22,23] and has been used as an experimental challenge to induce arousal in studies of gene-altered mice [26–28]. The simple presentation of a novel object into the home cage has also been found to alter sleep architecture [11], and novel object presentation has been used to promote arousal in sleep deprivation protocols [29,30]. Thus, cage change and novel object presentation in the home cage may provide convenient models for examining how mildly stressful changes and novelty in the environment influence sleep.

In the present study, we examined the relative changes in arousal and sleep that occur in response to changes in the sleeping environment in two mouse strains (C57BL/6J and BALB/cJ) that differ significantly in relative responsiveness to environmental stimuli. The changes examined included a complete cage change and the introduction of a novel object into a well-habituated home cage. We then assessed activity and sleep and EEG spectra to determine the effects on arousal.

2. Methods

2.1. Subject

The subjects were 7 BALB/cJ and 8 C57BL/6J male mice of approximately 10 weeks of age purchased from the Jackson Laboratory (Bar Harbor, Maine). The animals were individually housed upon arrival and for the duration of the experiment. Food and water were available ad libitum. Ambient room temperature was maintained at 24.5 ± 0.5 °C and lights were kept on a 12 : 12 cycle with lights on from 7:00 A.M. to 7:00 P.M. The mice received routine husbandry once per week at 9:00 A.M., which included a clean cage with fresh wood-chip bedding and raw nest building material (pulped virgin cotton fiber, Nestlet, Ancare corp. NY, approximately $5.0 \times 5.0 \times 0.6$ cm).

2.2. Surgery

The mice were surgically implanted with telemetry transmitters (DataSciences ETA10-F20) for recording EEG and activity as previously described [31]. Surgery was conducted with the mice under isoflurane (as inhalant: 5% induction; 2.0% maintenance) anesthesia. Screw electrodes were bilaterally implanted (A: 1.0, L: 1.0; P: 3.0, L: 3.0; relative to Bregma) for recording EEG. All procedures were conducted in accordance with the National Institutes of Health Guide for the Care and Use of Experimental Animals and were approved by Eastern Virginia Medical School's Animal Care and Use Committee (Protocol #02-022).

2.3. Experimental procedure

Implant surgery was performed two weeks after the mice arrived from the supplier and they were allowed a post-surgery recovery period of approximately 20 days. Between arrival and the start of recording, the mice received standard husbandry with cage change a total of five times. Five days after the last of these cage changes, uninterrupted baseline sleep was recorded for 2 days. Afterwards, sleep recording were obtained for 46 h immediately after cage change and cage change control, and after novel object and novel object control. Each treatment and control was performed at 9:00 A.M. (2 h following lights on). In the cage change condition, the mice were placed into a clean cage with fresh bedding and raw nesting material. For cage change control, they were removed from and placed back into the same cage 4 days following the experimental cage change (sixth after arrival). In the novel object condition, a 1 1/4″ PVC Tee was placed in the cage. For control, the cage was opened without placing the novel object. Novel object and novel object control were conducted 4 days after the seventh and eighth cage change, respectively.

The mice were housed and studied in the same room. Sleep could be recorded in 8 mice concurrently, and the study was conducted in two stages with 3 or 4 mice of each strain in each stage.

2.4. Determination of behavioral state

For recording sleep and activity, individual home cages were placed on a DataSciences telemetry receiver (RPC-1)