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A Correlational Analysis of the Recovery from Sleep Deprivation across a Panel of Inbred Mouse Strains

Author
Trotter, Damion

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A Correlational Analysis of Recovery from Sleep Deprivation across a Panel of Inbred Mouse Strains

A thesis submitted in partial satisfaction
of the requirements for the degree Master of Science
in Physiological Science

by

Damion Lamar Trotter

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ABSTRACT OF THE THESIS

A Correlational Analysis of Recovery from Sleep Deprivation across a Panel of Inbred Mouse Strains

by

Damion Lamar Trotter

Master of Science in Physiological Science

University of California, Los Angeles, 2022

Professor Ketema N. Paul, Chair

Sleep is known to be necessary for everyday life for humans. Although sleep is common across phylogeny, there still is much not known about sleep, including many of the genetic components that regulate it. In this study, we investigated 10 sleep phenotypes in 24 inbred mouse strains while looking at both spontaneous sleep conditions and recovery following six hours of sleep deprivation beginning at the light onset in a 24-hour light-dark cycle. We found that there were significant differences across strains in ten sleep phenotypes. We then tested the hypothesis that there are strain differences in the homeostatic ability to recover from sleep loss. Our findings suggested that there are strain differences in the recovery from sleep loss across different mouse strains. These findings suggest that sleep homeostasis is sensitive to the genetic differences across these inbred strains. This work furthers our understanding of the genetic mechanisms underlying sleep homeostasis.

The thesis of Damion Lamar Trotter is approved.

Arthur P. Arnold

Gina R. Poe

Christopher S. Colwell

Ketema N. Paul, Committee Chair

University of California, Los Angeles

2022

Dedicated to my family and friends

Who stood by me

And encouraged me to never give up

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Chapter 1: Introduction

1.1 What is Sleep?

Sleep is a period of dormancy exhibited by all known animals and is characterized by reduced responsiveness to external stimuli and reduced muscle activity. A key aspect of sleep is that it is easily reversible, unlike a coma or other disorders of consciousness. This prevalence across phylogeny denotes an evolutionary necessity for sleep, which is further substantiated by the fact that prolonged deprivation of sleep can lead to cognitive impairment (Alhola & Polo-Kantola, 2007), loss of bodily function (Goel et al., 2009), organ failure (Periasamy et al., 2015), and eventual death (Vaccaro et al., 2020). The impact of sleep loss on mortality has been reported in studies with dogs (Anderson et al., 2020), rats, mice, and flies (Vaccaro et al., 2020) as well as many other model organisms.

There are two major processes involved in sleep, Process C and Process S (Borbély et al., 2016). Process C, also known as the circadian process, is involved in the body's circadian regulation of internal biological processes and alertness. As a wake-promoting process, it is more active during the daytime and begins to dissipate during an animal's time for rest. Process C is critical also as it consolidates sleep and wake into distinct episodes. Process S is the process of sleep homeostasis. Sleep pressure builds up the longer and animal stays awake and dissipates when they enter a period of sleep.

Sleep is composed of two major stages: non-Rapid Eye Movement (NREM) and Rapid Eye Movement (REM). NREM sleep consists of three stages: N1, N2 and N3 (Patel et al., 2022). N1 sleep is the period of light sleep immediately transitioning from wakefulness and is characterized by slowing down of eye movement and muscle activity and lasts for about 5-10 minutes. N1 sleep is also when hypnic jerks occur,

when the body experiences false sensory phenomena such as a feeling of falling. N2 sleep involves periods of muscle contraction and relaxation. In N2 sleep, eye movement comes to an almost complete stop, the heart rate slows down, body temperature lowers, and the body begins to prepare for deep sleep. Following N2 sleep the body enters N3 sleep. N3 sleep is characterized by the presence of delta waves and there are no eye movements or muscle activity. REM sleep follows NREM sleep, and brain activity starts to increase similar to that of wakefulness. Dreams are formed and are present during this stage and REM begins around 90 minutes into sleep on average in humans. Both stages are important in different aspects. NREM is important for tissue regeneration (Eugene & Masiak, 2015) and strengthening of the immune system whereas REM sleep is important for memory consolidation (Peever et al., 2016) and both are important for learning (Tamaki et al., 2020).

1.2 How is Sleep Studied?

There are many different paradigms and models that can be used to study sleep in both humans and animals. Standard tools to measure sleep include electroencephalographs (EEGs) which are used to measure the activity of electrical brainwaves (Campbell, 2019), and electromyographs (EMGs) which are used to measure muscle activity (Oishi et al., 2016). EEGs are especially helpful when it comes to distinguishing between NREM and REM sleep as delta waves (.5-4 Hz) become more prevalent during NREM sleep. EMGs are a helpful tool that serve as an additional check when it is difficult to distinguish between wake and REM sleep, as the EEGs can look similar, but there should be a lack of muscle movement during REM as opposed to being awake. The process of using EEG and EMG to determine sleep stage is called polysomnography and most sleep-wake data in animal models is analyzed by scoring

the data manually. A number of labs have looked at automatic scoring (Barger et al., 2019; Gao et al., 2016; Rytkönen et al., 2011) but currently, there is no consistent mechanism for reliable sleep scoring, and as such manual scoring is still used in many labs.

A popular model organism to study sleep is the mouse. Mice are used to study sleep because genetic tools are more advanced in mice than in other organisms and mice have clearly defined phenotypes, specifically bouts of sleep which tend to last about 2-4 minutes on average (Toth & Bhargava, 2013). These short bouts also tend to help when trying to use mice as a model for sleep disorders such as insomnia, with which mouse strains like DBA/2J could be used as a potential model (Toth & Bhargava, 2013).

1.3 Sleep and Genetics

Sleep can differ between animal species, and even within the same species, but a major question that exists is the degree of genetic control of sleep homeostasis. Scientists have explored this in a myriad of ways. A popular purpose for studying sleep and genetics involves sleeping disorders and their potential heritability. A 2011 study (Sehgel & Mignot, 2011) conducted a review of sleep studies looking at genes and found that narcolepsy can be driven by genetic anomalies (Miyagawa & Tokunaga, 2019; Mignot, 1998) and may even be driven by ethnic components (Kornum et al., 2011). But the possible genetic contributions to sleep homeostatic mechanisms are not known.

1.4 Purpose

In this study, I compared the sleep/wake architecture of 22 different strains of inbred mice in both spontaneous and sleep deprivation conditions. Following this, I then analyzed how the sleep phenotypes of these strains differed between spontaneous and

recovery conditions. My central hypothesis is that there would be strain differences in sleep homeostatic mechanisms that would be reflected in underlying genetic differences between the strains.

Chapter 2: Materials and Methods

2.1 Animals

In order to assess the potential for a genetic component of sleep in adult male mice, 24 inbred mouse strains were analyzed. The strains studied were: 129/J (n = 7), A/J (n = 5), AKR/J (n = 7), BTBR T+ Itpr3tf/J (n = 11), BUB/BnJ (n = 7), C3H/HeJ (n = 4), C57BL/6J (n= 4), C57L/J (n = 7), C58/J (n = 7), CAST (n = 8), CBA/J (n = 6), CZECH/EiiJ (n = 3), DBA/2J (n = 5), FVB/NJ (n = 2), KK/HiJ (n = 8), MOLF/EIJ (n =5), NOD/ShilTj (n = 8), NZB (n = 2), PL/J (n = 5), PWD/PhJ (n = 4), SJL/J (n = 7), SM/J (n = 3), SWR/J (n = 3), and WSB/EiJ (n = 6) strains. All of the mice were maintained on a 12-hour light:12-hour dark schedule throughout the study. Food and water were provided ad-libitum and they were individually housed for two weeks prior to the experimental aspect of the study. All animals were purchased from Jackson Laboratories.

2.2 Phenotypes

For the purposes of this study, 10 sleep phenotypes were studied. These were NREM sleep, REM sleep, total sleep, number of bouts of NREM, duration of bouts of NREM, number of bouts of REM, duration of bouts of REM, number of bouts of total sleep, duration of bouts of total sleep, and number of bouts of arousal.

2.3 Surgical Methods

EEG and EMG electrodes were implanted in anesthetized mice. The heads were positioned using a head mount provided by Pinnacle Technologies and three electrodes

were implanted into the head [Figure 1]. The first electrode is implanted into the frontal area of the brain and the second (recording) and third (reference) electrodes are implanted into the intraparietal area. A fourth screw was used to serve as a ground.

2.4. EEG and EMG Recordings

Following the surgery, the mice are given a 14-day period to recover from surgery. Following that week, they were moved to the sleep recording suite and given time to accommodate to the new areas. They were then connected to the tether which is attached to the low-resistance commutator mounted over the cage [**Figure 1**] (provided by Pinnacle Technologies). Mice were able to freely roam their cage while becoming acclimated to their environment. Seven days after entering the sleep recording chambers, EEG and EMG began recording. The data was collected on a computer running Sirenia Acquisition software (Provided by Pinnacle Technologies). This software was developed solely for the purpose of recording sleep in animals, specifically rodents. The data was recorded for 24 hours in a baseline condition and subsequently 6 hours in a sleep deprivation condition followed by 18 hours of recovery.

2.5 Sleep Deprivation

After 24 hours of baseline recording, sleep deprivation was conducted in the first 6 hours of the light phase [ZT 0-6] across all studied mouse lines. Gentle handling was used to keep the mice awake either by the introduction of a novel object into the cage, disturbing the bedding, tapping on the cage, and when necessary, the mice were touched delicately. [**Figure 2**] During this period access to food was still allowed ad-libitum.

2.6 Sleep Scoring

Once the data was collected, it was classified by a trained observer. The classification process used data recorded by the EEG and EMG waves. Wake, NREM, and REM sleep were primarily determined by the frontal electrode and the EMG served to help differentiate between wake and REM sleep. This would be conducted in 10-second intervals. Artifacts (caused by movement, eating, drinking, and scratching) were excluded from the data set. Wake is denoted by a yellow color, NREM is denoted by blue, REM is denoted by red, and artifacts are denoted by white. [**Figure 3**] The baseline data and sleep recovery data were analyzed for each individual mouse across all the strains.

Most of the methods above were completed at the time that I started my project. I contributed to the manual analysis of the sleep records.

2.7 Statistics

Kruskal-Wallis ANOVAs were conducted to identify strain differences in phenotypes. A paired t-tests were conducted to observe within strain differences between the baseline conditions and the recovery conditions across all phenotypes. To compare the recovery from sleep loss across all the strains Pearson correlations were run (comparing the differences in baseline vs recovery sleep across strain). This approach has been used by prior researchers (Diessler et al., 2018).

Chapter 3: Results

I compiled, analyzed, and interpreted all of the data reported in this section.

3.1 Sleep Phenotypes across Strains

Across 24 strains, all the data for the phenotypes were collected and segmented into three 6-hour time periods, ZT 6-12, 12-18, and 18-24. ZT 0-6 was excluded from the

dataset since we are comparing sleep states between sleep-replete (spontaneous) and sleep-deprived mice, and ZT 0-6 was the period of sleep deprivation in the sleep-deprived group. In a 12-hr light:12-hr dark cycle, we examine light-phase phenotypes independently of dark-phase phenotypes. Since the light-phase phenotype in recovery is only six hours, we divided all phenotypes into six-hour time bins for ease of comparison. These kinds of time bins are standard in sleep research in animal models.

Kruskal-Wallis ANOVA revealed strain differences in all the phenotypes in each of the 6-hour studied windows in both the baseline condition and the recovery conditions **[Figure 4]** (NREM, REM, Total Sleep, number and duration of bouts of NREM, number and duration of bouts of REM, number and duration of bouts of total sleep, and number of bouts of arousal) with $p < 0.0001$ for every analysis, and for each phenotype there was a significant difference ($p<.05$) across strains in both baseline and recovery after analysis with a Kruskal-Wallis test. A Kruskal-Wallis test was performed because the number of animals in each strain were different.

3.2 **Between Strain Differences in Sleep Homeostasis**

For this experiment, we conducted within-mouse comparisons of baseline and recovery. We used only 22 strains because in two of the strains (NZB and FVB/NJ) only two mice shared the within-mouse condition. Within the strains, all of the data was collected into three 6-hour time periods (6-12, 12-18, and 18-24). ZT 0-6 was excluded from the data pool because there is no corresponding period for comparison in sleep-deprived mice. Mice that were present in the baseline condition but not in the sleep deprivation condition were excluded from the data pool. In addition, individual mice that were present in the sleep deprivation condition but not present in the baseline condition

were removed from the data pool. This was done to reduce possible data confounds as well as making within-mouse comparisons easier.

To see if there was a strain difference in the effect of sleep homeostasis across phenotypes, we first had to normalize our data. In order to do so, we ran Pearson correlations across three-time domains. Our goal was to determine whether the degree of coincidence between the baseline and recovery values within each strain changed significantly as a function of time [**Figure 5**]. The reason we looked for the Pearson coefficient is that it is one of the most common ways to analyze the relationship between two variables and it was also run in previous sleep studies across inbred mouse strains (Diessler et al., 2018). The higher the positive correlation between baseline and recovery the less robust the homeostatic response to sleep loss and vice versa. In that regard, the correlation is a way of normalizing of sleep homeostasis across strains with significant differences in absolute sleep phenotypes. In this regard, the correlations are an indirect measurement of sleep homeostasis as a function of time. This helps to compensate for the limitation of not having a direct measurement of sleep homeostasis across the strains. The reason we chose three time bins is that since the sleep deprivation is six hours, we expressed recovery in six-hour bins to accommodate the light-dark transition (light phase recovery is only six hours) while keeping the time comparisons consistent. We used a one-way repeated-measures ANOVA (with R-value as the repeated measure) to find potential differences in the correlation of baseline and recovery between three time domains across all the strains combined. This comparison is to determine if there is a significant difference in the correlation between baseline and recovery between the three time domain. In this

comparison, our sample size is the number of strains (22), our independent variable is the time domain (three), and our dependent variable is the R-value. We found that the correlations between baseline and recovery changed across the time bins. We found significant differences in correlation coefficients across time bins between baseline and recovery for two phenotypes: Number of Bouts of NREM ($p = 0.0181$) and Duration of Bouts of NREM ($p = 0.0156$) [**Figure 5a**]. We didn't find differences between strains in the correlation coefficients for NREM ($p = 0.1501$), REM ($p = 0.2781$), Total Sleep ($p = 0.2368$), DB of NREM ($p = 0.169$), Number of Bouts of REM ($p = 0.1027$), Duration of Bouts of REM ($p = 0.9711$), Number of Bouts of Total Sleep ($p = 0.348$) and Number of Bouts of Arousal ($p = 0.7582$).

When comparing whether there were any significant differences between baseline and recovery there was quite a variation with some strains not showing any significant differences between baseline and recovery across all three-time points and other strains demonstrating a variety of significant differences in each of the 6-hour time bins **[Figure 5b]**. This finding is true across all of the 10 listed phenotypes, although DB REM had the fewest significant differences shown between baseline and recovery. *This variation in recovery from sleep deprivation across strains suggests that the homeostat may be regulated by genetic mechanisms*.

Since we initially compared these phenotypes using relative data, via the Pearson R values, we also examined whether there would be any differences in the phenotypes across the strains using absolute values. We examined sleep fragmentation, which is often used as a measurement of sleep homeostasis. We took the four sleep fragmentation phenotypes (NREM Bouts, REM Bouts, Total Sleep Bouts, and Number

of Bouts of Arousal) of each animal in each strain, and we subtracted the recovery values from the baseline values in each of the studied 6-hour intervals [**Figure 6**]. We then ran a Kruskal-Wallis ANOVA to examine strain differences regarding this change between baseline and recovery. The analysis yielded that there were significant differences in this change between the strains. With the number of bouts of NREM there was a significance difference between all strains in ZT 7-12 ($p < 0.001$), 13-18 ($p < 0.001$) and 19-24 ($p = 0.0212$) [**Figure 6a**]. With the number of bouts of REM, a significant difference between strains was found in ZT 6-12 ($p < 0.0001$), 12-18 ($p = 0.0032$) but surprisingly not for 18-24 ($p = 0.1148$) [**Figure 6b**]. With the number of bouts of Total Sleep, a significant difference between strains was found in ZT 6-12 ($p < 0.0001$), 12-18 ($p = 0.0011$), and 18-24 ($p = 0.0286$) [**Figure 6c**]. Looking at the number of bouts of arousal, a significant difference between strains was found in ZT 6-12 ($p = 0.0018$), 12-18 ($p = 0.0014$), and 19-24 ($p = 0.0091$) [**Figure 6d**]. These findings suggest that *the homeostatic response to sleep loss is indeed genetically regulated, and that regulation is likely encoded by adjustments to sleep-wake fragmentation after sleep loss*.

Discussion

The mechanisms that underlie sleep homeostasis are currently not fully understood. To better understand how genetic heterogeneity contributes to sleep homeostasis, we analyzed data to examine differences between strains across 10 different phenotypic conditions (both in baseline and in recovery). We also examined differences within strains (between baseline and recovery) across 10 different phenotypes and to see whether there was a difference in sleep phenotype response between baseline and

recovery. All of the data was separated into three time periods: ZT 6-12, ZT 12-18 and ZT 18-24.

Differences in between-strain comparisons let us know which specific phenotypes have a high degree of genetic heterogeneity. The finding of strain differences would suggest that genetic differences (as opposed to environmental perturbations) underlie these variations in sleep phenotypes. In order to explore this, I conducted a between-strain analysis of variance across three time windows (ZT 6-12, 12-18 and 18-24) in their baseline condition. Subsequently, I conducted a between-strain analysis of variance across all three time windows in the recovery condition. In addition, I compared the sleep phenotypes across all strains in their baseline condition to their recovery condition across three different time bins to see if there was a phenotypic difference in the dissipation of sleep pressure. In order to do this, we ran Pearson's correlations to normalize the dataset for comparison.

Ten sleep phenotypes exhibited significant differences across strains during baseline and recovery conditions

For the between-strain analyses, there was a significant difference between the strains for all phenotypes in the baseline condition. For the between-strain analysis in the recovery condition, we also found a significant difference in all of the strains in every phenotype. These differences are illustrated in the graphs [**Fig. 4**] which show several examples of how different the strains are from each other. Prior studies also substantiate this evidence as different strains are expected to spend different amounts of time sleeping and displaying sleep phenotypes such as NREM sleep (Hoekstra et al., 2019) and REM sleep (Niwa et al., 2018). *These data demonstrate robust strain*

difference among all 10 sleep phenotypes in both the baseline and recovery conditions. They also indicate that several key sleep phenotypes are genetically influenced and suggest that future studies can interrogate these stains to look for specific genes that regulate sleep. However, it is important to note that the strain differences observed during baseline do not necessarily recapitulate the strain differences that occur during recovery.

In order to account for the effects of sleep loss on strain differences during recovery, we examined correlations between baseline and recovery phenotypes within strains. This provides a high throughput measurement of the ability of sleep deprivation to alter strain differences in these phenotypes. This also provides a novel and useful tool to examine sleep homeostasis, which is the ability to recover from sleep loss. This analysis will reveal whether or not there is a genetic component to sleep homeostasis across strains.

Two sleep phenotypes exhibited significant correlations between baseline and recovery across three-time windows

We ran a Pearson's correlation for the phenotypes between baseline and recovery for each animal in three different 6-hour intervals. The R-values gained from the statistical analysis were then compared across all the time intervals for each of the strains. The reason that we used Pearson's correlation is that the different phenotypes are expressed in different units, and all have different responses to sleep loss. In order to perform a comprehensive analysis of the responses to sleep loss across all phenotypes, we chose to apply a normalization that avoids biasing any of the specific phenotypes. Analyzing the recovery from sleep over time is the most efficient method to

detect the effects of sleep deprivation across a panel of numerous different phenotypes with different measurement criteria (Diessler et al., 2018). This statistical analysis revealed significant differences in 2 of the 10 phenotypes: Number of Bouts of NREM and Duration of Bouts of Total Sleep. The remaining 8 phenotypes did not yield any significant differences, as is compatible with the findings in (Diessler et al., 2018) and (Jan et al., 2020). This finding suggests that the genetic mechanisms that are responsible for the homeostatic ability to recover from sleep loss are not reflected in the genetic variation of most of the phenotypes under the current analysis. However, with the number of bouts of NREM and duration of bouts of total sleep showing a significant difference across the strains, this is a promising result for QTL mapping or genetic mapping. To date, few homeostatic sleep phenotypes that account for the differences between baseline and recovery have yielded promising genetic targets (Diessler et al., 2018; Franken et al., 2001; Maret et al., 2007). The finding that these differences in correlations for the number of bouts of NREM and duration of bouts of total sleep suggest that these *two specific phenotypes may yield valuable insights into the genes that regulate sleep homeostasis*.

Sleep-wake fragmentation is a promising measure of sleep homeostasis for genetic mapping studies

Few studies in mammals have examined sleep-wake fragmentation as a measure of sleep homeostasis, in order to conduct forward genetic approaches. When looking at the absolute values of sleep fragmentation, and the differences between baseline and recovery within each of the strains, we found significant differences in many of the strains in all of the phenotypes. This suggests that sleep deprivation produced

significant effects on sleep fragmentation in many inbred strains, but not all of them. However, when we examined recovery with respect to baseline sleep across strains, few phenotypes exhibited significant differences. This finding may provide insights into future studies that seek to explore the role of genetics and sleep homeostasis in mouse models.

We examined sleep phenotypes associated with sleep fragmentation as a measurement of sleep homeostasis. These phenotypes examined recovery relative to baseline. We found that among all homeostatic sleep fragmentation phenotypes, there were significant differences across strains (Fig. 6). In all the fragmentation phenotypes, there were more bouts (either in NREM, REM, Total Sleep or Arousal) in the baseline condition as opposed to the recovery condition but after ZT 12 the opposite becomes more apparent. This is the first inbred strain study focusing on sleep fragmentation as a measure of sleep homeostasis in mammals, and the glaring differences between strains is promising. The data suggests that sleep fragmentation may play a larger role in the genetic regulation of sleep homeostasis than previously thought and opens the door to future exploration of the potential genetic components underlying it.

The next step for this study utilizes a special mouse model that could help with trying to identify a potential genetic component of sleep homeostasis, namely the BxD mouse. An experiment in 2018 (Diessler et al., 2018) was run conducting QTL analysis on 33 BxD mice and they found that sleep traits in mice were heritable and could possibly even be identified in specific loci. The next step for this study is to record the BxD model in both the baseline and recovery conditions and add the BxD data with the rest of the strains. Then QTL analysis will be conducted between the 24 strains and an

investigation will be underway to find specific loci correlated with sleep traits. Other approaches to looking into strain differences, including the new data with the BxD model, could be looking into the Homer1a gene (Mackiewicz et al., 2008) which is associated with Fragile X syndrome or looking at a connection between sleep and Vitamin A signaling (Tafti, 2007).

There also has been several studies on sleep homeostasis which could provide the foundation for future research. Specifically, Dr. Liza Ashbrook (Ashbrook et al., 2020) found that genetic variations in humans could lead to a phenotype of short sleep (Familial natural short sleep) where people would only get 4.5-6 hours of sleep as a result of the DEC2 gene, P385R. Dr. Geraldine Mang and Dr. Paul Franken found that sleep homeostasis is likely to have a myriad of different pathways involved and that sleep homeostasis can vary by sex within specific animal strains (Mang, G. & Franken P., 2015). This data suggests that sleep homeostasis may be involved in other pathways regarding hormones. Dr. Maxime Jan found that the cortical expression of the core clock genes *Npas2* and *Clock* seemed to be driven by sleep-wake homeostasis and didn't seem to have a circadian drive (Jan et al., 2020). Research into sleep homeostasis and its potential mechanisms has great promise and there are a number of different approaches to better understand it. Bettering our understanding of the genetic components of sleep has the potential to help us better understand how sleep disorders functions and possibly even assist in developing treatments for them.

Figure Legends

Figure 1: Head Mount and Commutator

Provided on the left is an image of how the mice look after a complete surgery with the head mount sticking upwards. On the right is an image of the commutator that connects to the head mount to relay EEG data to the computer.

Figure 2: Sleep Deprivation Container and Example Novel Object

On the left is an image of the mouse cage during sleep deprivation. They would have bedding, food and water and would be kept awake by gently moving the cage, introducing a novel object (right image) or disturbing bedding. A novel object like a paintbrush would be of great assistance as it would allow for disturbing of the bedding without having to place my hand inside the cage.

Figure 3: An Example of Scored Sleep-Wake Architecture

This image showcases how the sleep-wake architecture of a 30-second epoch is scored using both EEG and EMG. Wake is yellow, NREM is blue, and REM is red as color coding helps with identification when going through a file. The EMG is beneath the EEG and shows movement during the wake period.

Figure 4: Comparison of Strain Differences among all 12 Sleep Phenotypes in both Baseline and Recovery Conditions.

4a. Comparison of Strain Differences in NREM in the baseline and recovery Conditions.

A one way ANOVA was run across all strains in NREM ZT 6-12, 12-18, and 18-24 which found significant differences in NREM ($p< 0.001$) for all time points across both baseline and recovery.

4b. Comparison of Strain Differences in REM in both the Baseline and Recovery Conditions.

A one way ANOVA was run across all strains in ZT 6-12, 12-18, and 18-24 in baseline and recovery, yielding significance in in REM at all time points ($p < 0.0001$).

4c. Comparison of Strain Differences in Total Sleep in both the Baseline and Recovery Conditions.

A one-way ANOVA was run comparing all strains in baseline and recovery for ZT 6-12, 12-18 and 18-24. The test showed significant differences in Total Sleep amongst the strains ($p < 0.001$).

4d. Comparison of Strain Differences in Number of Bouts of NREM in both the Baseline and Recovery Conditions.

In order to see if there were strain differences in the number of bouts of NREM we performed a Kruskal-Wallis ANOVA in ZT 6-12 ($p < 0.0001$), 12-18 ($p <0.0001$) and 18-24 ($p <0.0001$) and found that the differences between strains were significant. This was also true in the recovery condition.

4e. Comparison of Strain Differences in Duration of Bouts of NREM in both the Baseline and Recovery Conditions.

A significant difference across strains during duration of bouts in baseline was found in ZT 6-12 ($p < 0.0001$), 12-18 ($p < 0.0001$) and 18-24 ($p < 0.0001$). A significant difference across strains during recovery was found in ZT 6-12 ($p < 0.0001$), 12-18 ($p < 0.0001$) and 18-24 ($p < 0.0001$).

4f. Comparison of Strain Differences in Number of Bouts of REM in both the Baseline and Recovery Conditions.

A significant difference across strains in number of bouts of REM during baseline was also found in ZT 6-12 ($p < 0.0001$), 12-18 ($p < 0.0001$) and 18-24 ($p < 0.0001$) according to a one way ANOVA. A significant difference across strains during recovery was found in ZT 6-12 ($p < 0.0001$), 12-18 ($p < 0.0001$) and 18-24 ($p < 0.0001$) according to a one way ANOVA.

4g. Comparison of Strain Differences in Duration of Bouts of REM in both the Baseline and Recovery Conditions.

A significant difference across strains in duration of Bouts of REM during baseline was also found in ZT 6-12 ($p < 0.0001$), 12-18 ($p < 0.0001$) and 18-24 ($p < 0.0001$) according to a one way ANOVA. A significant difference across strains during recovery was found in ZT 6-12 ($p < 0.0001$), 12-18 ($p < 0.0001$) and 18-24 ($p < 0.0001$) according to a one way ANOVA.

4h. Comparison of Strain Differences in Number of Bouts of Total Sleep in both the Baseline and Recovery Conditions.

A significant difference across strains in number of bouts of total sleep during baseline was also found in ZT 6-12 ($p < 0.0001$), 12-18 ($p < 0.0001$) and 18-24 ($p < 0.0001$)

according to a one way ANOVA. A significant difference across strains during recovery was found in ZT 6-12 ($p < 0.0001$), 12-18 ($p < 0.0001$) and 18-24 ($p < 0.0001$) according to a one way ANOVA.

4i. Comparison of Strain Differences in Duration of Bouts of Total Sleep in both the Baseline and Recovery Conditions.

A significant difference across strains in duration of bouts of total sleep during baseline was also found in ZT 6-12 ($p < 0.0001$), 12-18 ($p < 0.0001$) and 18-24 ($p < 0.0001$) according to a one way ANOVA. A significant difference across strains during recovery was found in ZT 6-12 ($p < 0.0001$), 12-18 ($p < 0.0001$) and 18-24 ($p < 0.0001$) according to a one way ANOVA.

4j. Comparison of Strain Differences in Number of Bouts of Arousal in both the Baseline and Recovery Conditions.

A significant difference across strains in number of bouts of arousal during baseline was also found in ZT 6-12 ($p < 0.0001$), 12-18 ($p < 0.0001$) and 18-24 ($p < 0.0001$) according to a one way ANOVA. A significant difference across strains during recovery was found in ZT 6-12 ($p < 0.0001$), 12-18 ($p < 0.0001$) and 18-24 ($p < 0.0001$) according to a one way ANOVA.

Figure 5: Tables Comparing Strains across Three 6 hour Time Bins

5a: Tables Comparing the r-values of Strains across Three 6 hour Time Bins

These tables show the correlation between baseline and recovery for each strain of mouse in each of the six-hour time bins. They are organized (from left to right) as such:

NREM, REM, Total Sleep, Number of Bouts of NREM, Duration of Bouts of NREM, Number of Bouts of REM, Duration of Bouts of REM, Number of Bouts of Total Sleep, Duration of Bouts of Sleep and Number of Bouts of Arousal.

5b: Tables Comparing the p-values of Strains across Three 6 hour Time Bins

These tables show the correlation between the baseline and recovery for each of strain of mouse in each other the six hour time bins. They are organized similar to that of figure 6a. Significance is color-coded in these tables with green being signficant at $p < 0.05$, yellow being significant at $p < 0.01$, and red being significant at $p < 0.001$.

Figure 6: Analysis of Baseline - Recovery in Sleep Fragmentation Phenotypes between Strains

6a. Analysis of Baseline – Recovery in Sleep Fragmentation between Strains in Number of Bouts of NREM

With the number of bouts of NREM there was a significance difference between all strains in ZT 7-12 ($p < 0.001$), 13-18 ($p < 0.001$) and 19-24 ($p = 0.0212$).

6b. Analysis of Baseline – Recovery in Sleep Fragmentation between Strains in Number of Bouts of REM

With the number of bouts of REM, a significant difference between the baseline and recovery of all strains was found in ZT 6-12 ($p < 0.0001$), 12-18 ($p = 0.0032$) but surprisingly not for 18-24 ($p = 0.1148$).

6c. Analysis of Baseline – Recovery in Sleep Fragmentation between Strains in Number of Bouts of Total Sleep

With the number of bouts of Total Sleep, a significant difference between baseline and recovery was found in ZT 6-12 ($p < 0.0001$), 12-18 ($p = 0.0011$), and 18-24 ($p = 0.0286$).

6d. Analysis of Baseline – Recovery in Sleep Fragmentation between Strains in Number of Bouts of Arousal

Looking at the number of bouts of arousal, a significant difference between baseline and recovery across the strains were found in ZT 6-12 ($p = 0.0018$), 12-18 ($p = 0.0014$), and 19-24 ($p = 0.0091$).

Figures

Figure 1: Head Mount + Commutator

Figure 2: Sleep Deprivation Set Up

Figure 3: An Example of Scored Sleep-Wake Architecture

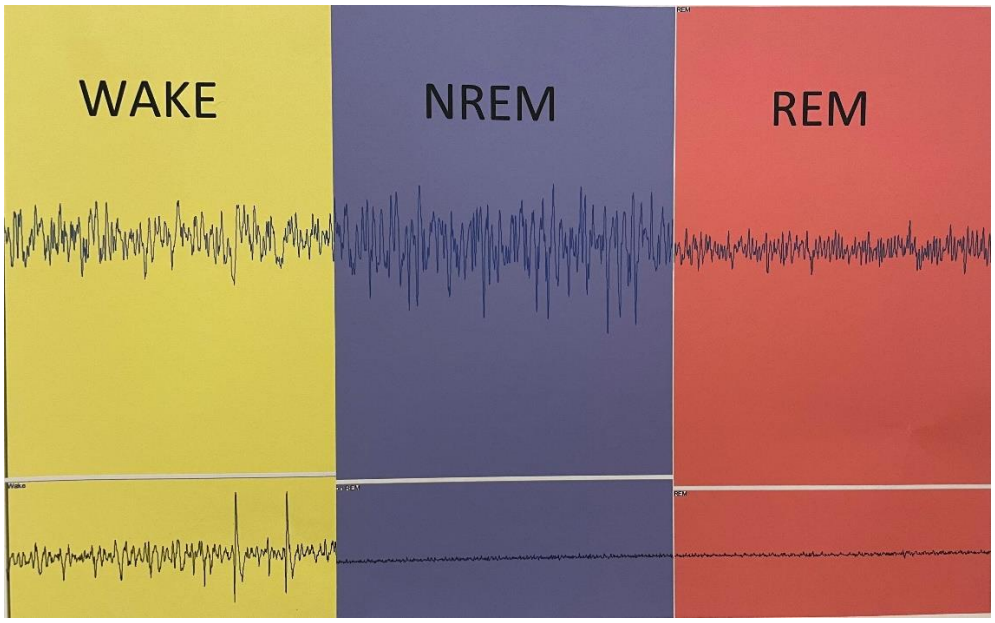
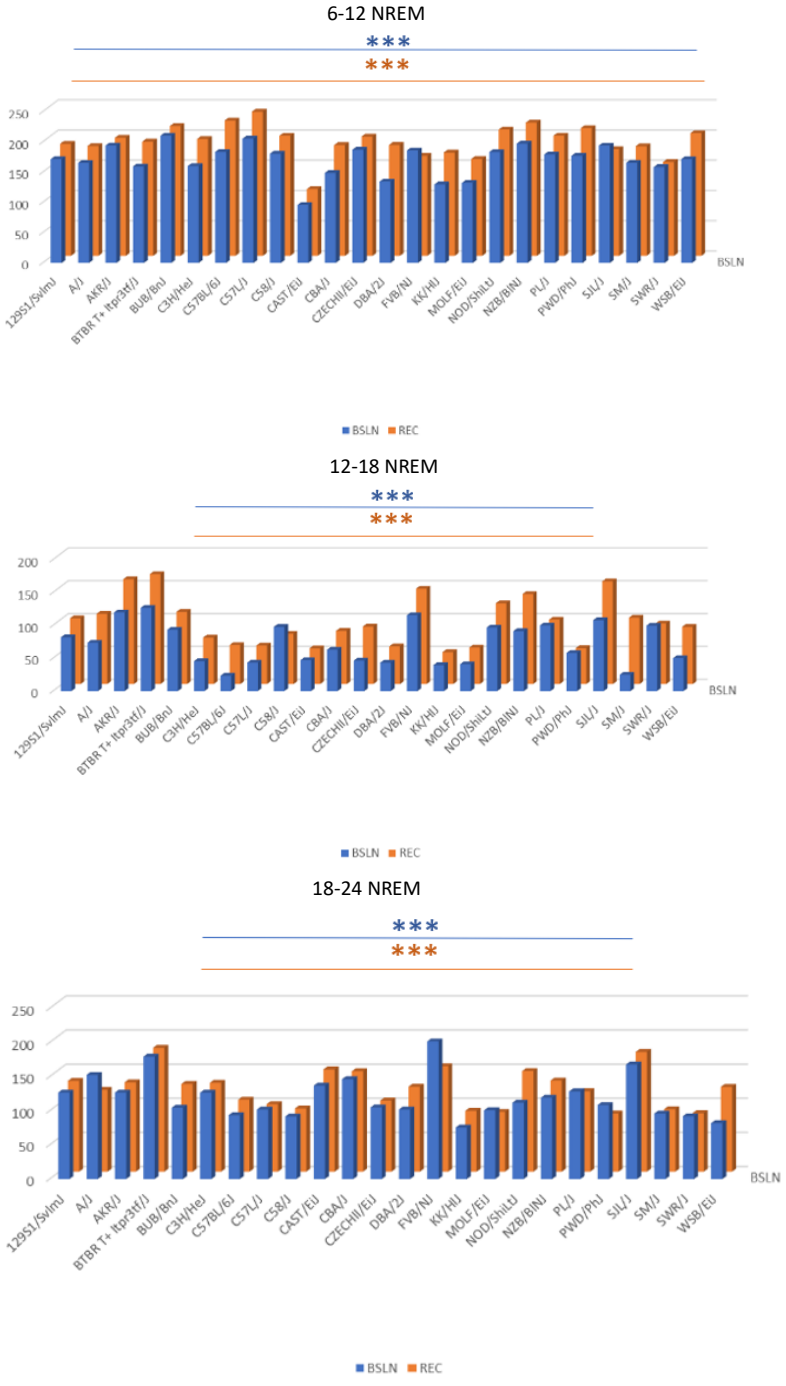
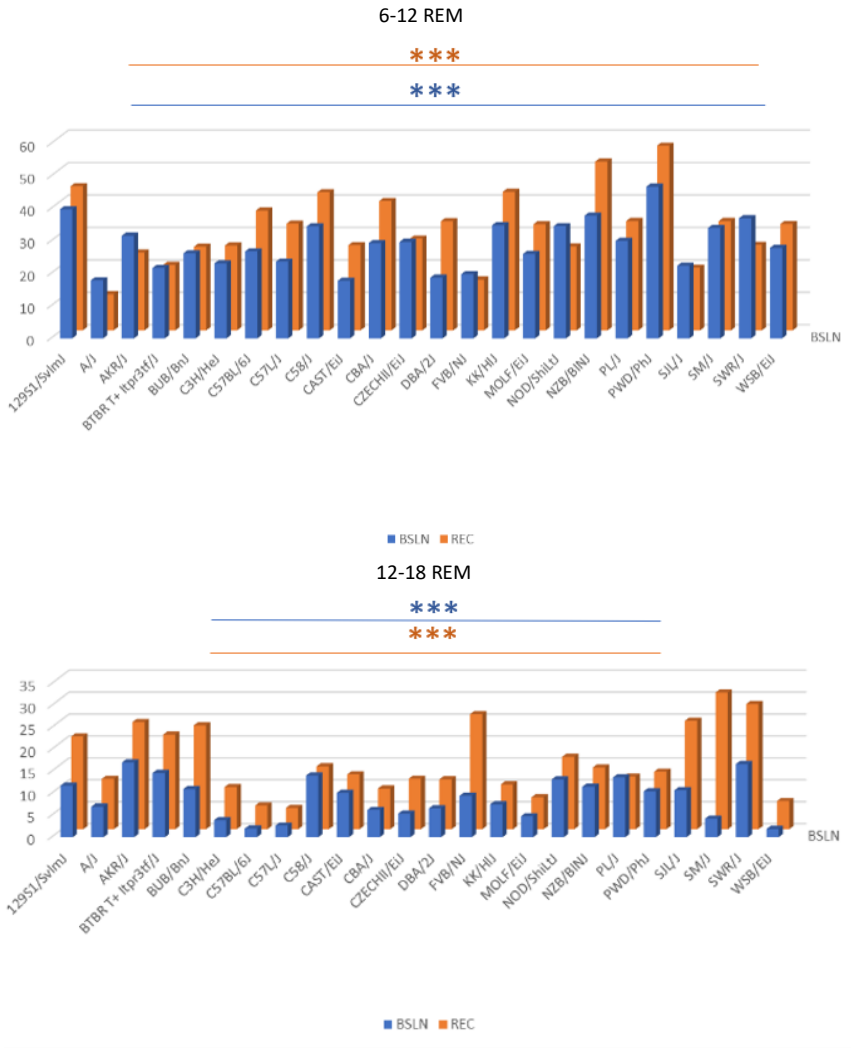


Figure 4: Comparison of Strain Differences among all 10 Sleep Phenotypes in both Baseline and Recovery Conditions

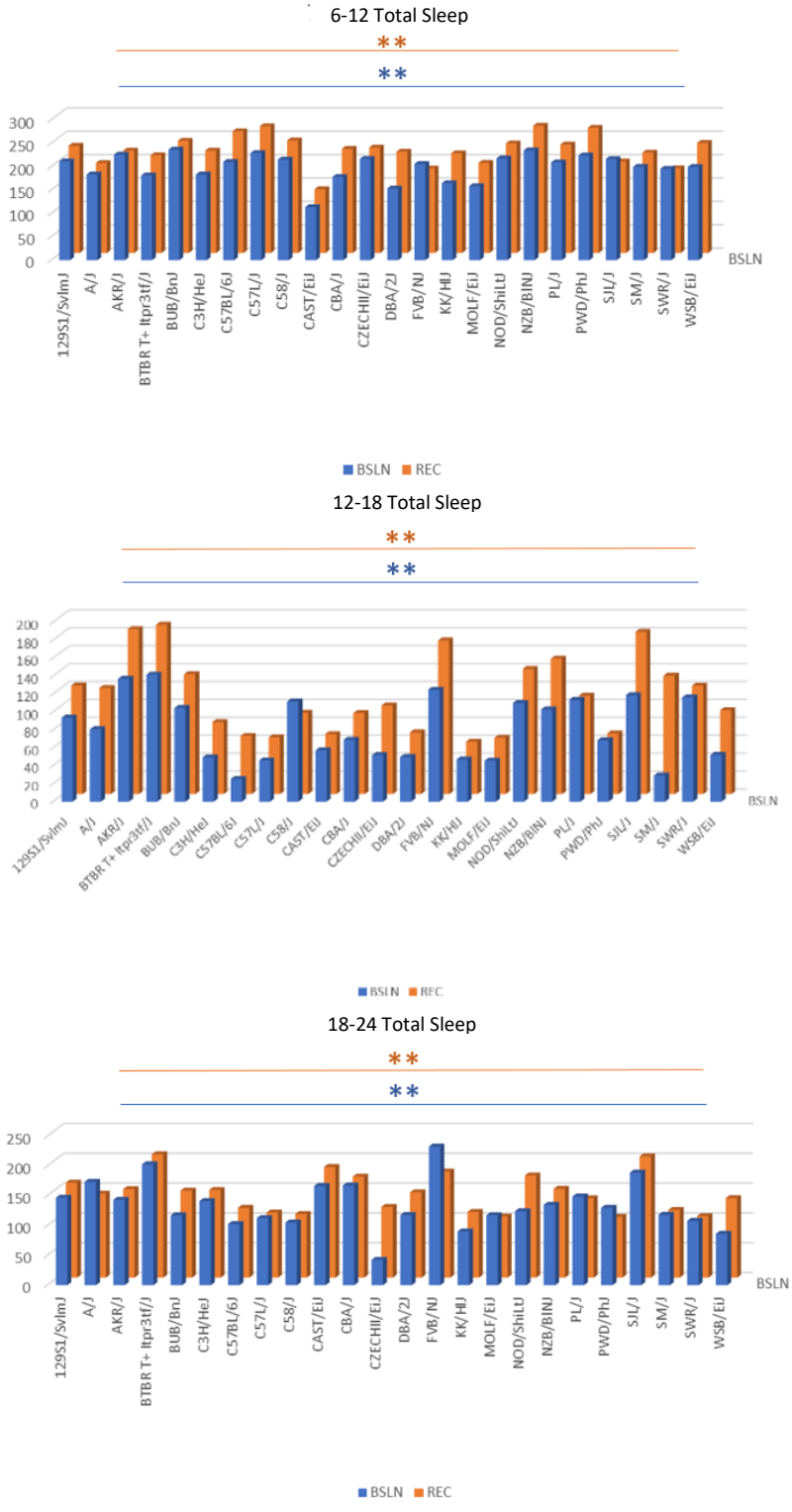
4a. NREM



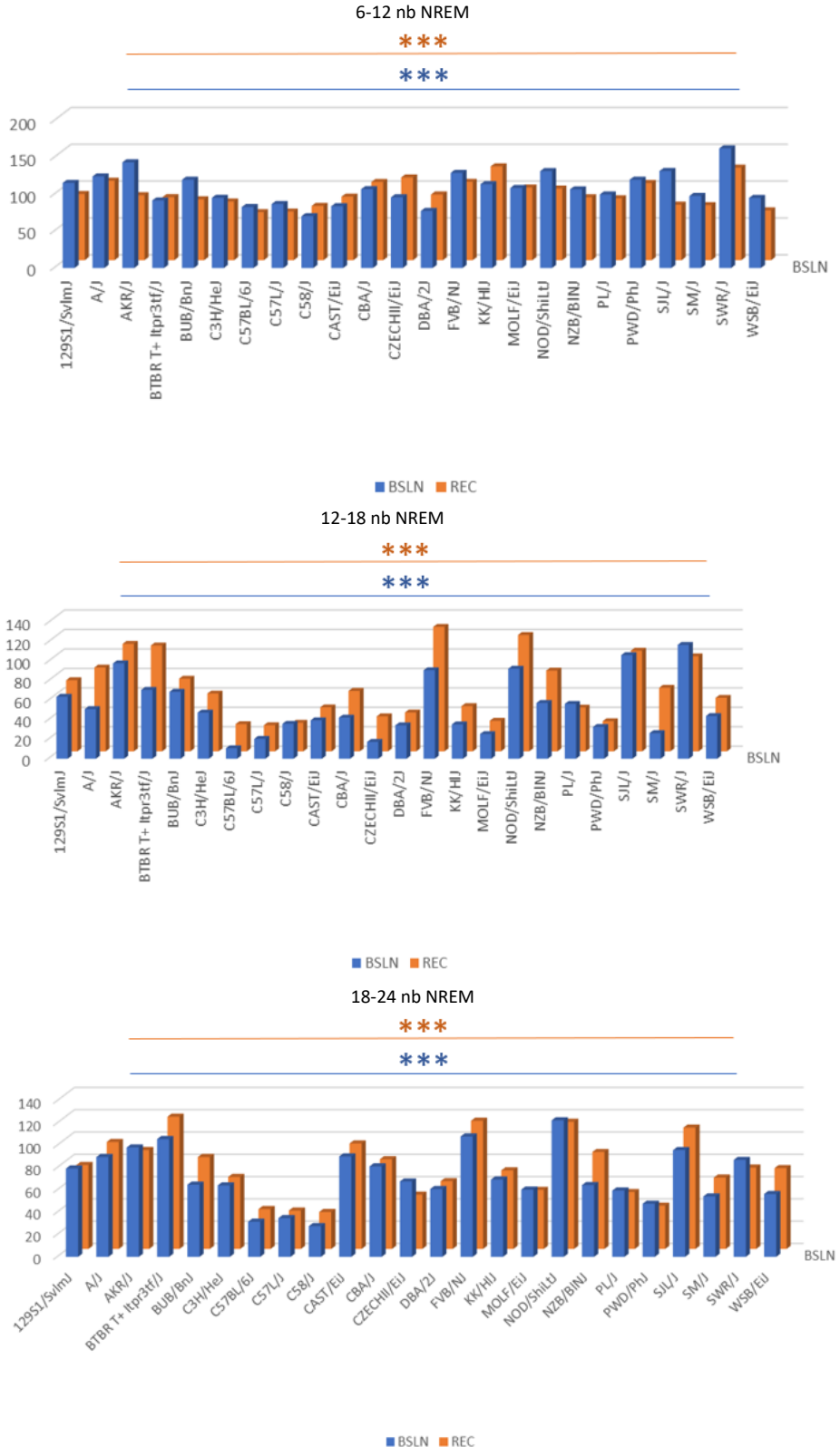
4b. REM


6-12 REM
***
***
60
50
40
30
20
10
0
BSLN
129S1/SvImJ
A/J
AKR/J
BTBR T+ Itpr3tf/J
BUB/BnJ
C3H/HeJ
C57BL/6J
C57L/J
C58/J
CAST/EiJ
CBA/J
CZECHII/EiJ
DBA/2J
FVB/NJ
KK/HlJ
MOLF/EiJ
NOD/ShiLtJ
NZB/BINJ
PL/J
PWD/PhJ
SJL/J
SM/J
SWR/J
WSB/EiJ
BSLN
REC
12-18 REM
***
***
35
30
25
20
15
10
5
0
BSLN
129S1/SvImJ
A/J
AKR/J
BTBR T+ Itpr3tf/J
BUB/BnJ
C3H/HeJ
C57BL/6J
C57L/J
C58/J
CAST/EiJ
CBA/J
CZECHII/EiJ
DBA/2J
FVB/NJ
KK/HlJ
MOLF/EiJ
NOD/ShiLtJ
NZB/BINJ
PL/J
PWD/PhJ
SJL/J
SM/J
SWR/J
WSB/EiJ
BSLN
REC
18-24 REM
***
***
60
50
40
30
20
10
0
BSLN
129S1/SvImJ
A/J
AKR/J
BTBR T+ Itpr3tf/J
BUB/BnJ
C3H/HeJ
C57BL/6J
C57L/J
C58/J
CAST/EiJ
CBA/J
CZECHII/EiJ
DBA/2J
FVB/NJ
KK/HlJ
MOLF/EiJ
NOD/ShiLtJ
NZB/BINJ
PL/J
PWD/PhJ
SJL/J
SM/J
SWR/J
WSB/EiJ
BSLN
REC

4c. Total Sleep

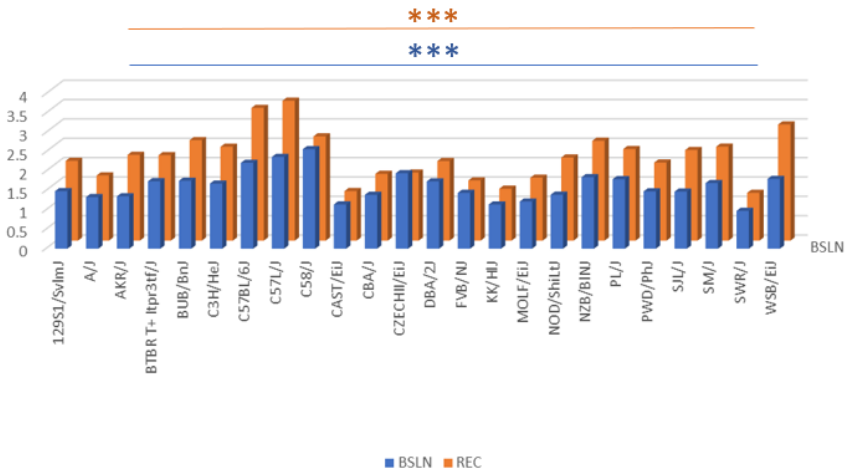


4d. Number of Bouts of NREM

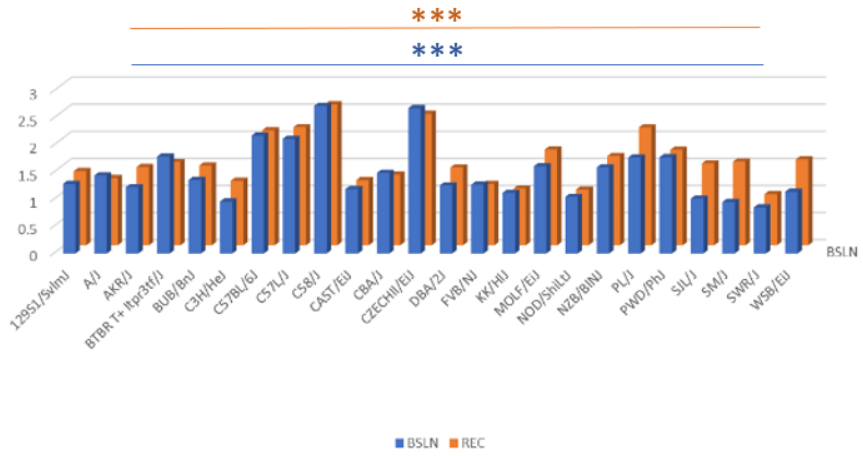


4e. Duration of Bouts of NREM

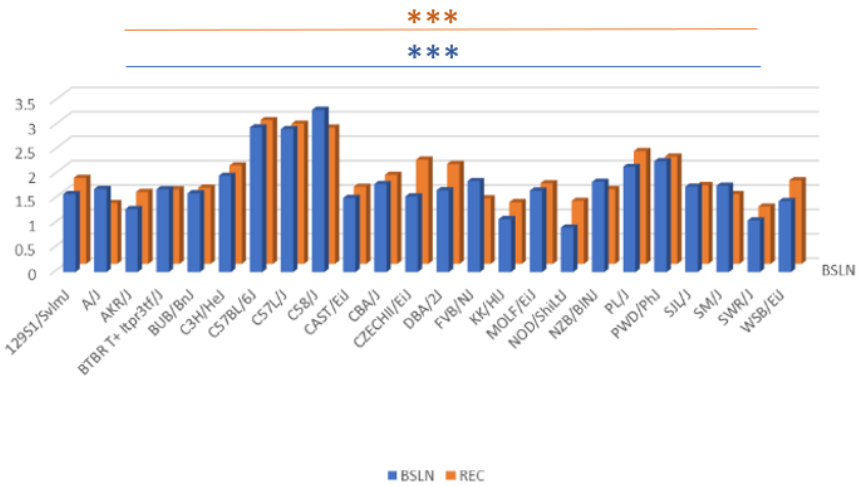
6-12 db NREM



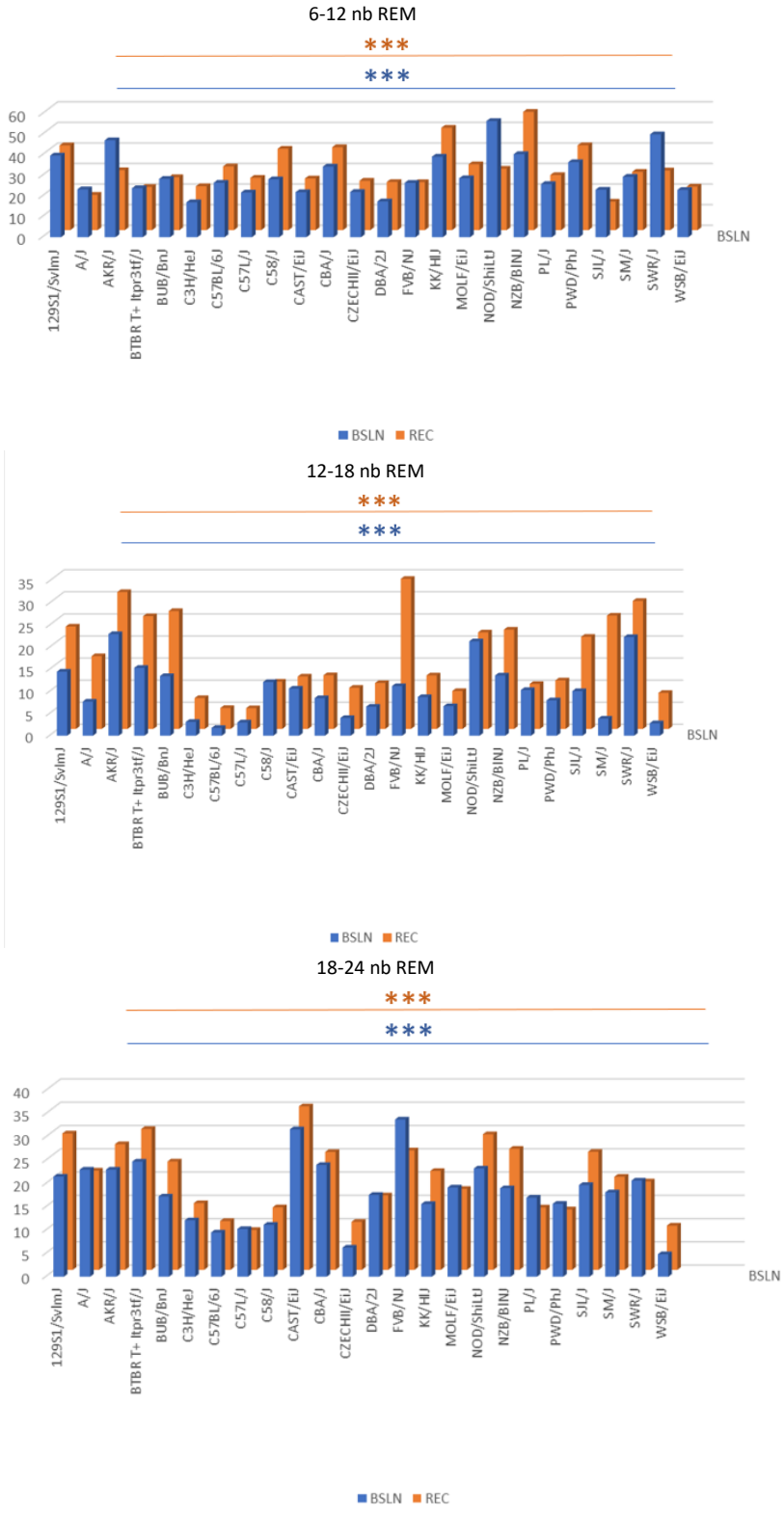
12-18 db NREM



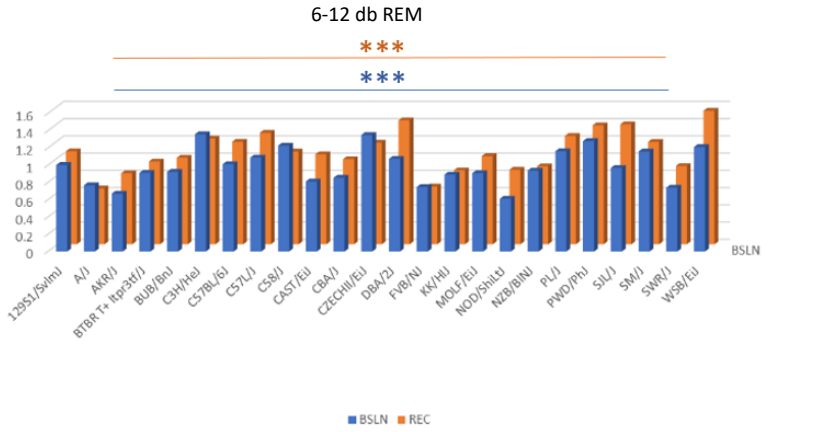
18-24 db NREM

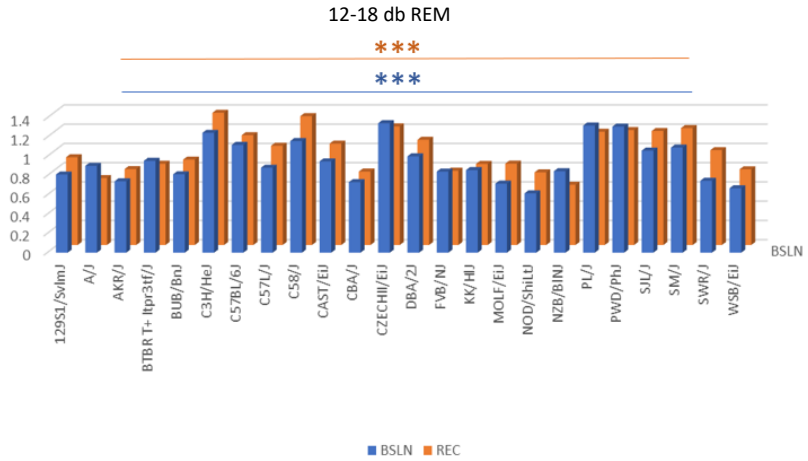


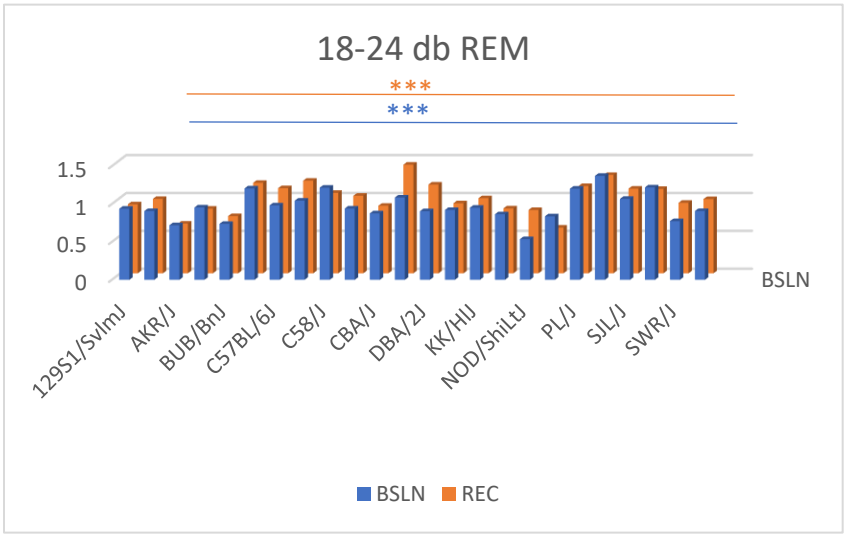
4f. Number of Bouts of REM



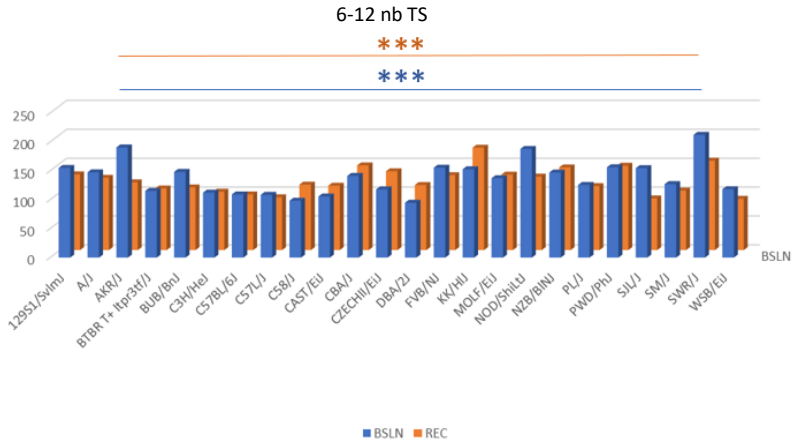
4g. Duration of Bouts of REM

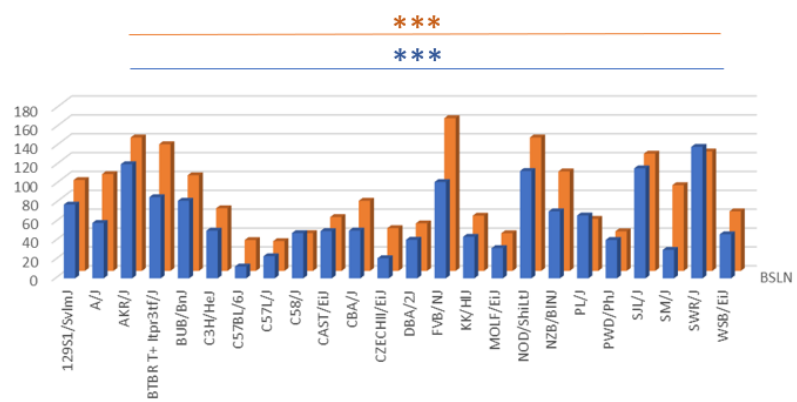


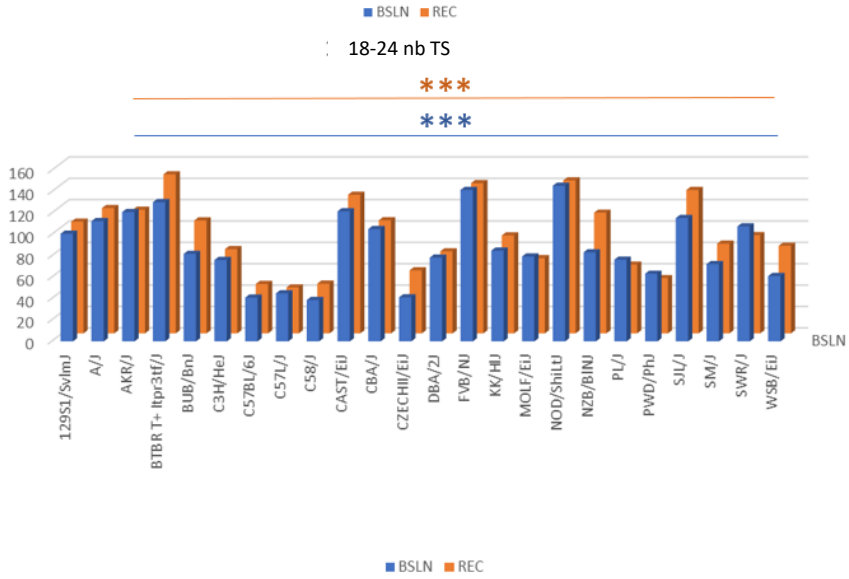




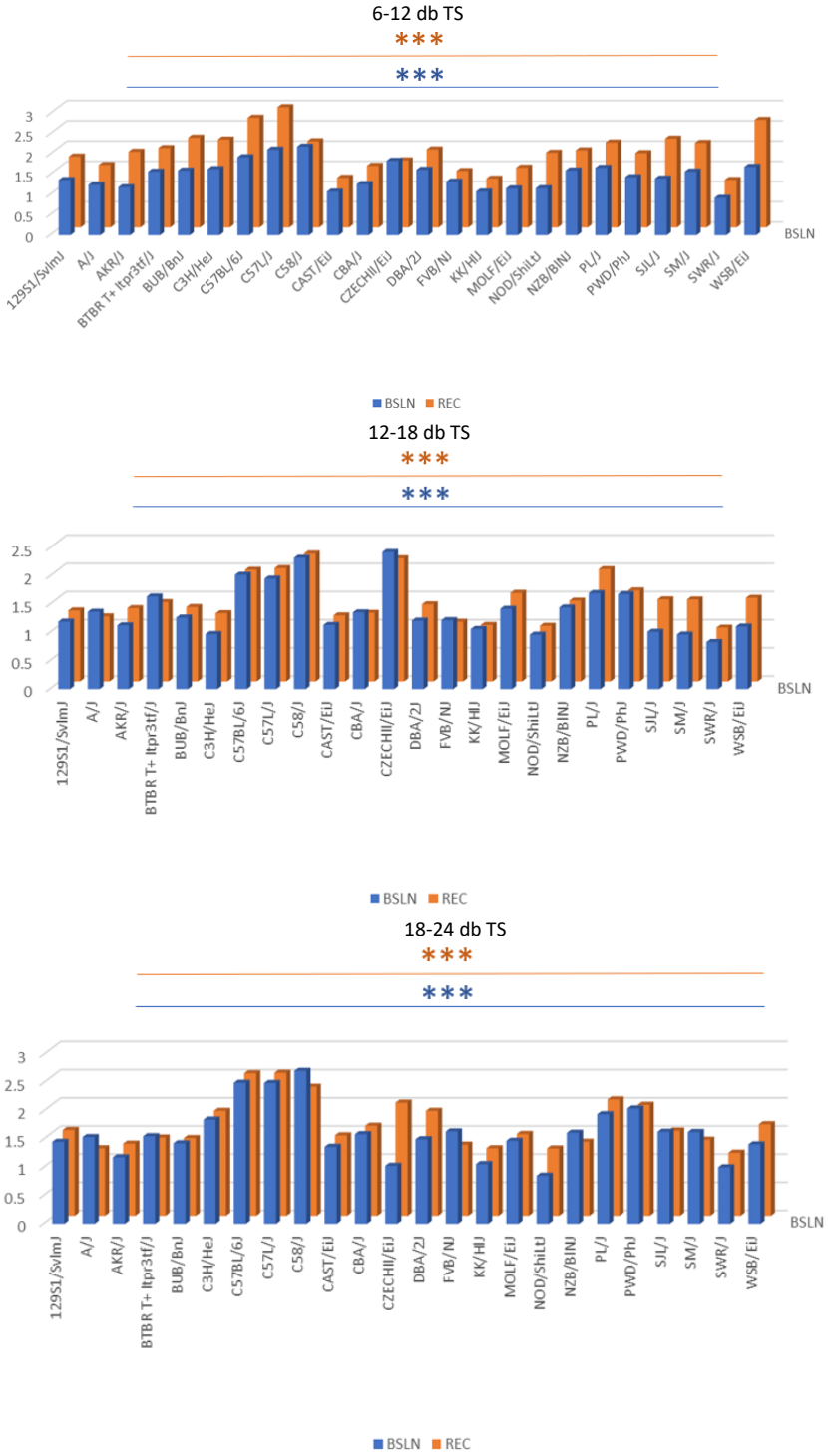
4h. Number of Bouts of Total Sleep







4i. Duration of Bouts of Total Sleep



4j. Number of Bouts of Arousal

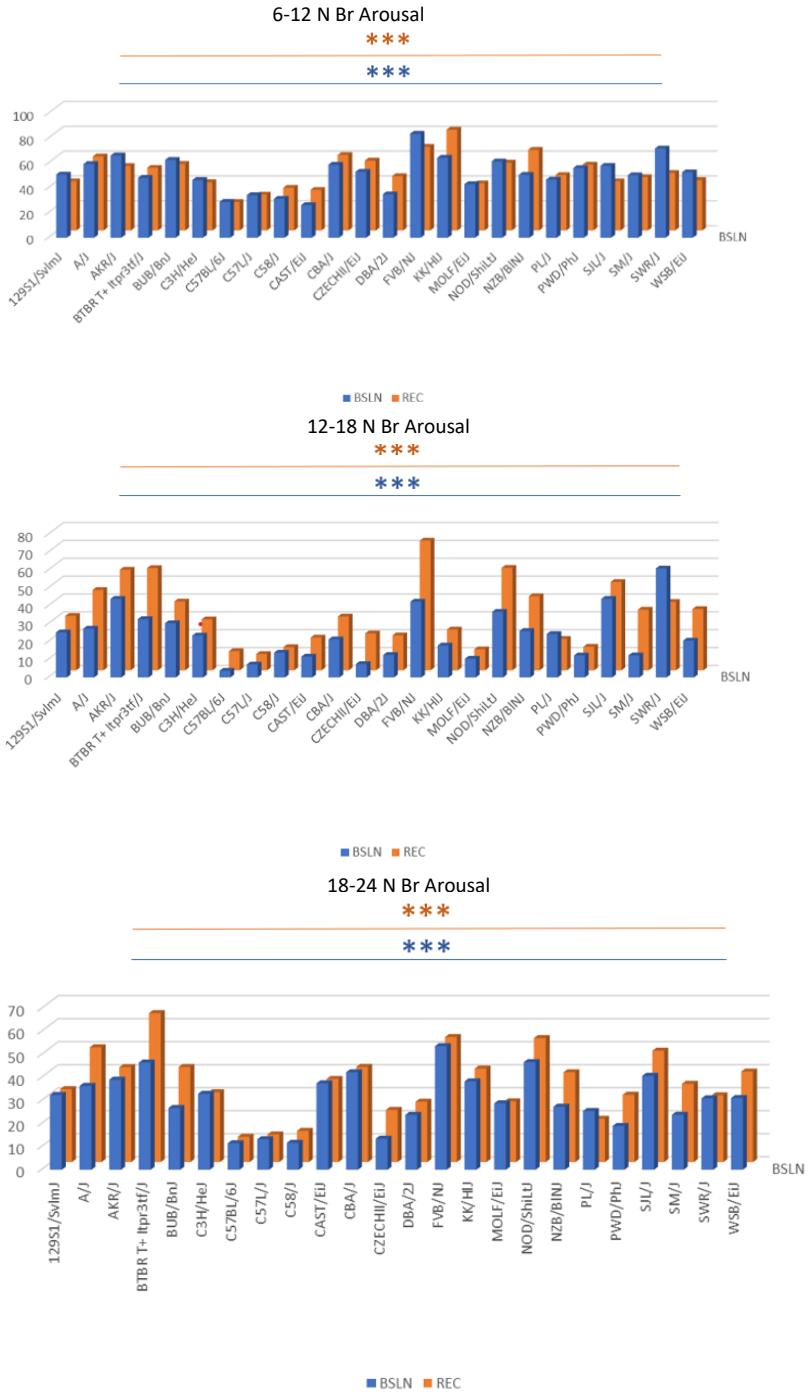


Figure 5: Tables Comparing Strains across Three 6 Hour Time Bins

Figure 5a: Tables of R Values Comparing Strains across Three 6 Hour Time Bins

NREM

Strain	(06-12)	(12-18)	(18-24)
129S1/SvIm	0.39855	0.44489	-0.17498
A/J	0.1157	0.73019	-0.21365
AKR/J	-0.19972	0.64947	0.4864
BTBR T+ Itp	0.66189	0.58469	-0.08677
BUB/BnJ	0.90738	0.56914	0.86361
C3H/HeJ	-0.55311	0.75641	0.72412
C57BL/6J	-0.88169	-0.53145	0.72806
C57L/J	0.37196	0.9458	0.70072
C58/J	0.04058	0.0676	0.9382
CAST/EiJ	0.74539	0.45379	-0.04654
CBA/J	0.81365	0.9285	0.64229
CZECHII/Ei	0.63601	-0.5241	0.83014
DBA/2J	0.61514	0.75479	0.93144
KK/HlJ	0.27386	0.70157	0.2779
MOLF/EiJ	0.00744	0.99327	0.4939
NOD/ShiLtJ	0.25591	0.7772	0.45127
PL/J	0.94318	0.76887	0.89819
PWD/PhJ	0.86913	0.59117	0.88
SJL/J	0.41503	-0.10833	-0.2484
SM/J	0.89728	0.90733	0.08299
SWR/J	0.81706	0.96533	0.73506
WSB/EiJ	0.94876	0.78514	0.8646

REM

Strain	(06-12)	(12-18)	(18-24)
129S1/Svl	0.37597	0.10711	0.62694
A/J	0.64547	-0.66284	-0.48452
AKR/J	0.52796	0.18318	0.76821
BTBR T+ I	0.06385	0.15321	0.58721
BUB/BnJ	0.51343	0.06216	0.79977
C3H/HeJ	-0.52915	0.86243	0.61978
C57BL/6J	0.34684	0.69573	0.87297
C57L/J	0.77432	0.90457	0.2466
C58/J	0.60581	0.7729	0.94982
CAST/EiJ	0.62495	0.56534	0.57103
CBA/J	0.68037	0.86499	0.6436
CZECHII/E	0.95694	-0.92447	0.55492
DBA/2J	0.98285	0.75235	0.83623
KK/HlJ	0.79783	0.69286	0.32487
MOLF/EiJ	0.8952	0.92384	0.61384
NOD/ShiL	-0.15318	0.69825	0.80674
PL/J	0.96071	-0.43265	0.75736
PWD/PhJ	0.2376	0.79143	0.68414
SJL/J	-0.37847	0.84201	0.09236
SM/J	-0.31985	0.99978	-0.75939
SWR/J	-0.95122	0.28947	-0.8508
WSB/EiJ	0.83389	-0.16607	0.45474

TS

Strain	(06-12)	(12-18)	(18-24)
129S1/Svl	0.36333	0.33898	-0.05642
A/J	-0.01155	0.47096	-0.37448
AKR/J	-0.11496	0.62466	0.6715
BTBR T+ I	0.60277	0.5427	0.01372
BUB/BnJ	0.89278	0.38093	0.86911
C3H/HeJ	-0.71317	0.90671	0.67678
C57BL/6J	-0.74073	-0.37818	0.74346
C57L/J	0.26927	0.94394	0.66668
C58/J	0.6282	0.86305	0.77192
CAST/EiJ	0.70273	0.43651	0.2783
CBA/J	0.78043	0.94459	0.67194
CZECHII/E	0.62968	-0.60752	0.94209
DBA/2J	0.80435	0.76565	0.92198
KK/HlJ	0.44679	0.71525	0.28507
MOLF/EiJ	0.26748	0.99029	0.51167
NOD/ShiL	-0.0123	0.77702	0.53785
PL/J	0.90044	0.73986	0.89021
PWD/PhJ	-0.93867	0.13228	0.85123
SJL/J	0.23181	-0.02762	-0.38949
SM/J	0.92064	0.93769	-0.60345
SWR/J	0.8041	0.97602	0.76741
WSB/EiJ	0.91587	0.76508	0.83022

NB NREM

Strain	(06-12)	(12-18)	(18-24)
129S1/SvIm	-0.31645	0.29301	-0.31585
A/J	0.309759	0.448425	0.928879
AKR/J	0.373728	0.298311	0.077278
BTBR T+ Itp	0.25045	0.569608	-0.42569
BUB/BnJ	0.701481	0.42222	0.596672
C3H/HeJ	0.931925	0.812535	0.681135
C57BL/6J	0.728309	0.652377	0.371032
C57L/J	0.908843	0.886705	0.819313
C58/J	0.711417	0.536075	0.929525
CAST/EiJ	0.717776	0.563641	0.382106
CBA/J	0.978289	0.793793	0.796424
CZECHII/EiJ	0.914318	-0.24019	0.993134
DBA/2J	-0.19242	0.988509	0.154453
KK/HlJ	0.795752	0.847166	0.004025
MOLF/EiJ	-0.26041	0.939263	0.63876
NOD/ShiLtJ	0.850537	0.765571	0.860623
PL/J	0.639957	0.371993	0.90798
PWD/PhJ	0.765987	0.955114	0.996655
SJL/J	0.089669	-0.01908	-0.12394
SM/J	-0.9519	0.732331	-0.82603
SWR/J	-0.16733	0.991442	0.907831
WSB/EiJ	0.8955	0.59254	0.816575

DB NREM

Strain	(06-12)	(12-18)	(18-24)
129S1/SvIm	-0.05278	0.536276	-0.219
A/J	0.811568	-0.05647	0.319427
AKR/J	-0.05465	-0.00733	-0.11056
BTBR T+ I	-0.17853	-0.27171	-0.28176
BUB/BnJ	0.93063	0.395392	0.613869
C3H/HeJ	0.455358	0.603989	0.703244
C57BL/6J	0.941619	-0.09038	0.874788
C57L/J	0.425395	0.810639	0.021482
C58/J	0.619238	0.304463	-0.15618
CAST/EiJ	0.617477	0.426902	0.176294
CBA/J	0.923639	0.849693	0.829141
CZECHII/E	0.996268	0.918459	-0.04812
DBA/2J	-0.13352	0.425685	0.650417
KK/HlJ	0.35315	0.513164	0.445149
MOLF/EiJ	0.069386	0.845389	0.396553
NOD/ShiLt	0.758003	0.43672	0.719282
PL/J	0.495705	0.832864	0.97316
PWD/PhJ	0.612382	0.96736	0.545335
SJL/J	0.360571	0.634926	-0.32138
SM/J	0.999566	0.062221	0.306849
SWR/J	-0.6202	-0.3651	0.876782
WSB/EiJ	0.942881	0.914601	-0.45242

NB REM

Strain	(06-12)	(12-18)	(18-24)
129S1/SvI	0.365399	0.395926	0.434836
A/J	0.521951	-0.18798	-0.89348
AKR/J	0.44664	0.429838	0.760891
BTBR T+ I	0.229524	0.609523	0.119323
BUB/BnJ	0.565708	0.571718	0.363069
C3H/HeJ	0.993399	0.994039	-0.3143
C57BL/6J	0.885134	0.242065	0.824131
C57L/J	0.37368	0.893728	0.292588
C58/J	0.300369	0.563463	0.920747
CAST/EiJ	0.452818	0.580977	0.481942
CBA/J	0.594053	0.975227	-0.07297
CZECHII/E	-0.14286	-0.86603	0.755929
DBA/2J	0.432549	0.86267	0.516025
KK/HlJ	0.582532	0.520389	0.252965
MOLF/EiJ	0.892178	0.762161	0.010183
NOD/ShiLt	0.132167	0.765332	0.590561
PL/J	0.717607	0.774913	0.75585
PWD/PhJ	0.279553	0.839109	0.60553
SJL/J	0.098943	0.839516	0.859449
SM/J	0.802955	0.995567	-0.05241
SWR/J	-0.67193	0.06647	-0.77771
WSB/EiJ	0.505514	0.160645	0.475247

DB REM

Strain	(06-12)	(12-18)	(18-24)
129S1/SvI	-0.25358	-0.07301	0.165311
A/J	0.760644	0.811263	-0.00261
AKR/J	0.186465	-0.09294	0.526389
BTBR T+ I	0.322632	0.781001	0.453637
BUB/BnJ	0.545954	0.358376	0.74312
C3H/HeJ	-0.10439	0.887977	0.281144
C57BL/6J	0.737542	0.282104	0.470843
C57L/J	-0.04239	0.473331	0.118235
C58/J	0.368457	-0.14595	0.733407
CAST/EiJ	0.096222	0.0248	0.704827
CBA/J	0.043367	0.805072	0.414105
CZECHII/E	0.983046	-0.98381	0.804818
DBA/2J	0.616514	0.18207	0.184585
KK/HlJ	0.617553	0.784777	0.680785
MOLF/EiJ	0.423039	0.889889	0.64248
NOD/ShiLt	0.517399	0.082968	0.16938
PL/J	0.909526	0.8784	0.085929
PWD/PhJ	0.316442	0.185966	0.61993
SJL/J	0.301519	0.467953	0.606898
SM/J	0.523797	-0.41324	0.893161
SWR/J	0.680885	0.750487	-0.88396
WSB/EiJ	0.746109	-0.23389	0.347767

NB TS

Strain	(06-12)	(12-18)	(18-24)
129S1/SvIm	-0.05493	0.08042	-0.15321
A/J	0.134066	0.683366	0.914969
AKR/J	0.42278	0.590358	0.708354
BTBR T+ Itp	0.341582	0.688705	-0.25333
BUB/BnJ	0.612038	0.451449	0.506327
C3H/HeJ	0.961814	0.863965	0.761728
C57BL/6J	0.817491	0.518407	0.475546
C57L/J	0.926081	0.892491	0.738533
C58/J	0.839883	0.51344	0.937485
CAST/EiJ	0.776596	0.489126	0.385752
CBA/J	0.954273	0.793706	0.571544
CZECHII/EiJ	0.980481	-0.29785	0.978983
DBA/2J	-0.00917	0.972643	0.180925
KK/HlJ	0.684169	0.775705	0.095601
MOLF/EiJ	-0.52479	0.925644	0.438493
NOD/ShiLtJ	0.726233	0.898004	0.783001
PL/J	0.597719	0.555523	0.886612
PWD/PhJ	0.735344	0.936959	0.047377
SJL/J	0.038928	0.169428	0.404779
SM/J	0.453921	0.903799	-0.97073
SWR/J	-0.15435	0.783382	0.047377
WSB/EiJ	0.613746	0.525765	0.907463

DB TS

Strain	(06-12)	(12-18)	(18-24)
129S1/SvI	-0.09438	0.408294	-0.31313
A/J	0.788485	0.253697	0.428191
AKR/J	-0.11411	-0.10446	0.407348
BTBR T+ I	-0.17303	-0.0931	-0.20148
BUB/BnJ	0.896229	0.452446	0.46375
C3H/HeJ	0.539686	0.703629	0.776882
C57BL/6J	0.975786	0.862461	0.899368
C57L/J	0.693472	-0.09644	0.338499
C58/J	0.673533	0.326001	0.357128
CAST/EiJ	0.561595	0.514387	0.177783
CBA/J	0.941229	0.906875	0.626347
CZECHII/E	0.996106	0.526144	-0.4632
DBA/2J	0.648088	0.031858	0.617934
KK/HlJ	0.188649	0.257975	0.28667
MOLF/EiJ	-0.38089	0.872057	0.505435
NOD/ShiLt	0.74959	0.246124	0.652459
PL/J	0.551671	0.926661	0.929652
PWD/PhJ	0.633279	0.76707	0.987522
SJL/J	0.299704	0.661183	-0.0617
SM/J	0.980693	0.519853	0.471471
SWR/J	-0.64442	-0.4678	0.647828
WSB/EiJ	0.928068	0.690323	0.038251

N B Ar

Strain	(06-12)	(12-18)	(18-24)
129S1/SvI	-0.17176	0.538473	0.305233
A/J	0.020758	0.709306	0.120681
AKR/J	0.653031	0.379946	-0.24014
BTBR T+ I	0.395141	0.70395	0.424995
BUB/BnJ	0.72008	0.203719	0.695123
C3H/HeJ	0.832284	0.725555	0.412068
C57BL/6J	0.259481	0.933368	0.720438
C57L/J	0.743346	0.691489	0.866181
C58/J	0.926905	0.27073	0.673547
CAST/EiJ	0.821531	0.101482	0.44549
CBA/J	0.896396	0.864594	0.768369
CZECHII/E	0.762875	-0.73241	0.863365
DBA/2J	0.073229	0.98555	0.141162
KK/HlJ	0.920158	0.880374	0.359976
MOLF/EiJ	0.573945	0.845378	0.929546
NOD/ShiLt	0.139931	0.80591	0.832738
PL/J	0.65028	-0.57971	0.679971
PWD/PhJ	-0.6787	0.996838	0.981348
SJL/J	-0.21008	0.006796	0.234903
SM/J	0.831157	-0.82199	-0.06102
SWR/J	0.256257	-0.88385	0.936244
WSB/EiJ	0.41787	0.713984	0.715679

Figure 5b: Tables of P Values Comparing Recovery-Baseline in Strains across Three 6 Hour Time Bins

NREM

Strain	(6-12)	(12-18)	(18-24)
129S1/SvImJ	0.3758	0.3172	0.7075
A/J	0.853	0.1613	0.7301
AKR/J	0.6677	0.1144	0.2684
BTBR T+ Itpr	0.0265	0.0589	0.7997
BUB/BnJ	0.0048	0.1824	0.0122
C3H/HeJ	0.4469	0.2436	0.2759
C57BL/6J	0.1183	0.4685	0.2719
C57L/J	0.4113	0.0013	0.0795
C58/J	0.0722	0.0153	0.0753
CAST/EiJ	0.0338	0.2587	0.9129
CBA/J	0.0579	0.0075	0.169
CZECHII/EiJ	0.5612	0.6488	0.3765
DBA/2J	0.2694	0.1403	0.0213
KK/HlJ	0.5116	0.0525	0.5052
MOLF/EiJ	0.9905	0.0007	0.3977
NOD/ShiLtJ	0.5407	0.0232	0.2617
PL/J	0.0161	0.1287	0.0384
PWD/PhJ	0.1309	0.4088	0.12
SJL/J	0.3545	0.8172	0.5912
SM/J	0.2911	0.2762	0.9471
SWR/J	0.3912	0.1681	0.4743
WSB/EiJ	0.0039	0.0643	0.0263

REM

Strain	(6-12)	(12-18)	(18-24)
129S1/SvImJ	0.4059	0.8192	0.1319
A/J	0.2395	0.2227	0.4082
AKR/J	0.2232	0.6942	0.0437
BTBR T+ Itpr	0.8521	0.6529	0.0575
BUB/BnJ	0.2386	0.8947	0.0308
C3H/HeJ	0.4708	0.1376	0.3802
C57BL/6J	0.6532	0.3043	0.127
C57L/J	0.041	0.0051	0.594
C58/J	0.1494	0.0416	0.0011
CAST/EiJ	0.0976	0.1442	0.1393
CBA/J	0.1369	0.0261	0.1679
CZECHII/EiJ	0.1875	0.249	0.6255
DBA/2J	0.0027	0.1423	0.0776
KK/HlJ	0.0177	0.0568	0.4324
MOLF/EiJ	0.0401	0.0249	0.2708
NOD/ShiLtJ	0.7172	0.0541	0.0155
PL/J	0.0093	0.4668	0.1381
PWD/PhJ	0.7624	0.2086	0.3159
SJL/J	0.4025	0.0175	0.8439
SM/J	0.7927	0.0133	0.451
SWR/J	0.1997	0.813	0.3522
WSB/EiJ	0.0391	0.7532	0.3649

TS

Strain	(6-12)	(12-18)	(18-24)
129S1/SvImJ	0.4231	0.457	0.9044
A/J	0.9853	0.4233	0.5346
AKR/J	0.8061	0.1337	0.0986
BTBR T+ Itpr	0.0497	0.0845	0.9681
BUB/BnJ	0.0068	0.3992	0.0111
C3H/HeJ	0.2868	0.0933	0.3232
C57BL/6J	0.2593	0.6218	0.2565
C57L/J	0.5593	0.0014	0.1019
C58/J	0.1308	0.0124	0.042
CAST/EiJ	0.0782	0.3275	0.5456
CBA/J	0.067	0.0045	0.1438
CZECHII/EiJ	0.5664	0.5843	0.2177
DBA/2J	0.1008	0.1313	0.0259
KK/HlJ	0.2671	0.0461	0.4937
MOLF/EiJ	0.6635	0.0011	0.3782
NOD/ShiLtJ	0.9769	0.0233	0.1691
PL/J	0.0371	0.1529	0.0429
PWD/PhJ	0.0613	0.8677	0.1488
SJL/J	0.617	0.9531	0.3878
SM/J	0.2553	0.2259	0.5876
SWR/J	0.4053	0.1397	0.4431
WSB/EiJ	0.0103	0.0763	0.0408

NB NREM

Strain	(6-12)	(12-18)	(18-24)
129S1/SvImJ	0.4893	0.5236	0.4901
A/J	0.612	0.4488	0.0225
AKR/J	0.4089	0.5158	0.8692
BTBR T+ Itpr	0.4576	0.0674	0.1918
BUB/BnJ	0.079	0.3454	0.1573
C3H/HeJ	0.0681	0.1875	0.3189
C57BL/6J	0.2717	0.3476	0.629
C57L/J	0.0046	0.0078	0.0241
C58/J	0.073	0.2148	0.0024
CAST/EiJ	0.045	0.1457	0.3502
CBA/J	0.0007	0.0594	0.0579
CZECHII/EiJ	0.2655	0.8456	0.0746
DBA/2J	0.7565	0.0015	0.8041
KK/HlJ	0.0182	0.0079	0.9925
MOLF/EiJ	0.6722	0.0178	0.246
NOD/ShiLtJ	0.0074	0.0268	0.0061
PL/J	0.2448	0.5375	0.033
PWD/PhJ	0.234	0.0449	0.0033
SJL/J	0.8484	0.9676	0.7912
SM/J	0.1983	0.4769	0.3812
SWR/J	0.893	0.0833	0.2755
WSB/EiJ	0.0158	0.2152	0.0474

DB NREM

Strain	(6-12)	(12-18)	(18-24)
129S1/SvImJ	0.9105	0.2146	0.6371
A/J	0.0954	0.9281	0.6003
AKR/J	0.9074	0.9876	0.8135
BTBR T+ Itpr	0.5994	0.419	0.4012
BUB/BnJ	0.0023	0.38	0.1426
C3H/HeJ	0.5446	0.396	0.2968
C57BL/6J	0.0584	0.9096	0.1252
C57L/J	0.3414	0.027	0.9635
C58/J	0.1381	0.5067	0.7381
CAST/EiJ	0.1029	0.2915	0.6762
CBA/J	0.0085	0.0322	0.0413
CZECHII/EiJ	0.055	0.2589	0.9694
DBA/2J	0.8305	0.4748	0.2347
KK/HlJ	0.3908	0.1934	0.2691
MOLF/EiJ	0.9117	0.0713	0.5087
NOD/ShiLtJ	0.0293	0.2793	0.0443
PL/J	0.3957	0.0799	0.0053
PWD/PhJ	0.3876	0.0326	0.4547
SJL/J	0.4269	0.1255	0.4821
SM/J	0.0188	0.9604	0.8015
SWR/J	0.5741	0.7621	0.3194
WSB/EiJ	0.0048	0.0106	0.3677

NB REM

Strain	(6-12)	(12-18)	(18-24)
129S1/SvImJ	0.4202	0.3793	0.3296
A/J	0.367	0.7621	0.0411
AKR/J	0.3151	0.3358	0.047
BTBR T+ Itpr	0.4972	0.0465	0.7268
BUB/BnJ	0.1856	0.1799	0.4234
C3H/HeJ	0.0066	0.006	0.6857
C57BL/6J	0.1149	0.7579	0.1759
C57L/J	0.409	0.0067	0.5243
C58/J	0.5128	0.1878	0.0033
CAST/EiJ	0.2599	0.131	0.2265
CBA/J	0.2137	0.0009	0.8907
CZECHII/EiJ	0.9087	0.3333	0.4544
DBA/2J	0.467	0.0598	0.3734
KK/HlJ	0.1297	0.1861	0.5455
MOLF/EiJ	0.0418	0.1342	0.987
NOD/ShiLtJ	0.7551	0.0269	0.1232
PL/J	0.1723	0.1238	0.1394
PWD/PhJ	0.7204	0.1609	0.3945
SJL/J	0.8328	0.0181	0.0132
SM/J	0.4065	0.06	0.9666
SWR/J	0.5309	0.9577	0.4328
WSB/EiJ	0.3063	0.7611	0.3408

DB REM

Strain	(6-12)	(12-18)	(18-24)
129S1/SvImJ	0.5832	0.8764	0.7232
A/J	0.1354	0.0956	0.9967
AKR/J	0.6889	0.8429	0.2248
BTBR T+ Itpr	0.3332	0.0045	0.1611
BUB/BnJ	0.2049	0.4299	0.0556
C3H/HeJ	0.8956	0.112	0.7189
C57BL/6J	0.2625	0.7179	0.5292
C57L/J	0.9281	0.2834	0.8007
C58/J	0.4161	0.7549	0.0607
CAST/EiJ	0.8207	0.9535	0.0509
CBA/J	0.935	0.0533	0.4143
CZECHII/EiJ	0.1174	0.1147	0.4045
DBA/2J	0.2681	0.7695	0.7663
KK/HlJ	0.1028	0.0211	0.0631
MOLF/EiJ	0.4779	0.0431	0.2424
NOD/ShiLtJ	0.1891	0.8451	0.6884
PL/J	0.0322	0.05	0.8907
PWD/PhJ	0.6836	0.814	0.3801
SJL/J	0.5111	0.2896	0.1484
SM/J	0.649	0.7288	0.297
SWR/J	0.5232	0.4596	0.3097
WSB/EiJ	0.0885	0.6556	0.4994

NB TS

Strain	(06-12)	(12-18)	(18-24)
129S1/SvImJ	0.9069	0.8639	0.743
A/J	0.8298	0.2034	0.0294
AKR/J	0.3447	0.1629	0.0748
BTBR T+ Itpr	0.3039	0.0191	0.4523
BUB/BnJ	0.1441	0.3092	0.2462
C3H/HeJ	0.0382	0.136	0.2383
C57BL/6J	0.1825	0.4816	0.5245
C57L/J	0.0027	0.0069	0.058
C58/J	0.018	0.2386	0.0018
CAST/EiJ	0.0234	0.2187	0.3453
CBA/J	0.0031	0.0594	0.236
CZECHII/EiJ	0.126	0.8075	0.1308
DBA/2J	0.9883	0.0054	0.7709
KK/HlJ	0.0613	0.0237	0.8218
MOLF/EiJ	0.3639	0.0241	0.4601
NOD/ShiLtJ	0.0413	0.0025	0.0216
PL/J	0.2871	0.331	0.045
PWD/PhJ	0.2647	0.063	0.9698
SJL/J	0.934	0.7165	0.3677
SM/J	0.7	0.2815	0.1544
SWR/J	0.9013	0.427	0.9698
WSB/EiJ	0.195	0.284	0.0124

DB TS

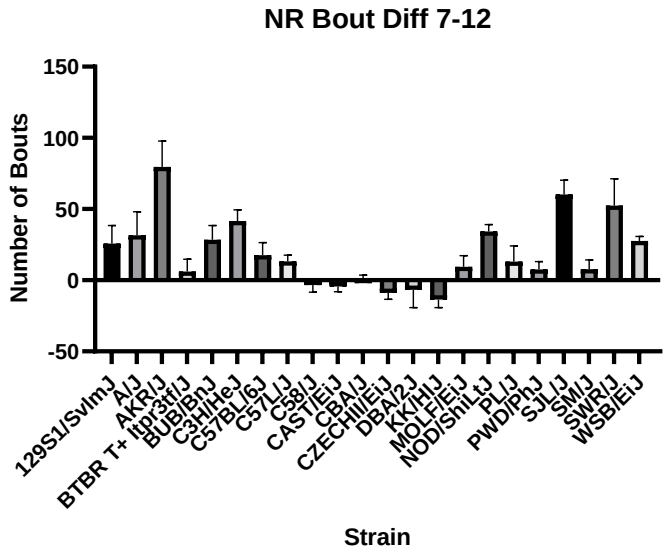
Strain	(06-12)	(12-18)	(18-24)
129S1/SvImJ	0.8405	0.3632	0.4941
A/J	0.113	0.6805	0.472
AKR/J	0.8075	0.8236	0.3644
BTBR T+ Itpr	0.6109	0.7854	0.5525
BUB/BnJ	0.0063	0.308	0.2946
C3H/HeJ	0.4603	0.2964	0.2231
C57BL/6J	0.0242	0.1375	0.1006
C57L/J	0.084	0.8558	0.4577
C58/J	0.0972	0.4755	0.4316
CAST/EiJ	0.1475	0.1921	0.6736
CBA/J	0.0051	0.0126	0.1833
CZECHII/EiJ	0.0562	0.6473	0.6934
DBA/2J	0.2369	0.9594	0.2666
KK/HlJ	0.6546	0.5373	0.4912
MOLF/EiJ	0.527	0.0539	0.385
NOD/ShiLtJ	0.0323	0.5568	0.0795
PL/J	0.3351	0.0236	0.0222
PWD/PhJ	0.3667	0.2329	0.0125
SJL/J	0.5137	0.1058	0.8954
SM/J	0.1253	0.652	0.6874
SWR/J	0.5542	0.6901	0.5514
WSB/EiJ	0.0229	0.3097	0.9513

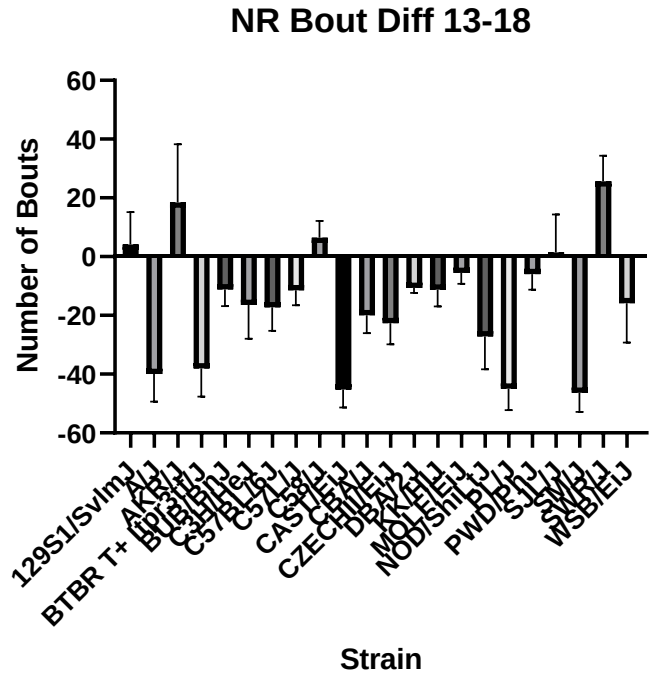
N B Ar

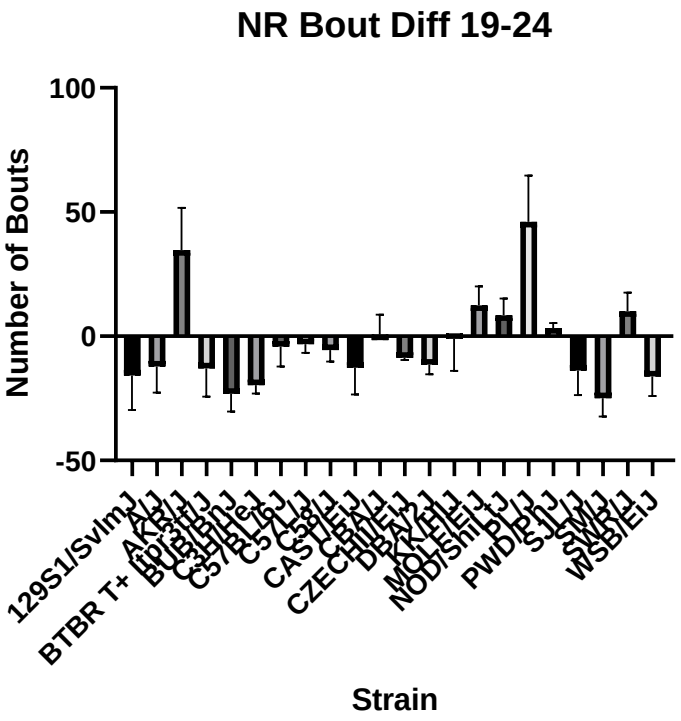
Strain	(06-12)	(12-18)	(18-24)
129S1/SvImJ	0.7127	0.2124	0.5056
A/J	0.9736	0.1797	0.8467
AKR/J	0.1118	0.4005	0.604
BTBR T+ Itpr	0.2291	0.0156	0.1926
BUB/BnJ	0.068	0.6613	0.083
C3H/HeJ	0.1677	0.2744	0.5879
C57BL/6J	0.7405	0.0666	0.2796
C57L/J	0.0555	0.0853	0.01117
C58/J	0.0027	0.5571	0.0972
CAST/EiJ	0.0124	0.811	0.2686
CBA/J	0.0155	0.0263	0.0743
CZECHII/EiJ	0.4476	0.4768	0.3367
DBA/2J	0.9068	0.0021	0.8209
KK/HlJ	0.0012	0.0039	0.3811
MOLF/EiJ	0.3116	0.0713	0.0222
NOD/ShiLtJ	0.741	0.0157	0.0103
PL/J	0.2348	0.3056	0.2066
PWD/PhJ	0.3213	0.0032	0.0187
SJL/J	0.6512	0.9885	0.6121
SM/J	0.3754	0.3857	0.9611
SWR/J	0.835	0.3099	0.2286
WSB/EiJ	0.4097	0.111	0.1098

Figure 6: Absolute Differences in Sleep Fragmentation

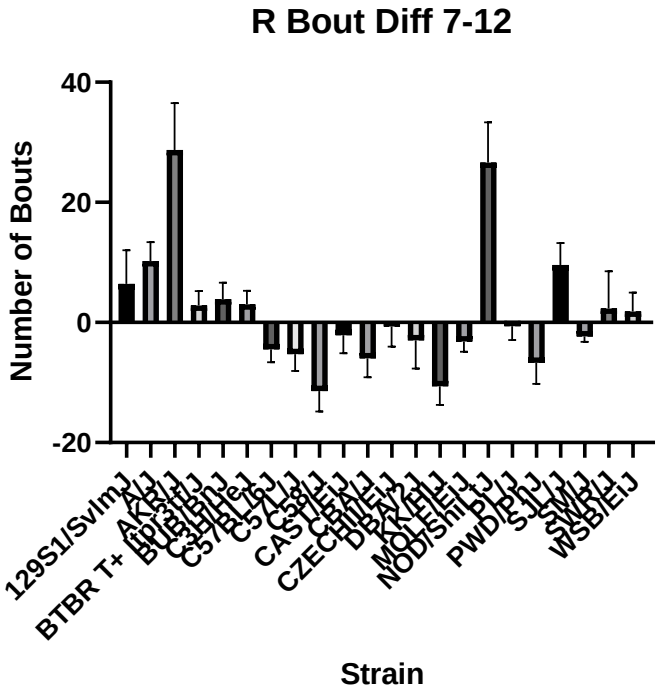
6a. Number of Bouts of NREM

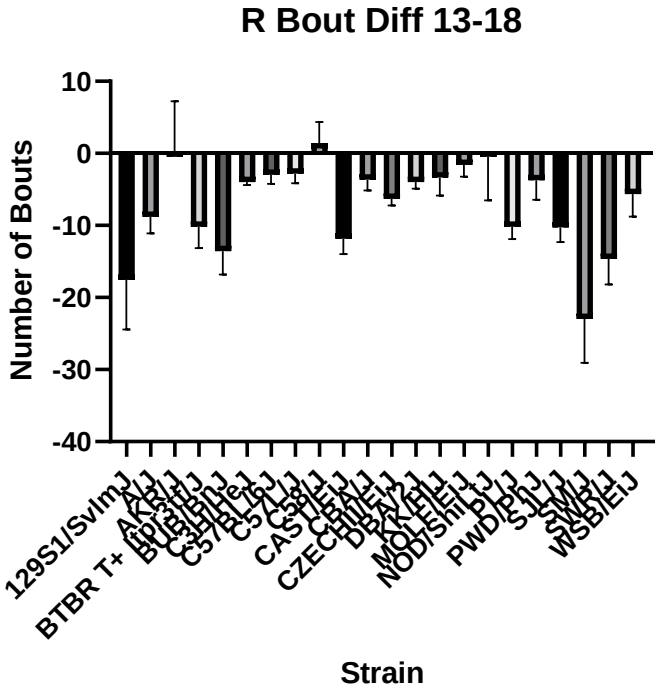


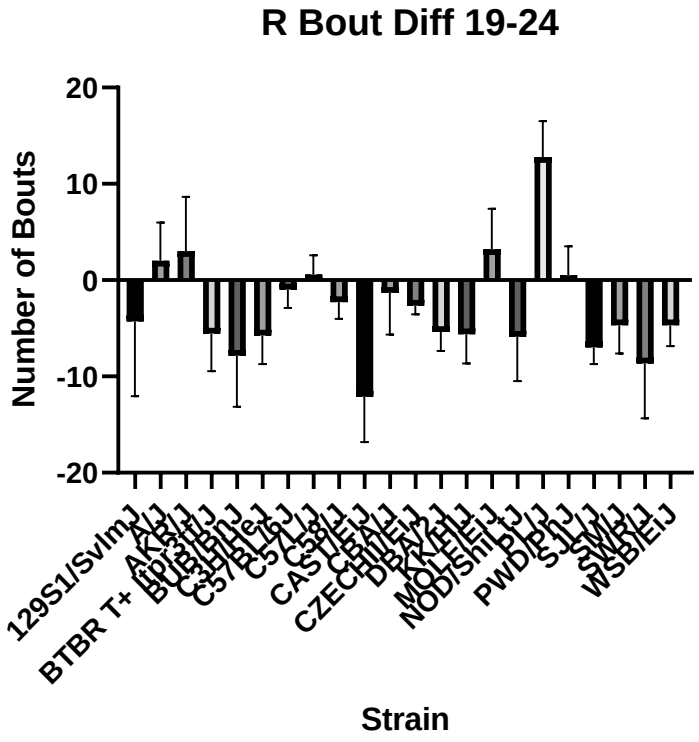



NR Bout Diff 19-24
Number of Bouts
100
50
0
-50
129S1/SvImJ
A/J
AKR/J
BTBR T+ Itpr3tf/J
BUB/BnJ
C3H/HeJ
C57BL/6J
C57BL/10J
C57L/J
CAST/EiJ
CBA/J
CZECHII/EiJ
DBA/2J
KK/HlJ
MOLF/EiJ
NOD/ShiLtJ
NZB/BlNJ
PWD/PhJ
SJL/J
SM/J
SWR/J
WSB/EiJ
Strain

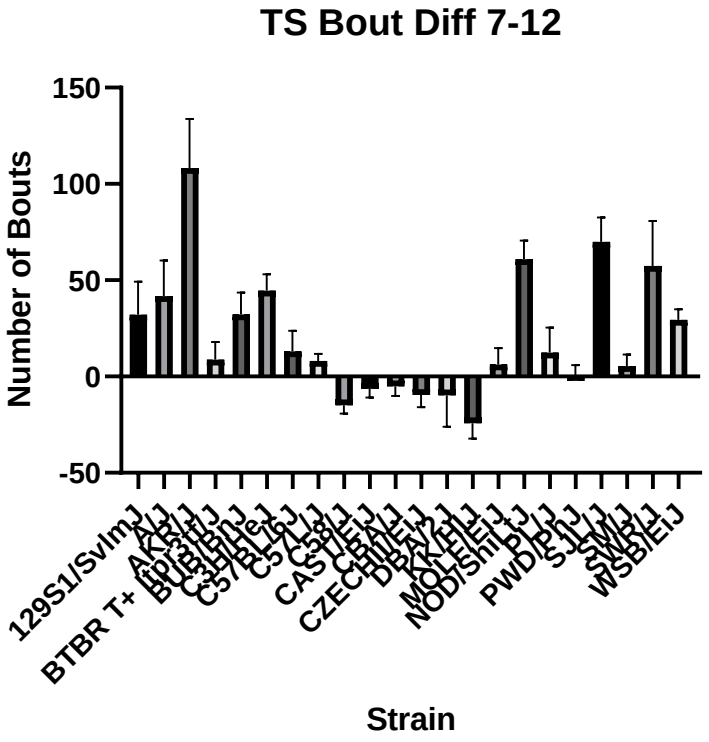
6b. Number of Bouts of REM

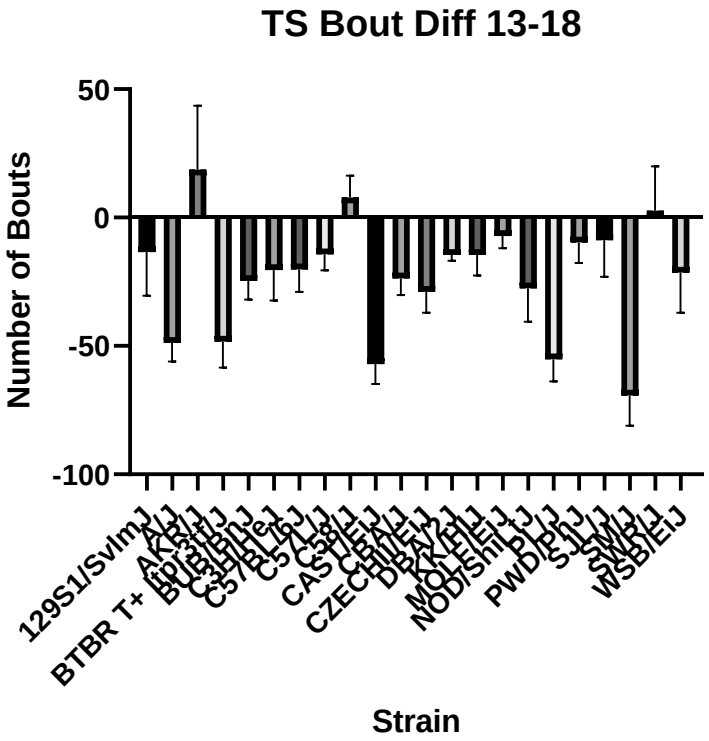


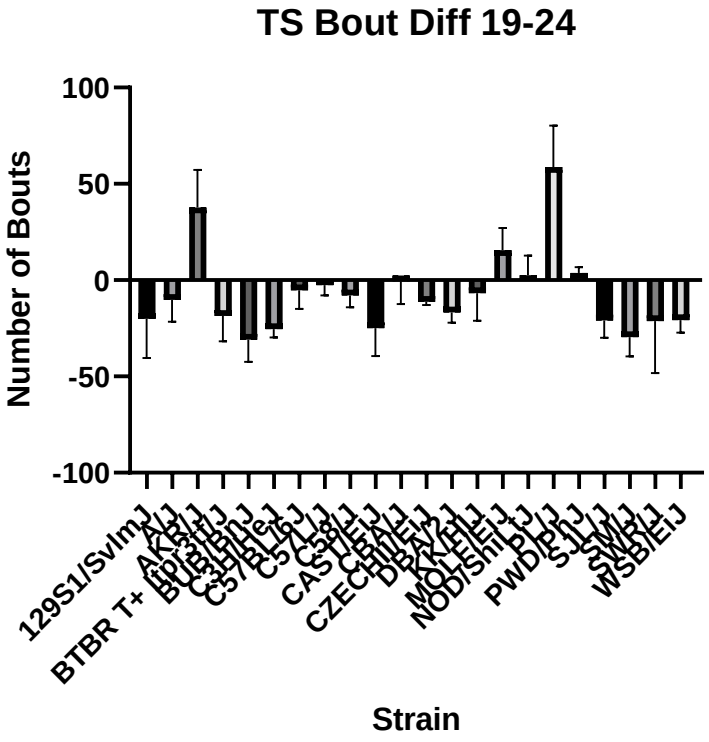



R Bout Diff 19-24
Number of Bouts
20
10
0
-10
-20
129S1/SvImJ
AJ
AKR/J
BTBR T+ Itpr3tf/J
BUB/BnJ
C3H/HeJ
C57BL/6J
C57L/J
C58/J
CAST/EiJ
CBA/J
CZECHII/EiJ
DBA/2J
FVB/NJ
KK/HlJ
MOLF/EiJ
NOD/ShiLtJ
PJ
PWD/PhJ
SJL/J
SM/J
SWR/J
WSB/EiJ
Strain

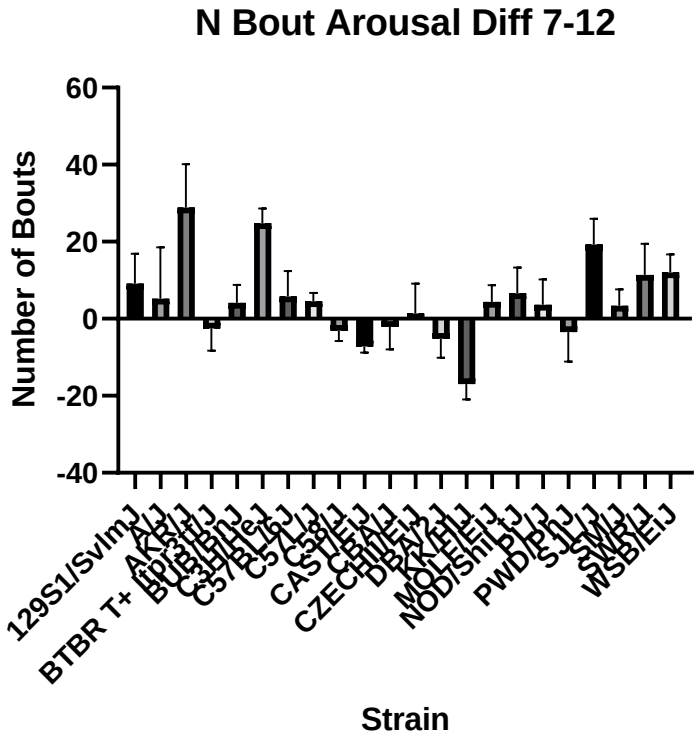
6c. Number of Bouts of Total Sleep

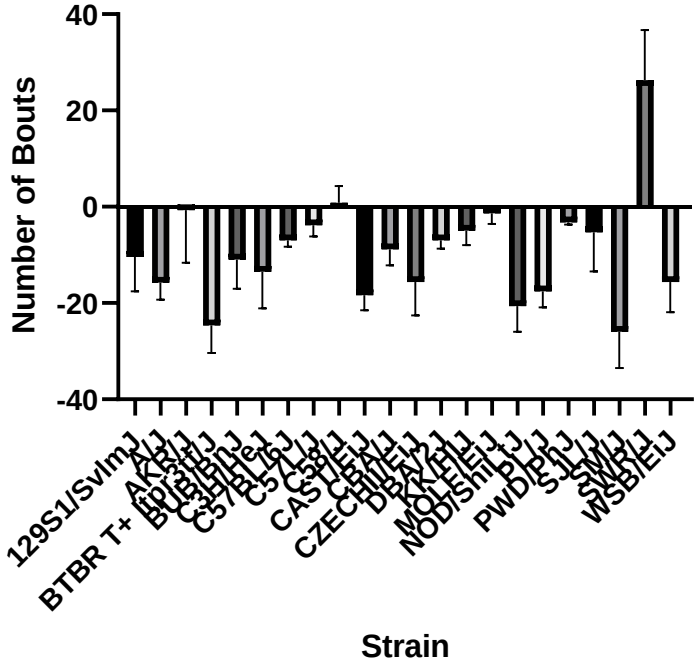


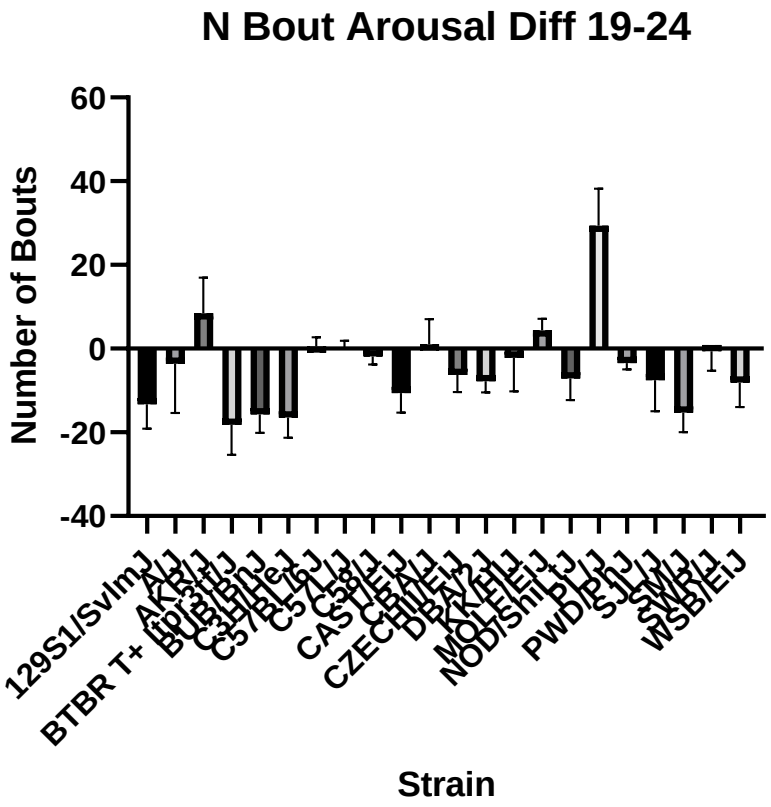



TS Bout Diff 19-24
Number of Bouts
100
50
0
-50
-100
129S1/SvImJ
A/J
AKR/J
BTBR T+ Itpr3tf/J
BUB/BnJ
C3H/HeJ
C57BL/6J
C57L/J
C58/J
CAST/EiJ
CBA/J
CZECHII/EiJ
DBA/2J
KK/HlJ
MOLF/EiJ
NOD/ShiLtJ
PWD/PhJ
SJL/J
SM/J
WSB/EiJ
Strain

6d. Number of Bouts of Arousal






N Bout Arousal Diff 19-24
Number of Bouts
60
40
20
0
-20
-40
129S1/SvImJ
A/J
AKR/J
BTBR T+ Itpr3tf/J
BUB/BnJ
C3H/HeJ
C57BL/6J
C57L/J
C58/J
CAST/EiJ
CBA/J
CZECHII/EiJ
DBA/2J
KK/HlJ
MOLF/EiJ
NOD/ShiLtJ
PL/J
PWD/PhJ
SJL/J
SM/J
SWR/J
WSB/EiJ
Strain

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