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This study investigates DBP gene expression levels between the ZT10 and ZT14 time points, and the effect of jet lag on gene expression.

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A study of the *Reverb* gene expression in the SCN under normal day length

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ABSTRACT

Introduction: The circadian rhythm is the body's natural mechanism that regulates the sleep-wake cycle in repeated 24-hour periods. It regulates several body functions, and is controlled by the body's master clock, the suprachiasmatic nucleus (SCN). In the SCN, circadian genes such *as Per1, Cry1, Clock, REVERB* and *Bmal* help regulate sleep and behavior controls. The *REVERB* gene is known as a regulator of circadian rhythm and metabolism. It is also vital for the transcription of the clock gene *Bmal1* and the absence of *Bmal1* has shown to impair temporal patterns of locomotor behavior, sleep-wakefulness cycle, and food intake in mice. Jetlag is experienced when desynchronization happens between the biological and body clocks. Jetlag has been associated with conditions such as disturbed sleep, fatigue, difficulty concentrating, and gastrointestinal issues. This study determines the effect of jetlag on the expression of the *REVERB* gene. **Methods:** Gene expression levels of *REVERB* were evaluated under normal day length, jetlag and control (non-jetlag) conditions at ZT10 and ZT14 time points in C57BL/6NCrl adult mice using qPCR. **Results:** *REVERB* expression was downregulated at ZT14 compared to ZT10 under non-jet lag conditions. However, under jetlag conditions, *REVERB* expression was upregulated at ZT14 compared to ZT10. Also, *REVERB* was upregulated at ZT10 and ZT14 under jetlag conditions compared to controls (non-jetlag). **Conclusions:** Our results suggest that the expression of *REVERB* varies between ZT10 and ZT14 time points and is upregulated by jet lag conditions. Understanding the molecular variation of *REVERB* can help to elucidate the mechanisms used by the biological clock to adapt to jetlag.

INTRODUCTION

An essential aspect of how the body maintains itself is the circadian rhythm. The circadian rhythm is the body's natural clock that controls sleep as well as different functions in the body such as our metabolic processing, and regulation of hormones (Duez and Stales, 2009). This rhythm is controlled by the body's master clock, the suprachiasmatic nucleus (SCN). In the SCN, there are specific genes that contribute to the temporal or circadian regulation of sleep as well as behavior control such as *Per 1, Per 2, Cry 1, and CLOCK* (Zhang *et al*., 2014). One of the main functions of the *REVERB* gene is to regulate circadian rhythm and metabolism (Duez and Stales, 2009). Another crucial function of *REVERB* is the transcription of *Bmal1,* another clock gene. *REVERB* and *Bmal1* partner to activate the transcription of other clock genes and the absence of Bmal1 has been shown to impair temporal patterns of locomotor behavior in mice, sleep-wakefulness cycle, and food intake in mice (Guillaumond *et al*., 2005; Mieda *et al*., 2017). Jetlag, a widely known disruptor of circadian rhythm, is typically experienced during travel when desynchronization happens between the biological and body clocks. Physiological dysfunctions related to jet lag include disturbed sleep, fatigue, difficulty concentrating, and gastrointestinal issues (Mayo Clinic, 2020).

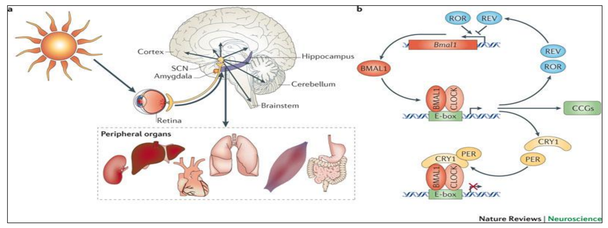


Figure 1. The circadian clock in mammals (Kondratova and Kondratov, 2012)

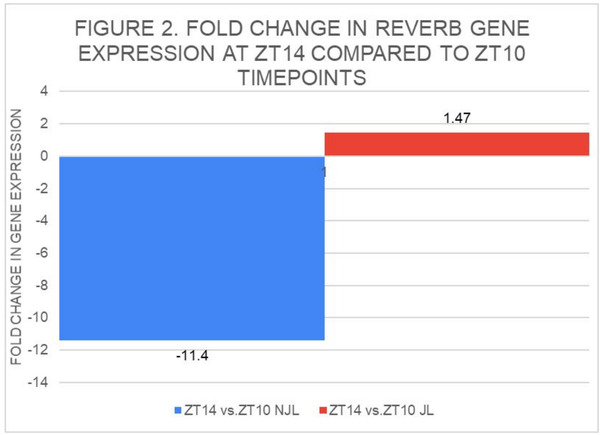
RESEARCH STATEMENT/.OBJECTIVE

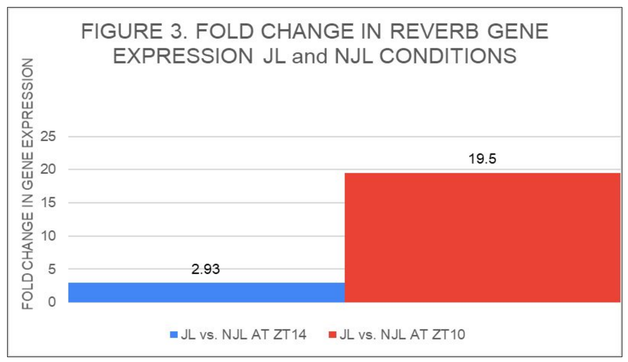
The aim of this study is to determine the effect of jet lag on the expression of the *REVERB* gene, a significant molecular component of the circadian clock.

METHODS

Gene expression levels were evaluated under jetlag and control (non-jetlag) conditions and at the ZT10 and ZT14 time points in C57BL/6NCrl adult mice using qPCR. Total RNA was extracted from tissue lysates, and used to synthesize cDNA. cDNA samples were processed using a PowerUp SYBR green PCR kit and QuantStudio 5 instrument. The absolute quantification method was used for data analysis, and data were normalized using the 18S gene.

RESULTS





DISCUSSION

Our findings confirm previous reports where *REVERB* expression in the SCN followed similar gene expression patterns to ours under LD conditions (*Onishi et al. 2002*). In that study, *REVERB* expression was found to be higher than that of other genes (*Per 1, Per 2, Bmal1*) (*Onishi et al. 2002*). Both studies showcase the high importance that *REVERB* has in regulating the circadian rhythm in mammals. One of the limitations of our study was sample size which may explain the lack of statistical significance observed in our results.

CONCLUSION

This study showed that the expression of *REVERB* varies between ZT10 and ZT14 time points and is affected by jet lag conditions. These results are impactful for individuals who are constantly in a jetlagged state due to their occupation or life circumstance.

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