Effects of Caloric Restriction on Circadian Rhythms in Knockout Mice

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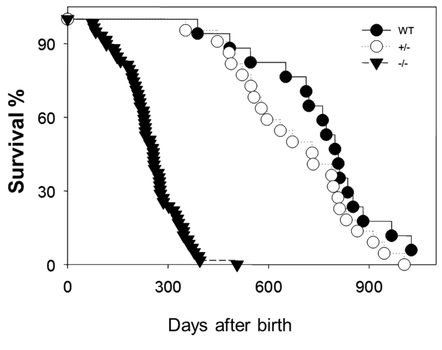
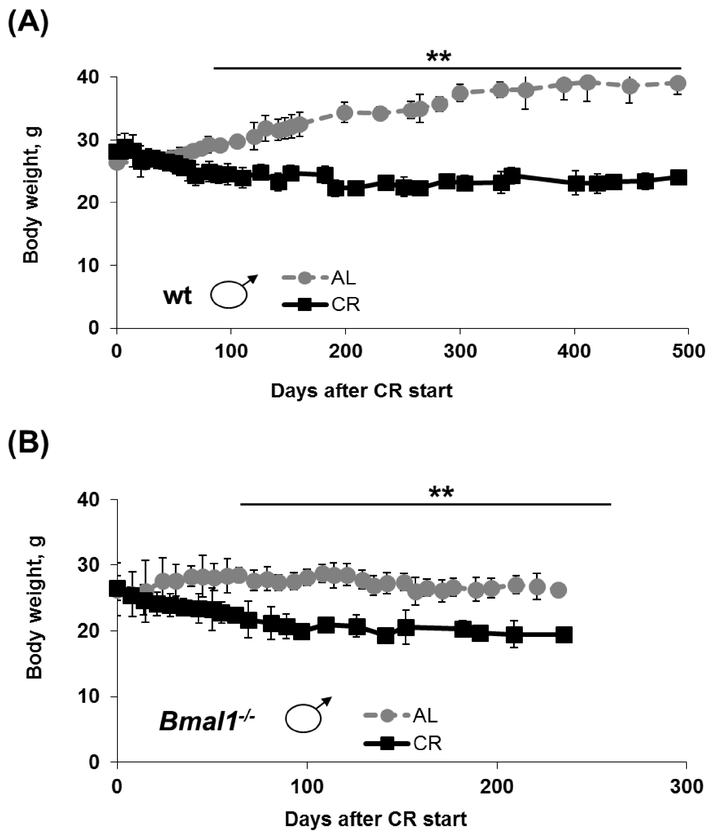
Abstract:

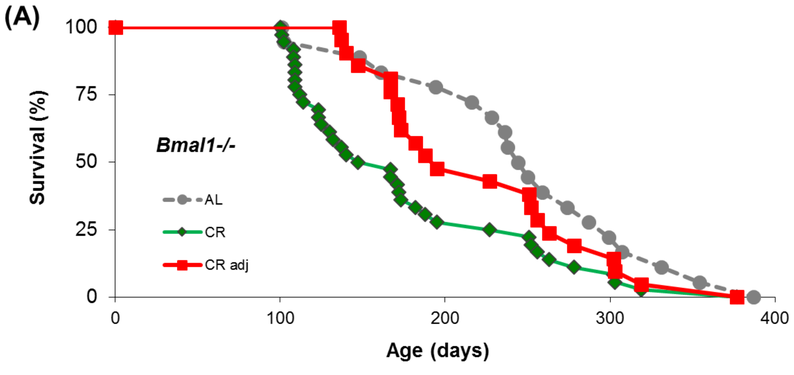
Circadian rhythms are 24–hour rhythms existing in organisms ranging from bacteria to humans that govern activity levels, behavior, and gene expression. While an endogenous 24-hour clock persists in the absence of stimuli, it can be altered by exposure to stimuli such as light or a feeding schedule in a process called entrainment. Constant disruption of the circadian rhythm has been shown to reduce lifespan, increase rates of obesity, diabetes, and cancer, and can contribute to mental disorders such as depression, which is particularly relevant as many people work unpredictable hours. Caloric restriction has been known for years to increase lifespan, but in knockout mice for BMAL1, a gene controlling the circadian clock, have decreased lifespan and abnormal behavior. Knockout mice on a variety of feeding regimens (Ad Libitum, Time Restricted, and Fasting) were compared to control mice also on a variety of feeding regimens, and found that caloric restriction only increased lifespan in control mice, without affecting knockout mice. This indicates that caloric restriction has a significant effect on the circadian system, and can help in development of new treatments for circadian rhythm disorders.



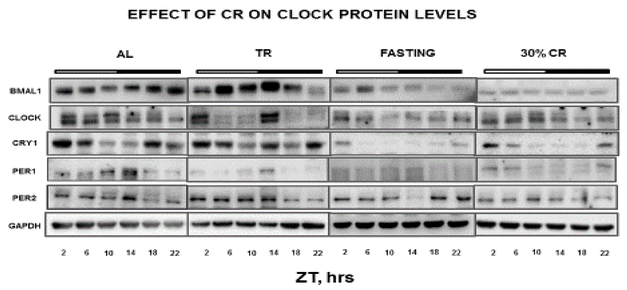
- Wild type and BMAL1 carriers have approximately the same lifespan, while knockout mice age at an accelerated rate.



Effects of Caloric Restriction on body weight in wild type and knockout mice



Caloric restriction has no effect on lifespan in Knockout mice



Effect Of Calorie Restriction On CLOCK Protein Levels

Conclusion:

- A functioning BMAL1 gene is necessary for Calorie Restriction to have a beneficial effect on a mouse's lifespan
- Functioning Circadian clock genes such as BMAL1 are necessary for a healthy lifespan in mice

Sources:

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- *CLOCK-mediated acetylation of BMAL1 controls circadian function; Jun Hirayama1, Saurabh Sahar1, Benedetto Grimaldi1, Teruya Tamaru2, Ken Takamatsu2, Yasukazu Nakahata1 & Paolo Sassone-Corsi; Department of Pharmacology, School of Medicine, University of California, Irvine, 92697-4625 Irvine, California, USA; Department of Physiology, Toho University, Faculty of Medicine, Tokyo 143-8540, Japan*