

# A Sirtuin 1 haplotype influences homeostatic sleep parameters in young healthy men

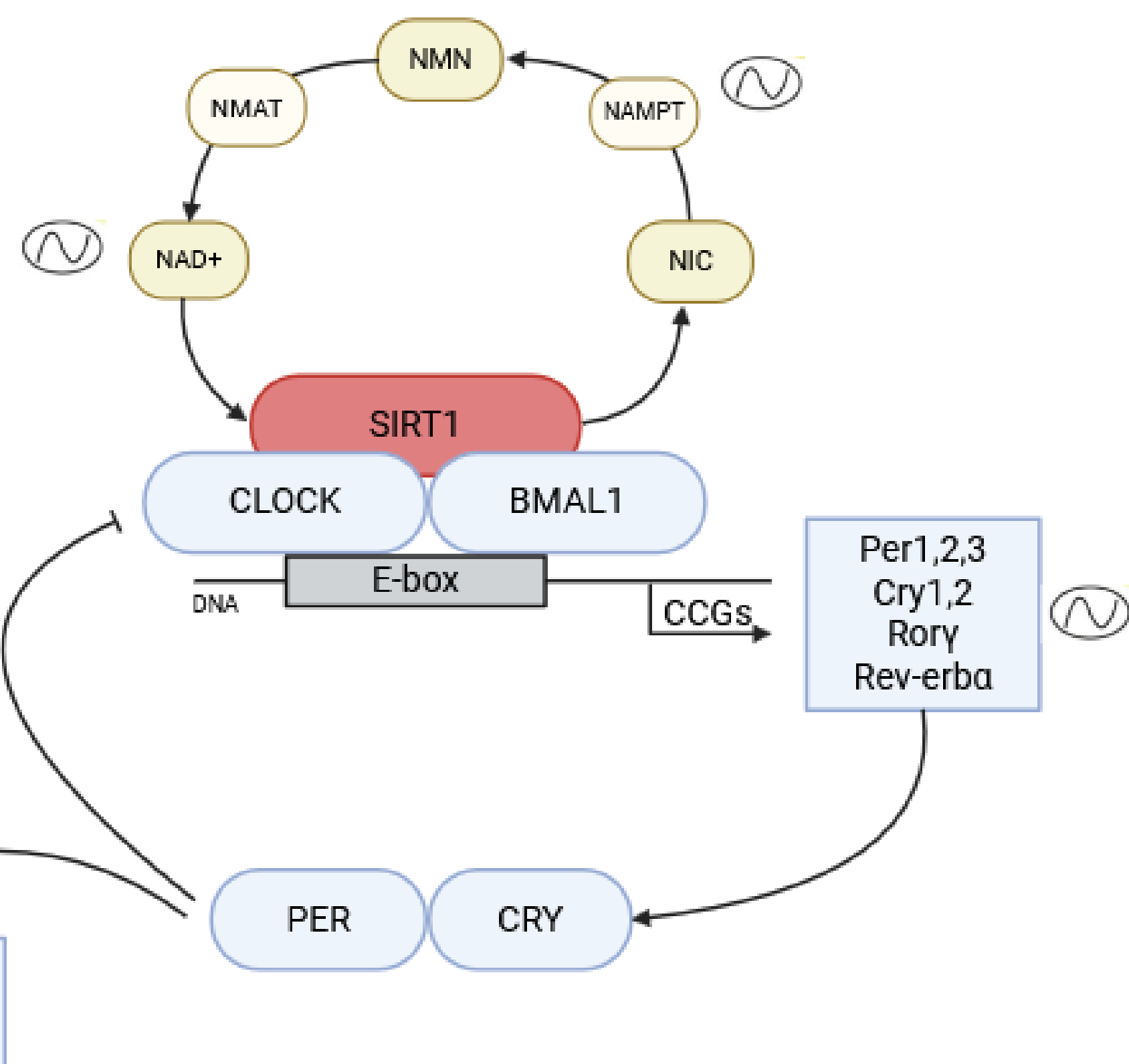
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## Introduction

Sirtuin 1 (SIRT1) plays a central role in the circadian transcription of several core clock genes in a nicotinamide adenine dinucleotide (NAD<sup>+</sup>) dependant manner, thus linking cell metabolism to sleep-wakefulness regulation. Studies in animals and human suggest a bidirectional interaction between circadian rhythmicity and sleep homeostasis. However, the molecular mechanisms underpinning this interplay remain poorly understood. We hypothesize that sleep need is driven by the energetic cost of cellular metabolism, with clock genes acting as energy sensors. Therefore, variants in key genes that are both regulated by cellular metabolism and modulate clock activity may influence sleep homeostasis. We assessed the association between slow wave energy (SWE), a validated and highly heritable metric for sleep pressure dissipation during slow wave sleep, and a *SIRT1* haplotype in a large cohort.

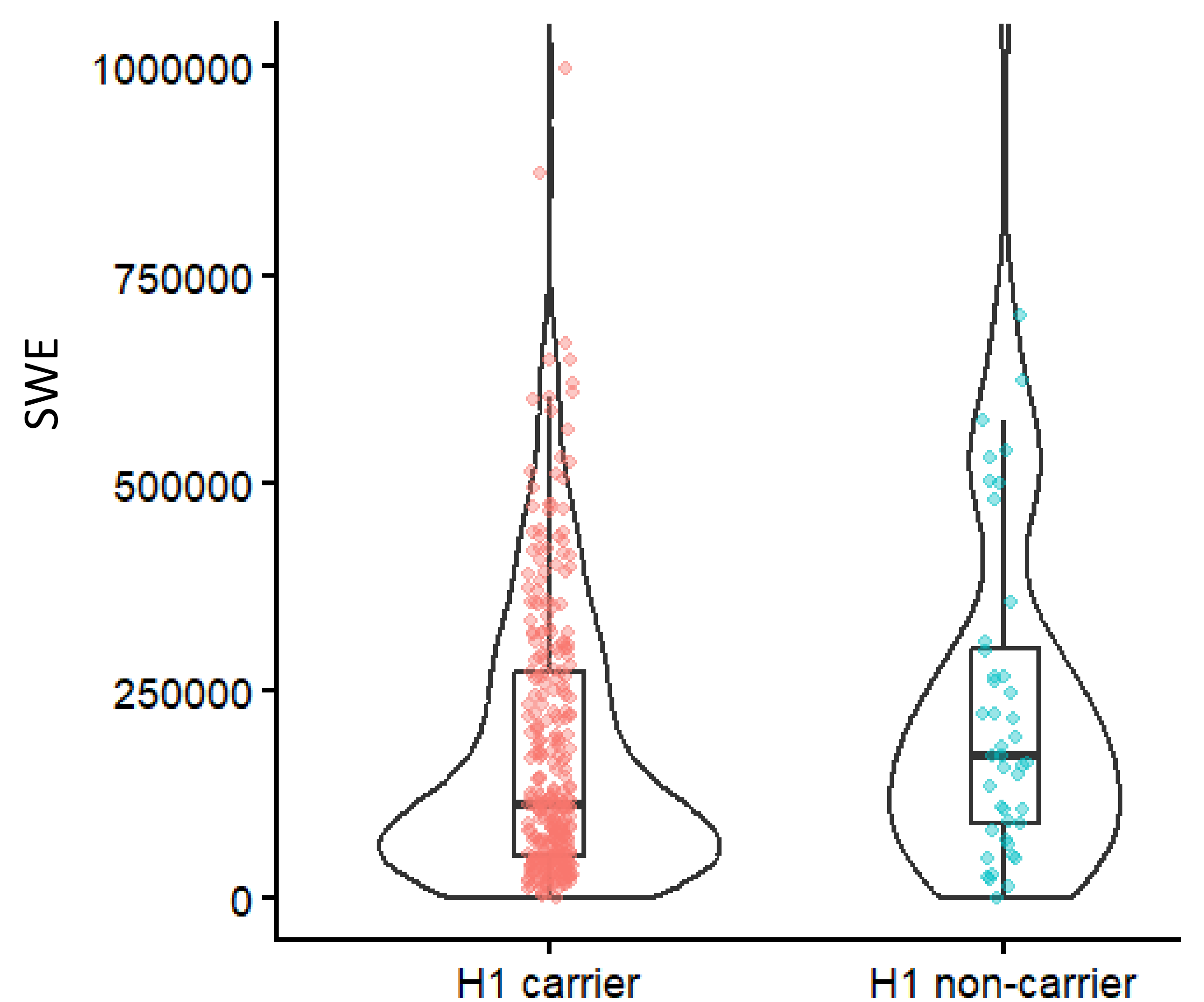


## Methods

360 young Caucasian men (18-30 years, mean age=22.09±2.71 years) underwent in-lab EEG recording of habitual sleep. Sleep staging was realised with a validated automatic algorithm (ASEEGA, PHYSIP, France). SWE was then computed as the cumulated overnight power in the delta frequency band (0.5-4 Hz) during N2 and N3 stages and outliers (Z-score≥4) were removed. Genomic DNA was extracted from blood and used for genome-wide genotyping. SNPs in *SIRT1* gene (+2kb upstream) were retrieved and a three SNP (rs3758391-rs35706870-rs932658) haplotype was identified: CAC (major), TCA and TAA. Associations between sleep parameters and haplotype were explored with generalized additive models (GAMLSS), adjusting for relevant covariates.

## Results

GAMLSS analysis indicated that individuals who were non-carriers of the major CAC allele (n=44) showed significantly higher SWE compared with CAC-carriers ( $\beta \approx 37600$ ,  $p < 0.02$ ). Despite the narrow age-range of the sample, the analyses also yielded a significant negative association between SWE and age ( $\beta \approx -7100$ ,  $p < 0.0001$ ).



## Discussion

The results suggest a SIRT1-dependant variation of the ability to dissipate sleep pressure in young healthy individuals. In the future, we will assess the role of this haplotype in the variation of other sleep metrics, such as the rate of sleep pressure dissipation, and brain microstructure.

## References

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