**Title:** TEMPORAL SERIES OF HUMAN ACTIVITY AND GENETICS: ASSOCIATION AMONG SLEEP PROFILES, BIOLOGICAL RHYTHMS, AND *PER3* GENE

Authors: Juliana Viana Mendes, Maria Augusta Medeiros Andrade, Ana Amélia Benedito-Silva, Mario Pedrazzoli

**Introduction:** The molecular mammalian circadian clocks are genes that work as endogenous oscillators [1] and have their expression modulated every 24 hours. The modulation of the genetic expression is essential to the physiological processes, such as the sleep/wake cycle. *PER3* is a clock gene that shows polymorphisms that have been associated with human sleep and circadian phenotypes. Rare are studies that explore these phenotypes using a technique that allows to monitor them for several days in real-life conditions, like actigraphy.

**Objective:** This study aimed to compare the sleep and circadian profiles of the *PER3*<sup>4/4</sup> and *PER3*<sup>5/5</sup> individuals through actigraphy in real-life conditions (during the lockdown established for the COVID-19 pandemic).

**Methods:** A sample of 513 university students between 18 and 30 years old was enrolled in the research. All subjects were genotyped for the *PER3* gene *VNTR* polymorphism [2]. From the initial sample of 513, 81 individuals with homozygous genotype (*PER3*<sup>4/4</sup> or *PER3*<sup>5/5</sup>) were invited to have activity records under actigraphy monitoring. The monitoring step has happened during the lockdown established for the COVID-19 pandemic. The subjects were invited to wear the actigraph device (ActTrust AT0503, Condor Instruments, São Paulo, SP, Brazil) for at least 14 consecutive days. The proportional integration mode (PIM) algorithm was used to derive a measure for user activity from acceleration readings. The PIM data with epochs of 60 seconds were integrated every hour to generate 24 epochs of 3600 seconds each day.

**Results:** The comparison between  $PER3^{4/4}$  e  $PER3^{5/5}$  revealed that sleep onset and offset were later in the  $PER3^{5/5}$  group on the weekdays (p=0,015; p=0,004, respectively) and weekends (p=0,022; p=0,041, respectively). Although sleep onset and offset were different, sleep duration did not differ between groups. Moreover, despite the phase of sleep being later in the  $PER3^{5/5}$  group, we found no differences in social jet lag (p=0,823). The individuals  $PER3^{5/5}$ , on average, expressed a more unstable (p=0,032) and more fragmented (p=0,035) rest/activity rhythm.

**Discussion:** The new lifestyle including more screen time exposure [3-5] and less physical activity [4,5] added to the environmental challenges established by the lockdown, may have created a context that reflects the results of the *PER3*<sup>5/5</sup> group showed in this study.

**Conclusions:** To the best of our knowledge, this is the first study that shows the association among sleep, circadian profiles, and genotypes of the *PER3* gene *VNTR* polymorphism through actigraphy in real-life conditions.

## Main references:

[1] Takahashi J. S. (2017). Transcriptional architecture of the mammalian circadian clock. *Nature reviews. Genetics*, *18*(3), 164–179. <u>https://doi.org/10.1038/nrg.2016.150</u>

[2] Ebisawa, T., Uchiyama, M., Kajimura, N., Mishima, K., Kamei, Y., Katoh, M., Watanabe, T., Sekimoto, M., Shibui, K., Kim, K., Kudo, Y., Ozeki, Y., Sugishita, M., Toyoshima, R., Inoue, Y., Yamada, N., Nagase, T., Ozaki, N., Ohara, O., Ishida, N., ... Yamauchi, T. (2001). Association of structural polymorphisms in the human period3 gene with delayed sleep phase syndrome. *EMBO reports*, *2*(4), 342–346. <u>https://doi.org/10.1093/embo-reports/kve070</u>

[3] Salfi, F., Amicucci, G., Corigliano, D., D'Atri, A., Viselli, L., Tempesta, D., & Ferrara, M. (2021). Changes of evening exposure to electronic devices during the COVID-19 lockdown affect the time course of sleep disturbances. Sleep, 44(9), zsab080. <u>https://doi.org/10.1093/sleep/zsab080</u>

[4] Guo, Y. F., Liao, M. Q., Cai, W. L., Yu, X. X., Li, S. N., Ke, X. Y., Tan, S. X., Luo, Z. Y., Cui, Y. F., Wang, Q., Gao, X. P., Liu, J., Liu, Y. H., Zhu, S., & Zeng, F. F. (2021). Physical activity, screen exposure and sleep among students during the pandemic of COVID-19. Scientific reports, 11(1), 8529. <a href="https://doi.org/10.1038/s41598-021-88071-4">https://doi.org/10.1038/s41598-021-88071-4</a>

[5] Giuntella, O., Hyde, K., Saccardo, S., & Sadoff, S. (2021). Lifestyle and mental health disruptions during COVID-19. Proceedings of the National Academy of Sciences of the United States of America, 118(9), e2016632118. <u>https://doi.org/10.1073/pnas.2016632118</u>