

Previews

Taking the time for our bodies: How wearables can be used to assess circadian physiology

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Consumer wearables, such as smart watches, are a promising tool for monitoring circadian health in “real world” settings. Bowman et al. demonstrate that circadian signals can be accurately captured through heart rate data obtained from wearables, opening up new possibilities for population-level studies on heart rate and circadian rhythm.

Circadian rhythm is the cyclical change in behavior and/or physiology established through a combination of an internal clock and external stimuli, with a period of approximately 24 h (Vitaterna et al., 2001). Circadian rhythm disruptions are associated with various diseases such as dementia, diabetes, depression, and sleep disorders. Therefore, developing accurate and scalable methods to measure circadian rhythm is a critical step for developing improved monitoring and intervention methods. The current gold standard method of monitoring circadian rhythm is through repeated measures of biomarkers such as melatonin levels, core body temperature, and rest-activity cycles (Reid, 2019). However, these measurements can be inconvenient, cumbersome, and sometimes invasive, making them impractical in a real-world scenario. For that reason, researchers have been exploring alternatives that can reliably track circadian rhythm by using unobtrusive sensing modalities that include actigraphy, wrist temperature, light exposure, and heart rate (Madrid-Navarro et al., 2018; Reid, 2019).

The rapid adoption of wearables in recent times, with 21% of people in the US owning smartwatches (Vogel 2020), provides an opportunity to monitor physiological and activity characteristics of an individual continuously and in real-world scenarios. Utilizing wearables to measure and track aspects of health and wellness (e.g., heart rate, steps, sleep duration, etc.) has gained popularity and attention among healthcare researchers because of the unobtrusiveness, convenience,

and low-cost nature of these devices, as well as the ability to collect large datasets longitudinally outside of a clinical setting. Despite such potential, new challenges have arisen surrounding the analysis of these large and often noisy datasets, particularly because wearable devices and their corresponding software and algorithms often lack interpretability and generalizability. One overarching challenge to interpretability is uncovering and addressing confounding variables. As an example, we and others have demonstrated that the accuracy of some sensors and algorithms are affected by variables including race/ethnicity (Bent et al., 2020; Sjoding et al., 2020), physiological condition (Dunn et al., 2021; Shcherbina et al., 2017), and behavioral patterns like work and sleep schedules (Erickson et al., 2021; Marino et al., 2013). Another overarching challenge is the generalizability, or extensibility of the technology to new settings because of differences in the technology’s development and validation phase as compared with its real-world deployment, which can result in lower accuracy in the deployment phase of the models. For example, sleep detection algorithms developed by using data from people with typical sleep habits fail to generalize in a real-world deployment on shift workers (Erickson et al., 2021; Marino et al., 2013) as well as individuals with certain physiologic or pathophysiological conditions (pregnancy, sleep apnea, etc.). For these reasons, substantial research is needed to ensure that the implementation of wearables to monitor health is interpretable and generalizable.

Reporting in a recent issue of *Cell Reports Methods*, work from Dr. Daniel Forger and colleagues at the University of Michigan acknowledges these challenges by focusing on the interpretable and generalizable application of wearables to monitor daily physiology in real-world settings (Bowman et al., 2021). In particular, the authors investigated how accurately we can track circadian rhythms of heart rate (CRHR) by using ambulatory wearable data in the daily environment of shift-workers (i.e., medical interns). They developed a statistical method to extract key physiological parameters from wearable data, including basal heart rate, the amplitude of CRHR, and circadian phase. They purposefully investigated the effects of possible confounders of heart rate such as the direct effects of activity and the effects of meals, posture, and stress on heart rate to understand how we should interpret CRHR estimated from wearables. The team tested their models in estimating and tracking these parameters in a real-world deployment from a wearable dataset consisting of over 130,000 days of wearable heart rate and activity data from more than 900 medical interns. They were able to identify both the underlying CRHR and processes accounting for short-term dynamics in heart rate, again including posture, meals, stress, and other external factors. The method was implemented in real-time in the “Social Rhythms” iPhone and Android apps, which anonymously collects data from wearable users and provides analysis based on their method.



The findings demonstrate that CRHR can be passively assessed by using heart rate and activity measurements from common wearable devices in real-world settings. This approach is inherently scalable and will therefore enable future population-level studies. Another important finding is the demonstration that long-term measurements from wearable data can be utilized to generate personalized phase response curves (PRCs) (Khalsa et al., 2003) of CRHR to activity. Generating PRCs from wearable data alone is in notable contrast to the traditional extensive, costly, and laborious clinical PRC protocol (Khalsa et al., 2003) and will provide an opportunity to understand how activity affects phase shifts in CRHR on a day-to-day basis in real-world settings. Importantly, this also opens up possibilities to understand what is normal variation (due to activity or circadian rhythm) and what is abnormal variation in heart rate, which is a crucial step to monitoring cardiovascular disease.

This study provides new insights into the circadian rhythm dynamics that can be captured by wearables, and additionally highlighted the difference in CRHR compared with dim light melatonin onset (DLMO), a gold-standard biomarker of the circadian rhythm. These differences are physiologically expected, given that CRHR and DLMO are known to originate from two distinct places in the body (D'Souza et al., 2021). The authors have demonstrated that CRHR dynamics are distinct from those of sleep-wake or physical activity patterns because of rotating shifts and that they vary greatly among individuals. They also showed that activity has a longer-lasting effect on CRHR as compared with that of DLMO. The phase and amplitude of the CRHR found here closely match with previous studies involving a constant routine protocol (Vandewalle et al., 2007).

Although the approach is promising, there are a few limitations that must be addressed before this methodology can be translated into a general solution to monitor CRHR in real-world scenarios. The study demographic is skewed in terms of age, considering that the study cohort consists of medical interns only. Future studies should investigate whether similar methods work in other age groups,

in populations with specific physiological conditions (e.g., pregnancy), and in persons with other occupations that can disrupt the sleep-wake cycle and are associated with disease incidence (e.g., police, firefighters, etc.) (Rivera et al., 2020). Another limitation here is the exclusion of sleep data to avoid the effect of sleep on heart rate as a potential confounding variable to circadian rhythm. This choice is reasonable but misses some potentially interesting and significant analyses and discoveries surrounding sleep and CRHR. Moreover, sleep/wake labels from consumer devices are often inaccurate (Chinoy et al., 2021), particularly in the context of non-standard sleep timing (as is the case for medical interns), and this muddles the reliability of the sleep phases and sleep midpoints used in this study.

Regardless of these limitations, it is conceivable that the adoption and implementation of consumer wearables to monitor health will continue to grow, and the work from Bowman et al. (2021) successfully addresses many urgent needs for further development in this field. In this context, efforts are needed both from researchers and industry to establish the field of wearables in monitoring daily physiology with interpretable and generalizable algorithms.

DECLARATION OF INTERESTS

The authors declare no competing interests.

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