Sleep Medicine Reviews 33 (2017) 70–78

Contents lists available at ScienceDirect

Sleep Medicine Reviews

journal homepage: www.elsevier.com/locate/smrv

CLINICAL REVIEW

The role of race and ethnicity in sleep, circadian rhythms and cardiovascular health

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ARTICLE INFO

Article history:
Received 1 March 2016
Received in revised form
25 May 2016
Accepted 27 May 2016
Available online 3 June 2016

Keywords:
Admixture
Health disparities
Cardiovascular disease
Circadian rhythm
Sleep

SUMMARY

In recent years, strong evidence has emerged suggesting that insufficient duration, quality, and/or timing of sleep are associated with cardiovascular disease (CVD), and various mechanisms for this association have been proposed. Such associations may be related to endophenotypic features of the sleep homeostat and the circadian oscillator, or may be state-like effects of the environment. Here, we review recent literature on sleep, circadian rhythms and CVD with a specific emphasis on differences between racial/ethnic groups. We discuss the reported differences, mainly between individuals of European and African descent, in parameters related to sleep (architecture, duration, quality) and circadian rhythms (period length and phase shifting). We further review racial/ethnic differences in cardiovascular disease and its risk factors, and develop the hypothesis that racial/ethnic health disparities may, to a greater or smaller degree, relate to differences in parameters related to sleep and circadian rhythms. When humans left Africa some 100,000 years ago, some genetic differences between different races/ethnicities were acquired. These genetic differences have been proposed as a possible predictor of CVD disparities, but concomitant differences in culture and lifestyle between different groups may equally explain CVD disparities. We discuss the evidence for genetic and environmental causes of these differences in sleep and circadian rhythms, and their usefulness as health intervention targets.

Introduction

Anatomically modern humans first emerged from Africa some 100,000 years ago and began to colonise the other continents. There are reasons to hypothesise that differences in parameters related to circadian rhythms and sleep evolved as groups of humans gradually moved away from the equatorial zone in the direction of the poles and settled there [1], just as the different light conditions favoured a loss of skin pigmentation. Indeed, polymorphisms in specific genes have been reported to associate with photoperiod, and signatures of positive selection detected [2]. After millennia of gradual expansion, our species has experienced some profound rapid changes during the last few centuries [3]. Voluntary and forced migration has moved individuals and groups from the environments to which their ancestors had adapted over generations into different environments and living conditions, where previously separate populations are now undergoing an unprecedented and accelerating degree of admixture.

The last few centuries have also been characterised by the gradual transition from an agrarian to an industrial society, which has afforded unprecedented benefits as well as novel challenges to human health. This transition, where the major causes of death have shifted from nutritional deficiency and infectious disease to degenerative chronic disease — cardiovascular disease (CVD), diabetes, and cancer — has been named “the epidemiologic transition” [3]. This transition is still ongoing in many countries and regions. An important contributor to this increase in chronic diseases is change in diet. Our behavioural drives evolved to maximise intake of precious energy-rich nutrients whenever available, but today, many of us have almost unrestricted access to high-calorie foods.

Parallel to the epidemiologic transition, affordable electricity has emerged, which first enabled us to keep our homes lit regardless of the external photoperiod, and then provided us with endless

Abbreviations: CHD, chronic heart disease; CVD, cardiovascular disease; HPA, hypothalamus-pituitary-adrenal; MI, myocardial infarction; OSA, obstructive sleep apnoea.

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http://dx.doi.org/10.1016/j.smrv.2016.05.004
1087-0792/

Glossary of terms

Admixture	a mixture of different ancestries present within individuals in a population
Ancestral informative marker (AIM)	a set of polymorphisms at a particular locus which has different frequencies between populations of different geographical origin
Endophenotype	a distinct phenotype with clear genetic connections
Race/ethnicity	two often conflagrated terms, referring to varying degrees to geographical ancestry, physical appearance, and cultural and religious factors. In the context of this review, any and all aspects of these are referred to under this binomial

options for work and distractions at any hour of the night and the day. This has long been considered to have caused a decrease in the length and a shift in the timing of sleep. A recent study of hunter-gatherer societies [4] showed less total sleep in a community that had recently been connected to the electrical grid than in a community that had not. And whilst there is no reliable evidence suggesting a decrease in average sleep time during recent decades, there is stronger evidence that the proportion of short sleepers has increased [5] and that there has been a significant decrease in sleep amongst adolescents [6,7]. It can also be hypothesised that the intensive forced mass migration of Africans to Northern and (even more prominently) Southern latitudes of the Americas [8] may, in addition to the social inequalities rooted in the aftermath of slavery, also convey physiological maladaptations to high-amplitude photoperiods that need to be understood in order to be mitigated [1]. The situation is further complicated by socioeconomic stratification of racial/ethnic groups within societies, making it complex to disentangle to which extent observed differences are caused by genetic traits or states associated with environmental variables.

In public health terms, the most dramatic fallout of the epidemiological transition has been an increase in CVD, which is now the main cause of disability and death in the modernised world. The global cost of CVD is around US$900 billion, and, as the world population ages, this figure is set to rise to over US$1000 billion by 2030 [9]. CVDs include a number of diseases of the heart and circulation such as coronary heart disease and stroke, alongside hypertensive, inflammatory, and rheumatic heart disease. A fundamental need to understand the root causes of CVD prevalence remains, and much of our knowledge about prevention is owed to the pioneering Framingham study [10]. This longitudinal cohort study identified a number of potentially modifiable risk factors — high levels of cholesterol and triglycerides, hypertension, diabetes, high adiposity, obesity, smoking, unhealthy diet, and lack of physical activity. Although the vast majority of the Framingham cohort consists of middle class individuals of European descent, the main findings of the study have been confirmed, and gained universal acceptance [11]. Although treatment for CVD has also improved considerably over the last decades, CVD remains a major cause of morbidity, and the well-known principle that prevention is better than cure holds true for CVD, particularly as the accessibility of pharmacological or surgical interventions is neither universal nor without risk. Nonetheless, current modifiable risk factors for CVD, such as diet and physical activity, are notoriously difficult to change. Therefore, there is a pressing public health need to understand whether other potentially modifiable targets may also reduce CVD risk, particularly among groups disproportionately burdened by disease. Here, we discuss the case for sleep and circadian rhythms as modifiable targets. This discussion probably defines at least as many gaps in current knowledge (summarised in the research agenda) as it fills. The aim of this review is not only to identify the differences between different groups of people which could potentially be attributed to genetically determined physiological differences, but also to convey an appreciation of the many non-genetic factors, such as environment or culture, that could potentially explain the same observations wholly or in part. Either way, it is intended that the review will help make the case for additional research that includes novel population groups and methodologies.

Circadian rhythms and sleep and their importance to human health

Endogenously generated through transcriptional and post-transcriptional networks of specific clock genes, circadian rhythms enable organisms to actively anticipate, as opposed to passively react to, the predictable changes that occur across the 24-hour day:night cycle. In real-life conditions, circadian rhythms are continuously *entrained* by external signals, known as *Zeitgebers*, most prominently by light. Circadian rhythms are of fundamental importance to human health. Prominent effects on the body include an impact on sleep–wake cycles, hormone release, body temperature, and metabolism. Continuous entrainment of the circadian clock is required not only because of the variability in photoperiod in non-equatorial regions, but also because the internal period length of the oscillator is not exactly the combined length of a day and a night. In humans, it shows a normal distribution around an average of 24.2 h [12]. Modern life, however, does not replicate the daily patterns of our ancestors, around which the entrainment mechanisms of *Zeitgebers* evolved. We spend often considerable amounts of time indoors, and many of us work shifts with nocturnal and/or irregular hours. Thus, our 24/7 society induces a high prevalence of social jetlag, a discrepancy between endogenous circadian clocks and socially imposed external ones [13].

The circadian phase of physical inactivity is augmented by sleep, a specialised programme of reversible uncoupling from external stimuli involving different stages defined by specific electrophysiological signatures. Sleep is closely linked to circadian rhythms. In addition to its profound and obvious behavioural manifestations, sleep and its transition into and out of wakefulness also have manifestations on the molecular and physiological level that are independent of the effects of circadian rhythms on both metabolic and endocrine function [14].

The relationship between circadian rhythms, sleep and cardiovascular disease

Circadian rhythm and cardiovascular health

Circadian rhythms have been associated with CVD and its risk factors, including diabetes (which is outside of the scope of this review) and obesity, on multiple levels. Cardiomyocyte metabolism is under circadian control [15], and circadian and diurnal rhythms are, in turn, observed in blood pressure, heart rate, and platelet aggregability, as well as in the incidence of multiple categories of CVD [16]. This has inspired multiple lines of investigation of the relationship between circadian disruption and cardiovascular risk factors and health outcomes.