Circadian Rhythms: Does Burning the Midnight Oil Leave You Weak?

Article · July 2016

DOI: 10.1016/j.cub.2016.06.027

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Circadian Rhythms: Does Burning the Midnight Oil Leave You Weak?

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http://dx.doi.org/10.1016/j.cub.2016.06.027

A new study shows that nocturnal light exposure rapidly disrupts the central circadian clock as well as reduces motor performance and bone health. These findings provide a striking example of the costs of living in a disrupted light/dark cycle.

As we warm up our world, we are also lighting up the night skies (Figure 1). In an evolutionary instant, the widespread use of artificial lighting both inside and outdoors has transformed the photic environment within which we live. There are clearly many economic and quality of life benefits to living in a world in which light comes on with a flick of a switch. But there is a growing appreciation of the costs which have to be considered in balance with the benefits [1–3]. Some of the most compelling examples of costs come from studies of metabolic syndrome. In animal models, the genetic or environmental disruption of the circadian system disrupts glucose regulation [4–6]. Similarly, laboratory studies where healthy participants were exposed to circadian misalignment provided causative evidence for a deleterious impact on diabetes risk and cardiovascular function [7–9]. So for both mice and humans, sleep and circadian disruption hinders glycemic control and compromises our health.

New work reported in this issue of *Current Biology* by Lucassen *et al.* [10] provides evidence that a disrupted photic environment may be a major challenge to musculoskeletal health. Experimentally, they looked at the impact of disrupting the circadian system by placing mice in continuous light (LL) for six months while longitudinally following a number of measures of motor performance and bone health. The authors confirmed that this treatment disrupted rhythms in behavior as well as increased weight and blood glucose, as has been previously shown. Importantly, the authors were able to carry out long-term neuronal recordings from the central circadian clock, embodied in the suprachiasmatic nucleus (SCN), and demonstrate that the LL treatment greatly reduced rhythmicity as measured by neural activity. This LL treatment reduced skeletal muscle function (forelimb grip strength, wire-hanging duration, and grid hanging duration), caused bone deterioration, and induced a transient pro-inflammatory state. After the mice were returned to a standard light/dark (LD) cycle, the SCN neurons rapidly recovered their normal high-amplitude rhythm, and many of the parameters returned to age-appropriate levels. These findings strongly suggest that a disrupted circadian rhythm reversibly induces detrimental effects on multiple biological processes involved in motor function.

Those who would like a detailed mechanistic understanding of how LL alters muscle physiology will have to wait for future studies. The authors did demonstrate that SCN neural activity is disrupted by this treatment [11] and argue that these changes in neural activity mediate the impact of LL. The electrical activity rhythms that are the hallmark feature of the central clock appear to be vulnerable to the impact of aging and neurodegeneration [12]. With a reduction of the output signal from the central clock, the circadian network consisting of circadian oscillators found throughout the body would lose their normal pattern of synchrony. Disorganized clocks cause a number of undesirable effects throughout the body [13] including altering the function of key organ systems including the heart, pancreas, liver, and lungs, as well as the brain. Still the

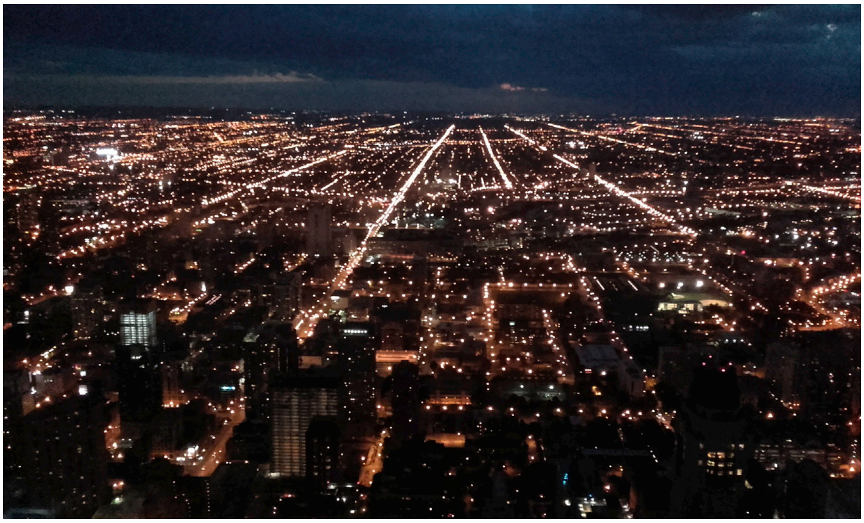

Figure 1. The biological cost of 'lighting up' our night skies.
Driven by economics and convenience, we are filling our nights with light. New work from Lucassen *et al.* [10] provides evidence that nocturnal light exposure rapidly disrupts the central circadian clock as well as reduces motor performance and bone health. (Photo courtesy of A. Olde Engberink.)

specific factors that underlie the impact on musculoskeletal health in this study are not known.

Previous studies have linked circadian rhythms with muscle function by examining mice with mutations in their core clock genes. A large number of genes in the skeletal muscle and bones are expressed in a circadian pattern, and these genes participate in a wide range of functions [14]. When circadian rhythms are genetically disrupted, the observed effects on skeletal muscle include fiber-type shifts, altered sarcomeric structure, reduced mitochondrial respiration, impaired muscle function, disrupted bone formation and arthropathy [15–17]. One concern with this body of work is that clock genes are transcriptional regulators and removing the genes may well have developmental as well as pleiotropic consequences. To this point, many of the well characterized consequences of the loss of *Bmal1* disappear in a conditional, adult-only, knock out line [18]. However, in the case of the musculoskeletal system, this does not appear to be the concern. The loss of *Bmal1* solely from adult skeletal muscle results in reductions in specific tension, increased muscle fibrosis, cone calcification, and decreased joint collagen without changes in activity levels [19]. So these genetic studies complement the present study which used light as a disruptor of the circadian system, and both support the hypothesis that a functional circadian system is essential for musculoskeletal health.

So this new work from Lucassen *et al.* [10] is the latest of a series of important studies which indicate that disrupting the sleep/wake cycle with light at night compromises our health [3–5,20]. As our understanding of the molecular and genetic underpinnings of circadian oscillations has progressed, it is increasingly clear that the function of cells and tissues within our body can vary with the daily cycle. Disruptions in this timing system are a common symptom of many diseases and difficulty sleeping at night is one of the most common clinical complaints when people see their physicians. While constant light is not common, it is experienced by some of the most vulnerable members of our society including pre-term infants, patients in intensive care units and the elderly in nursing homes. Based on our understanding of the circadian system, light sources with a strong blue emission, like Metal Halide and white LEDs, should be avoided during the night while light sources emitting warmer wavelengths would be less disruptive. While changing our use of light at night may be a long-term goal, taking care of the photic environment in healthcare settings is likely a cost-effective way to improve health and speed recovery and would seem to be a reasonable first step.

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Neuroscience: Impaired Decision-Making in Parkinson's Disease

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http://dx.doi.org/10.1016/j.cub.2016.05.075

When making decisions we combine previously acquired knowledge with the available current information to optimize our choices. A new study shows that Parkinson patients are impaired in using their prior knowledge leading to suboptimal decisions when current information is ambiguous.

Parkinson's disease is a common neurological disorder affecting several million people worldwide [1]; it is considered a 'movement disorder' causing, amongst other symptoms, an abnormal slowing of movements, which has been largely related to deficiency of the neurotransmitter dopamine [2]. In recent years, it has become increasingly clear that Parkinson's disease patients not only exhibit problems executing movements but also show marked impairments when deciding which movement to perform [3]. A new study by Basso and colleagues [4], reported in this issue of *Current Biology*, sheds new light on this impairment by demonstrating that patients with Parkinson's disease have great difficulties in using prior, that is previously learned, information to guide their decisions during perceptual decision-making.

What Is Perceptual Decision-Making?

Consider the activity of picking cherries to eat: in sunlight, the decision whether or not to pick a cherry is relatively simple, because you can clearly see the colour of the fruit. Once dusk has fallen, however, this decision becomes more challenging: you need more time to deliberate and are more likely to make a mistake. It turns out that this behaviour can be described by a relatively simple model [5,6]. For ease, we consider decisions between two alternatives (Figure 1A). If choice A and choice B are equally likely, evidence starts to accumulate exactly from the middle between boundary A (indicating the decision for A) and boundary B (decision for B) and drifts towards choice A or choice B over time depending on the cues received. If these are clearly in favour of A, the evidence will quickly drift towards boundary A (high drift rate), resulting in fast and accurate decisions. But if the cues are less clear, evidence will only drift slowly towards A or B (low drift rate), leading to slower and, because the evidence accumulation process is noisy, less accurate choices.

In the study by Basso *et al.* [4], Parkinson's disease patients and healthy, age-matched participants had to judge whether the orientation of a presented stimulus was leftwards or rightwards. In some trials, the orientation was clearly visible, while there was no clear orientation in other trials. Overall, patients performed the task well, indicating that they understood the task instructions, were able to discriminate leftwards from rightwards orientations, and could perform the movement to indicate their choice. Thus, both patients and healthy people chose the correct response with high accuracy when the orientation of the stimuli was clear, and performed at around chance level when the stimuli were unclear. A strong difference between the two groups became evident only when the authors assessed how participants made use of any prior knowledge about which choice was more likely to be correct when stimuli were unreliable.

How Can Prior Knowledge Guide Our Choices during Uncertainty?

When we have to make a decision, but are faced with ambiguous information, it often