

FINAL

Transcript of

Professor Shadab Rahman

Innovators in Healthcare

17 April online

Introduction

Thank you for having me, delighted to be here.

Today, I'll talk about the impact of dynamic lighting schedules. And by dynamic lighting schedule, we'll just define it upfront. I mean, lighting that changes across the day, changes in terms of the spectral content, the intensity, and the timing of that sequence.

So, for example, having blue-enriched light during the day and then turning to blue-depleted light and dimmer light in the evening. Specifically, we'll talk about the impact of that on helping the circadian system optimise its adaptation to changes in sleep-based schedules associated with shift work. I have a few disclosures, but nothing directly related to the work that I'm presenting today.

Risks of shift work and link with circadian misalignment.

So we all know that shift work is associated with a whole host of different adverse health effects, physiological effects ranging from accidents and injuries, 54 % increase in the odds of injury, mood and burnout, cardiometabolic impacts, increased risk of cardiovascular disease, effects on reproduction, especially in women, and then obviously inflammation as well.

And what underlies these adverse physiological effects is primarily circadian misalignment. We hear a lot about circadian and I'll briefly touch on what we mean by circadian.

But, very simplistically, in the aligned state, which is hopefully our typical daily state, we are normally sleeping at night when the body is promoting sleep based on its endogenous 24-hour timing.

We are awake and working during the day. In contrast, in the misaligned state, this would be the case of shift workers, they're sleeping during the day when the sun is up and our bodies are actually indicating or promoting wakefulness, whereas they're working at night. So they're

really fighting their sleep drive to stay awake and work. And so it's quite understandable that in that situation the chances of making errors and accidents go up significantly.

So in all the different physiological endpoints, health endpoints that do show adverse changes in response to shift work, you can see behind them all the different components are circadian-regulated. So this is just an exemplary few studies that I've listed here, but this has been corroborated with different groups.

Circadian component of mood

If you look, for example, just at mood itself, you can see across the day, there's a circadian oscillation. So it's high at some times and it's lower at other times during the day. So when shift work induces this circadian misalignment, it disrupts the daily timing or the near 24-hour timing of these underlying physiological processes.

Mechanism of circadian entrainment

I'll just very quickly dive into the machinery, the clock machinery that regulates circadian rhythms. The clock is a collection of neurons, about 6,000 to 10,000 in humans, and it is connected directly to the eye. So it receives the light input. There's a dedicated neural pathway, the retinohypothalamic track, that carries that signal to the SCN.

But importantly, the signal then reaches various other neural centres in the brain that regulate neuroendocrine responses, neurobehavioral responses, alertness, and sleepiness. But it's also important to recognise that this signal doesn't necessarily have to go through the biological clock. It can go directly to other parts of the brain. For example, it goes to the habenula, which directly regulates mood and other regions in the brain as well. So it can have a direct impact.

So light exposure can at the same time induce direct acute changes in physiological endpoints and at the same time change the circadian timing of these physiological processes. And from the brain, it then travels down to the peripheral organs as well. So when it comes to circadian timing, it's composed of a molecular clock that is present in almost every cell in the body. And that clock, the clock in the brain and the clock in the peripheral organs, the molecular machinery is the same. But for light to reach the peripheral clocks, our current understanding is that it has to go through the central clock. It sits right above the optic chiasm in all mammals, including humans.

We're not going to get into the details of all of this, but just to show a quick video: this is this clock oscillating every 24 hours. So each oscillation getting brighter and darker in one day. And this is gene expression in the SCN in mice. And you can see how well it oscillates with a constant period across multiple days.

Early proof of link between circadian entrainment and bright light

This is a seminal study that was done by Dr. Gene Duffy with Dr. Chuck Czeisler back in '96, so more than two decades ago now.

But this was a very elegant study to show that in humans, light exposure is the principal time cue the main environmental stimulus that sets the timing of the central biological clock, located in the suprachiasmatic nucleus that I just showed you. So they studied individuals in four different groups or four different conditions. And again, without getting into the full details in the interest of time, basically they contrasted dim lighting versus bright lighting. And by bright lighting, I mean 10,000 lux of white light and dim lighting was less than three lux of white light. Individuals received these two different lighting conditions either during the early part of the night or the late part of the night in a simulated shift work protocol. So you can see the black bars are indicating sleep. Normally, when they come into the lab, the first three days, they sleep at night. And then they switch to a night shift protocol where they're sleeping during the day. And so they're either getting light in the early part of the night or the late part of the night.

This shows that it's tracking the circadian clock, the time of the circadian clock in these individuals. And you can see that group one and three across the three assessment points, which is really over a period of two weeks, they don't really shift much. Whereas groups two and four shift a lot. Group four advances, group two delays and that corresponds to this group and this group.

The important point here is that their central clock advanced or delayed or shifted only when they were exposed to bright light, not when they were exposed to dim light.

Light is main cue for central clock

And this becomes important because we often think, what about just changing the timing of sleep? Does that impact the circadian system? What about our feeding schedules? Does that impact the circadian system? And the clear answer from these sorts of studies, and this has been replicated as well, is that no, for the central clock in humans, it really responds just to light.

Even when you shift other things, because in this case, they were doing a simulated shift work, they did shift their sleep, break timing, they did shift their meal schedules, their activity, but because they did not receive the bright light, the central clock did not shift.

We and others are doing a lot of work in terms of understanding how things like meal timing impact the circadian system. But what we are recognising is that meal timing does not impact the central clock; it impacts peripheral clocks.

But that's a whole different discussion. Maybe we can do a different presentation another day. Today, we'll focus on the central clock, which then synchronises all the other peripheral clocks.

The main cue for setting its time is light exposure.

Dynamic lighting v static lighting, facilitated adaptation to shift work and improved sleep

With that in mind, I'll jump into some dynamic lighting schedule work that we've been doing. I'll start off with a set of studies that we did in the lab under very controlled conditions. So we were trying to explore the impact of dynamic lighting schedules. Our typical exposure to light is very static, for artificial light at least. It's not changing in spectral composition nor is it changing in intensity very much. But you can make the lighting more efficient and effective if you control or regulate the spectrum, the intensity and the timing of that light exposure.

So that's what we were trying to test. We did this in 44 healthy, relatively young individuals. And the different types of lights that we used were primarily LED-based or fluorescent-based. I can get into the details later on, but primarily, there was blue-depleted, dim lighting for pre-bedtime. And then for the daytime, we tried different types of blue-enriched lighting at different intensities. And there was the control lighting of the fluorescent, static fluorescent lighting.

I'm not going to get into all the different protocols, but we tested six different protocols, which either advanced individuals or delayed individuals in their simulated shift work protocols. There were four consecutive night shifts in each of these protocols. And we even tried different things, like giving an intermittent light exposure or introducing exercise along with light exposure. Because there are often questions like: 'Do you have to get exposed to blue-enriched lighting to shift the clock for the entire duration that you're awake, or can you get strategically timed bouts of bright light exposure and then the rest of the time you can just stay in indoor lighting?' So we were trying all of that.

And bottom line, what we found was that it's much easier to delay individuals than it is to induce advances, even when you're using optimised lighting with dynamic schedules. However, within the delay protocol, we found that even with the addition of things like exercise, the ideal condition is when you have blue-enriched bright lighting timed to induce the delay for the entire duration. So you want a continuous light exposure instead of intermittent or even room light exposure that we normally get.

In other words, for the circadian system to adjust to the shifted schedule, a dynamic lighting schedule certainly facilitates that.

And this has consequences. So, for example, when we measured sleep using polysomnography, which is the gold standard objective method of measuring sleep, we see that indeed the ones who adapt more, which were the ones using the dynamic lighting

schedule, have significantly better sleep. So, almost an hour more asleep in the adapted individuals compared to the non-adapted individuals.

It changes sleep architecture as well, but primarily it's reducing the amount of wakefulness after falling asleep initially. So, circadian adaptation is attenuating sleep fragmentation, which has major cardiometabolic consequences and other health consequences as well.

From the lab to the space station

So, taking it outside of the lab, we partnered up with NASA. We went into one of their space analogue-research-analogue environments at Herod's Johnson Space Centre. In this protocol, it wasn't really shift work necessarily, but we studied a model of chronic variable sleep restriction. Essentially, individuals would get eight hours of sleep on the weekends, but on the weekdays, they only got five hours of sleep for five consecutive days. So it's more similar to what the average individual faces in their regular lives when we are trying to cram our social schedules, our work schedules during the weekday. And so we tend to truncate our sleep or get less sleep during the weekdays and then we try and catch up on the weekends.

Static v dynamic lighting in 45-day mission, aligning sleep with optimal circadian phase, improved neurobehavioural performance,

So that's what we were studying, the impact of that on the circadian system, and really contrasting what happens if you have a standard static lighting schedule during the day as compared to a dynamic lighting schedule that was blue-enriched and bright during the day. And then three hours before bedtime, it started to yellow and dim. And then an hour before bedtime, it was the dimmest and most blue-depleted, or short-wavelength-depleted.

And the impact of that is that first of all, in the dynamic lighting schedule across the 45-day mission, the individuals on average, when you look at the circadian clock, remain pretty stable. There was a delay, but importantly, even when individuals were delayed on average, it was within their habitual sleep period. In contrast, when they're in the static lighting schedule, the typical indoor room lighting schedule, they delay such that across the 45-day mission, their circadian timing gets later and later, such that it's outside of their habitual sleep period.

And when we looked at their sleep using diaries in this case, sleep diaries, we found that in the dynamic lighting schedule, 93 % of the sleep episodes were in the aligned state. So sleep was occurring at the optimal circadian phase. In contrast, in the standard lighting schedule, only 43 % were aligned, the rest being misaligned. So clearly, a dynamic lighting schedule is beneficial when you have a shifted sleep week schedule, either one that's in a shift work protocol or in our weekend transitions that we typically face.

And we've taken this all the way up to the International Space Station. They had to change their fluorescent lighting; they were getting LED lighting for energy efficiency, and then we

collaborated and said, 'Hang on a second, why don't we introduce dynamic lighting schedules there as well?'

Static v dynamic lighting in a care home facility - falls, self-reported sleep and cognitive decline in residents with dementia

We also tested the impact of dynamic lighting schedules in a care home facility. You may have seen me present this before. The primary outcome was falls. We looked at four different care homes, a pair of care homes within each parent company. Within each pair, one got an upgraded lighting system with dynamic lighting schedules, and the other remained as a static control. We looked at about 758 different residents with over 120,000 patient-bed-days.

The primary outcome measure was falls. The bottom line is that with the dynamic lighting schedule, there was a significant 43 % reduction in the rate of falls. So the improvements that we see in sleep, depression, and cognition do translate to harder outcomes, such as falls and specifically a reduction in falls.

Energy reduction

And of course, for those who are interested, an independent report that was generated by PNNL found an improvement in energy efficiency ranging between 60% to 75 % with the dynamic lighting schedule as well.

Summary: Significant return on investment from dynamic lighting in line with circadian physiology

So, just to summarise, I think we all recognise that circadian misalignment has a whole host of adverse physiological and health effects.

There are different reasons for circadian misalignment, but for humans, the central clock is most sensitive to the light-dark schedule.

Optimising the light-dark schedule, primarily by implementing a dynamic lighting schedule that is in line with the sleep and circadian physiology that we know, does facilitate circadian adaptation. That has a significant value and return on investment when you look at the different outcomes, reducing circadian misalignment, improving safety, productivity, et cetera. So there's a higher ROI with the implementation of these dynamic lighting schedules in work fields.

So I'll just finish up by acknowledging my wonderful collaborators, the institutions that have supported this work, the funding agencies, and most importantly, all the different research participants and the technical staff that have facilitated this work.

Thank you very much for your attention.

Question: real life has many random variables - do lab studies translate?

John Bullock (21:47)

I'd like to pick up on a comment from Peter Thorns, which is about the random nature of human life. We have our organized life pattern, like we go home, we go to work, but there are also other sorts of things happening in between. And do we have any sense of how that random pattern impacts the data that you're collecting?

Answer: by and large, results do translate

Shadab Rahman (22:20)

Yes, so that's a great question. Certainly, sleep in the circadian system is a multi-dimensional system. As much as we would like to say that light is the only thing that affects it, many other things from our random life affect the system, even if it's indirect effects.

So for example, this is what I say to a lot of individuals that you can have the best lighting in your room. But if you happen to watch a movie or read a book with minimal light exposure, but it had disturbing content or it had very exciting content, once you turn off the lights, you did everything right. But once you've turned out the lights, you're going to wonder and think about that movie or that book. And that's going to impact how quickly you fall asleep or how well you sleep across the night.

So, yes, certainly our daily life events impact these systems, independent of light or with light. And that's why we do both the control lab studies, where all of this randomness is removed or controlled. We also do field studies in applied settings to see if what we find in the lab translates to the field. By and large, they do. So the effects of dynamic lighting schedules and sleep and circadian-informed lighting are robust enough to have benefits even with all the random changes that we experience in our daily lives.

Thank you.