THE DISTURBANCE OF THE CIRCADIAN RHYTHM IN WESTERN SOCIETY

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- 3 Our aim
- 4 What is a wicked problem?
- 5 The problem explained
- 6 The Biological domain
- 12 The Psychological domain
- **18** The Social domain
- 24 The Problem Mapped Out
- **25** What now?
- 26 Want to learn more?

OUR AIM

This magazine is a product of the *Wicked Challenges in Health* honours course at the University of Amsterdam (UvA). We are an interdisciplinary group of second-year bachelor honours students. Our academic backgrounds are in psychology, sociology, medicine, and health and life sciences. We are not experts in circadian-related fields and we hence encourage you to approach this magazine with a critical, yet open mind.

This magazine aims to give a very brief *introduction* to this problem. As such, we chose to make this magazine accessible for both those with no knowledge of the problem and those with specialised knowledge within an area of the problem. We hope this magazine can function as informative to those who are unfamiliar with the problem and is broadening to those who already have experience with it.

We believe in the wickedness, importance, and urgency of this problem.



SPECIAL THANKS TO

In our exploration of the wicked problem, several experts were kind enough to let us interview them. These experts range from academic researchers to experience-experts to professionals. These interviews have been integrated throughout the magazine and have been a great contribution to our project. They shine a light on the different aspects of the problem, and it should be noted that comments made reflect the personal opinions of those interviewed and were edited for clarity and length, with permission.

We would like to thank all interviewees for their time, information and especially their enthusiasm.

What is a wicked problem?

If you Google "what is a wicked problem?" you'll find any number of sources and pictures bringing up different aspects of a wicked problem drawn from the original conceptualization by Rittel and Webber (1973) (1). With the evolution of the concept, wicked problems all vary in nuance, but the mainstays of the ten properties can be boiled down to two key themes. Firstly, the problems themselves have numerous ambiguous properties and are practically impossible to define due to the innumerable interactive factors inherent to a problem that is wicked.

The second key theme is presented by exploring the implications of the first theme: how can you solve a problem that no one knows how to define and with many different significant areas? Well, the simple answer is that wicked problems are never completely solved and that every solution based on one field has overreaching consequences on another, sometimes in contrast to the general interests of other field(s). Effectively, both the problem definition and the solution are too complex and multifaceted to tackle the problem as conventional empirical methods have taught us. As many fields as possible must be accounted for, or we risk exacerbating the wicked problem.



What are these possible fields then? These fields are an interconnected, complex maze of systems working both in tandem and against one another. Another way to refer to them is as *complex adaptive systems* (CAS). This theory is used to try to understand, and unravel the complexity of wicked problems by laying out the systems it can have an impact on. These systems are not only complex, but *adaptive*, meaning that they change over time, much in the same vein as our society.

In this magazine, we assert that the Disturbance of the Circadian Rhythm in Western Society is a Wicked Problem and will demonstrate its "wickedness" throughout three domains (The Biological domain, The Psychological domain, and The Social domain). Each domain starts with an introduction page substantiated by our literature research. Followed up by interviews of both experts in studying the circadian rhythm as well as experts in experiencing its disturbance.

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THE PROBLEM EXPLAINED

The problem explained

What is the circadian rhythm?

The circadian rhythm is composed of many cellular oscillators located in the hypothalamic suprachiasmatic nucleus (SCN) within the hypothalamus (1). Together they regulate many physiological processes in humans in 24-h patterns. For instance, sleep, metabolism, hormone secretion, and neurobehavioral processes (2). The internal cyclic clock is synchronised to the environment by external cues known as "zeitgebers" (from German, "time givers") (3). The most significant zeitgeber in mammals is light, though polygenic variations, age and environmental factors like food intake and work conditions, also play a role in an individual's circadian rhythm. The disturbance of the circadian rhythm is a public health concern, as it is known to have negative impacts on health.

Additionally, modern technology such as phone screens -that emit light- and lifestyles - such as shift work- are disturbing circadian synchrony in an increasing number of people (3). Though medical, lifestyle, and social interventions can alleviate some of these issues, growing research on circadian effects, variability and sensitivity suggests that there is not one simple solution. In order to minimise the impact of circadian misalignment on health broader social changes may be necessary.

Why Western Society?

We chose to focus on western society for one important reason: scope. Disturbance of the circadian rhythm can impact a vast number of the human population. As long as a human has the capability of sleeping, their circadian rhythm can be disturbed. The scope and implications of investigating this are far too large for us. Narrowing it down to western society allows us to examine the disturbance with more familiar terms and customs. This also prevents us from misrepresenting or misinterpreting other customs far different than the ones we have experienced during our lives.

Our Domains

We have chosen to present our findings from the view of three separate, yet linked, domains. Our investigation begins with the very zoomed-in biological domain, where we attempt to understand what systems in the body interact with the circadian rhythm. Next, we will expand our horizons by delving into the psychological domain. Here we will observe the cognitive functions and different disorders that impact the circadian rhythm and may cause disturbances. Lastly, we will zoom out from the human body and attempt to understand the social domain, with which the body interacts. In the final section, we will attempt to outline societal causes for why it can be difficult for humans to sleep properly even as relatively healthy individuals.

Within all three domains, there is no true definition of the problem and no realistically employable solutions, even on their own. It is, however, important to note that the subjects discussed within the domains and the domains themselves are only the tip of the iceberg. Under the surface, there are many more systems, institutions, causes, explanations, and outcomes that we may not necessarily even be able to conceive of at this moment.

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The Biological Domain

We will start by looking at the biological domain and talk about chronobiology, the main driving force behind the research on the circadian rhythm, and several systems that the circadian rhythm impacts within our bodies.

Chronobiology is still quite a new research topic, but it has been getting more and more attention. The circadian rhythm is generated by molecular circadian clockwork and clock genes. These genes are regulated by the suprachiasmatic nucleus (SCN), which is a part of the brain located in the hypothalamus. The SCN receives light from the photosensitive ganglion cells in the retina and synchronises the peripheral tissue clocks (1). Because it regulates the circadian rhythm of all cells in the body, it has a lot of impact on several processes in the body. Misalignment of the circadian rhythm can lead to adverse effects, such as inflammation and cardiovascular disease, and is associated with the development of metabolic syndrome (MetS), cancer, cardiovascular disease, Alzheimer's disease, and cognitive impairment.

One of the most striking processes that is influenced by the circadian rhythm is the sleep and wake cycle. Melatonin and cortisol release influence this cycle, with a peak of melatonin in the middle of the night and a peak of cortisol at the time of awakening. Oscillations of these hormones are regulated by clock genes. The circadian rhythm is influenced by daily exposure to chronic synchronizers, the most important one being light. With changes in the pattern of light exposure, such as changing between time zones, the SCN can be reset to later or earlier phases. This adaptation is a slow process and is more difficult in the case of shift work, as they are still exposed to the external factors promoting a dayoriented schedule. Due to the irregularity of many people's schedules, like switching between day and night shifts for shift workers, their endogenous circadian system cannot adapt accordingly. This results in people sleeping when their melatonin levels are low and their cortisol levels are high, which can cause a low quality of sleep (2).



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The SCN regulates the circadian rhythm of the peripheral cells via endocrine and neuronal pathways. It is closely related to several hormonal systems, such as melatonin, the hypothalamicpituitary-adrenal (HPA) axis and epinephrine (3,4). Circadian misalignment has been shown to have a negative effect on the metabolism, such as an impaired glucose tolerance and cardiovascular disease (5,6).

The circadian rhythm can also orchestrate the activity of the innate and adaptive immune system. This can be done by upregulation or downregulation of certain clock proteins, which will act as transcription factors. Transcription factors are molecules that affect the expression of certain genes in our DNA. Next to these clock genes, the DNA can also be methylated or acetylated to impact the expression of certain inflammatory proteins. The interaction between the circadian clock and the immune system works in both ways. Studies have shown that misalignment of the circadian rhythm can lead to severe disease (7).

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Next to light exposure, nutrition is an important factor, with the timing of food consumption being especially important. The metabolism as well has a circadian rhythm, meaning that there are certain time frames where the body expects to receive food and process it. If food intake takes place at different times this can lead to high levels of glucose, insulin, and triglyceride lipids (fat) and a decrease of energy. This dysregulation can harm the metabolism and result in metabolic diseases. An example of this dysregulation in daily life is fasting, especially in religious contexts like Ramadan.

It is widely known that shift workers are at higher risk of obesity, hypertension, and cardiovascular disease. This could be due to the misalignment of the circadian rhythm causing high glucose and lipid levels in the blood that can contribute to these complications (8,9).

We've seen the importance of the SCN and processes that can impact circadian rhythm, so now we'll gain deeper insight into the biology of it all with researcher Tom de Boer.



Tom de Boer

Tom is an associate professor at the University of Leiden and works at the university's medical centre. He has a PhD in biology and write his thesis on the relation between hibernation and sleep. He has been involved in the field of sleep for a very long time, starting with his first postdoc study in the USA, where he studied the working mechanisms of REM* sleep and its relation to post-traumatic stress disorders. After this, he did another postdoc in Zurich where he worked with different knock-out mouse models to search for genes involved in sleep. Eventually, he moved to a lab in Leiden, which gave him the ability to measure the electrophysiology in the SCN and use EEG**. This allows him to investigate the interaction between sleep and the circadian rhythm.

What's the two-process model of sleep?

"On one side you have, sleep homeostasis (S), and on the other side, the circadian clock (C). We did not fully understand sleep homeostasis until now. The longer you are awake, the sleepier you feel and the longer you have been awake, the deeper you will sleep. So there's something that keeps track of the time and compensates for that in the sleep. And that is what you can call a homeostatic process [...] There's an upper limit that is allowed, and there's a lower limit that is allowed. And it turns out that if you do experiments, these upper and lower limits are not fixed. They fluctuate with the circadian cycle which means that during the wake phase, this sort of upper limit of your homeostasis is fluctuating and at some point, your homeostatic process reaches this upper limit and then you fall asleep. Then it goes down and it reaches the lower limit and you wake up"



* Rapid eye movement ** Electroencephalogram

What have you been researching recently?

"We do some fundamental research on the working mechanisms of caffeine on the [biological] clock and sleep because recently, it has been noticed that caffeine not only influences sleep, but that caffeine can also influence the speed of your circadian clock. Apparently, it may be the case that when you chronically use caffeine, which a lot of people do, your clock becomes slower, which is very interesting, so we have done some experiments in that direction recently."

"CHRONIC USE OF CAFFEINE COULD POSSIBLY SLOW DOWN YOUR CIRCADIAN CLOCK"

What do you think are the most important causes of the disturbance of the circadian rhythm nowadays?

Well, I think it's funny that it has improved because of the COVID-19 pandemic. But before that, there was apparently quite some pressure for people to sleep shorter and to make longer working days and having fun after. Of course, one of the main reasons [for the disturbance] is artificial light (ie. phone and computer screens). You sort of give the signal to your brain, now there's still plenty of light; don't go to sleep yet. I think this one is the most important at the moment. Also, I think there is a group of people who feel the need to have long working days because they are in competition. There's also the shift worker problem. There's a one size fits all approach. Now everybody needs to follow the same shift protocol. And this may work for some and not for others. We know that we have morning types and evening type people. I think in Germany there's now an initiative to try and ask or measure the chronobiological preference of their workers and adapt it, and see where they would fit best. I think that may be a better approach than the one size fits all approach. But it's not the final solution because there will always be people that work outside their comfort zone in that respect, and particularly when you're young, you probably think 'it's not a problem. But you see that there are more problems with obesity, diabetes, and other things that are increased because of the circadian disruption.

Do you think using melatonin can help with misalignment of the circadian rhythm?

"Melatonin is used by many people to sleep better. However, the pure chronobiologists, they'll say that's rubbish. Melatonin is a synchronizer, and it will not make you more sleepy. But if you take it on a regular basis, it may be that your clock works better. Particularly when you take it at the same time of day, every day in the evening. And eventually, you may also sleep better because you take melatonin on a regular basis. But, you should only take melatonin if you do not produce enough melatonin by yourself and that is something that you can check. I mean there are several clinics that can take samples of your saliva and see whether you have enough production of melatonin, because if you produce enough melatonin, then a melatonin pill is not the solution. "

What did you find about the impact of nutrition on the circadian rhythm in your (young/middle aged) mouse model?

"[...] we came to the conclusion that if they eat a high caloric diet they can live under a higher sleep pressure. They do not seem to sense it [sleep pressure]. They sleep less. They do not suffer from it except for becoming very fat and their slow wave activity getting higher with the same amount of sleep. So they seem to live under a higher sleep pressure. And the interesting thing is that if you look at humans who sleep less, they tend to go for high caloric foods and they get hungrier. So, they will go for the chips and cola with sugar and chocolate with sugar, etc. That's the stuff that they crave. That's also one of the reasons why some of people are a bit obese because it starts with not having enough sleep and then feeling hungry and eating. And in these mice, we turned that around. We forced them to eat a high fat diet, but they didn't get anything else, and then they seem to be able to cope better with a higher sleep pressure. Which I thought was interesting, because it seems to fit with what happens to humans that are seep depriving themselves, as they tend to go for high fat, high caloric diets and cope with the situation as well."

Your study showed that animals that are sleep deprived have a reduced response to light and reduced amplitude of the circadian clock. Might there be a vicious cycle?

"Shifting the rhythm is more difficult when people sleep for shorter durations. So it also seems to apply to humans that if you are sleep deprived you are not able to adapt very well to the light-dark cycle. Which could mean that you end up in a vicious cycle. If you keep up this low level of sleep and or maybe also when you are not having full bright light during the day, then you may get into trouble at some point when your sleep-wake rhythm starts to move around. It basically again makes you sleep worse."

''THAT'S ALSO ONE OF THE REASONS WHY SOME PEOPLE ARE OBESE, IT STARTS WITH NOT HAVING ENOUGH SLEEP AND THEN FEELING HUNGRY AND EATING.''

If you apply your research more broadly, where do you see that this circadian rhythm disturbance is manifesting most obviously in our society?

I don't want to exaggerate, but in principle, it is important in every clinical application that you do. There may be a circadian part in it. [For instance] if you give medication, it may work better in the morning than in the afternoon. This is the same for pain killers, but also for cancer treatment. [...] But more in general, if you look at plants and flowers that we grow, they are all working with the light-dark cycle somehow and trying to influence the growth of plants by changing the day length and things like that. So if you want to exaggerate, it's really everywhere. However, where it can is relevant, and can make relevant steps is in the clinic. Answering questions like: How and when do you apply your medication?



EXPLAINING THE MAP

As we close on the first domain, we want to broadly explain a few points and systems on the mindmap to help it be more digestible. We will continue to do this with each domain.

When the circadian rhythm is disturbed it can have an effect on the way people consume certain substances, like food, alcohol, and tobacco. This often means that people will consume foods high in sugars and fats and substances such as alcohol and tobacco. The consumption of this diet may lead to diabetes, obesity, a higher BMI, high cholesterol levels, and metabolic syndromes. It is also known that people with a late chronotype are more prone to substance use (for more info visit page 12). The timing of food consumption is also regulated by the circadian rhythm and eating at different times can have several effects such as gaining weight.

Disruption of the circadian rhythm may also lead to dysregulation of hormonal processes. Leptin and insulin, both hormones involved in hunger regulation, can rise in levels. These high levels may lead to insulin and leptin resistance and therefore an increased risk of obesity and diabetes. Melatonin is a hormone that is very important in the regulation of the circadian rhythm and induction of sleep. When the circadian rhythm is disrupted this will lead to a decrease in melatonin levels.

The immune system is also involved with the circadian rhythm with a mutual influence. Once misalignment of the circadian rhythm occurs this can lead to malfunction of the immune system and therefore the development of several diseases (page 7 has more info on this).

The more direct consequences of a disturbed circadian rhythm are lower sleep quality, lower alertness, lower performance, and higher chances of hypertension. Nowadays more people start using substances such as melatonin, valerian, and modafinil in order to get to sleep. This medicalisation of sleep seems to be a trend, and as noted by Tom de Boer: sleep medication only functions under specific circumstances, for specific types of people.



THE NEW WICKED PROBLEM | 11

The Psychological Domain

Individuals can be organised into a spectrum of chronotypes. Chronotypes refer to the differences in the circadian rhythm and timing of an individual's functions. The spectrum of chronotypes contains two extremes: late/evening chronotype and early/morning chronotype (6). People with a later chronotype appear more prone to substance use, eg, alcohol and nicotine, and mental disorders, eg, depression and anxiety (1,2). This is attributed to these individuals sleeping outside their circadian rhythm. Our societal rhythms may be putting these individuals at risk (2).

Individuals' cognitive functions are impacted by their circadian rhythm and chronotypes. While sleep deprivation alters cognitive functions, time of day is also influential, in turn influenced by sleep quality and quantity (3). It is thought that these fluctuations in functions, especially attention, is related to the scheduling of, and accidents occurring during, night shifts (4).

These fluctuations disproportionately influence individuals with more extreme chronotypes and increase their risk of developing psychological disorders. So far, several disorders have been linked to sleep and/or circadian rhythm (disturbance); eg, depressive disorders, bipolar disorders, sleep disorders and Alzheimer's disease (AD).

Depressive and bipolar disorders include sleep disturbances in their symptomatology, and regarding AD, there is a correlation between the development and progression of the disorder and the disturbance of the circadian rhythm. Gretchen et al (2022) (5) found supporting evidence that the clearance of the protein amyloid beta, a protein which aggregates in AD, is a daily oscillatory process regulated by the circadian clock. A disruption in the circadian rhythm can cause a disruption in the regulation of the immune cells that are responsible for the clearance of amyloid beta (5).

The clearance of certain proteins and substances is not only important in the development of AD but also in other neurodegenerative disorders, such as Parkinson's disease (PD). The removal of these proteins from the cerebrospinal fluid (CSF) is regulated via the glymphatic system, which is a waste clearance pathway of the brain. It allows the clearance of waste proteins and other substances. Sleep disorders can cause dysfunction in the glymphatic system as it is more effective during sleep, peaking in the mid-rest phase (6,7). The malfunction of the glymphatic system can result in the progression of such neurodegenerative disorders (6,8).

The following interviews will help elaborate on the impacts of mental health on circadian rhythm disturbance and how light therapy broadens the available psychological treatments.

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Mees

Mees is a Dutch university student in his early 20's. He describes his problems sleeping in relation to his depression, and how he turned to over-the-counter substances in an effort to combat these problems.

Could you give some background on your history of problems sleeping?

"I wasn't necessarily always a difficult sleeper. Before I could sleep easily under different circumstances, with noise etc. At school you had a good rhythm. Every day you were expected to be there at 08:45, and if you were late you had to go get a note so then while waking up wasn't fun, it went pretty okay. In the evenings I would get tired more often, and going to sleep was easier than it is now. Living alone as a student, my rhythm is different than it used to be at school. The times you are expected to be somewhere vary. There are days that you are expected to rise early, or that you go out at night or watch television or game. Those are the small things that influence my rhythm. But I didn't see those things as a problem at that time.

Now I do see myself as having a problem. This coincided with depressive thoughts and I went to a psychologist for this. These sleeping problems kept getting worse and my rhythm became more dysregulated. It became normal for me to fall asleep at 04:00 and that my eyes were very heavy and my body was tired after a week of having to get up around 07:00 or 08:00. Then, my rhythm was very disturbed.

I think that when it was dysregulated, I also had less trust because I went to bed later and thought 'it's not going to happen anyways' [falling asleep]. And I would just watch the ceiling and there was more chance for unpleasant thoughts, so I would push back sleep. I know it's not a good idea to use screens, but it was a distraction from those thoughts until I had to sleep, but I know it's not a natural means. So that's how it's been for that past [year]."

What do you think the biggest reasons are for your dysregulated rhythm?

"The biggest reasons are that I have depression and especially at night, without distractions, there are thoughts and fear of panic attacks. Even if they don't happen, you are still worried about them, in the silence and dark. That is, I think, the biggest reason. "Another reason is, and I have also done some research on this, that you shouldn't use screens before you sleep. I try not to do this; I will listen to an audiobook or a podcast. But I still think it has an influence.

I also think that you lose confidence in your sleeping after lying awake for all those nights. You give up and think 'I could try to lie in bed at 11:00 or 12:00 but I know it won't work', so then I push it back. The main reasons would then be the confidence and panic attacks, but also the dysregulated rhythm happening when you sleep until noon and your body hasn't had sleep."

You used to and still use certain substances to try to sleep. What are these and how did you find them?

"The first thing was melatonin, which my mum had on her nightstand. I have used it, but I doubt whether it did anything. You could use a lot because the pills were quite small, and I did sometimes have the idea that I was calmer because of it but I did not feel anything change physically. You wonder "When will this work? When will I fall asleep?" but its not that type of substance. It's not that powerful. Sometimes I wondered if it even did anything or if it was a placebo effect, that thats why i was calmer. I did use a few packets but I did not think that it was very useful.

I also used Valerian and am not really sure what it is or what it's made of but my parents had also bought a packet of that and I thought "I'll also try that". It's similar to melatonin, that it may help a little but it didn't really help me.

I also, without prescription, used cannabis to try and sleep. I try not to become dependent on it but it is often tempting, because it does give you a calmer mood and there I noticed that cannabis was better for getting to sleep. I have read that sleep quality does get worse after cannabis, but for me falling asleep became easier and this was my biggest problem. When I am asleep I do not easily wake up [...] When I sleep, it is quite stable."

Do you see a trend in how sleep substances are used?

"I do have the idea that it's quite normalised, in the sense that a lot of people have it on their nightstand and that some also use it without sleep problems, more out of habit. I do not know if that's damaging, probably not so. I do have an idea that a lot of people use it and its normalised.

What has also been normalised, I've noticed, is having a chaotic week. It's quite weird, for example, that I have my Monday volleyball training until 23:45 where I also need to take some time to bike back [home]. The life of a student is also quite focussed on being dysregulating. The starting time of a borrel [a Dutch social gathering over drinks] and ending time, do not connect well to the 08:30 or 08:45 times that you are expected to be at university. I have sometimes also taken exams at 08:30 in the morning when I had a lot of problems sleeping, and I know that is the time of day I function the worst.

The life of a student and expected times and expectations seem out of balance. This is of course, partly our own choice but it is also not good it seems for our rhythms."

Would you want this to be changed?

"It's difficult because there are also people in the morning that thrive. We can't say that we will do more later activities so we can all sleep in. That is not a solution. I do think that those issues, like early exams and lectures, should be more flexible or later."

"I AM NOT VERY AWARE OF WHAT EXACTLY ALL THE SUBSTANCES DO.

I WOULDN'T KNOW WHICH EFFECT WAS FROM THE SUBSTANCES AND WHICH FROM THE SLEEP DEBT."



"THE PRODUCT SHOULD NOT TRY TO BE THE ANSWER. YOU SHOULD SEE HOW EFFECTIVE IT IS FOR YOURSELF, BECAUSE FOR ME IT WAS NOT REALLY."

THE PSYCHOLOGICAL DOMAIN



Emma

Emma Visser & Oana Georgiana Rus-Oswald



Oana Georgiana

Emma and Georgiana are neuroscientists involved with the BioClock consortium, where they are investigating the use of light therapy as treatment for depression. Emma is a PhD student at TU Eindhoven, looking at the effectiveness, response predictors, and mechanisms of light therapy.

Oana Georgiana is a postdoctoral researcher affiliated with the University of Leiden, and has a background in psychology and neuroimaging. She will be taking brain scans of participants in the project.

In our simultaneous interview, they detail the potential of light therapy and their thoughts on the disturbance of the circadian rhythm.

What types of depressive disorders does your research involve?

"We already have a light café where the treatment is already implemented in regular care at Geestelijke Gezondheidszorg in Eindhoven (GGzE). So what we know from the literature is that light therapy is, especially effective for seasonal affective disorders, also known as winter depression. That is already known and not a new fact, hence it is also part of the clinical guidelines to use light therapy for seasonal affective disorder. For all other depressive disorders like unipolar or bipolar depression, there seems to be positive effects, however the studies are not conclusive yet. More studies with bigger samples and which evaluate long term effects of light therapy in these disorders are needed.

The patients for this project come from the GGzE in Eindhoven and the LUBEC Leiden University Medical Centre.

"FOR ALL OTHER DEPRESSIVE DISORDERS, LIKE NON-SEASONAL DEPRESSION, BIPOLAR, WE HAVE SEEN ALL POSITIVE EFFECTS IN THE STUDIES, BUT IT'S NOT CONCLUSIVE YET"

What does the process of light therapy look like?

Here at the GGzE Eindhoven, we do treat those patients [with seasonal depressive disorder, unipolar and bipolar depression] with light therapy. [...] And we see really good results with it as well. So right now everyone who has mild to moderate depressive symptoms, and is willing, receives this therapy. [...] Your general practitioner or psychiatrist gives you a referral for light therapy and then you can get the light treatment in the café setting.

The light café is like a regular café, so you really can order a cup of coffee, read a book, do whatever, just that additionally you have these light lamps in front of which you sit. You need to make an appointment every day at the same time, in the morning, for at least a week. And then you go to this café and you sit in front of the lamp for thirty minutes, and you can talk to other people and socialise.

After thirty minutes you leave, you go about your day and the next day you come back and do it again for thirty minutes. After one week we assess how it worked the patient. [...]

The treatment length is between one week and three weeks depending on how well it is accepted and how and if symptoms decreased.



Can you get professional help at the café as well?

"You can also talk with a therapist who, if needed, can give you insights into how its best to adapt your sleep/wake schedules and implement physical activity during the day as well. This is important because it is known that depressive patients usually have a disturbed day-night rhythm, for example some cannot get out of bed in the morning. In these situations, suggestions like: avoiding screen light from mobile phones in the night, having a regular sleep hour time and a regular wake up time in the morning can be useful. This is done individually and adapted to the patient's needs.

And maybe an important thing to mention is, [...] the light therapy is always in the morning.

This is key, as the exposure to light is there to not only improve your mood, but also to trigger your awakeness level. If one would use it later in the day, it would disturb again your sleep pattern by making you sleep later and by this disturbing your day-night rhythm, which in case of depression needs to be regulated. Therefore, avoiding light at night is also an important element in therapy."

What will your research process look like?

"In our upcoming study we will use this framework of light café just in a more standardized manner and in a big sample of patients. We will assess a lot of contributing factors such as mood, sleep quality but also biological markers from saliva samples and brain scans, to see what effects this therapy has on the patient. These assessments will be performed before and after the intervention and even more important in some follow-up sessions (some weeks later) to be able to see if this effect is also maintained on a long run."

"WE ARE JUST NOW STARTING TO REALIZE HOW IMPORTANT IT [THE CIRCADIAN RHYTHM] IS"



What is the effect of light pollution on people?

"[We are] not experts in this, right, so [we] are speculating here. There are other people in BioClock who have way more experience with light building and similar topics. In mental health, of course, it is important to keep a steady rhythm, especially for people who are really sensitive to disturbances.

People with depression already have a disturbed biorhythm and having additionally the light pollution as a contributing factor might disturb their day-night rhythm even more. Hence avoiding it with the available resources is for sure a good idea.

So then it is important to not be disturbed by light in the evening because it improves your sleep quality and to sleep in a really dark room. There are studies out right now that [show] even if you sleep in a completely dark room and you have your laptop monitor and there is one little light bleeping, that it impairs your sleep quality by I think something like 30%. Just one little blip of light that really decreases your sleep quality, and sleep is so important for mental health that I think that that's something that the light pollution really has done."

THE PSYCHOLOGICAL DOMAIN: MAPPED OUT



The circadian rhythm, especially when disturbed, influences both those with and without psychological disorders. Cognitive functioning is especially impacted when one's rhythm is disturbed, and it is difficult to find a cognitive function not impacted by either sleep (deprivation) or the circadian rhythm. In addition to conscious functioning being impacted, one's neurobiological systems also feel the impact of a disturbed circadian rhythm, in turn (likely being involved in) exacerbating

and/or altering the risk of developing a disorder, such as Alzheimer's. Depending on someone's chronotype, and how they manage their sleep-wake rhythm, they may be at an increased risk for developing mental disorders, especially substance use disorders. Mood and anxiety disorders have symptomology relating to sleep disturbance, but there is not yet a conclusive reason for why sleep and these disorders are interrelated.

The full implications of altered cognitive functioning are too vast to cover, however in the following section, within the social domain, we will cover some of the main causes and effects hereof.





Lastly, we will zoom out and see how the circadian rhythm is disturbed and impacted by forces outside of the body.

While our circadian rhythm is determined by internal and external cues, social time is mainly established by social obligations such as work, religion (i.e., prayer times), school and social events. The term social jetlag (SJL) is used to describe the misalignment between social time and circadian rhythm. In industrialised countries, two-thirds of the studying/working population experiences social jetlag, often for several years.

Shift work and circadian misalignment

The effects of SJL have also been researched in shift workers. Due to their working schedule, they must periodically re-adjust their wake-up and bedtimes to be able to be present at their morning, evening, or night shifts. As these shifts are (usually) assigned regardless of the individuals' chronotype the shift workers can experience up to three hours of SJL (2,3). A shift worker working night shifts and sleeping during the day suffers a state of rhythmic disturbance similar to that of a traveller who flies rapidly across several time zones (1). Individuals differ greatly in their degree of tolerance to shift work, and there is evidence to suggest that circadian physiology substantially affects an individual tolerance to work shifts and factors. Factors such as gene-environment interactions, chronotype, the phase angle of entrainment, racial/ethnic differences, and daily pattern of light and darkness. The organisation of work schedules and the complete adaptation of the circadian rhythm to night shifts would only occur in a minority (<3%) (1). The effects of working outside of the conventional daytime hours cause a substantial increase in sleepiness, sleep complaints, increased health risks, impaired vigilance, and an increase in the risk of accidents (50-100%) (1).

THE SOCIAL DOMAIN

Described for the first time in 2006, a lot of research has been done to try and comprehend the effects of social jetlag on human physiology. Still to this day, our understanding of social jetlag and the circadian rhythm is very limited. However, due to its high prevalence, social jetlag is becoming a primary concern for public health (3). Even a small increase in health risk will have a significant impact on public health, and no single countermeasure can completely alleviate the circadian and sleep-wake disturbances shift workers present (1). Therefore, both social and individual strategies should be applied to counteract the adverse effects of SJL.

Alongside the influence of SJL, another disturbance that occurs in the social domain is people attempting to customise their circadian rhythm through medicalised or even commercialised means (4). Medicalisation refers to, in this case, circadian rhythm, becoming viewed as a medical issue while it was not warranted before. Similarly, commercialisation is creating an industry from something that was not before. These concepts are not mutually exclusive and can be one and the same. An example of this is advertisements for melatonin. Other examples of products that fall under one or both categories are specialised mattresses, modafinil, and caffeine products.



Caffeine can exacerbate disrupted circadian cycles as we saw that caffeine shifts the circadian rhythm backward, causing a person to sleep later. It is not realistic to remove caffeine products altogether, as this would have farranging implications for the people working in those businesses, and remove a substance arguably useful to many people.

In the interview with Alexander and Jynthe, we will further expand on the methods used to help shift workers and the struggles of shift workers.

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THE SOCIAL DOMAIN



Alexander van Eekelen

Alexander heads the Dutch branch of the CIRCADIAN company, a consulting company aiding in the optimisation of shift work in terms of safety, health, and employee performance. Alexander is also involved in research involving shift work, and completed his PhD in physiological psychology at the University of Amsterdam, after investigating human circadian rhythmicity in stress reactivity. He is primarily involved in consulting shift work operations.

If you had to summarise the ultimate goal of CIRCADIAN and its consultants, what would that be?

"In the Western world, anywhere between 15% and 20% of the people work in shifts. That's a lot of people. And shift work poses an extra burden for everyone involved. Resulting in increased risks when it comes to health and also safety. So the ultimate goal is actually to help people. Just to see if we can be of any assistance to these people, to help them get through their shift work career just a little bit better and a little bit safer. The goal is to help people also to [discover] how we can translate scientific knowledge into practical solutions. [...] There is no golden rule in this area, because the root cause of all of these increased risks, we can't take that away. The only real solution is that everyone works from 09:00 to 17:00, and is at home at 18:00 to eat their dinner. That's the only real solution, so that's not going to happen."

What kinds of solutions are possible?

"The cause of risks involved in shift work is because of a few basic, fundamental things.

It's caused by circadian misalignment in combination with sleep deprivation. The root cause of shift work risks is physiological. It's a disruption of your biological system. That's the root cause. If that's the core of the problem, then the solution should be found right next to that.

The solution then should be to minimise that disruption, to minimise circadian misalignment, and to minimise disturbed sleep. So interventions, health and safety interventions, should always be focused on: how can we minimise these disruptions? From science we know that there are two main areas that we can use to do that, and these two areas are light and nutrition. You can use light interventions and nutrition interventions when it comes to shiftwork populations to at least mitigate or minimise this type of disruptions. We [CIRCADIAN] work with both of these areas. If you look at at circadianlight.com, you learn that we developed LED lighting that can filter out the bioactive blue components in the existing lighting during the night and add bioactive blue during the day. So during the day you can use that to synchronise the biological clock and at night you can use that blue depleted light to make sure that there's no hormonal disbalance caused by bioactive blue during that particular period. So you can use light and then you can use nutrition interventions [...] making use of the chrononutrition principles when it comes to meal timing, meal frequency, and also meal composition[...]"

"SO WHAT'S THE NEXT BEST THING? WE'RE ALWAYS LOOKING FOR THE NEXT BEST THING.

WHICH, IN MY PERSONAL OPINION, MAKES IT MORE INTERESTING, BECAUSE IT'S A CHALLENGE. MAYBE IT'S A WICKED CHALLENGE, BUT IT'S A CHALLENGE."

What is your opinion on people doing shift work using things like caffeine or other drugs to try to sleep?

"If you look at shift work related health issues: disturbed sleep but also the risk of developing diabetes type 2, gaining weight, cardiovascular issues, most of these health risks are lifestyle related.

So if that's true then you could speculate on the fact [that] these risks can, at least partially, be reversed by changing your lifestyle. One of the things that I do in my work is to provide shift workers with lifestyle information. I give what we call a managing shift work lifestyle training, for shift workers, in which I explain that there are actually changes that you can make to your behaviour that can already improve your sleep, [...] nutrition habits, and other lifestyle related and health risk related issues, in contrast to just maintaining lifestyle problems and only using meds to dampen that effect.

In the past, research has shown, for example, that when you provide people with shift work related insomnia with cognitive behavioural therapy just to teach them about sleep hygiene, sleep restriction and regularity in their bed times [...] That that information is superior to what any sleep medication can can do in terms of improving their sleep. So changing your behaviour for the better, in this case to improve your sleep, is always superior to sleep medication for example.

Should we be trying to change our shift work society, or is it an inevitability?

"I think it's eminent to think about the future of shift work and the future of our 24/7 economy. At certain levels, I think shift work is inevitable for years to come. When you look at healthcare, for example, if I break my leg in the middle of the night I'd like to get picked up by an ambulance and taken to a hospital, not to wait until the next morning. But on the other hand, I've had numerous examples of people working in night shifts where I thought 'What are you doing here? There's no work, you're just sitting around.' [...] And when you ask the question 'Why are these people here?' [They respond] 'Yeah, well you know, that's what we do.' I think it's always a good idea to stay critical and to look critically at working nights."

YOU ARE THE BEST SLEEP AID THERE IS. THERE'S NO PILL ON THE MARKET AT THIS TIME THAT CAN REPLACE WHAT YOU CAN DO WITH TWEAKING YOUR BEHAVIOUR WHEN IT COMES TO YOUR [...] SLEEP'

Are there other areas where you see problems arise due the shift away from circadian rhythm?

"If you zoom out then you can see increasingly that the influence of our so-called 24/7 economy has its impact on public health. We know that one out of six people experience problems with sleep on a regular basis and we know from research that this has a direct impact on lifestyle related health issues, like obesity, diabetes types too. If the whole COVID crisis has taught us one thing, it is that these lifestyle related health issues can have a real impact on the susceptibility of people towards virus infections.

And the fact that our work hours and our workplaces are becoming more and more flexible. [...] You can see that the keyword in all of this is structure and regularity, corny, as it may sound. But we as humans really, really rely on regularity and structure. The more our activities are planned in a structural way across the day, the better our biological clock stays in its place and the better we function, the better we sleep, the better we perform the next day.

There are a number of influences right now that really eat away that structure, and that regularity, and you see people suffer from that when it comes to sleep. But also in terms of their diet. People just don't have this regular three-meal structure anymore; where they eat breakfast, lunch and dinner at about the same times every day. They just munch away when they have the chance. On the surface it looks like it adds to our freedom, to choose what we do at the time that we choose to do it. But learn more and more that it comes with a price: a health price."

THE SOCIAL DOMAIN



Jynthe works as a nurse and experiences several night shifts each month. She details how she experiences these shifts and their impact on her life and health.

What kind of hours do you sleep when you have a night shift?

"The day before the night shift I try to stay up as long as possible till 02:00 or 03:00. Then I will sleep for six to seven hours and wake up at 09:00. During the day, I will go work out or do something fun till dinner. After dinner I will sleep for a few hours untill 21:00. At 23:00 my night shift begins.

After my shift I will be home at 08:30 and eat something like yoghourt. Then I tend to sleep till about 13:30. After a night shift, I'll fall into a deep sleep.

We have these night shifts three nights in a row, but sometimes you will have more."

"I don't get to sleep during my night shift. For doctors it's different. They have to complete seven night shifts and get seven free days afterwards. They can also sleep whenever. I do get my seven to eight hours of sleep, just not in one go."

How do you feel during a night shift?

"At 04:00 I will have an energy dip, maybe because we eat at around 02:30 or 03:00. I feel this dip after my food has settled. I experience these during my day shifts as well, but these feel different. I feel like this [night shifts] goes against your biological clock. You need to sleep but you no longer feel tired."

"A night shift is much calmer. You speak to family, help people go to the bathroom and keep an eye on the people that are not doing well. You also watch a lot of tv and walk through the wards. In the morning you do a morning walk and give antibiotics

The night shifts can also get heavy, because you work with two coworkers instead of seven during the day."

"I feel like my brain is worse during a night shift, in sleep mode or something. I feel less sharp, but whenever there is a crisis my brain turns on. So when it's not necessary my brain is turned off. One time I wrote an essay during my night shift. The next day I read it back and could not believe the things I wrote. I was amazed.

During the day you have more tasks to do. But I enjoy night shifts. I have never fallen asleep."

What does your eating look like during a night shift?

"I feel like I eat healthier. Between 02:30 and 03:00, I have a bite to eat. I tend to eat lighter foods like crackers and a bouillon. This is because I can get nauseous if I eat more. What I find weird is that I drink a lot during night shifts. I don't drink coffee, so I drink tea. Some co-workers drink coffee and/or coke [and] eat candy or full meals."

How do you deal with your changing sleep schedule?

"After three night shifts you get two free days. After those two free days I feel well, but [...] the mornings are hard. I feel tired but have slept enough. I have my blackout curtains and use a sleep mask to help me sleep.

Most people sleep until dinner the day after a night shift, but everybody has created their own routine."

THE SOCIAL DOMAIN: MAPPED OUT



We see all the subjects branching from the social domain as possible causes for disturbance of the circadian rhythm. As shown earlier, shift work inherently creates disturbances in the circadian rhythm. With problems inherent to the practice, this can create a demand for shift workers to survive their working environment. There's an appeal to sleeplessness by advertising energy drinks to help individuals stay awake and stay vigilant in their work as we saw in Jynthe's interview when she talked of her coworkers drinking coffee or soda during their shifts. Another answer to the inherent problems are companies designed to help shift managers create better routines with companies.

Looking outside of shift work, religious activity, school, and social jetlag are all capable of disturbing the circadian rhythm. Religious events such as Ramadan can be sources of disturbance through fasting and nightly prayer. School work and stress caused from studying is also capable of disturbance through a standard of hard work sometimes necessitated by their family or peers. Students may resort to drinking caffeine or using other stimulants to increase or maintain performance. Social jetlag is an ever-present member of disturbance in all of these social aspects, because social life simply does not always align to our biological time.



THE NEW WICKED PROBLEM | 23



WHAT NOW?

Are you also astounded by the interconnectedness of this problem? We are as well! Mapping out this problem does not result in a simple mindmap with few connections between the main domains, but in a maze of interwoven influences and effects. Rather than just displaying the complexity of the issue, it also demonstrates that this problem is truly wicked.

Wicked problems are defined by two main themes: 1) the problem has numerous properties and it is practically impossible to define due to the many inherent factors; 2) the problem can not be solved, as one field has overreaching consequences on another. With the disturbance of the circadian rhythm, many different fields are involved and it is quite hard to define the problem. The different domains that we have included in our project are just a small part of the fields and factors that are involved. We have artificially separated these domains, but it is quite clear that they are in constant interaction. Because of the many interwoven domains that are involved in the problem, it is impossible to find a solution that works for all the different factors. For example, if we focus on changing health interventions, it is most likely that our current economic systems will suffer, as we live in a 24/7-society that requires people to work nights shifts or inconsistent hours. We see this inter-field interaction reflected in the interviews as well. There is a shared awareness of the wicked problem but there is no consensus on future interventions.

Our project is only the tip of the iceberg, and there is much more to the problem than is described here. Chronobiology is a relatively young and developing field of research. Therefore there is not always conclusive evidence for everything, especially when it comes to the working mechanisms. The goal of our project is to raise awareness for this wicked problem and inspire more people to research chronobiology, or related areas, as it is a promising field of research. There is still much more to be uncovered.



WANT TO LEARN MORE?

To learn more about the experts we interviewed, and the wicked problem, visit these websites:

Circadian.com

Bioclockconsortium.org

Circadianlight.com

To learn more about wicked problems:

Watch the documentary Koyaanisqatsi

Read Dillemas in a General Theory of Planning by Rittel and Webber

Feel free to contact our group through WickedCircadian@gmail.com

THE NEW WICKED PROBLEM APRIL 2022